

# **THE ANTIMICROBIAL RESISTANCE PATTERNS OF URINARY TRACT INFECTIONS (UTIs) IN A SOUTH AFRICAN PUBLIC HOSPITAL**

UNIVERSITY OF THE  
WITWATERSRAND,  
JOHANNESBURG



**Benhilda Jaji**

**May 2021**

Supervised by: Ms. Stephanie Leigh-de Rapper, Professor Sandy van  
Vuuren and Dr. Neelaveni Padayachee

# DECLARATION

---

I, Benhilda Jaji, declare that this dissertation is my own work. It is being submitted in fulfilment for the degree of Master of Pharmacy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.



03 May 2021

---

**Benhilda Jaji**

---

**Date**

# ABSTRACT

---

**Introduction:** Urinary tract infections (UTIs) are amongst the most common types of bacterial infection in public hospitals and the second most common reason for empirical antibiotic treatment. Optimal treatment could decrease morbidity and mortality in women, also battling the ongoing crises of increasing antibiotic resistance. The aim of this study was to determine antimicrobial resistance patterns of UTIs in the study hospital, in order to recommend an effective treatment protocol and infection management practices.

**Method:** This study was conducted on 200 urine samples collected from outpatient departments of the study hospital. The antimicrobial susceptibility patterns of isolated bacteria were determined by disk diffusion method (Kirby–Bauer). Bacterial isolates were identified using the MicroScan.

**Results:** A total of 238 bacterial isolates were found in uncomplicated UTIs. Among them, the most predominant bacteria were *Escherichia coli* (43.6%). A total of 194 bacterial isolates were found in complicated UTIs, where similarly *E. coli* (31.2%) was the most predominant bacteria encountered. Antibiotic susceptibility patterns showed that almost all of the isolates were resistant to at least one antibiotic. Highest resistance percentage of the isolates in uncomplicated UTIs was observed in cephalexin (96.2%) followed by co-trimoxazole (91.3%). Highest resistance percentage of the isolates in complicated UTIs was observed in cephalexin and co-trimoxazole (100%).

**Conclusion:** This study provides evidence for an updated treatment protocol, hence, providing valuable tools for antimicrobial stewardship in South Africa. Knowing the resistance levels is key to effective and cost-effective empirical prescribing. Co-trimoxazole resistance rates are 100%, in which case a single 3 g dose of fosfomycin is likely to be the most cost-effective treatment option.

# DEDICATION

---

I dedicate this thesis to the Almighty God, my dear parents Mr. Francis Jaji and Mrs. Mirriam Jaji, my brother and sisters, for their sacrifices, continued encouragement and support which has made me what I am today.

# ACKNOWLEDGEMENTS

---

I would like to thank my supervisor, Ms. Stephanie Leigh for the encouragement, guidance, patience and enthusiasm throughout the course of this research. Thank you for being a hands-on supervisor.

To my co-supervisors, Professor Sandy van Vuuren and Dr. Neelaveni Padayachee, thank you for the many hours, efforts, and advice. Your wisdom and insight concerning this study are greatly appreciated. Thank you!

To Phumzile Moerane and Londiwe Dube, our hard-working laboratory technicians, thank you for your assistance behind the scenes. Your positive contributions and advice in the laboratory were indispensable.

To the study hospital and national health laboratory services staff, I appreciate your assistance in the data collection and identification period. Thank you for sharing your wisdom with me.

A big thank you to Tinevimbo Hove for the continual encouragement, support and for being my strength during these years. A gigantic thank you to Primrose Jaji for reading my thesis a million times, making sure that there were no grammatical errors. Thank you for being so supportive, I really appreciate.

Thank you to Adcock Ingram Holdings and the Medical Faculty Research Endowment Fund for their generous financial support towards this research. I would also like to acknowledge the University of the Witwatersrand for the resources provided for my research. Thank you!

Most importantly, I express my sincere appreciation to my parents and the entire family for their patience, love, support, encouragement, prayers throughout my educational pursuit and daily life.

# TABLE OF CONTENTS

---

|                                                  |           |
|--------------------------------------------------|-----------|
| Declaration.....                                 | 1         |
| Abstract.....                                    | 2         |
| Dedication .....                                 | 4         |
| Acknowledgements.....                            | 5         |
| Table of Contents .....                          | 6         |
| List of Figures.....                             | 7         |
| List of Tables.....                              | 9         |
| List of Equations .....                          | 10        |
| List of Abbreviations.....                       | 11        |
| <b>CHAPTER ONE – INTRODUCTION.....</b>           | <b>16</b> |
| 1.1. Urinary tract infections.....               | 13        |
| 1.2. Epidemiology and pathogenesis of UTIs ..... | 13        |
| 1.2.1. Classification of UTIs .....              | 16        |
| 1.2.2. Risk factors for UTIs.....                | 17        |
| 1.3. Available treatment for UTIs .....          | 19        |
| 1.3.1. Fluoroquinolones .....                    | 19        |
| 1.3.2. Trimethoprim-Sulfamethoxazole .....       | 20        |
| 1.3.3. Penicillins .....                         | 21        |
| 1.3.4. Cephalosporins .....                      | 21        |
| 1.3.5. Aminoglycosides .....                     | 22        |
| 1.3.6. Tetracyclines .....                       | 22        |
| 1.3.7. Fosfomycin.....                           | 23        |
| 1.3.8. Nitrofurantoin .....                      | 23        |

|                                                                |               |
|----------------------------------------------------------------|---------------|
| 1.4. The reoccurrence of UTIs.....                             | 24            |
| 1.5. Antimicrobial resistance patterns.....                    | 25            |
| 1.6. Pharmacoeconomics: Costing.....                           | 26            |
| 1.7. Aim.....                                                  | 27            |
| 1.7.1. Study objectives.....                                   | 27            |
| 1.7.2. Study design.....                                       | 28            |
| <br><b>CHAPTER TWO – CLINICAL SAMPLING.....</b>                | <br><b>31</b> |
| 2.1. Introduction.....                                         | 30            |
| 2.2. Ethics.....                                               | 30            |
| 2.3. Setting.....                                              | 31            |
| 2.4. Methods.....                                              | 31            |
| 2.4.1. Participants: Inclusion criteria.....                   | 31            |
| 2.4.2. Participants: Exclusion criteria.....                   | 32            |
| 2.5. Patient selection.....                                    | 33            |
| 2.5.1. Urine sample collection.....                            | 33            |
| 2.5.2. Urine Dipstick.....                                     | 34            |
| 2.5.3. Point of care tests.....                                | 35            |
| 2.5.3.1. Blood glucose test.....                               | 35            |
| 2.5.3.2. Pregnancy test.....                                   | 36            |
| 2.6. Data analysis.....                                        | 37            |
| 2.7. Results and Discussion.....                               | 38            |
| 2.7.1. Patient demographics: complicated vs uncomplicated..... | 38            |
| 2.7.2. Dipstick, blood glucose and pregnancy test results..... | 39            |
| 2.7.3. Patient demographics: Underlying conditions.....        | 40            |
| 2.7.4. Patient symptoms.....                                   | 41            |

|                    |    |
|--------------------|----|
| 2.8. Summary ..... | 42 |
|--------------------|----|

## **CHAPTER THREE – CULTURING, SUSCEPTIBILITY TESTING AND IDENTIFICATION..... 44**

|                         |    |
|-------------------------|----|
| 3.1. Introduction ..... | 43 |
|-------------------------|----|

|                    |    |
|--------------------|----|
| 3.2. Methods ..... | 43 |
|--------------------|----|

|                                      |    |
|--------------------------------------|----|
| 3.2.1. Urine sample collection ..... | 43 |
|--------------------------------------|----|

|                               |    |
|-------------------------------|----|
| 3.2.2. Agar preparation ..... | 44 |
|-------------------------------|----|

|                                     |    |
|-------------------------------------|----|
| 3.2.3. Urine sample culturing ..... | 44 |
|-------------------------------------|----|

|                                      |    |
|--------------------------------------|----|
| 3.2.4. Single colony culturing ..... | 45 |
|--------------------------------------|----|

|                                            |    |
|--------------------------------------------|----|
| 3.2.5. Macro morphology descriptions ..... | 45 |
|--------------------------------------------|----|

|                                                   |    |
|---------------------------------------------------|----|
| 3.2.6. Antimicrobial susceptibility testing ..... | 46 |
|---------------------------------------------------|----|

|                                                                 |    |
|-----------------------------------------------------------------|----|
| 3.3. Culture identification by MicroScan testing procedure..... | 47 |
|-----------------------------------------------------------------|----|

|                                  |    |
|----------------------------------|----|
| 3.4. Results and discussion..... | 50 |
|----------------------------------|----|

|                                                                         |    |
|-------------------------------------------------------------------------|----|
| 3.4.1. Complicated and uncomplicated UTIs: Urine sample culturing ..... | 50 |
|-------------------------------------------------------------------------|----|

|                                                                     |    |
|---------------------------------------------------------------------|----|
| 3.4.2. Uncomplicated UTIs: Macro morphology of micro-organisms..... | 52 |
|---------------------------------------------------------------------|----|

|                                                        |    |
|--------------------------------------------------------|----|
| 3.4.4 Uncomplicated UTIs: culture identification ..... | 58 |
|--------------------------------------------------------|----|

|                                                                                                |    |
|------------------------------------------------------------------------------------------------|----|
| 3.4.3. Uncomplicated UTIs: Antimicrobial susceptibility patterns and resistance patterns ..... | 59 |
|------------------------------------------------------------------------------------------------|----|

|                                                                   |    |
|-------------------------------------------------------------------|----|
| 3.4.5. Complicated UTIs: Macro morphology of micro-organisms..... | 62 |
|-------------------------------------------------------------------|----|

|                                                       |    |
|-------------------------------------------------------|----|
| 3.4.7. Complicated UTIs: culture identification ..... | 68 |
|-------------------------------------------------------|----|

|                                                                      |    |
|----------------------------------------------------------------------|----|
| 3.4.6. Complicated UTIs: Antimicrobial susceptibility patterns ..... | 69 |
|----------------------------------------------------------------------|----|

|                    |    |
|--------------------|----|
| 3.5. Summary ..... | 71 |
|--------------------|----|

## **CHAPTER FOUR –CLINICAL PHARMACY..... 71**

|                         |    |
|-------------------------|----|
| 4.1. Introduction ..... | 73 |
|-------------------------|----|

|                    |    |
|--------------------|----|
| 4.2. Methods ..... | 73 |
|--------------------|----|



|                                                                                                                                                                             |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 4.2.1. Retrospective review of patient files.....                                                                                                                           | 73                                  |
| 4.2.2. Antibigram.....                                                                                                                                                      | 74                                  |
| 4.3. Results and discussion.....                                                                                                                                            | 75                                  |
| 4.3.1. Uncomplicated UTI: Patient file review.....                                                                                                                          | 76                                  |
| 4.3.2. Complicated UTIs: Patient file review.....                                                                                                                           | 82                                  |
| 4.3.3. Analysis of risk factors in complicated and uncomplicated UTIs .....                                                                                                 | 87                                  |
| 4.4. Selection of antibiotics according to classifications .....                                                                                                            | 88                                  |
| 4.4.1. Uncomplicated UTI: Antibigram .....                                                                                                                                  | 86                                  |
| 4.4.2. Complicated UTI: Antibigram .....                                                                                                                                    | 90                                  |
| <b>CHAPTER FIVE –CONCLUSION.....</b>                                                                                                                                        | <b>91</b>                           |
| 5.1. Overview .....                                                                                                                                                         | 94                                  |
| 5.2. The study aims achieved.....                                                                                                                                           | 94                                  |
| 5.2.1. Objective 1: To determine the antimicrobial resistance patterns of confirmed UTI infections within identified patients seeking treatment at the study hospital... 94 |                                     |
| 5.2.2. Objective 2: To determine the likelihood of past urinary tract Infection and past treatment practices in the management of these infections. ....                    | 95                                  |
| 5.2.3. Objective 3: To suggest a treatment policy and infection management protocols for UTIs.....                                                                          | 96                                  |
| 5.3. Strengths of the study .....                                                                                                                                           | <b>Error! Bookmark not defined.</b> |
| 5.4. Limitations of the study.....                                                                                                                                          | 96                                  |
| 5.5. Contribution to knowledge .....                                                                                                                                        | 98                                  |
| 5.6. Recommendations .....                                                                                                                                                  | <b>Error! Bookmark not defined.</b> |
| 5.6.1. Policy .....                                                                                                                                                         | <b>Error! Bookmark not defined.</b> |
| 5.6.2. Clinical practice .....                                                                                                                                              | <b>Error! Bookmark not defined.</b> |
| 5.7. Summary and conclusion .....                                                                                                                                           | 99                                  |

# LIST OF FIGURES

---

|                                                                                                                |           |
|----------------------------------------------------------------------------------------------------------------|-----------|
| <b>CHAPTER 1.....</b>                                                                                          | <b>16</b> |
| <b>Figure 1. 1:</b> Movement of bacteria in the urinary system (Adapted from: health.clevelandclinic.org)..... | 16        |
| <b>Figure 1. 2:</b> A workflow schematic showing summary of study objectives.....                              | 30        |
| <br>                                                                                                           |           |
| <b>CHAPTER 2 .....</b>                                                                                         | <b>31</b> |
| <b>Figure 2. 1:</b> Urine dipstick testing .....                                                               | 35        |
| <b>Figure 2. 2:</b> Blood glucose test procedure.....                                                          | 36        |
| <b>Figure 2. 3:</b> Pregnancy test procedure .....                                                             | 37        |
| <b>Figure 2. 4:</b> The frequency of symptom distribution.....                                                 | 42        |
| <br>                                                                                                           |           |
| <b>CHAPTER 3.....</b>                                                                                          | <b>44</b> |
| <b>Figure 3. 1:</b> Step by step procedure of the methodology .....                                            | 49        |
| <b>Figure 3. 2:</b> An overview of the colonies obtained after sample culturing.....                           | 51        |
| <b>Figure 3. 3:</b> Number of samples per patient group with the same morphologies in uncomplicated UTIs.....  | 57        |
| <b>Figure 3. 4:</b> Number of samples per patient group with the same morphologies in complicated UTIs .....   | 65        |

# LIST OF TABLES

---

|                                                                                                                                                                                                               |               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| <b>CHAPTER 1.....</b>                                                                                                                                                                                         | <b>16</b>     |
| <b>Table 1. 1:</b> Antibiotics costs for the treatment of UTIs in South Africa (Data of Medicine Prices) (accessed on 6 August 2020).....                                                                     | 26            |
| <br><b>CHAPTER 2 .....</b>                                                                                                                                                                                    | <br><b>31</b> |
| <b>Table 2. 1:</b> Blood glucose results descriptions.....                                                                                                                                                    | 35            |
| <b>Table 2. 2:</b> Patient demographics for complicated and uncomplicated UTIs .....                                                                                                                          | 38            |
| <b>Table 2. 3:</b> Point of care testing in complicated and uncomplicated UTIs.....                                                                                                                           | 40            |
| <b>Table 2. 4:</b> Underlying conditions in complicated and uncomplicated UTIs .....                                                                                                                          | 41            |
| <br><b>CHAPTER 3.....</b>                                                                                                                                                                                     | <br><b>44</b> |
| <b>Table 3. 1:</b> The morphologies for samples showing identical macro morphological characteristics in uncomplicated UTIs .....                                                                             | 52            |
| <b>Table 3. 2:</b> The identified micro-organisms in uncomplicated UTIs .....                                                                                                                                 | 58            |
| <b>Table 3. 3:</b> The antimicrobial susceptibility patterns were undertaken for all 238 samples and results attained demonstrated similar patterns for each group. This is a summary per patient group ..... | 59            |
| <b>Table 3. 4:</b> The morphologies for samples showing identical macro morphological characteristics in uncomplicated UTIs .....                                                                             | 62            |
| <b>Table 3. 5:</b> The identified micro-organisms in complicated UTIs .....                                                                                                                                   | 66            |
| <b>Table 3. 6:</b> The antimicrobial susceptibility patterns were undertaken for all 194 samples and results attained demonstrated similar patterns for each group. This is a summary per patient group ..... | 67            |

|                                                                                                         |               |
|---------------------------------------------------------------------------------------------------------|---------------|
| <b>CHAPTER 4.....</b>                                                                                   | <b>71</b>     |
| <b>Table 4. 1:</b> Risk factors, number of infections and treatment outcomes in uncomplicated UTIs..... | 74            |
| <b>Table 4. 2:</b> Risk factors, number of infections and treatment outcomes in complicated UTIs.....   | 80            |
| <b>Table 4. 3:</b> Age adjusted risk factors in complicated and uncomplicated UTIs .....                | 83            |
| <b>Table 4. 4:</b> Antibigram for uncomplicated UTIs.....                                               | 85            |
| <b>Table 4. 5:</b> Antibigram for complicated UTIs.....                                                 | 87            |
| <br><b>CHAPTER 5.....</b>                                                                               | <br><b>91</b> |
| <b>Table 5. 1:</b> Summary of the thesis and results obtained .....                                     | 92            |

# LIST OF ABBREVIATIONS

---

|        |                                                                 |
|--------|-----------------------------------------------------------------|
| %      | Percent                                                         |
| µl     | Microliter                                                      |
| AIDS   | Acquired Immune Deficiency Syndrome                             |
| CFU    | Colony forming units                                            |
| CLSI   | Clinical and Laboratory Standards Institute                     |
| Cm     | Centimetres                                                     |
| EML    | Essential Medicines List                                        |
| G      | Grams                                                           |
| H      | Hours                                                           |
| HIV    | Human Immunodeficiency Virus                                    |
| HLA    | Human leukocyte antigen                                         |
| Mg     | Milligram                                                       |
| Mg/dl  | Milligrams per decilitre                                        |
| Mmol/L | Millimoles per litre                                            |
| Min    | Minute                                                          |
| ml     | Millilitre                                                      |
| MSU    | Mid-stream urine sample                                         |
| NHLS   | National Health Laboratory Services                             |
| R      | Rand                                                            |
| STG    | Standard Treatment Guidelines                                   |
| STI    | Sexually transmitted infection                                  |
| TSA    | Tryptone Soya agar                                              |
| UTI    | Urinary tract infection                                         |
| WHO    | World Health Organization                                       |
| ZOI    | Zone of inhibition                                              |
| SAAGAR | South African Expert Advisory Group on Antimicrobial resistance |

# CHAPTER 1

## INTRODUCTION

---

### 1.1. Urinary tract infections

Urinary tract infections (UTIs) are a collective term that describes the microbial invasion of any part of the urinary tract, which consists of the kidneys, ureter, bladder and urethra (Tan and Chlebicki, 2016). The urinary tract can be divided into the upper and lower urinary tract. Lower urinary tract infections are regarded to be superficial as they effect the mucosal layer and entails infection of the urethra or bladder, while upper urinary tract infections involve infection of the prostate, the ureter, the kidney and intra-renal and perinephric abscesses signifying invasion of tissue (Haslund *et al.*, 2013). The presentation of UTIs symptoms range from pain, incontinence, needing to pass urine frequently, discomfort passing urine, burning or stinging when passing urine, constant lower abdominal ache, difficulty urinating and slow stream of urine (Iskander, 2018).

### 1.2. Epidemiology and pathogenesis of UTIs

Urinary tract infections are the most frequently encountered infections by clinicians, with an estimated global incidence of no less than 150 million patients annually (Tessema *et al.*, 2020). In a South African study, 143 patients were diagnosed clinically with UTI by nurses and clinicians. However, only 28 of these patients were positive for UTIs of Gram-negative bacterial aetiology based on further urine analysis, giving a prevalence of 19.6% (Kubone *et al.*, 2020). Men who are younger than 50 years of age, have shown to have an approximated incidence of UTI of 0.0005 to 0.0008 per person per year compared with the prevalence of 0.5 to 0.7 per person per year for younger women (Tessema *et al.*, 2020). In South Africa, UTIs were most common in the 18 to 28-year age group which could be due to higher sexual activities, as it is reported that highest sexual activities were observed in women between the ages of 18 and 39 (Kubone *et al.*, 2020). Females are more prone to UTIs with reported occurrence greater than males. The majority of the patients with UTIs in a study in

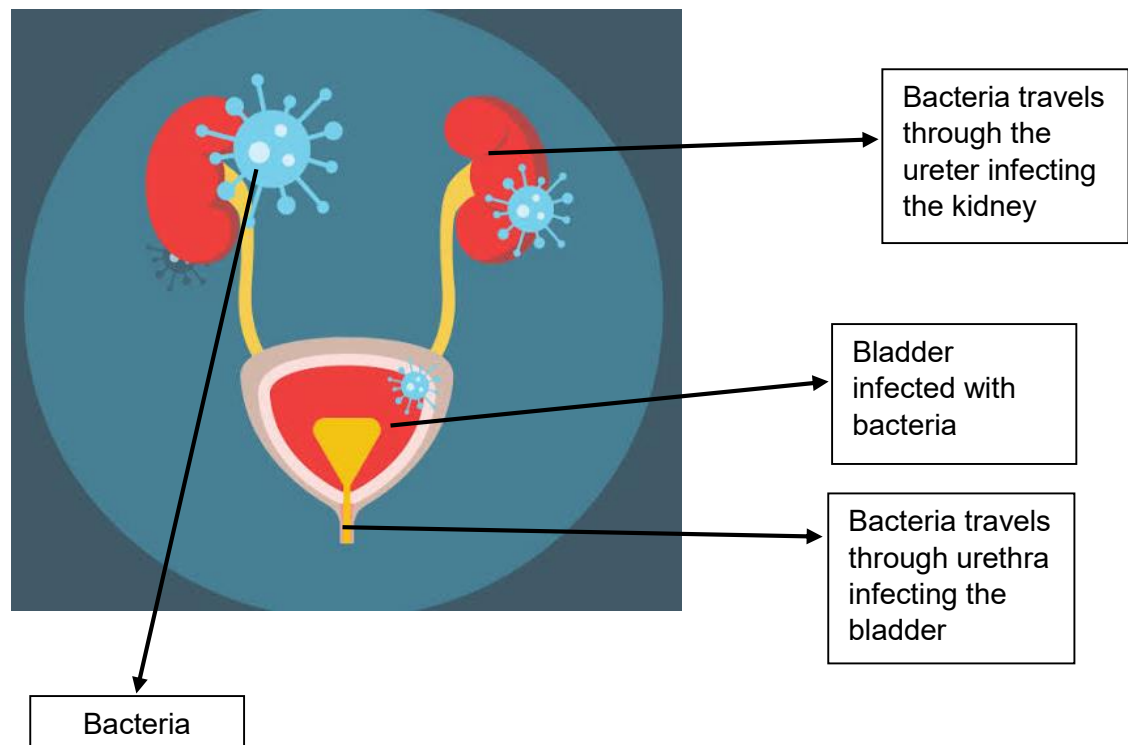
South Africa were females (75%), which was expected as UTIs are more common in females mainly because of their anatomical and physiological characteristics (Sadler *et al.*, 2017). Up to 40% of women will develop UTI at least once during their lives, and a significant number of these women will have recurrent urinary tract infections (Lin *et al.*, 2016). The female urethra is prone to colonization when compared to males due to the close proximity of the urethra to the anus, its short length of  $\pm 4$  cm and its termination beneath the labia (Vasudevan, 2014). The anal triangle is important regarding the pathogenesis of UTI and sources of infection in females (Lin *et al.*, 2016). The anal triangle consists of the anus, the surrounding tissue and the resident microflora which may infect the urinary tract through the short urethra and the close proximity between the rectal and vaginal regions in women (Henn, 2010). Micro-organisms may reach the urinary tract by means of lymphatic or haematogenous spread. There is experimental and clinical evidence to show that in the vast majority of UTIs, access is gained through the ascent of the urethra into the bladder, especially by micro-organisms of enteric origin such as *Escherichia coli* and other Enterobacteriaceae (Henn, 2010). Bowel residing enteric Gram-negative bacilli will colonize the periurethral skin and distal urethra before and during episodes of bacteriuria in females who are prone to the development of cystitis, that is, inflammation of the bladder. (Alkhyat and Al-Maqtari, 2014). Infections in the urinary tract initially present as cystitis and ascends the ureters to the kidneys and are the pathways for most renal parenchymal infections (Sadler *et al.*, 2017). The ascending infection route provides a reasonable explanation for the higher incidence of UTIs in women as opposed to men and for the increased infection risk in hospitalized patients following catheterisation (Flores-Mireles *et al.*, 2015).

*Escherichia coli*, a Gram-negative bacterium belongs to the Enterobacteriaceae family, is accountable for 70-95% of acute uncomplicated lower and upper UTIs (Bezuidenhout, 2017). The remaining 20% of UTIs are commonly caused by bacteria such as *Proteus* spp., *Klebsiella* spp., *Enterococcus faecalis*, *Staphylococcus saprophyticus*, with occasional infections associated to *Enterobacter* spp. and yeasts *Escherichia coli*, a Gram-negative bacterium belongs to the Enterobacteriaceae family, is accountable for 70-95% of acute uncomplicated lower and upper UTIs (Bezuidenhout, 2017). These micro-organisms, including *Serratia* spp. and

*Pseudomonas* spp., may be regarded of much greater significance in infections associated with urological manipulation, obstruction, calculi infections and reoccurrences (Riley *et al.*, 2012).

Additional sources support these findings with the most commonly encountered uropathogens identified worldwide as *E. coli* (75%); *K. pneumoniae* (6%); *S. saprophyticus* (6%) and *Proteus* spp. (13%) among others (Ghaima *et al.*, 2018). Other studies show that Enterococci and *S. aureus* are common causes of UTIs in patients with previous surgery, renal calculi and instrumentation (Leekha, Terrell and Edson, 2011). According to a South African study, all the 26 *E. coli* isolates were tested for their susceptibility to 17 antibiotics. Twenty-two (84.6%) of these isolates were resistant to at least one of the antibiotics tested in the current study. The highest resistance was observed to ampicillin 20 (76.9%) while the lowest resistance (7.1%) was to amoxicillin/clavulanic acid (Kubone *et al.*, 2020). The vaginal microbiota is a dynamic and often critical factor in this pathogenic interplay, because changes in the characteristics of the vaginal microbiota resulting in the loss of normally protective *Lactobacillus* spp, increase the risk of UTI (Stewardson *et al.*, 2015). Most peri-urethral bacteria enter a structurally normal bladder through a process of urethral massage by means of sexual intercourse *Escherichia coli*, a Gram-negative bacterium belongs to the Enterobacteriaceae family, is accountable for 70-95% of acute uncomplicated lower and upper UTIs (Bezuidenhout, 2017). Except for the distal urethra which contains resident microflora, the normal genitourinary tract is considered sterile and to be protective against UTIs (Flores-Mireles *et al.*, 2015). Figure 1.1 shows how bacteria travel through the urinary system.





**Figure 1. 1:** Movement of bacteria in the urinary system (Adapted from: [health.clevelandclinic.org](http://health.clevelandclinic.org)).

### 1.2.1. Classification of UTIs

Infections of the urinary tract are traditionally classified into uncomplicated and complicated in nature (Wagenlehner *et al.*, 2011). Uncomplicated UTIs occur when there are no functional or anatomical anomalies in the urinary tract, that is, no renal functional impairment and no concomitant disease that would promote the UTI (Tan and Chlebicki, 2016). Complicated UTIs occur mainly in persons with structural or functional abnormalities (Tan and Chlebicki, 2016). They are associated with risk factors such as urinary obstruction or retention, spinal cord injuries, immunosuppression, renal failure, transplantation and the presence of foreign bodies (Sofia *et al.*, 2019). Infections are further classified based on clinical schedule of the UTIs based on frequency of occurrence. Single-episode occurs only once, whereas in recurrent UTIs, patients have repeated episodes of infection (Flores-Mireles *et al.*, 2015). Reoccurrences of UTI may be due to reinfections by the same or a different urinary pathogen (Hickling, Sun and Wu, 2015).

### 1.2.2. Risk factors for UTIs

Common factors associated with the development of UTIs include poor hygiene, sexual intercourse, use of certain types of medication such as glibenclamide which is an anti-diabetic agent, spermicide use or diaphragms, delay in post-coital micturition, obesity, low levels of vaginal oestrogen, or a history of recent UTI (Barber *et al.*, 2013).

Sexual intercourse in women seems to be important in the pathogenesis of UTIs and there is a temporary association with the onset of cystitis, due to the fact that sexual intercourse causes the introduction of bacteria into the bladder (Sofia *et al.*, 2019). Approximately 20-30% of pregnant women with asymptomatic bacteriuria will subsequently develop pyelonephritis (Sadler *et al.*, 2017). In pregnancy, the predisposition to infection of the upper tract may be ascribed to decreased urethral tone, decreased urethral peristalsis and temporary incompetence of the vesicourethral valves (Storme *et al.*, 2019). Although the majority of UTIs in pregnancy are asymptomatic, the mother is placed at high risk for low birth weight, hypertension, maternal anaemia, thrombosis, stillbirth and abortion (Grabe *et al.*, 2015). Therefore, pregnant women should be screened for asymptomatic UTIs in the first trimester and treated, if positive (Grabe *et al.*, 2015).

Obstruction which impedes the free flow of urine, whether it is caused by a tumour, strictures, stone or hypertrophy of the prostate, may result in hydronephrosis, resulting in an enhanced frequency of developing a UTI (Sofia *et al.*, 2019). This may lead to rapid renal tissue destruction when an infection is superimposed on urinary tract obstruction (Sofia *et al.*, 2019). The initiating cause of infections might be due to catheter use for drainage of the bladder or due to prolonged stasis of urine in the bladder (Odoki *et al.*, 2019). Vesicourethral reflux is defined as retrograde flow of urine from the cavity of the bladder back up into the ureters and sometimes reaching into the renal pelvis during voiding, which may be due to elevated pressure in the bladder (Odoki *et al.*, 2019). The reflux of bacteria hence, an upper urinary tract infection is facilitated by an anatomically impaired vesicourethral junction (Sheerin and Glover, 2019).

Risk factors associated with UTIs are specifically concerning in patients with underlying health concerns, including pregnant or immunocompromised patients. Significant adverse health outcomes may occur following UTI infection in these populations with the possibility of developing pre-eclampsia in pregnant women, while immunocompromised patients and patients undergoing organ transplant, have a higher rate of developing bacteraemia (Odoki *et al.*, 2019).

Human Immunodeficiency Virus (HIV) Infection and Acquired Immune Deficiency Syndrome (AIDS) are known to cause urinary tract infections in patients who are predisposed to infection (Odoki *et al.*, 2019). When the CD4 count declines to less than 200/mm<sup>3</sup> the risk of opportunistic infections rises dramatically (Sheerin and Glover, 2019). The reported incidence of UTIs in patients with HIV/AIDS is between 7–50% (Sadler *et al.*, 2017). Patients with HIV/AIDS can experience the typical lower urinary tract symptoms, for example dysuria and polyuria, even though several patients are asymptomatic (Sheerin and Glover, 2019). Pyuria (the presence of pus in urine) has been noted in up to 52% of HIV patients who are diagnosed with UTIs (Sheerin and Glover, 2019).

Diabetes mellitus, even when well regulated, correlates to a higher frequency of asymptomatic bacteriuria. Diabetic patients are more prone to get UTIs due to frequent urination and high blood sugar levels (Sadler *et al.*, 2017). High blood sugar levels give a favourable growth environment to the pathogens. Also, diabetic patients may have poor circulation, which reduces the ability of white blood cells to travel in the body and fight off any kind of infection (Sadler *et al.*, 2017). One random controlled trial demonstrated that eradicating asymptomatic bacteriuria did not reduce the risk of symptomatic UTI and infectious complications in patients with diabetes mellitus (Vasudevan, 2014). Furthermore, untreated UTIs did not correlate to diabetic nephropathy. Screening and treatment of UTIs in well-controlled diabetes mellitus patients is therefore not recommended. However, poorly regulated diabetes is a risk factor for symptomatic UTI and infectious complications (Tai *et al.*, 2013).

### 1.3. Available treatment for UTIs

In public hospital settings in South Africa, the approach by healthcare professionals to the treatment of UTIs, is informed and guided by Standard Treatment Guidelines (STG) and Essential Medicines List (EML) which was last revised in 2018 (National Department of Health, 2018). These guidelines provide practitioners in public healthcare settings with diagnostic criteria and the associated expected treatment of these infections. The current treatment of UTIs in these settings include the use of antimicrobial agents such as ciprofloxacin, amoxicillin, fosfomycin, trimethoprim-sulfamethoxazole and nitrofurantoin (National Department of Health, 2018).

#### 1.3.1. Fluoroquinolones

Ciprofloxacin is a fluorinated quinolone whose activity is mainly Gram-negative even though it is a broad spectrum antibiotic. Currently in South Africa ciprofloxacin is used to treat a broad range of clinical conditions, among them UTIs, upper respiratory tract infections as well as prophylaxis for neutropenic patients (National Department of Health, 2018). Fluoroquinolones are widely distributed with good penetration and is therefore considered as the preferred empiric drug choice especially in the treatment of reoccurring UTIs for both male and female patients when there is a high resistance to other antibiotics (Lewis *et al.*, 2013). Of the fluoroquinolone class, ciprofloxacin is the most potent against Gram-negative bacilli, notably against the *Enterobacter* spp. (Linhares *et al.*, 2013). Uncomplicated UTIs are treated with ciprofloxacin for three days and complicated UTIs are treated with amoxicillin (pregnant women) for seven days, according to the STG and EML (National Department of Health, 2018).

*Escherichia coli* is the most commonly associated bacteria to UTIs and has developed resistance to ciprofloxacin (Reis *et al.*, 2016). The extensive use of ciprofloxacin has led to the development of ciprofloxacin resistant strains (Sofia *et al.*, 2019). The resistance of ciprofloxacin depends on the ability to select resistant mutants, its ability to reach concentrations that are able to avoid the resistance selection and its ability to act against mutant bacteria generated during previous treatments with other fluoroquinolones (Kubone *et al.*, 2020). Ciprofloxacin is a useful antibiotic for the treatment of UTIs, however, resistance should be monitored meticulously. Patients

infected with *S. saprophyticus*, on the other hand, are more prone to treatment failure when given a single dose of fluoroquinolone (Hooton *et al.*, 1999). Treatments that are seven days or longer do not add any therapeutic benefit but increase side effects that require further medical intervention and cost (Kubone *et al.*, 2020).

Fluoroquinolones are well tolerated, though side effects are gastrointestinal disturbances such as abdominal pain, nausea and vomiting, however, the concomitant use of ciprofloxacin and glibenclamide (an antidiabetic agent) can result in hypoglycaemia (National Department of Health, 2018).

### **1.3.2. Trimethoprim-Sulfamethoxazole**

The combination of trimethoprim and sulfamethoxazole, also known as co-trimoxazole has been used extensively as a broad-spectrum antibiotic (Reis *et al.*, 2016). The therapeutic effectiveness of this combination has decreased due to the emergence of widespread resistance (Kubone *et al.*, 2020). Therapeutic levels of co-trimoxazole are attained in bile, cerebrospinal fluid, prostatic tissue and vaginal secretion. Therefore, co-trimoxazole may be used in the treatment of bacterial prostatitis and the elimination of Enterobacteriaceae and Pneumococci surrounding the urethral orifice and those inhabiting the vaginal walls. This results in markedly reduced bacterial numbers, hence diminishing the chance of reinfection (Kubone *et al.*, 2020). Resistance rates of *E. coli* bacterial isolated from female outpatients have shown a 17.5% resistance against co-trimoxazole (Sheerin and Glover, 2019). The three days or longer regimen was more successful than the single dose therapy, for co-trimoxazole in most trials conducted (Lewis *et al.*, 2013). Co-trimoxazole is extensively used in South Africa to treat UTIs in immunocompromised patients and this has led to increased bacterial resistance against this agent (Kubone *et al.*, 2020). Uncomplicated UTIs are treated with co-trimoxazole for seven days, according to the STG (National Department of Health, 2018). The use of co-trimoxazole and oral antidiabetic agents leads to the potentiation of hypoglycaemic effects of sulfonylureas (Linhares *et al.*, 2013). The side effects of both co-trimoxazole are hypersensitivity reactions and gastrointestinal disturbances (National Department of Health, 2018).

### **1.3.3. Penicillins**

Penicillins are used for broad-spectrum activity against Gram-positive and Gram-negative micro-organisms. The combination of clavulanic acid with amoxicillin has extended the sensitivity spectrum of amoxicillin against the production of beta-lactamases, especially in resistant Gram-negative bacteria, rendering them sensitive to penicillin (Lewis *et al.*, 2013). Due to the fact that beta-lactam levels in the urine can be attained, at recommended doses, penicillin can be used after sexual intercourse in the prophylaxis of reoccurring urinary tract infections (Beyene and Tsegaye, 2011). According to the STG, pregnant women with UTIs are treated with amoxicillin, for seven days (National Department of Health, 2018). The most common side effects are gastrointestinal disturbances and a macular rash which increases in the presence of leukaemia, lymphoma and renal impairment (National Department of Health, 2018).

The therapeutic value of penicillin is increasingly limited due to the development of resistance. The combination of amoxicillin with clavulanic acid has restored effectiveness against many beta-lactamase producing organisms (Ghaima *et al.*, 2018).

### **1.3.4. Cephalosporins**

Cephalosporins are broad-spectrum semi-synthetic beta-lactam antibiotics with a mechanism of action similar to that of penicillins. Third generation cephalosporins exhibit significant activity unlike penicillins in treating UTIs (Bhattacharya *et al.*, 2013). Patients who are admitted to the hospital for a UTI, are often infected with an organism that is resistant to cephalosporins (Rezaee and Abdinia, 2015). Enterobacteriaceae and Enterococci were found to be resistant to cephalosporins (George *et al.*, 2015). Cephalexin, cephadrine and cefaclor are used as alternative treatment regimens in patients who are allergic to penicillin even though they are not as effective as other antibiotics (Manikandan *et al.*, 2011). Other side effects include, neurotoxicity, nephrotoxicity and gastrointestinal disturbances (National Department of Health, 2018).

### 1.3.5. Aminoglycosides

Aminoglycosides inhibit bacterial synthesis by binding to the 30s ribosomal subunits thereby causing inhibition of protein synthesis in the bacterial cell (George *et al.*, 2015). Aminoglycosides are known to concentrate in the urine and with known susceptibility to the bacterial isolate may be used to treat UTIs (Van Schoor, 2015). Aminoglycosides are active against many Gram-negative bacilli including *Pseudomonas* spp and mycobacteria species, while they are ineffective against anaerobes (Van Schoor, 2015). Due to the high concentration of bacteria in urine, smaller dosages of the aminoglycosides are often used to treat UTIs, than those used for the treatment of a systemic infection (Barry *et al.*, 2017). According to a study by Moyo *et al.* (2010), single-dose aminoglycoside therapy appears to be an effective treatment option for lower UTIs in non-septic patients, with minimal toxicity. The study also notes that additional research would be beneficial to confirm efficacy for pyelonephritis. Greater concern is the increasing resistance of aminoglycosides for the management of UTIs (Rezaee and Abdinia, 2015). When resistance to first-line UTI agents is endemic, aminoglycosides may serve as beta-lactam and fluoroquinolone-sparing options (Moyo *et al.*, 2010). Aminoglycosides are used as alternative treatment regimens in patients who are allergic to penicillin (Lichtenberger and Hooton, 2011). The most common side effects are nephrotoxicity and ototoxicity. They have direct toxic effects on the renal tubular cells related to duration of therapy and dosages (National Department of Health, 2018).

### 1.3.6. Tetracyclines

In most patients with intact renal function, *P. aeruginosa* can be eliminated in 85% of cases with oral tetracyclines (Ghaima *et al.*, 2018). The clinical effectiveness of tetracyclines interestingly, was highest with *P. aeruginosa* and somewhat less effective when compared against *E. coli*. Therapy with tetracyclines, therefore, carries a significant risk of bacterial resistance should the next re-infection of the urinary tract occur (Ghaima *et al.*, 2018). Tetracyclines are also used as an alternative treatment when treating UTIs in patients who are allergic to penicillin (Ghaima *et al.*, 2018). The most common side effects are gastrointestinal disturbances which are usually dose

related such as nausea, vomiting, flatulence, epigastric pain, photosensitivity and nail discolouration (National Department of Health, 2018).

### **1.3.7. Fosfomycin**

Derived from a phosphoric acid, fosfomycin is considered to be bactericidal and a broad-spectrum antibiotic (Lewis *et al.*, 2013). It is mainly used in acute uncomplicated UTIs by sensitive *E. coli* in women, and children over five years of age (Sofia *et al.*, 2019). After a single dose of fosfomycin, therapeutic concentrations in the urine are provided for up to 36 hours (Kubone *et al.*, 2020). As one of the few oral treatment options available in Europe for catheter associated UTIs due to extended spectrum beta-lactamase producing *E. coli*, fosfomycin is now being used more frequently (Sofia *et al.*, 2019). Fosfomycin is also used for prophylaxis in diagnostic and surgical transurethral procedures in adult men (Sofia *et al.*, 2019). Fosfomycin is promptly excreted in the urine and very low levels are found in tissues, making it an excellent choice for UTIs (Tan and Chlebicki, 2016). The increased prevalence of multi-drug resistant Enterobacteriaceae limits available treatment options for UTIs (Lewis *et al.*, 2013). The lack of new antibiotics provide good rationale for using older antibiotics, such as fosfomycin, because it has shown to retain some activity against multi-drug resistant bacteria (Sraboni, Program and Sciences, 2018). Fosfomycin is used as an alternative for patients who cannot adhere to taking medication for long periods and in patients who are allergic to penicillin (Kubone *et al.*, 2020). Common side effects are gastrointestinal disturbances such as nausea, diarrhoea and vomiting. A less common side effect is the development of a skin rash (National Department of Health, 2018).

### **1.3.8. Nitrofurantoin**

Nitrofurantoin is recommended for short-term prophylaxis in women with reoccurring UTIs (Lewis *et al.*, 2013). A study revealed that nitrofurantoin is a cost effective oral drug with good patient compliance (Konar *et al.*, 2014). Within its therapeutic range it has no grave adverse effects (Konar *et al.*, 2014). Nitrofurantoin, although used in the treatment of UTIs, has elevated concerns regarding increased resistance patterns (Lichtenberger and Hooton, 2011). It has been established that the majority of nitrofurantoin resistant bacteria were Gram-negative (*K. pneumoniae* demonstrating



30.8% resistance) and Gram-positive bacteria (*Enterococcus* spp.) (Kubone *et al.*, 2020). Nitrofurantoin is used as an alternative in patients who are allergic to penicillin (Sofia *et al.*, 2019).

#### **1.4. The reoccurrence of UTIs**

Three aetiologies exist for reoccurring UTIs, that is, persistence, reinfection with the original pathogen and reinfection with a different pathogen (Moyo *et al.*, 2010). In women, the majority of reoccurring urinary tract infections are as a result of reinfection of the or due to persistence with the original pathogen in the faecal flora (Kubone *et al.*, 2020).

Reoccurring urinary tract infections are common among healthy women. Women with normal urinary tracts (structurally), experience this at some point in the course of their life (Lin *et al.*, 2016). Some women, however, may be predisposed toward the development and recurrence of UTIs through certain genetic and biological factors (Henn, 2010). Additionally, the inadequate secretion of immunoglobulin A and the reduced expression of the receptor for interleukin (IL)-8 are examples of other genetic mediators which may play a role in reoccurring urinary tract infections (Henn, 2010).

A report in a primary health care setting shows that 44% of the women who present with a UTI, experience a second infection in the space of one year (Saeed *et al.*, 2017). A number of risk factors and behavioural modifications have been identified by Grabe *et al.* (2015), which may be associated with or even prevent reoccurring urinary tract infections. Suggested identifiable risk factors which have been shown to increase the risk of reoccurring urinary tract infections are the reduced intake of fluids, habitual delayed post-coital urination, back to front wiping after defecation, douching, the wearing of occlusive underwear, sexual intercourse, spermicidal use, having a new sex partner and having an UTI during childhood (Grabe *et al.*, 2015). In addition, malnutrition, poor hygiene and a low socioeconomic status are associated with UTI and these factors are rife in rural settings (Aiyegoro *et al.*, 2007). Reoccurring infections of the urinary tract are also associated with antimicrobial resistance (Bates *et al.*, 2014).

## 1.5. Antimicrobial resistance patterns

Antimicrobial resistance is defined as the resistance of bacterial microorganisms to antimicrobial medicines that were previously effective for treatment of infections (World health organization, 2017). It occurs naturally over time but is accelerated by the inappropriate use of antimicrobial medicines in the health sectors, lack of access to health services, including to diagnostics and laboratory capacity (World health organization, 2017). As outlined in the treatment protocols for UTIs in South Africa, many available treatments are subject to reduced efficacies associated with antimicrobial resistance.

Both *E. coli* and *K. pneumoniae* were found to have a resistance rate of >20% to ciprofloxacin, amoxicillin, co-trimoxazole and nitrofurantoin. For this reason, the authors of the study recommended amoxicillin-clavulanate as the first-choice for empirical treatment (Lin *et al.*, 2016). Another study revealed that the most frequent therapeutic choice in private facilities for the treatment of UTIs was ciprofloxacin (50,3%), followed by fosfomycin (17,9%), amoxicillin/clavulanic acid (15,2%), cefuroxime (6,6%), cefpodoxime (4,6%), levofloxacin (4,0%) and amoxicillin (1,3%) (Tessema *et al.*, 2020). The increasing resistance due to an overconsumption of broad-spectrum antibiotics, referring in particular to fluoroquinolones and cephalosporins, has led to the parallel development of co-resistance to other antibiotics (Grabe *et al.*, 2015).

It is important to narrow down treatments from broad-spectrum empiric therapy to narrow-spectrum targeted antibiotics (de-escalation), which are less likely to lead to resistance (Bates *et al.*, 2015). A practice that is sorely lacking is the sampling of cultures for susceptibility testing (Bates *et al.*, 2015). Resistant *E. coli* strains producing extended-spectrum beta-lactamases such as CTX-M enzymes often occur in the community (Reis *et al.*, 2016). Because this organism is regarded as the most common bacterial isolate to cause UTIs, the choice of antimicrobials used to treat these infections are diminishing (Reis *et al.*, 2016).

## 1.6. Pharmacoeconomics: Costing

Guidelines in the treatment of UTIs are governed by the cost of medication versus benefit analysis. According to STG, ciprofloxacin is the drug choice in the management of UTIs as it is cheaper as compared to fosfomycin. However, fosfomycin is more beneficial as compared to ciprofloxacin to manage UTIs. Urinary tract infections due to pathogenic strains of *E. coli* result in significant morbidity, mortality and increased healthcare costs. Unnecessary and inappropriate antibiotic prescribing increase the risk of side effects and the development of antibiotic resistance, while wasting resources due to the increase in costs to treat UTIs (Tessema *et al.*, 2020). In South Africa, the costs of antibiotics used to treat UTIs are provided in Table 1.1.

**Table 1. 1:** Antibiotics costs for the treatment of UTIs in South Africa (Data of Medicine Prices) (accessed on 6 August 2020) (<https://health-e.org.za>)

| Antibiotic                          | Days of treatment | Cost per course   |                |
|-------------------------------------|-------------------|-------------------|----------------|
|                                     |                   | Originator (Rand) | Generic (Rand) |
| Ciprofloxacin 500 mg                | 3                 | 139.86            | 61.78          |
| Fosfomycin 3 g                      | 1                 | 277.01            | -              |
| Amoxicillin 500 mg                  | 5                 | -                 | 51.03          |
| Cephalexin 500 mg                   | 7                 | -                 | 60.56          |
| Co-trimoxazole 960 mg               | 7                 | 195.76            | 70.24          |
| Amoxicillin-clavulanic acid 1000 mg | 5                 | 756.21            | 435.72         |
| Nitrofurantoin 50 mg                | 7                 | 937.02            | -              |

**Key:** -: Not commercially available.

In South Africa, the cost per course of nitrofurantoin (R937.02) and fosfomycin (R277.01) show that they are expensive treatment options but are considered more effective in the management of UTIs (Sadler *et al.*, 2017). Co-trimoxazole 960mg which is taken twice a day for three to seven days is estimated to be the most cost effective treatment (R70.24 per UTI resolved) (Tessema *et al.*, 2020). Of the listed antibiotics in Table 1, generic prices are generally cheaper in treating UTIs as compared to the originator. For example, ciprofloxacin, the cost per course is R139.86 (originator) and R61.78 (generic) therefore the originator price is double the generic price. Current treatment guidelines have profound implications, limiting potential oral choices to ciprofloxacin, amoxicillin and trimethoprim-sulfamethoxazole, with cephalexin cautiously included as its resistance is approximately 19% in the population

(Sheerin and Glover, 2019). Health economic analysis suggest that empirical treatment driven by applied knowledge of the resistance rates in the local population delivers a more effective therapeutic option, without an increase in costs (Sheerin and Glover, 2019). Therefore it is important to accurately diagnose the UTI in order to treat effectively and thereby reduce costs of treatment (Sheerin and Glover, 2019).

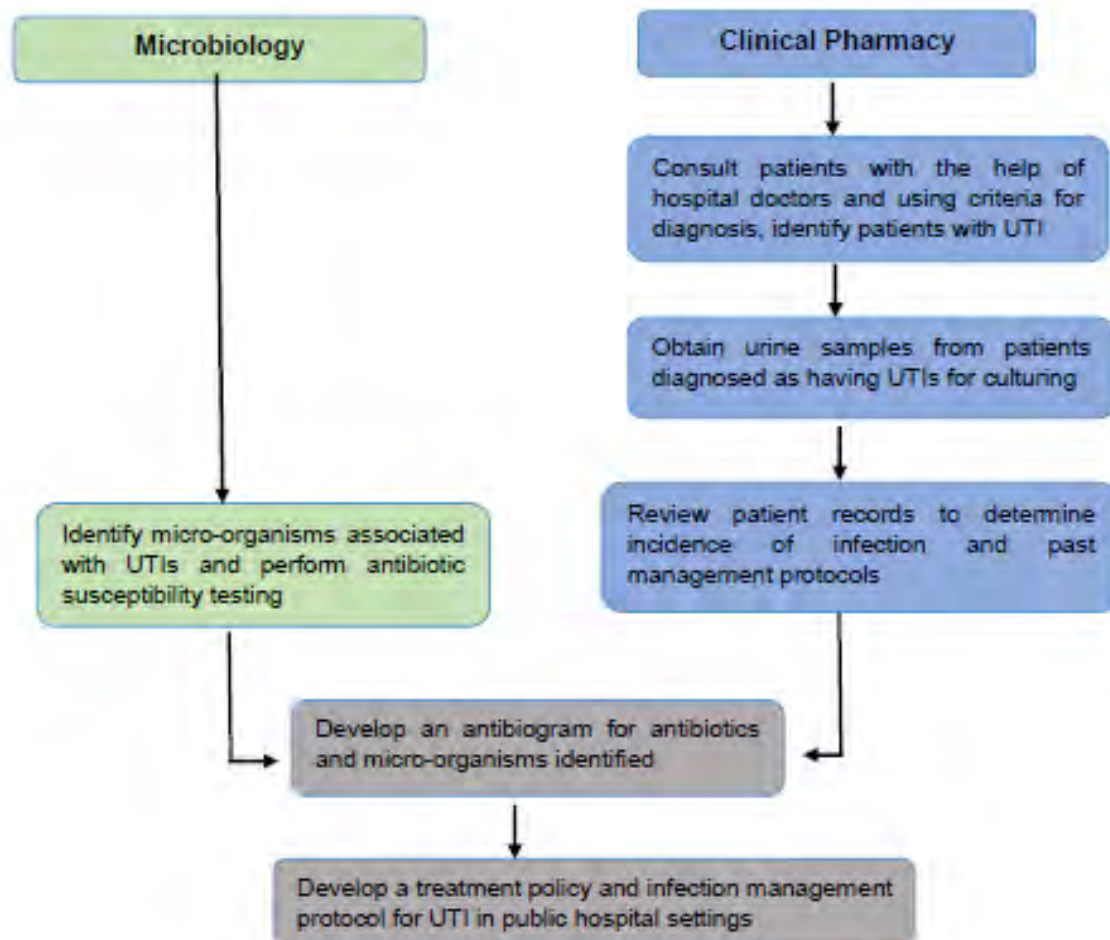
### **1.7. Aim and objectives**

The aim of this study was the determination of antimicrobial resistance patterns of UTIs in a selected public hospital in Johannesburg, in order to suggest an effective treatment protocol as well as a protocol on infection management practices.

**The study objectives were then subdivided into the following;**

- To determine the antimicrobial resistance patterns of confirmed UTI infections within identified patients seeking treatment at the study hospital.
- All patients gave oral and written consent (Appendix B). In order to select complicated and uncomplicated UTI patients, blood glucose tests and pregnancy tests were carried out as well as checking their file to confirm the details. Complicated refer to pregnant patients and uncomplicated refer to non-pregnant patients.
- Taking samples and isolating bacteria responsible for the UTI.
- Antibiotic susceptibility testing
- Identification of micro-organisms from isolated bacteria.
- To determine, through review of patient records, the likelihood of past urinary tract Infection and to determine past treatment practices in the management of these infections.
- To suggest a treatment protocol and infection management practices for UTIs in the study hospital based on findings of all the objectives.

A flow chart (Figure 1.2) presents how the study was systemically conducted.



**Figure 1. 2:** A workflow schematic showing summary of study objectives

### 1.7.1. Study design

This study consists of two phases which includes the experimental quantitative study and retrospective review. Experimental quantitative study design is applied when results are measured before and after treatment to establish causality (Tai *et al.*, 2013). This therefore entails identifying the causative organism and determining the rate of reoccurrence of infection (Tai *et al.*, 2013). The second component of the study, the retrospective review, is defined as a type of research design where pre-recorded patient-centred data is analysed to answer research questions (Linhares *et al.*, 2013).

### **1.7.2. Outline of the dissertation**

Chapter one discussed the background, literature review and rationale for this study. The literature review provides a detailed overview of research conducted and results published regarding UTIs. The available treatments for the treatment of UTIs are discussed, also the reoccurrence, antimicrobial resistance patterns and pharmacoeconomics. This chapter also includes the stated research question together with the aim and objectives of the study including the study design.

Chapter two will explain the methodology followed in selecting patients. The method followed in collecting the data with specific data collection instruments will be explained. The data analysis, as well as the validity of the data will be discussed.

Chapter three will include culturing, susceptibility testing and identification of the bacterial isolates. The methodology for each process is also outlined in this chapter as well as the results, discussion and summary of the findings.

Chapter four is the clinical pharmacy chapter. The retrospective review of patient data will be collected and it will outline the methodology followed in collecting the data. Guidelines for the treatment of UTIs will be made by analysing the data for chapter three and four.

Chapter five will start with an overview of the study, followed by ensuring that data collected pertaining to the objectives are analysed and discussed. The chapter concludes the study with a discussion on the limitations of the study, recommendations made and a conclusion.

## **CHAPTER 2**

### **CLINICAL SAMPLING**

---

#### **2.1. Introduction**

The choice of urine sampling in UTIs may highly impact the accuracy of the diagnosis hence leading to under or overtreatment (Vasudevan, 2014). The main concern is that if handling of urine samples is done inadequately, the risk of contamination increases therefore the patient is diagnosed and treated inaccurately (Sheerin and Glover, 2019). Sampling accuracy increases when the sample size increases therefore it is important to determine safe sample sizes in order to obtain reliable data (Sofia *et al.*, 2019).

This chapter aims to identify and categorise patients seeking treatment for UTIs at the study hospital. Patient demographics, dipstick, blood glucose and pregnancy testing were sourced and recorded on the data collection tool (Appendix H).

#### **2.2. Ethics**

Ethics was obtained from the Human Research Ethics Committee (HREC) of the University of the Witwatersrand (clearance certificate number M180645) (Appendix A). This consent was granted based on the provision of patient confidentiality and safety by using key numbers for identification of all participants (for example A001, A002) on the participant collection tool and thus, information given could not be traced to their names. The patient information leaflet was given to the patient before getting consent to participate in the study. Oral and written consents (Appendix B) were obtained from the hospital and participants before starting the study.

The safety of the principal investigator was ensured by carrying out the work in collaboration with, and under the guidance of the nurses and laboratory staff that had the necessary knowledge for handling infectious samples. Protective wear including

laboratory coats, scrubs, face masks and gloves were provided, to minimize the risk of exposure to infectious micro-organisms.

### 2.3. Setting

This study was conducted in a selected public hospital with 781 843 persons as an average patient population per year. The sample size (n) was calculated using the standard statistical formula for sample size determination as provided in Equation 1 (Odoki *et al.*, 2019).

$$n = \frac{z^2 P(1-P)}{d^2}$$

n=sample size

z=stats for CI (CI=z.d)

P= expected prevalence (in proportion to 1)

d= precision d= (0.5(1-P))

**Equation 1**

The sample size calculated amounted to 200 cases for data collection. One hundred pregnant and one hundred non-pregnant women constituted the sample population, in order to include uncomplicated and complicated UTI cases. Participation from patients was done on the day of urine collection and no follow-up visits from the patient were required.

### 2.4. Methods

#### 2.4.1. Participants: Inclusion criteria

Participants were of female gender due to the predominance of UTIs associated with this cohort (Sofia *et al.*, 2019). Patients between 18 and 50 years of age were selected due to the need for legal consent and an increased incidence of UTIs in older cohorts (Sheerin and Glover, 2019). Urine that met the criteria for UTIs, that is, demonstrated at least two out of four for leucocytes, protein, blood and/or nitrites was identified using



urine dipsticks. Patients who had not taken antibiotics two weeks before the consultation were included in the study as antibiotics will not be concentrated in the urine sample, therefore the pathogen can be identified (Lewis *et al.*, 2013). Patient samples were included if they were of a pure isolate with a minimum of three colonies isolated making them eligible for this study (Sadler *et al.*, 2017). Urinary tract infections symptoms present (nausea, urge to urinate, vomiting, burning feeling upon urinating, frequent urinating, urine discolouration) were identified and classification made as to whether infection was considered symptomatic or asymptomatic (Lewis *et al.*, 2013). Asymptomatic UTIs occur when there is the presence of bacteria in the urine specimen but without symptoms suggestive of a UTI (Storme *et al.*, 2019b). Symptomatic UTIs occur when there is the presence of bacteria in urine with the presence of symptoms (Sheerin and Glover, 2019). Complicated UTIs were identified as patients who were pregnant or had high blood glucose levels. Uncomplicated UTIs were identified as non-pregnant patients or with blood glucose levels. patients Most episodes of UTIs are considered to be uncomplicated infections when occurring in otherwise healthy non-pregnant women (Dadzie *et al.*, 2019). A complicated UTI can occur in either the upper or lower urinary tract, but is accompanied by an underlying condition which increases the risk of therapy failing The absence of symptoms did not prohibit the patient from participating in the study (Sadler *et al.*, 2017). Invitation to participate was only done if the patient met the requirements of the study and then provided with a Patient Information Sheet (Appendix I), alongside a Patient Informed Consent form (Appendix B).

#### **2.4.2. Participants: Exclusion criteria**

The study excluded male patients due to their low incidence of UTIs (Sheerin and Glover, 2019). Women on their menstrual periods were excluded as samples could provide a positive result for blood on the dipstick with no positive urinary tract infection (Sadler *et al.*, 2017). Patients with urinary tract abnormalities (ranging from mild to asymptomatic malformations such as a double ureter or minimal ureteral pelvic obstructions to severe life threatening pathologies like renal dysplasia) were excluded due to increased prevalence of infection linked to this cohort (Sheerin and Glover, 2019). These abnormalities were identified from the patient file data. Patients who

were diagnosed with a sexually transmitted infection (STIs) were excluded as the treatment for STIs includes multiple antibiotics (Dolinsky *et al.*, 2017).

## **2.5. Patient selection**

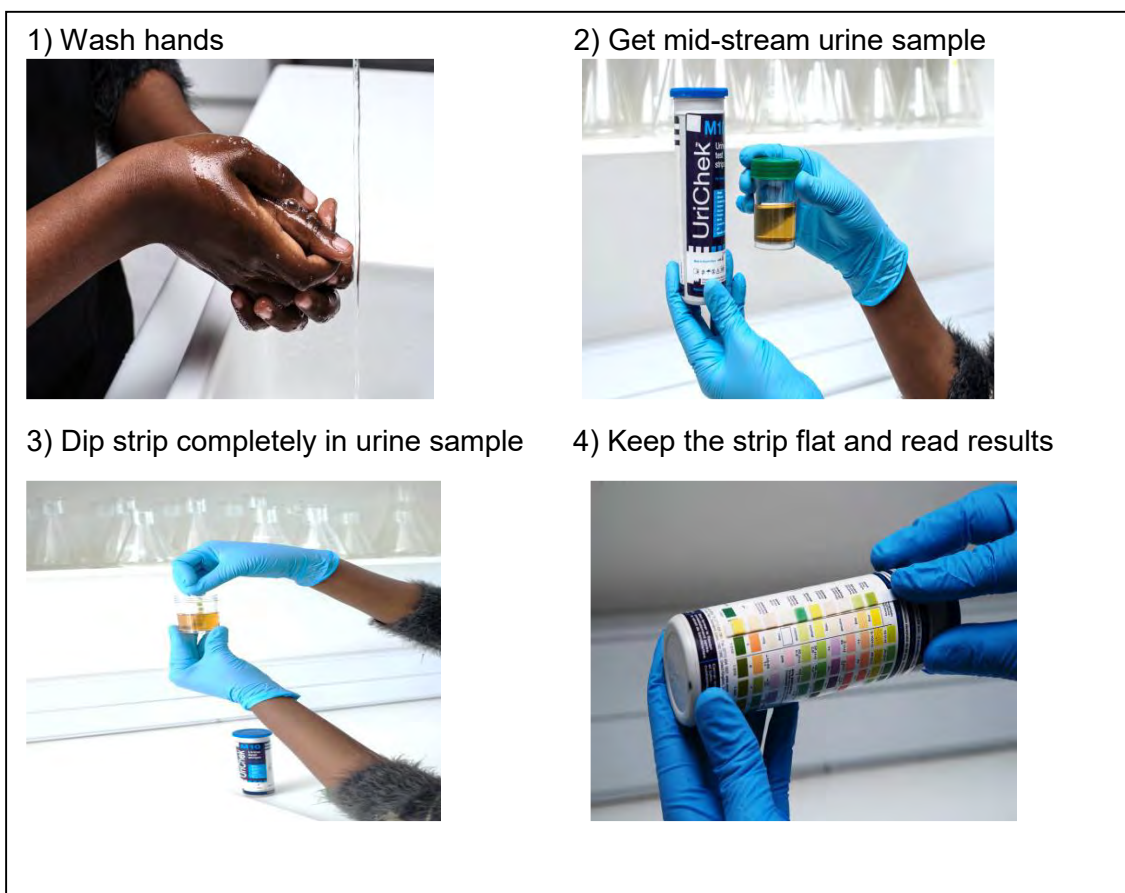
Patients were first identified after checking the symptoms of UTIs with the help of professional nurses. Patients who presented with symptoms mentioned in Section 2.4.1 were identified as potential study candidates. The patients were then asked if they would like to participate in the study following provision of study information. Upon positive affirmation of consent to participate, candidates were educated on how to provide a midstream urine sample. Upon return of the sample, dipstick testing was carried out and if found to be positive for midstream UTI, i.e. demonstrates at least two out of four for the criteria for protein, blood, leucocytes or nitrites, patients were then enrolled in the study. Point of care testing, an investigation taken at the time of consultation with instant availability of results to make immediate decisions about patient care, was applied in order to classify the patient as having a complicated or uncomplicated UTI.

### **2.5.1. Urine sample collection**

The patients were educated on how to collect mid-stream urine samples to prevent contamination. Before collecting urine samples, the patient was required to wash their hands with soap and water. A pre-labelled urine collection cup (labelled with a specific key for a specific patient, for example A001, etc) with the preservative, buffered boric acid was opened just before urinating, and then immediately recapped tightly. The patient was informed to void the first portion of the urine stream into the toilet and the mid-stream in the container to avoid contamination. The inside of the container did not come into any contact with any of the body parts, clothes or external surfaces. The pre-labelled urine container was placed in a cooler box with ice packs for transportation to the Department of Pharmacy and Pharmacology Microbiology Laboratory for specimen culturing. The urine specimens were cultured within the first twenty-four hours.

### 2.5.2. Urine Dipstick

Urine dipstick testing is a frequent method used for diagnostic testing if there is clinical evidence that a patient has the symptoms of a UTI (Dadzie *et al.*, 2019). Urine dipstick detects nitrites (metabolic product of typical pathogens of the urinary tract), leukocyte esterase, blood (a marker of inflammation) and protein, as the presence of these is indicative of a UTI (Sadler *et al.*, 2017). The dipstick test was conducted by immersing the dipstick fully in the urine sample for two minutes and allowing it to absorb the urine. The colour panels on the dipstick change based on the content of the urine sample. The dipstick was then removed from the sample and laid flat on an absorbent towel. After approximately five minutes and the results were read by comparing each colour on the dipstick to the normal ranges that are specified on the urine dipstick bottle. Samples that had a positive mid-stream urine for UTI, which demonstrated at least two out of four for the criteria for proteins, blood, leucocytes or nitrites were automatically eligible for the study. Figure 2.1 demonstrates the salient steps undertaken for a urine dipstick analysis.



**Figure 2 1:** Urine dipstick testing

### 2.5.3. Point of care tests

Blood glucose and pregnancy tests were performed on the whole sample size.

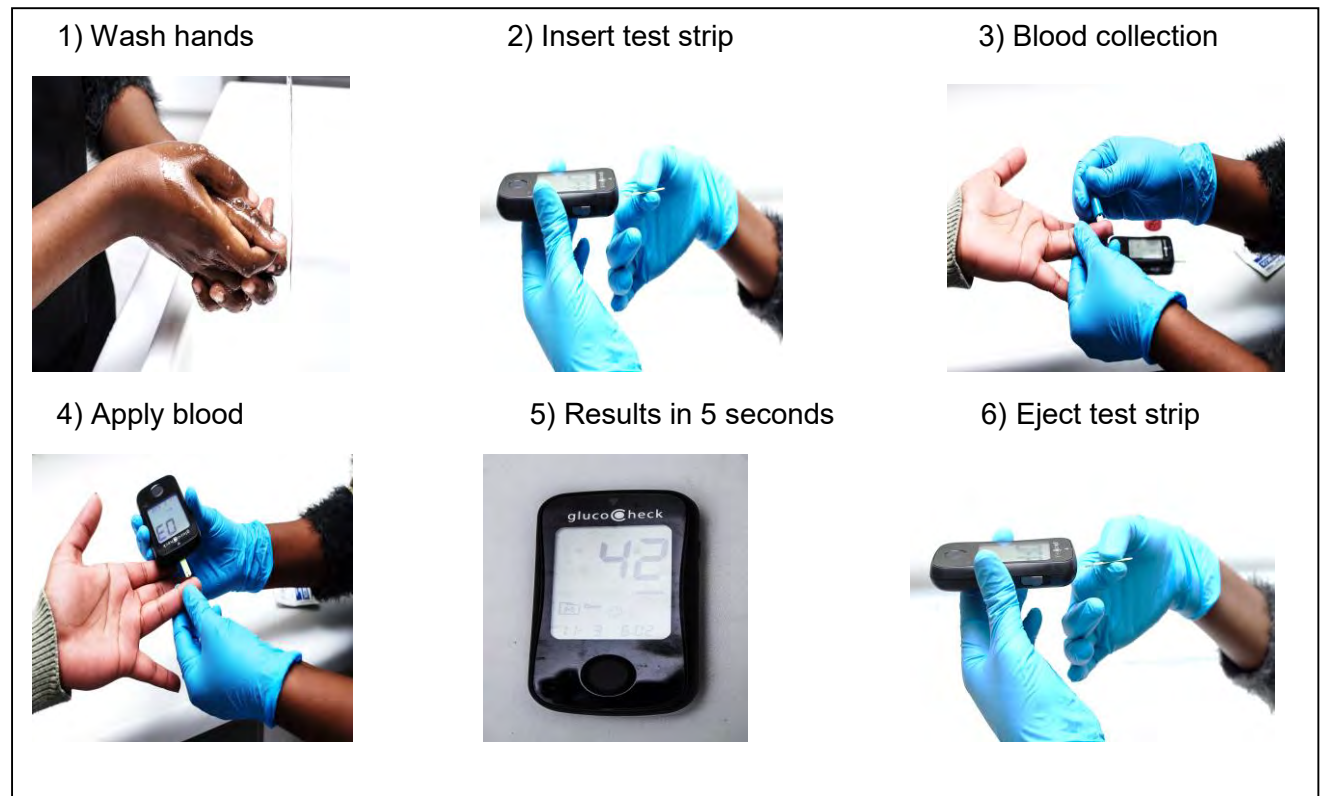
#### 2.5.3.1. Blood glucose test

Diabetic patients presenting with a UTI are classified as complicated in infection due to the association with this co-morbidity (Sadler *et al.*, 2017). The equipment needed (disposable latex gloves, alcohol swab, lance device, reagent strip and a calibrated blood glucose meter) were gathered. Hand hygiene was performed in the form of hand washing with Hibiscrub and wearing disposable latex gloves in order to prevent the transfer of micro-organisms. An alcohol swab was used to clean the puncture site on the patient which reduces the transmission of micro-organisms. The GlucoCheck reagent strip (HomeMed, South Africa) was removed from the container and immediately sealed with the container cap so that the remaining strips do not get exposed to environmental factors. The reagent strip was then placed in the GlucoCheck glucometer (HomeMed, South Africa). The appropriate puncture site, which are the sides of the finger (as there are less nerve endings) was selected and the skin puncture was performed. The skin was gently squeezed above the site. It is important to not touch the site as it may cause contamination. The droplet of blood needs to be large enough to cover the test pad on the reagent strip. The second drop of blood was transferred to the test pad and the blood droplet was absorbed for accurate results. The results were reviewed in five seconds and documented. This data was used to determine the patient's treatment plan. The blood glucose testing procedure was interpreted as the patients' blood glucose level (Table 2.1).

**Table 2. 1:** Blood glucose result descriptions

| Glucose level                                                      | Indication                             |
|--------------------------------------------------------------------|----------------------------------------|
| Below 5.5 mmol/L (below 99 mg/dL)                                  | Normal glucose level                   |
| From 5.6-6.9 mmol/L (100-125 mg/dL)                                | Prediabetes (impaired fasting glucose) |
| 7.0 mmol/L (126 mg/dL) and above on more than one testing occasion | Diabetes                               |

If the blood glucose level was higher than normal, the patient was referred to the clinic doctor. Figure 2.2 demonstrates the method undertaken for a glucose point of care test.

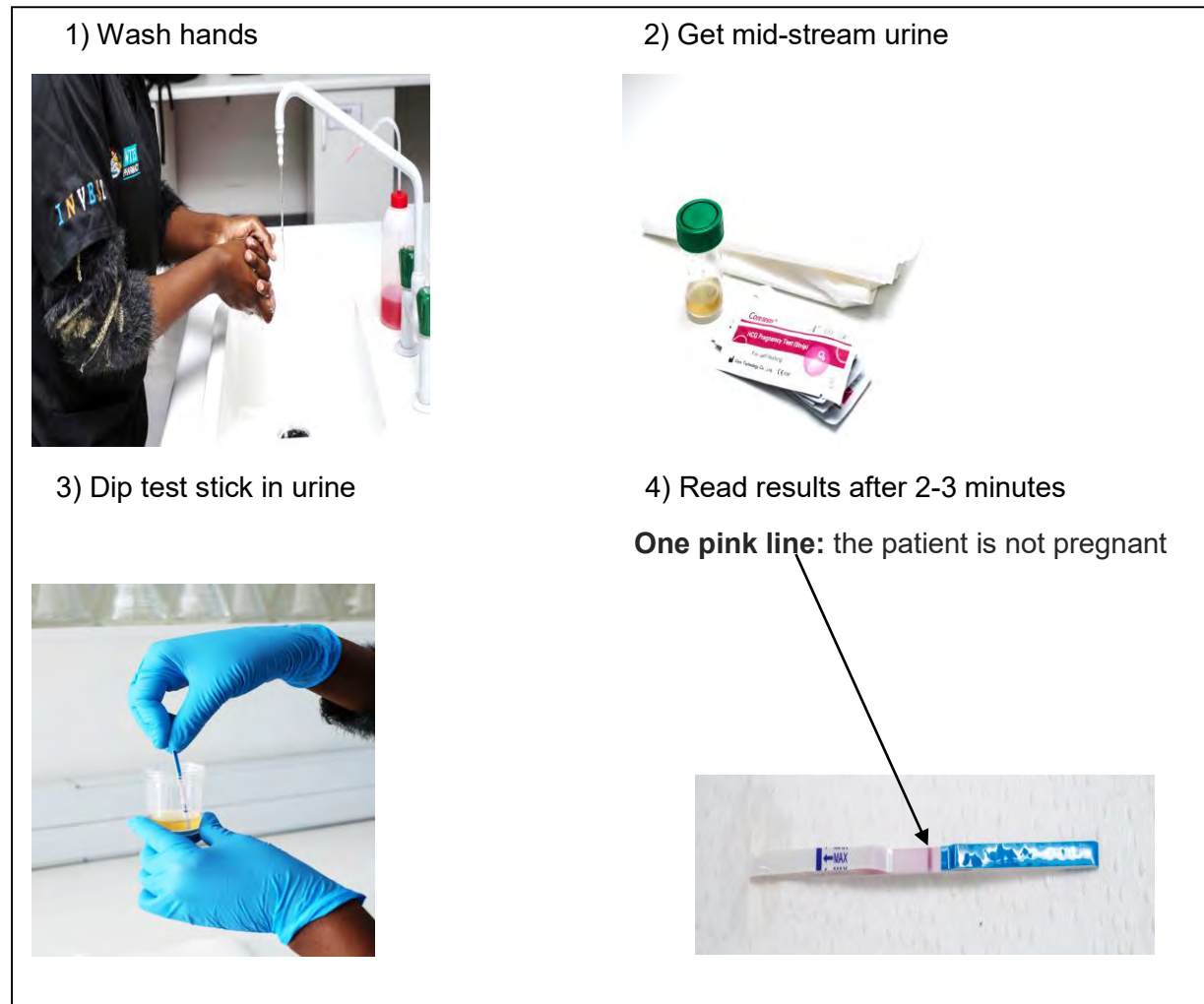


**Figure 2.2:** Blood glucose test procedure

### 2.5.3.2. Pregnancy test

Pregnant patients presenting with a UTI, are classified as complicated due to the management associated with this infection (Singh *et al.*, 2014). Certain antibiotics such as ciprofloxacin and trimethoprim-sulfamethoxazole cannot be given to pregnant patients as they may cause birth defects to the child, hence it is important to test for pregnancy in all female participants. The absorbent end of the test stick (Care Technology, UK) was dipped into the sample of urine that was separated from the urine sample cup and held for 10 seconds. The urine was first separated into a urine specimen jar in order to avoid contamination. The test stick was then laid on a flat surface for two minutes before reading the results. Once the waiting time had passed,

the test stick was checked for the results and interpreted as pregnant if two lines are formed and non-pregnant if only one line forms. If pregnant, the patient was referred to the clinic doctor for further assessments and the sample included in the study. Figure 2.3 demonstrates the process followed for pregnancy determination.



**Figure 2. 3:** Pregnancy test procedure

## 2.6. Data analysis

The initial descriptive analysis of the results was completed based on the obtained data from eligible participants. For instance, demographic features of the included participants were described, such as the patient sex, age, and the study design. Data analysis was applied using computerized software such as, Microsoft Excel, statistics and data (STATA). STATA was used to manage and analyse large data sets. The sample size used for this study was calculated to present 25% of the hospital patients

seen at the study hospital per year. Correlations between antimicrobial resistance patterns with known antibiotic susceptibility (with 95% confidence intervals) in complicated and uncomplicated UTIs calculated using a random-effects meta-analysis model. The effect size was considered statistically significant at 5% level ( $p < 0.05$ ) if the value of the pooled variance was within 95% confidence interval (CI) (Sadler *et al.*, 2017).

## 2.7. Results and Discussion

### 2.7.1. Patient demographics: complicated vs uncomplicated

On enrolment to the study, participant age was recorded on the allocated patient information leaflet using the descriptive key for confidentiality. Table 2.2 shows the ages of the enrolled participants to the study.

**Table 2. 2:** Patient demographics for complicated and uncomplicated UTIs

| Age                             | Uncomplicated UTI | Complicated UTI |
|---------------------------------|-------------------|-----------------|
| 16-27                           | 52                | 49              |
| 28-38                           | 41                | 48              |
| 39-50                           | 7                 | 3               |
| <b>Total number of patients</b> | 100               | 100             |

A total of 200 clinical urine samples were collected after considering the inclusion and exclusion criteria. The accuracy of the urine test in diagnosing UTIs was studied from the representative samples of uncomplicated (non-pregnant) and complicated (pregnant) patients. Low socioeconomic status, advanced age and high parity among others are factors associated with UTIs in women (Sadler *et al.*, 2017). In a study conducted in Ethiopia, 367 women who were pregnant with symptomatic or asymptomatic UTIs were examined throughout the study period. From the results obtained in this study, the 16-27 age group had more UTI incidences than the 28-38 and 39-50 age groups. This was consistent with the study that identified that the minimum and maximum ages of 17 and 39 years, respectively in pregnant women with

a higher UTI incidence in the 25-39 age group (Tessema *et al.*, 2020). The minimum and the maximum age of the pregnant women were 17 and 39 years respectively with mean age was 25.8. The predominant age group was 20–24 years, the majority of the group of study participants are at their second and third trimester of pregnancy with no significance variation with the rate of UTIs (Tessema *et al.*, 2020). In another study, a 184 urine samples were collected in four months. The mean age was  $48.5 \pm 12$  years (Kidwai *et al.*, 2017). 83(45.6%) patients were between 45-60 years (Kidwai *et al.*, 2017).

### 2.7.2. Dipstick, blood glucose and pregnancy test results

On the day of enrolment, dipstick, blood glucose and pregnancy tests were conducted and recorded on the patient information leaflet. Table 2.3 shows point of care test results of the enrolled participants to the study.

**Table 2 3:** Point of care testing in complicated and uncomplicated UTIs

| Point of care testing       | Uncomplicated UTI (%) | Complicated UTI (%) |
|-----------------------------|-----------------------|---------------------|
| Leucocytes (leuco/ $\mu$ L) | 100                   | 100                 |
| Nitrites                    | 93                    | 96                  |
| Protein (g/L)               | 76                    | 69                  |
| Blood (Ery/ $\mu$ L)        | 34                    | 41                  |
| Diabetes (mmol/L)           | 13                    | 21                  |
| Pregnancy                   | 0                     | 100                 |

In this research the sensitivity of urine dipstick (nitrate and leukocyte esterase in combination) was 93% and 100% respectively in uncomplicated UTIs and 96% and 100% in complicated UTIs which is similar to the study by (Tessema *et al.*, 2020), where the sensitivity of the dipstick test resulted in 98.9% and 86.7% respectively. In South Africa the most health care facilities use dipstick analysis to determine if a patient has a UTI but according to other studies, dipstick tests have poor sensitivity to



detect UTIs (Dadzie *et al.*, 2019, Mambatta *et al.*, 2015). A study revealed that pregnant women are at a higher risk of getting UTIs, starting in week six and hitting the highest point during weeks 22 to 24. Another study revealed that the sensitivity of dipstick tests of leukocyte esterase was 50% for pregnant women with asymptomatic UTI and 71.4% for pregnant women with symptomatic UTIs respectively (Tessema *et al.*, 2020).

### 2.7.3. Patient demographics: Underlying conditions

Co-morbidities and risk factors were recorded on the day of enrolment on the allocated patient information leaflet (Appendix H). Table 2.4 shows the co-morbidities and risk factors of the enrolled participants to the study.

**Table 2. 4:** Co-morbidities and risk factors in complicated and uncomplicated UTIs

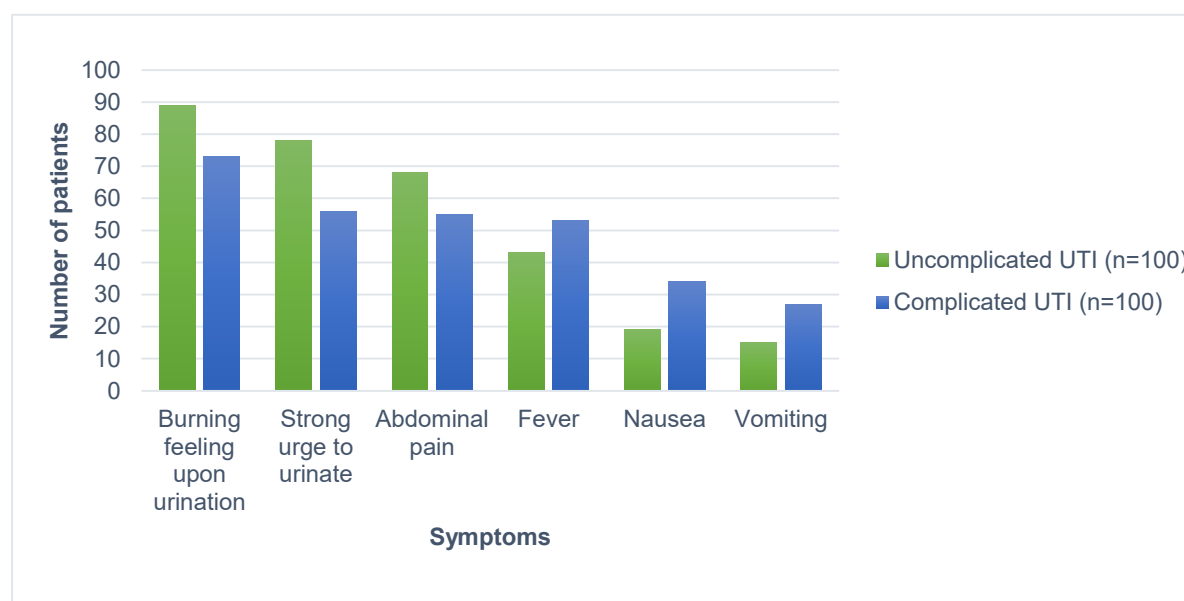
| Co-morbidity or risk factor                         | Uncomplicated UTI (%) | Complicated UTI (%) |
|-----------------------------------------------------|-----------------------|---------------------|
| HIV                                                 | 27.3                  | 14.7                |
| Co-trimoxazole usage as prophylaxis in HIV patients | 23.8                  | 26.7                |
| Diabetes mellitus                                   | 16.9                  | 27.3                |
| Urine catheterisation                               | 31.2                  | 18.7                |
| Use of spermicide                                   | 6.5                   | 0.0                 |
| Urinary incontinence                                | 13.0                  | 2.7                 |
| Hypertension                                        | 5.2                   | 9.3                 |

Previous studies noted that the substantiated risk factors for UTIs are frequent sexual intercourse, use of spermicide, history of UTI infections, immunocompromised patients and family history (Tan, 2019). Diabetic mellitus is a common chronic condition in South Africa. In adults aged between 21 to 79 years, 7% have diabetes in South Africa and that is 3.85 million people (Tessema *et al.*, 2020). The global prevalence of diabetes has nearly doubled and equally affects both men and women (Bash *et al.*, 2016). The presence of hypertension during pregnancy especially linked

to genetic factors may increase the chances of getting UTIs (Tan, 2019). Diabetic women are predisposed to an increased risk of developing UTI. This predisposition results from many factors such as glycosuria, adherence of bacteria to the uroepithelium and dysfunction of the immune system (Bash *et al.*, 2016). The overall prevalence of diabetes in this study was 18.29%. In this study, HIV positive patients (23.8% uncomplicated and 26.7% complicated) were on co-trimoxazole for prophylaxis, however they had reoccurrences of UTIs which may be due to resistance.

#### 2.7.4. Patient symptoms

Symptoms were recorded on the day of enrolment on the patient information leaflet. Figure 2.4 shows the symptoms of the enrolled participants to the study.



**Figure 2 4:** Complicated and uncomplicated UTIs: symptom distribution.

When a patient develops a UTI, the lining of the bladder and urethra are irritated which cause lower abdomen pelvic pain (Tan and Chlebicki, 2016). Burning and pain when urinating is the most common symptom (Sofia *et al.*, 2019). The patient can feel a strong urge to urinate but only get a few drops because of bladder irritation (Sheerin and Glover, 2019). Kidney infections on the other hand cause nausea, vomiting, fever and upper back pain (Tessema *et al.*, 2020). Kidney infections need to be treated at

once because they can spread into the blood and cause life-threatening infections (Tan and Chlebicki, 2016).

## **2.8. Summary**

- The age group 16-27 had more UTI incidences.
- Leucocytes were found in 100% of the patients who participated in the study.
- All the patients who were pregnant presented with complicated UTIs.
- The majority of the patients had a burning feeling upon urination as a major symptom.
- Most patients with complicated UTIs had diabetes mellitus.

## **CHAPTER 3**

# **CULTURING, SUSCEPTIBILITY TESTING AND IDENTIFICATION**

---

### **3.1. Introduction**

Among urinary tract infection causing pathogens, bacterial resistance has been steadily progressing over the last three decades. Available data confirms that the increase in resistance to commonly used antibiotics is a consequence of inappropriate use of antimicrobial agents (Vasudevan, 2014). The development of resistance among the pathogens responsible for UTI is an issue of serious concern and requires immediate attention in order to derive a suitable remedy to overcome the problem (Sadler *et al.*, 2017).

This chapter aims to isolate pathogens, identify, and determine the antimicrobial resistance patterns in samples from confirmed urinary tract infections within patients seeking treatment at the study hospital. Urine samples that were collected were cultured, antibiotic susceptibility testing undertaken, followed by the identification of micro-organisms causing the UTIs.

### **3.2. Methods**

#### **3.2.1. Urine sample collection**

The patient urine samples were collected as outlined in Chapter 2 (Section 2.7.1). During the collection process (in order to maintain cold conditions and the integrity of the sample), urine samples were stored on ice packs which were transported to the Pharmaceutical Microbiology laboratory within four to six hours where they were cultured.

### **3.2.2. Agar preparation**

Forty grams of Mueller Hinton agar (Oxoid, Thermofisher Scientific) was suspended in 1 liter of distilled water. The mixture was autoclaved at 121°C for 30 min and cooled to 45-50°C. Fifty milliliters of 5-10 % sheep's blood (South African Vaccine producers; Modderfontein, South Africa) was added aseptically. Fifteen to twenty milliliters of the ready media were poured in to sterile petri dishes. The sealed petri dishes were left standing for 30 min to solidify. The culture media plates were stored upside down at 2-8°C to reduce contamination and were kept for up to 16 weeks provided there was no change in the appearance of the medium to suggest contamination, hemolysis, or deterioration. Quality control was managed in the laboratory by swabbing the sheep's blood onto Mueller Hinton agar, incubated at 37°C for 24 hrs and checked for growth, if there was no growth then the blood was considered sterile.

### **3.2.3. Urine sample culturing**

Contamination of samples was avoided when streaking by discarding urine samples that had not been cultured within 24 hrs of collection. All equipment used was sterile and autoclaved before use. Monitoring of the quality of specimens, sample preparation and testing, decontamination, reagents and equipment, and reviewing of results was done using established laboratory operating procedures. A 1 µl loop was used to inoculate the urine specimen onto Mueller Hinton agar enriched with 5% sheep's blood. The choice of blood agar for culturing of samples is due to the pathogenicity of foreign invaders associated with UTIs and the rich nutritional environment when compared to the Mueller Hinton media alone (Alkhyat and Al-Maqtari, 2014). The inoculated agar plates were incubated in an inverted position for 24 hrs at 37°C (aerobic and anaerobic conditions), following which they were inspected for bacterial growth. Microbiological evidence of a UTI was considered if there were greater than 10 identical bacteria colonies, i.e. over 100 colony-forming units (CFU) per plate.

The urine sample was reported as having no significant growth if there were less than 10 bacterial colonies and was excluded from the study. If one to three different types of bacterial colonies were present in an individual sample, the colonies were streaked onto separate blood agar plates to culture single colonies and then identified

separately. Urine samples were discarded if more than three bacterial colony types were identified as these samples might yield results not indicative of UTI infections.

#### **3.2.4. Single colony culturing**

The source plate (sampling from patient) was examined to identify the number types of single colonies. These were colonies which have significantly different macro morphology traits, that is, size, colour shape, elevation and margin. The agar plate was labelled with a key, for example A050 1, A050 2 etc in order to keep track of the type of colony being streaked and its association with the patient information. A platinum wire bacteriological loop was flamed, cooled and the source plate was opened. The edge of the first selected colony was touched to pick up a tiny sample and the primary streak was applied. The loop was reflamed and cooled as before, then a secondary streak was performed starting from the terminal end of the primary streak, sweeping across the top of the quadrant, cross streaking several times back and forth through the primary streak. The plate was rotated at 90° and cross streaked through the secondary streak, starting at the far end, working towards the primary streak, and filling the rest of the quadrant. The agar plates were incubated for 24 hrs at 37°C under aerobic conditions).

#### **3.2.5. Macro morphology descriptions**

During the process of separating mixed cultures into single colonies, each sample was given a key, for example, patient B054 had three mixed colonies, on separation they were labelled as B054 1, B054 2 and B054 3 etc. These were recorded for easy location and grouping identical colonies. The morphologies that were recorded were size, colour, shape, margin and elevation. Different types of bacteria will produce different colonies. Some colonies may be coloured, and some circular in shape, while others are irregular (Wagenlehner *et al.*, 2011). The size of single colonies is when the diameter of the colony is measured. They are divided into large (1 mm-3 mm), small (<1 mm), granulated and tiny (pinpoint colonies that are 10 times smaller than small colonies) (Aiyegoro *et al.*, 2007). The colour/pigmentation of colonies differ in different types of bacteria, i.e. some are white, grey, brown, yellow, red or purple. The different shapes of bacteria include round (circular), irregular, spreading, filamentous and

rhizoid colonies (Sadler *et al.*, 2017). The margin or boarder of the colonies shows the magnification of the shape, i.e. the edge of a colony. Examples of margins are entire, undulate and filiform. The elevation of colonies describes the side view of a colony and this can be observed by turning the petri dish sideways. Elevation can be described as being flat, raised, convex, umbonate and irregular (Alkhyat and Al-Maqtari, 2014). Therefore, colonies that had the same size, colour, shape, elevation and margin were grouped together with their respective key numbers. As a collective group, they were assigned a number to represent the typical morphology observed across all samples within the group.

### **3.2.6. Antimicrobial susceptibility testing**

The antimicrobial susceptibility patterns of bacterial isolates were determined by disk diffusion method (Kirby–Bauer) according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI, 2020). A transfer of 0.1 ml of bacterial culture (refer to Section 3.2.4 for the single colony culturing method) was applied to the surface of a Mueller Hinton agar plate enriched with 5% sheep's blood. Using a sterile spreader, the culture was spread evenly over the agar surface. Commercially prepared antibiotic disks (ciprofloxacin at 5 mcg, fosfomycin at 50 mcg, amoxicillin at 10 mcg, cephalexin at 30 mcg, trimethoprim-sulfamethoxazole at 25 mcg and amoxicillin/clavulanic acid at 20 mcg) all purchased from commercial suppliers (Thermofisher Scientific, South Africa), were then evenly dispensed onto the agar surface using a six space disk dispenser (Oxoid antimicrobial susceptibility disk dispenser, Thermofisher Scientific). These antibiotics were selected as they are the antibiotics of choice for the treatment of UTIs (Sadler *et al.*, 2017). In addition, nystatin (100 mcg), an antifungal agent, was selected as a control to confirm the bacterial origin of the test sample. Amoxicillin/clavulanic acid was not selected for uncomplicated UTIs because it is not indicated for treatment on STG but amoxicillin which is indicated was included. Inoculated agar plates were incubated in an inverted position for 24 hrs at 37°C (aerobic and anaerobic conditions). Following incubation, the zones of inhibition for each sample were measured. During incubation, the antibiotic diffuses outward from the disks, creating a gradient of antibiotic concentration in the agar such that the highest concentration is found close to the disk with decreasing concentrations further away. The zone around an antibiotic disk that has no growth is referred to as the zone

of inhibition since this gives the minimum antibiotic concentration sufficient to prevent growth of the test bacterial isolate. This zone of inhibition was measured in millimetres, using a pair of callipers, from the edge of the disk to the edge where microbial growth occurs. Three readings were obtained for each disk and the average was calculated. The study was done in duplicate. Susceptibility patterns are compared to breakpoints in order to define isolates as susceptible or resistant (CLSI, 2020).

### **3.3. Culture identification by MicroScan testing procedure**

The MicroScan WalkAway 96 (Dade-Behring, USA) system is a programmed system which incubates microtiter identification, interprets biochemical results through the use of a photometric or fluorogenic reader, and generates computerized reports. Forty bacterial isolates (16 groups associated to complicated UTIs and 24 groups associated to uncomplicated infections) were selected based on the grouped macro morphology results. Bacterial isolates with similar macro morphologies were grouped. From each group a representative bacterial isolate was selected and plated on Mueller Hinton agar with 5% sheep blood. The MicroScan WalkAway 96 system served as the reference method for identification (Sadler *et al.*, 2017). Prior to testing, the isolates were classified into two major categories of Gram-positive and Gram-negative bacteria by sub-culturing samples from the Mueller Hinton agar with 5% sheep's blood onto MacConkey agar and incubated for 24 hrs. MacConkey agar inhibits the growth of Gram-positive bacteria due to the presence of crystal violet and salts and Gram-negative bacteria grow well on MacConkey agar. Individual isolates of Gram-negative and Gram-positive bacteria were separated then inoculated into the WalkAway identification panels for rapid identification.

The rapid fluorogenic panels for identification of Gram-negative bacilli and Gram-positive bacteria used fluorogenic substrates (4-methylumbelliferone or 7-amino-4-methylcoumarin attached to a phosphate, sugar moiety, or amino acid) or fluorometric indicators (Setu *et al.*, 2017). Identification was based on hydrolysis of fluorogenic substrates, pH changes following substrate utilization, production of specific metabolic by products, or the rate of production of specific metabolic by products after 2 h of incubation. Fluorogenic panels provided a 3.5 to 7h identification result for Gram-



negative bacteria and a 3.5 to 15h identification result for Gram-positive bacteria. Identifications were accepted if the likelihood of that identification was greater than or equal to 85% (Sadler *et al.*, 2017). Figure 3.1 demonstrates the sequence of methodology from urine collection to microbial identification.

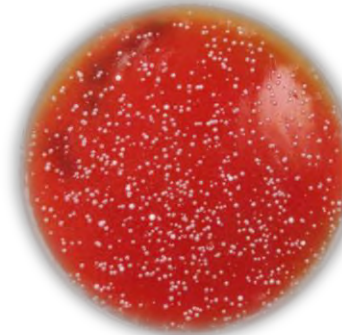
1) Urine sample collection



2) Culture in Mueller Hinton agar enriched with 5% sheep's blood



3) Results after incubating for 24 hrs at 37°C.



6) Culture identification using a MicroScan ([www.beckmancoulter.com](http://www.beckmancoulter.com))



5) Antimicrobial susceptibility testing



4) Separate mixed culture into single colonies



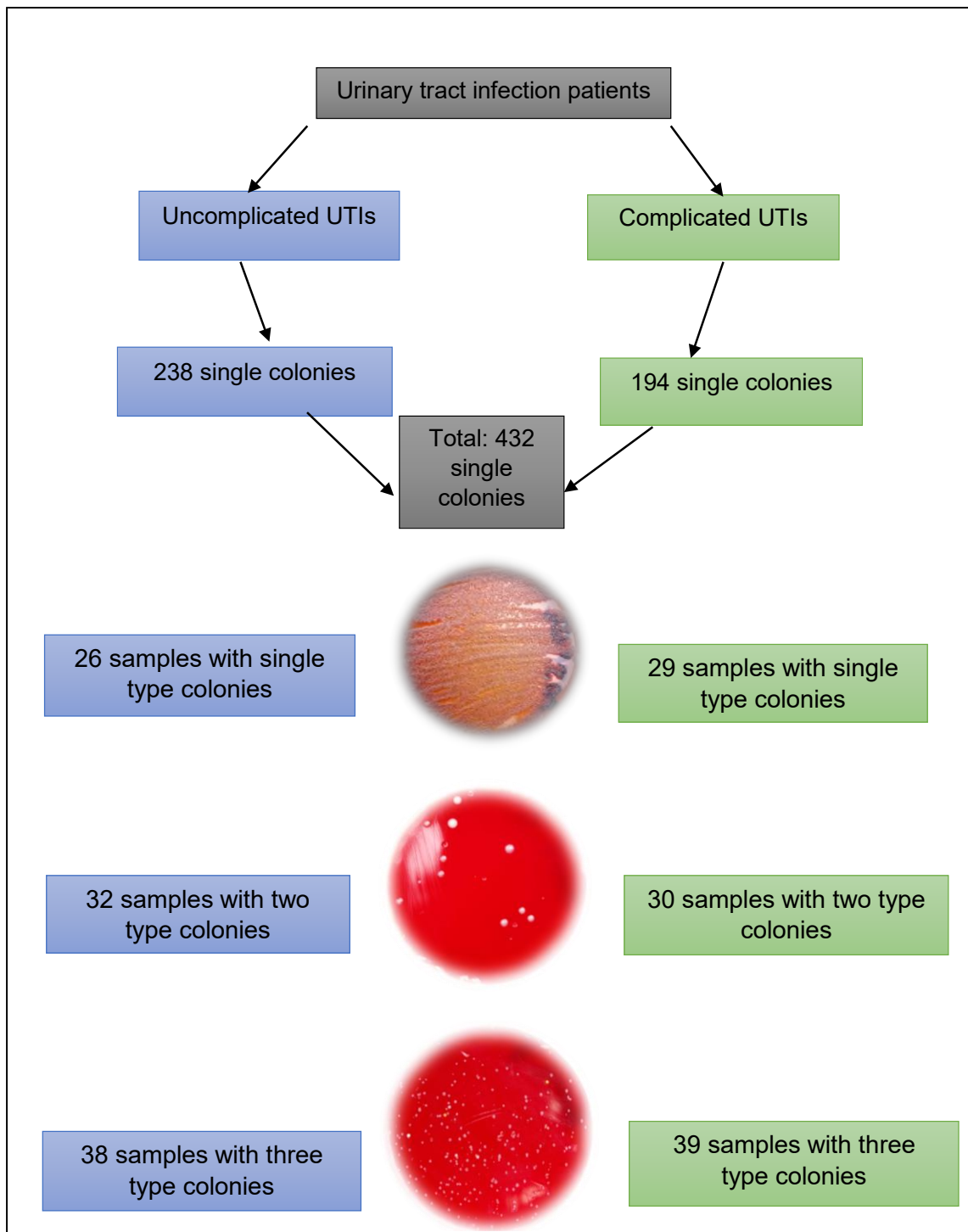
**Figure 3.1:** Step by step procedure of the microbiology methodology.

### **3.4. Results and discussion**

#### **3.4.1. Complicated and uncomplicated UTIs: Urine sample culturing**

Among the samples processed, all 200 urine samples showed bacterial growth which is in accordance with the reports of a previous study where an 90% positive culture from urinary tract infected patients was obtained (Sadler *et al.*, 2017). There were a total of 238 single colonies identified in uncomplicated UTIs and 194 single colonies identified in the complicated UTIs. The urine samples that were attained from the patients were cultured aseptically within 24 hours of collection.

The cultured samples either had one, two, three or multiple colony types (Figure 3.2).



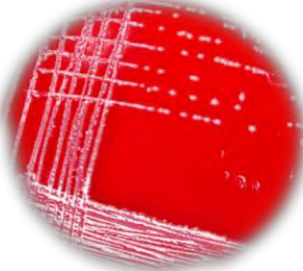
**Figure 3.2:** An overview of the colonies obtained after sample culturing.

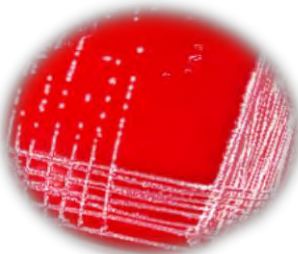
### 3.4.2. Uncomplicated UTIs: Macro morphology of micro-organisms

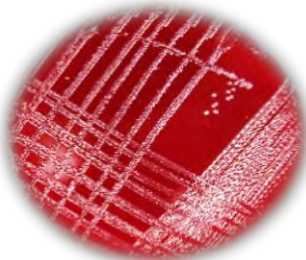
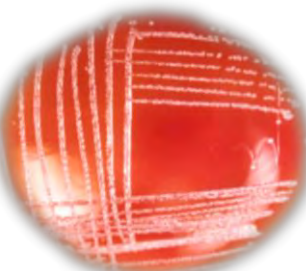
After separating mixed cultures into single colonies, the micro-organisms were analysed morphologically. Morphologies were determined for all 238 uncomplicated UTI samples (Appendix C). Table 3.1 shows the morphologies as grouped for samples showing identical macro morphological characteristics.

**Table 3.1:** The morphologies for samples showing identical macro morphological characteristics in uncomplicated UTIs.

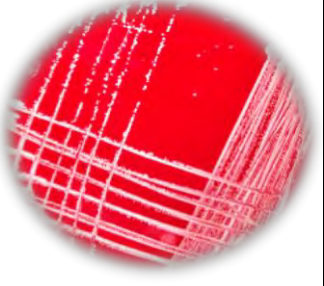
| Colony type                                                                         | Group ID | Description |        |                  |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|------------------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape            | Margin | Elevation |
|   | A1       | Large       | Cream  | Spreading colony | Entire | Flat      |
|  | A2       | Large       | Cream  | Spreading colony | Entire | Convex    |
|  | A3       | Large       | Cream  | Irregular        | Lobate | Convex    |

| Colony type                                                                         | Group ID | Description |        |                   |                  |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------------------|------------------|-----------|
|                                                                                     |          | Size        | Colour | Shape             | Margin           | Elevation |
|    | A4       | Small       | Grey   | Round             | Spreading colony | Convex    |
|   | A5       | Large       | Grey   | Irregular         | Entire           | Flat      |
|  | A6       | Large       | Grey   | Round             | Entire           | Convex    |
|  | A7       | Small       | Grey   | Round(not smooth) | Entire           | Flat      |

| Colony type                                                                         | Group ID | Description |        |           |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-----------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape     | Margin | Elevation |
|    | A8       | Large       | White  | Irregular | Lobate | Convex    |
|   | A9       | Small       | Grey   | Round     | Entire | Convex    |
|  | A10      | Small       | White  | Round     | Entire | Umbonate  |
|  | A11      | Large       | White  | Round     | Entire | Flat      |

| Colony type                                                                         | Group ID | Description |        |                  |                  |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|------------------|------------------|-----------|
|                                                                                     |          | Size        | Colour | Shape            | Margin           | Elevation |
|    | A12      | Small       | Grey   | Spreading colony | Entire           | Flat      |
|    | A13      | Small       | White  | Spreading colony | Spreading colony | Flat      |
|  | A14      | Small       | White  | Round            | Entire           | Flat      |
|  | A15      | Small       | White  | Round            | Entire           | Flat      |

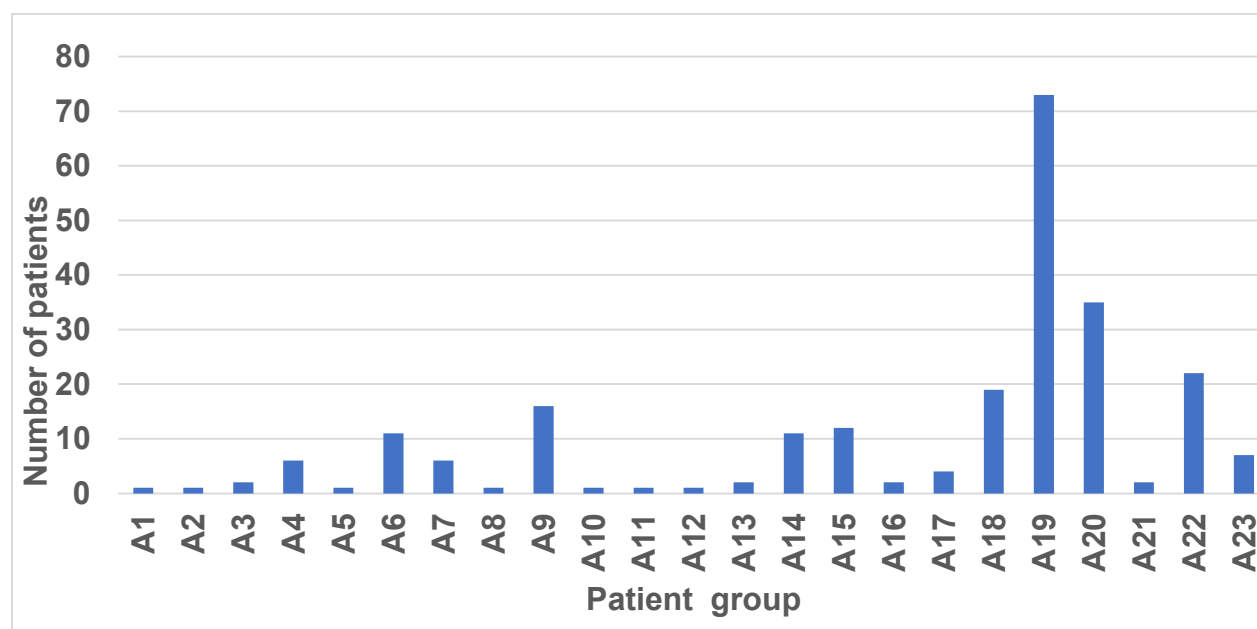


| Colony type                                                                         | Group ID | Description |        |       |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape | Margin | Elevation |
|    | A16      | Small       | Grey   | Round | Entire | Convex    |
|    | A17      | Small       | White  | Round | Entire | Convex    |
|  | A18      | Small       | White  | Round | Entire | Flat      |
|  | A19      | Small       | White  | Round | Entire | Flat      |

| Colony type                                                                         | Group ID | Description |        |       |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape | Margin | Elevation |
|    | A20      | Small       | White  | Round | Entire | Flat      |
|   | A21      | Small       | White  | Round | Entire | Convex    |
|  | A22      | Granulated  | Cream  | Round | Entire | Convex    |
|  | A23      | Small       | Yellow | Round | Entire | Flat      |

Pathogens with similar macro morphologies were grouped together and in uncomplicated UTIs, 23 groups were identified and given group numbers which are A1 to A23. Group A19 was determined as the most frequently isolated colony type.

This was followed by Group A20 then Group A22. Figure 3.3 shows the number of patients having samples showing identical macro morphological characteristics in uncomplicated UTIs.



**Figure 3.3:** Number of samples per patient group with the same morphologies in uncomplicated UTIs.

### 3.4.4 Uncomplicated UTIs: culture identification

The macro morphology and susceptibility results were used in grouping pathogens for identification. Twenty-three groups (A1-A23; Table 3.2) with similar macro morphology and susceptibility results in uncomplicated UTIs were selected for identification. Identification of the 23 groups is represented in Table 3.2. In uncomplicated infections, *E. coli* was determined as the most frequently isolated pathogen (43.5%) followed by *E. faecalis* (17.4%).

**Table 3.2:** The identified micro-organisms in uncomplicated UTIs.

| Identified pathogen     | Identified pathogens in uncomplicated UTI (%) |
|-------------------------|-----------------------------------------------|
| <i>Escherichia coli</i> | 43.6                                          |

| Identified pathogen                 | Identified pathogens in uncomplicated UTI (%) |
|-------------------------------------|-----------------------------------------------|
| <i>Enterococcus faecalis</i>        | 17.5                                          |
| <i>Enterococcus faecium</i>         | 8.8                                           |
| <i>Enterobacter</i> spp.            | 4.3                                           |
| <i>Staphylococcus haemolyticus</i>  | 4.3                                           |
| <i>Staphylococcus saprophyticus</i> | 4.3                                           |
| <i>Staphylococcus epidermidis</i>   | 4.3                                           |
| <i>Klebsiella pneumoniae</i>        | 4.3                                           |
| <i>Staphylococcus aureus</i>        | 4.3                                           |
| <i>Staphylococcus lugdunensis</i>   | 4.3                                           |

A previous study (Ahmed *et al.*, 2019), noted that the most commonly isolated micro-organisms from UTI infections were *E. coli* (27%), *K. pneumoniae* (12.4%), *P. mirabilis* (4.5%), *P. aeruginosa* (4.5%), *E. faecalis* (5.6%), and *S. saprophyticus* (3.4%) which was similar to this study. *Proteus* spp. was not identified in this research as it is mainly found in patients who are under long term catheterisation (Sofia *et al.*, 2019). According to Linhares *et al.* (2013), *E. coli* was the most commonly occurring micro-organism (64.3%), followed by *S. aureus* (21.4%) and *K. pneumoniae* (14.3%). In another study, Over 50% of the 958 pathogens tested were *E. coli* and *Klebsiella* spp. followed by *P. aeruginosa*, *Enterococcus* and *Enterobacter* spp. which was also similar to this study (Sadler *et al.*, 2017). In a recent study (Demarsh *et al.*, 2020), *E. coli* was the most common urinary isolate (61%), followed by *Klebsiella* spp. (15.1%), *Proteus mirabilis* (14%), *Enterobacter* spp. (5%) and *Serratia* spp. (2%).

### 3.4.3. Uncomplicated UTIs: Antimicrobial susceptibility patterns and resistance patterns

Antimicrobial susceptibility patterns and resistance patterns were determined for the isolates (Appendix F). The antibiotic demonstrating the highest susceptibility pattern, but moderate for uncomplicated UTIs ( $n = 238$ ) was fosfomycin (47.8%), followed by poor susceptibility rates with amoxicillin (26.1%) and ciprofloxacin (21.7%). The least susceptibility rate was found with cephalexin (3.8%) and trimethoprim-

sulfamethoxazole (8.7%). Breakpoints were used to check if antibiotics were sensitive or resistant to the pathogen identified. Breakpoint ranges were specific to the pathogen (CLSI, 2020). Table 3.3 shows the antimicrobial susceptibility patterns grouped with isolates having the same macro morphological characteristics.

**Table 3.3:** Antimicrobial susceptibility pattern summary per patient group for all 238 samples.

| Group ID | Susceptibilities (mm) |     |     |     |        |     |      |     |     |     | Pathogen identified               |
|----------|-----------------------|-----|-----|-----|--------|-----|------|-----|-----|-----|-----------------------------------|
|          | Cip                   | INT | Fos | INT | Amoxil | INT | Ceph | INT | TSX | INT |                                   |
| A1       | 2                     | R   | 25  | S   | 0      | R   | 0    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A2       | 9                     | R   | 24  | S   | 6      | R   | 8    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A3       | 26                    | S   | 24  | S   | 14     | S   | 8    | R   | 14  | S   | <i>Escherichia coli</i>           |
| A4       | 9                     | R   | 24  | S   | 0      | R   | 2    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A5       | 9                     | R   | 25  | S   | 0      | R   | 2    | R   | 3   | R   | <i>Escherichia coli</i>           |
| A6       | 10                    | R   | 24  | S   | 0      | R   | 3    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A7       | 4                     | R   | 9   | -   | 18     | S   | 6    | R   | 2   | R   | <i>Staphylococcus lugdunensis</i> |
| A8       | 9                     | R   | 26  | S   | 0      | R   | 14   | S   | 0   | R   | <i>Escherichia coli</i>           |
| A9       | 2                     | R   | 24  | S   | 0      | R   | 0    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A10      | 0                     | R   | 24  | S   | 0      | R   | 0    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A11      | 9                     | R   | 8   | R   | 14     | S   | 8    | R   | 0   | R   | <i>Escherichia coli</i>           |
| A12      | 16                    | S   | 0   | -   | 12     | S   | 7    | R   | 12  | S   | <i>Enterococcus faecalis</i>      |
| A13      | 15                    | S   | 9   | -   | 2      | R   | 6    | R   | 6   | R   | <i>Enterococcus faecalis</i>      |
| A14      | 8                     | R   | 0   | -   | 10     | S   | 2    | R   | 0   | R   | <i>Enterococcus faecalis</i>      |

| Group ID | Susceptibilities (mm) |     |     |     |        |     |      |     |     |     | Pathogen identified                 |
|----------|-----------------------|-----|-----|-----|--------|-----|------|-----|-----|-----|-------------------------------------|
|          | Cip                   | INT | Fos | INT | Amoxil | INT | Ceph | INT | TSX | INT |                                     |
| A15      | 4                     | R   | 6   | -   | 3      | R   | 4    | R   | 0   | R   | <i>Enterococcus faecalis</i>        |
| A16      | 15                    | S   | 2   | -   | 0      | R   | 2    | R   | 0   | R   | <i>Enterococcus faecium</i>         |
| A17      | 10                    | R   | 12  | -   | 19     | S   | 6    | R   | 0   | R   | <i>Staphylococcus haemolyticus</i>  |
| A18      | 2                     | R   | 26  | S   | 6      | R   | 0    | R   | 0   | R   | <i>Enterobacter spp.</i>            |
| A19      | 5                     | R   | 9   | -   | 2      | R   | 5    | R   | 0   | R   | <i>Staphylococcus saprophyticus</i> |
| A20      | 9                     | R   | 9   | -   | 2      | R   | 4    | R   | 0   | R   | <i>Staphylococcus epidermidis</i>   |
| A21      | 15                    | S   | 4   | R   | 3      | R   | 0    | R   | 0   | R   | <i>Enterococcus faecium</i>         |
| A22      | 9                     | R   | 24  | S   | 0      | R   | 8    | R   | 7   | R   | <i>Klebsiella pneumoniae</i>        |
| A23      | 5                     | R   | 9   | -   | 6      | R   | 2    | R   | 4   | R   | <i>Staphylococcus aureus</i>        |

**Key: Interpretation as per CLSI guidelines (CLSI, 2020):** INT: Interpretation, S: Susceptible, R: Resistant, Cip: Ciprofloxacin; Fos: Fosfomycin; Amoxil: Amoxicillin; Ceph: Cephalexin; TSX: Co-trimoxazole. Breakpoints: *E. coli* – cip (S>23; R<22); fos (S>24; R<23); amoxil (S>13; R<12); ceph (S>13; R<12); TSX (S>14; R<11). *E. faecalis* – cip (S>14; R<13); fos (-); amoxil (S>9; R<7); ceph (-); TSX (S>11; R<10). *E. faecium* - cip (S>14; R<13); fos (-); amoxil (S>10; R<8); ceph (-); TSX (S>11; R<10). *Enterobacter spp* – cip (S>26; R<24); fos (S>24; R<23); amoxil (S>14; R<13); ceph (S>14; R<13); TSX (S>14; R<11). *S. haemolyticus* – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>18; R<17); TSX (S>18; R<17). *S. saprophyticus* – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14). *S. epidermidis* – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14). *K. pneumoniae* – cip (S>26; R<24); fos (S>23; R<24); amoxil (S>14; R<13); ceph (S>14; R<13); TSX (S>14; R<11). *S. aureus* – cip (S>21; R<20); fos (-);

amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14). *S. lugdunensis* – cip (S>24; R<23); fos (-); amoxil (S>17; R<16); ceph (S>20; R<17); TSX (S>17; R<14). -: No commercial breakpoints available.

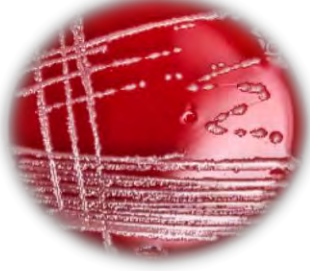
The antibiotic susceptibility of micro-organisms changes with time and is inconsistent in different regions (Ahmed *et al.*, 2019). A significant rise in resistance of micro-organisms to trimethoprim-sulfamethoxazole, cephalexin and amoxicillin has been established worldwide (Lichtenberger and Hooton, 2011). For some time, trimethoprim or sulfamethoxazole alone has been used extensively as an empirical therapy for UTIs caused by *E. coli*. Results of the study indicates that a ciprofloxacin resistance to other antimicrobials was slightly higher than reported in previous studies (Lin *et al.*, 2016). The study also noted highest susceptibility to trimethoprim-sulfamethoxazole which was inconsistent as there were 91% resistance patterns for trimethoprim-sulfamethoxazole in the study (Sadler *et al.*, 2017). Recent work points to considerable increases in the resistance of common uropathogens (Sofia *et al.*, 2019). The increased rates of resistance of *E. coli* in uncomplicated UTI to nitrofurantoin, pivmecillinam, and co-trimoxazole have been observed (Sofia *et al.*, 2019). At this higher level of resistance, and even at resistance levels as low as 30%, co-trimoxazole 200 mg twice daily was no longer the most cost-effective treatment. Assuming fosfomycin resistance is unchanged (to date, it has been rarely prescribed and there is some evidence that resistance rates to *E. coli* remain stable, fosfomycin 3 g once a day would be the most cost-effective option for empirical treatment (Ahmed *et al.*, 2019). Fosfomycin is primarily used in Spain, Germany, France, Japan, Brazil, and South Africa as an oral treatment UTIs (Silver, 2017). All the pathogens in this study showed resistance to at least two antibiotics, showing the presence of strong discriminating pressures from the antibiotics in the study hospital. A study by Lewis *et al.*, 2013, reports from South Africa, that *E. coli* as the common cause of UTIs and antibiotic resistance was high among the strains, which highlight the need for careful use of antibiotics.

#### **3.4.5. Complicated UTIs: Macro morphology of micro-organisms**

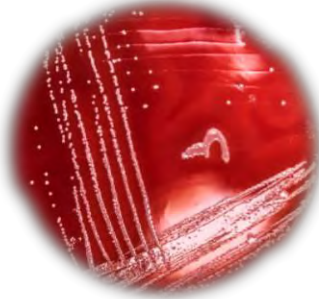
The morphologies of 194 complicated urinary tract infection samples were determined (Appendix D). Table 3.4 shows the morphologies as grouped for samples showing

identical macro morphological characteristics. Sixteen groups were identified and given group numbers B1 to B16.

**Table 3.4:** The morphologies for samples showing identical macro morphological characteristics in complicated UTIs.

| Colony type                                                                         | Group ID | Description |        |       |                  |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------|------------------|-----------|
|                                                                                     |          | Size        | Colour | Shape | Margin           | Elevation |
|    | B1       | Small       | Yellow | Round | Entire           | Flat      |
|  | B2       | Granulated  | Grey   | Round | Spreading colony | Convex    |
|  | B3       | Granulated  | Grey   | Round | Entire           | Flat      |

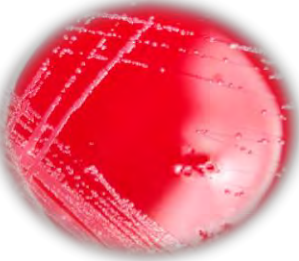
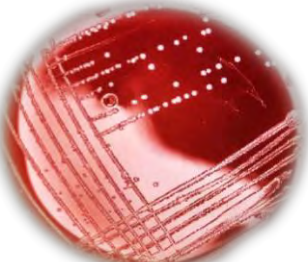


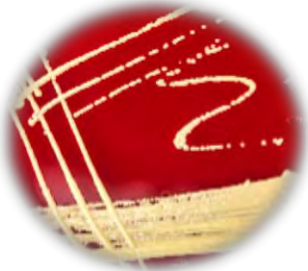
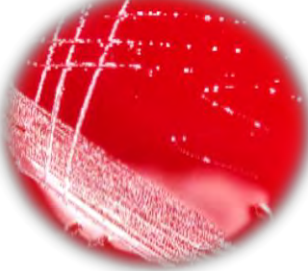
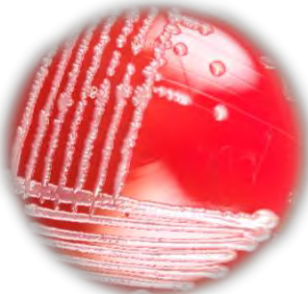
| Colony type                                                                       | Group ID | Description |        |       |        |           |
|-----------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                   |          | Size        | Colour | Shape | Margin | Elevation |
|  | B4       | Small       | Grey   | Round | Entire | Irregular |

| Colony type                                                                         | Group ID | Description |        |       |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape | Margin | Elevation |
|  | B5       | Small       | Yellow | Round | Entire | Flat      |
|  | B6       | Small       | Yellow | Round | Entire | Flat      |

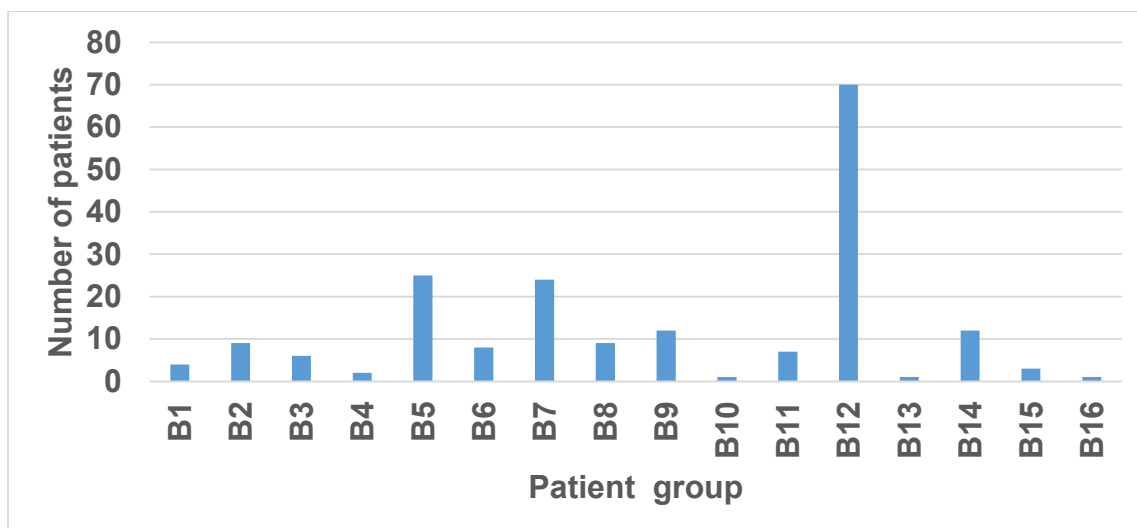
| Colony type                                                                        | Group ID | Description |        |       |        |           |
|------------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                    |          | Size        | Colour | Shape | Margin | Elevation |
|   | B7       | Small       | Cream  | Round | Entire | Flat      |
|  | B8       | Small       | Grey   | Round | Entire | Flat      |

| Colony type                                                                         | Group ID | Description |        |       |        |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|-------|--------|-----------|
|                                                                                     |          | Size        | Colour | Shape | Margin | Elevation |
|  | B9       | Small       | Grey   | Round | Entire | Flat      |

| Colony type                                                                         | Group ID | Description |        |                  |                  |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|------------------|------------------|-----------|
|                                                                                     |          | Size        | Colour | Shape            | Margin           | Elevation |
|    | B10      | Small       | White  | Spreading Colony | Spreading Colony | Convex    |
|    | B11      | Small       | White  | Round            | Entire           | Convex    |
|  | B12      | Small       | White  | Round            | Entire           | Flat      |

| Colony type                                                                         | Group ID | Description |        |                  |                  |           |
|-------------------------------------------------------------------------------------|----------|-------------|--------|------------------|------------------|-----------|
|                                                                                     |          | Size        | Colour | Shape            | Margin           | Elevation |
|    | B13      | Small       | Yellow | Round            | Entire           | Convex    |
|    | B14      | Small       | Yellow | Round            | Entire           | Convex    |
|  | B15      | Small       | White  | Round            | Entire           | Flat      |
|  | B16      | Granulated  | Grey   | Spreading Colony | Spreading Colony | Convex    |

Group B12 was determined as the most frequently isolated colony type, followed by groups B5 and B7. Figure 3.4 shows the number of patients for samples showing identical macro morphological characteristics in complicated UTIs.



**Figure 3.4:** Number of samples per patient group with the same morphologies in complicated UTIs.

#### 3.4.6. Complicated UTIs: culture identification

Sixteen groups with similar macro morphology and susceptibility results were selected for identification to represent each of the groups. In complicated UTIs, the most frequently isolated pathogens were *E. coli* (31.3%) and *S. aureus* (31.3%), followed by *E. faecalis* (18.8%). Table 3.5 demonstrates the frequency of micro-organisms in complicated UTIs.

**Table 3.5:** The identified micro-organisms in complicated UTIs.

| Identified pathogen                | Identified pathogens in uncomplicated UTI (%) |
|------------------------------------|-----------------------------------------------|
| <i>Escherichia coli</i>            | 31.2                                          |
| <i>Staphylococcus aureus</i>       | 31.2                                          |
| <i>Enterococcus faecalis</i>       | 18.8                                          |
| <i>Staphylococcus epidermidis</i>  | 12.5                                          |
| <i>Staphylococcus haemolyticus</i> | 6.3                                           |

A study from South Africa noted that *E. faecalis* was the most predominant Gram-positive micro-organism found (4%) (Kubone *et al.*, 2020). A total of 356 isolates of

enterococci were tested in all the geographical areas discussed in a study Asia-Western Pacific (Lin *et al.*, 2016). A study by Setu *et al.*, (2017) noted that major micro-organisms in UTIs were *E. coli*, followed by *S. aureus*, which is congruent with the current findings.

### 3.4.7. Complicated UTIs: Antimicrobial susceptibility patterns

The macro morphology and susceptibility results were used in grouping pathogens for identification. Sixteen groups (B1-B16; Table 3.7) with similar macro morphology and susceptibility results in uncomplicated UTIs were selected for identification. Identification of the 16 groups is represented in Table 3.6. The antibiotic showing the highest susceptibility patterns for complicated UTIs ( $n = 194$ ) was amoxicillin-clavulanic acid (93.8%), and poor susceptibility rate were fosfomycin (31.3%), amoxicillin (18.8%) and ciprofloxacin (6.3%). Breakpoint ranges were used to check if antibiotics were sensitive or resistant to the pathogen identified. Breakpoints were specific to the pathogen (CLSI, 2020).

**Table 3.7:** Antimicrobial susceptibility pattern summary per patient group for all 194 samples.

| Group ID | Susceptibilities (mm) |     |     |     |        |     |      |     |     |     |     |     | Pathogen identified          |
|----------|-----------------------|-----|-----|-----|--------|-----|------|-----|-----|-----|-----|-----|------------------------------|
|          | Cip                   | INT | Fos | INT | Amoxil | INT | Ceph | INT | TSX | INT | Aug | INT |                              |
| B1       | 11                    | R   | 12  | -   | 5      | R   | 7    | R   | 0   | R   | 9   | S   | <i>Staphylococcus aureus</i> |
| B2       | 11                    | R   | 24  | S   | 7      | R   | 8    | R   | 0   | R   | 8   | S   | <i>Escherichia coli</i>      |
| B3       | 9                     | R   | 26  | S   | 8      | S   | 7    | R   | 0   | R   | 16  | S   | <i>Escherichia coli</i>      |
| B4       | 5                     | R   | 24  | S   | 7      | R   | 7    | R   | 0   | R   | 8   | S   | <i>Escherichia coli</i>      |

| Group ID | Susceptibilities (mm) |     |     |     |        |     |      |     |     |     |     |     | Pathogen identified                |
|----------|-----------------------|-----|-----|-----|--------|-----|------|-----|-----|-----|-----|-----|------------------------------------|
|          | Cip                   | INT | Fos | INT | Amoxil | INT | Ceph | INT | TSX | INT | Aug | INT |                                    |
| B5       | 5                     | R   | 25  | S   | 6      | R   | 9    | R   | 0   | R   | 11  | S   | <i>Escherichia coli</i>            |
| B6       | 4                     | R   | 8   | -   | 7      | R   | 4    | R   | 2   | R   | 9   | S   | <i>Staphylococcus aureus</i>       |
| B7       | 5                     | R   | 9   | -   | 6      | R   | 2    | R   | 0   | R   | 18  | S   | <i>Staphylococcus aureus</i>       |
| B8       | 10                    | R   | 10  | -   | 4      | R   | 6    | R   | 0   | R   | 9   | S   | <i>Enterococcus faecalis</i>       |
| B9       | 4                     | R   | 6   | -   | 2      | R   | 7    | R   | 0   | R   | 13  | S   | <i>Enterococcus faecalis</i>       |
| B10      | 6                     | R   | 10  | -   | 11     | S   | 10   | R   | 8   | R   | 19  | S   | <i>Staphylococcus epidermidis</i>  |
| B11      | 11                    | R   | 12  | -   | 18     | S   | 7    | R   | 8   | R   | 18  | S   | <i>Staphylococcus haemolyticus</i> |
| B12      | 4                     | R   | 9   | -   | 7      | R   | 6    | R   | 0   | R   | 7   | R   | <i>Enterococcus faecalis</i>       |
| B13      | 15                    | S   | 9   | -   | 4      | R   | 3    | R   | 0   | R   | 9   | S   | <i>Staphylococcus aureus</i>       |
| B14      | 5                     | R   | 9   | -   | 6      | R   | 2    | R   | 7   | R   | 18  | S   | <i>Staphylococcus aureus</i>       |
| B15      | 9                     | R   | 10  | -   | 1      | R   | 4    | R   | 6   | R   | 10  | S   | <i>Staphylococcus epidermidis</i>  |
| B16      | 12                    | R   | 25  | S   | 6      | R   | 6    | R   | 4   | R   | 9   | S   | <i>Escherichia coli</i>            |

**Key: Interpretation as per CLSI guidelines (CLSI, 2020):** INT: Interpretation, S: Susceptible, R: Resistant, Cip: Ciprofloxacin; Fos: Fosfomycin; Amoxil: Amoxicillin; Ceph: Cephalixin; TSX: Co-trimoxazole; Aug: Amoxicillin-clavulanic acid. Breakpoints: *E. coli* – cip (S>23; R<22); fos (S>24; R<23); amoxil (S>13; R<12); ceph (S>13; R<12); TSX (S>14; R<11); Aug (S>7; R<6). *E. faecalis* – cip (S>14;

R<13); fos (-); amoxil (S>9; R<7); ceph (-); TSX (S>11; R<10); Aug (S>7; R<6). ***E. faecium*** - cip (S>14; R<13); fos (-); amoxil (S>10; R<8); ceph (-); TSX (S>11; R<10); Aug (S>7; R<6). ***Enterobacter spp*** – cip (S>26; R<24); fos (S>24; R<23); amoxil (S>14; R<13); ceph (S>14; R<13); TSX (S>14; R<11); Aug (S>7; R<6). ***S. haemolyticus*** – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>18; R<17); TSX (S>18; R<17); Aug (S>7; R<6). ***S. saprophyticus*** – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14); Aug (S>7; R<6). ***S. epidermidis*** – cip (S>24; R<23); fos (-); amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14); Aug (S>7; R<6). ***K. pneumoniae*** – cip (S>26; R<24); fos (S>23; R<24); amoxil (S>14; R<13); ceph (S>14; R<13); TSX (S>14; R<11); Aug (S>7; R<6). ***S. aureus*** – cip (S>21; R<20); fos (-); amoxil (S>18; R<17); ceph (S>20; R<17); TSX (S>17; R<14); Aug (S>7; R<6). ***S. lugdunensis*** – cip (S>24; R<23); fos (-); amoxil (S>17; R<16); ceph (S>20; R<17); TSX (S>17; R<14); Aug (S>7; R<6). -: No commercial breakpoints available.

The alarming finding was that ciprofloxacin, co-trimoxazole, cephalexin and amoxicillin were resistant to most of the strains tested. A deterioration in the activity of ciprofloxacin would be problematic in view of the ability of Gram-negative bacilli to obtain resistance to all classes of antimicrobials (Kubone *et al.*, 2020). Due to the prolonged use of co-trimoxazole in HIV patients to prevent opportunistic infections, this has led to development of resistance in UTIs. In this study, there was 100% resistance in patients who were on co-trimoxazole for prophylaxis. This study displays that resistance to ciprofloxacin continues to rise. Factors such as haemolysin production and presence of fimbriae in the *E. coli* may be linked with urovirulence. Moreover, these differences in sensitivity patterns of the isolates could be attributed to environmental factors such as practices of self-medication and indiscriminate misuse of antibiotics among the general population, which has favoured the emergence of resistance strains (Lin *et al.*, 2016). A study observed that 20.2% of the enrolled patients had a UTI resistant to trimethoprim-sulfamethoxazole (Demarsh *et al.*, 2020). A study noted that the broad-spectrum resistance of fosfomycin, including susceptibility against many important pathogens such as *S. aureus*, *S. epidermidis*, *S. pneumoniae*, *E. faecalis*, *E. coli*, *Proteus spp*, *K. pneumoniae* and *Enterobacter spp* was increasing (Silver, 2017).

### 3.5. Summary

- The number of colonies isolated per patient ranged between 1 to 4.



- In complicated and uncomplicated UTIs, three type colonies were mostly identified.
- In complicated and uncomplicated UTIs, *E. coli* (31.3% and 43.5% respectively) was identified as the most predominant micro-organism.
- The highest resistance was observed against cephalexin (100%, 96.2%) followed by co-trimoxazole (100%, 91.3%) in complicated and uncomplicated UTIs respectively.
- Amoxicillin-clavulanic acid (93.8%) was identified as the most sensitive antimicrobial agent in complicated UTIs.
- Fosfomycin (47.8%) was identified as the most sensitive antimicrobial agent in uncomplicated UTIs.

# CHAPTER 4

## CLINICAL PHARMACY

---

### 4.1. Introduction

A complicated UTI is associated with a structural or functional abnormality that increases the risk of treatment failure or serious complications (Lichtenberger and Hooton, 2011). The factors include foreign bodies, obstruction, neurogenic bladder, renal failure, renal transplantation, immunosuppression, drainage devices, and pregnancy (Lichtenberger and Hooton, 2011). Uncomplicated UTIs occur in young, otherwise healthy, non-pregnant women, whereas complicated UTIs occur in both sexes and any age group (Tan and Chlebicki, 2016). Understanding the risk factors associated with reoccurrences of UTIs can help physicians tailor prophylactic strategies to effectively reduce the potential for reoccurrence (Storme *et al.*, 2019b).

This clinical pharmacy chapter gives an overview into the patient reviews that were undertaken at the study hospital. The aim of this chapter is to determine, through the review of patient file reviews, the likelihood of past urinary tract infections as well as the past treatment practices in the management of UTIs. The findings from determining antimicrobial resistance patterns and reviewing of patient files were used to recommend a treatment protocol and infection management practices for UTIs at the study hospital.

### 4.2. Methods

#### 4.2.1. Retrospective review of patient files

Patient files have traditionally been compiled and maintained by healthcare professionals at study hospital in handwritten files that were put on shelves. More recently, the record taking involves scanning the documents and uploading them online under the patients' file number making them easy to locate. The protocol implemented was documented along with the number of infections treated and whether sample cultures were undertaken. In the urine collection process, patient file

numbers were recorded alongside the unique number assigned for each patient to maintain traceability and to maintain patients' confidentiality. The hospital file number was written in pencil on the patient collection tool and it was erased soon after reviewing the file.

Patient files were reviewed two weeks after sample collection as only following this period the patient file would have been scanned and uploaded online. Access was given to the database by the data capturing team on presentation of the ethics certificate as well as the letter from the Hospital Manager of the study hospital that the study was approved. Patient files were identified after punching in the hospital number for each patient for example GP010234238 and all the information and history of the patient would be processed. Patient files were reviewed because they can help in identifying the treatment patterns for urinary tract infections at study hospital and to determine the likelihood of previous UTIs. Retrospective review was done using the Orbit™ Document Management System 3.2 (Lee *et al.*, 2018). The pre-existing data was kept at the data base room at the study hospital. Patient file reviews are important as they help to improve quality of patient care, helps to inform healthcare providers of the deficiencies or successes in their practice and also helps to ensure that the records contain the basic data needed.

Twelve-month patient records (2018 to 2019) were used to identify previous infections and the causative pathogen, antibiotic used and frequency of UTIs. The information obtained was recorded on the patient collection tool for each patient and then entered into an Excel spreadsheet (Appendix F). On the Excel spreadsheet, the recorded information was the patient tool (identifier), date of infection, whether the urine was cultured, if so the micro-organism identified, indication if an antibiotic was prescribed and if so which treatment was prescribed for each patient. This information helped in the determination of the frequency of UTI infections and antibiotic prescribing patterns at the study hospital.

#### **4.2.2. Antibigram for UTIs**

An antibiogram is a general outline of antimicrobial susceptibility testing outcomes to a set of microbial agents (Jafri *et al.*, 2014). The profile was produced using

susceptibility testing results per micro-organism to a specific antimicrobial drug via disk diffusion as per Chapter 3. Antimicrobial effectiveness was determined by calculating the zone of inhibition. As a result, the antibiogram for the isolated pathogens was tested against amoxicillin, fosfomycin, ciprofloxacin, trimethoprim-sulfamethoxazole, cephalexin and amoxicillin/clavulanic acid (pregnant patients only) with the aim to create a hierarchy of antimicrobial effectiveness meant for policy development. The South African Expert Advisory Group on Antimicrobial resistance (SAAGAR) recommends several antibiotics for the treatment of UTIs (Dolinsky *et al.*, 2017). Antibiograms are used to guide clinicians and pharmacists when selecting the best empirical antimicrobial treatment in the event of pending susceptibility results or microbiology culture. They are also tools used to detect and monitor trends in antimicrobial resistance (Odongo *et al.*, 2013).

#### **4.2.3. Policy development for UTIs**

A diagnosis and management policy was prepared for the prescribing of UTIs. These guidelines were prepared by reviewing the susceptibility patterns, micro-organism identified and the antibiogram prepared aiming to suggest the best treatment for patients. To reduce the risk factors of UTIs, strategies such as evidence-based guidelines encompass patient identification and the diagnostic criteria. The ideal UTI policy is meant to guide physicians in all specialties, with attributes of guidelines of higher quality.

#### **4.3. Results and discussion**

The method used to categorize urinary tract infections is the retrospective medical record review method (Jafri *et al.*, 2014). Infections were categorized into either symptomatic, asymptomatic in order to generate treatment guidelines. Specific groups of people are at increased risk of urinary tract infection. Understanding individual and population-specific risk factors associated with reoccurring UTIs can help physicians tailor prophylactic strategies (Storme *et al.*, 2019b). Frequent sexual intercourse, age, vulvovaginal atrophy, immunodeficiency diabetes mellitus, spermicide-based contraception are validated factors for reoccurring UTIs (Kubone *et al.*, 2020; Setyorini, Tjempakasari and Mardiana, 2019).

#### **4.3.1. Uncomplicated UTI: Patient file review**

One-year data was reviewed for the 100 uncomplicated patients. In total, there were 216 antibiotics prescribed in one year for the 100 patients showing an average of at least one reoccurrence of the infection per patient. The prescribing patterns were dependent on the prescriber and the symptoms that the patient presents with at the hospital. The number of reoccurring infections was noted together with the risk factors that each patient has for uncomplicated UTIs (Appendix E). The treatment profiles for reoccurring infections were noted and the resistant patterns of the antibiotics was analysed based on the antimicrobial susceptibility patterns that were described in Chapter 3. Table 4.1 shows the risk factors, number of infections and treatment outcomes in uncomplicated UTIs.

**Table 4. 1:** Risk factors, number of infections and treatment outcomes in uncomplicated UTIs

| Patient ID | Risk factors      | Frequency of risk factors (%) | Number of reoccurring infections | Treatment provided               |                                              | According to STG | According to SAAGAR |
|------------|-------------------|-------------------------------|----------------------------------|----------------------------------|----------------------------------------------|------------------|---------------------|
|            |                   |                               |                                  | Current treatment                | Previous treatment                           |                  |                     |
| A1         | Diabetes          | 1(7.7)                        | 1                                | Ciprofloxacin 500mg PO 12 hourly | Amoxicillin 500mg tds 5 days                 | C                | C                   |
| A2         | HIV               | 3(14.3)                       | 1                                | Fosfomycin 3g single dose        | Amoxicillin/clavulanic acid 1g bd 5 days     | NC               | C                   |
| A3         | Diabetes          | 2(15.4)                       | 1                                | Fosfomycin 3g single dose        | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| A4         | Urine catheter    | 5(20.8)                       | 1                                | Nitrofurantoin 50mg tds 5 days   | Amoxicillin/clavulanic acid 375mg tds 5 days | NC               | C                   |
| A5         | HIV               | 3(14.3)                       | 1                                | Fosfomycin 3g single dose        | Amoxicillin/clavulanic acid 375mg tds 5 days | NC               | C                   |
| A6         | Use of spermicide | 2(40.0)                       | 1                                | Fosfomycin 3g single dose        | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| A7         | Urine catheter    | 4(16.7)                       | 1                                | Ciprofloxacin 500mg bd 5 days    | Amoxicillin 500mg tds 5 days                 | C                | C                   |

| Patient ID | Risk factors         | Frequency of risk factors (%) | Number of reoccurring infections | Treatment provided                       |                                                           | According to STG | According to SAAGAR |
|------------|----------------------|-------------------------------|----------------------------------|------------------------------------------|-----------------------------------------------------------|------------------|---------------------|
|            |                      |                               |                                  | Current treatment                        | Previous treatment                                        |                  |                     |
| A8         | HIV                  | 4(19.0)                       | 2                                | Amoxicillin/clavulanic acid 1g bd 5 days | Fosfomycin 3g single dose<br>Amoxicillin 500mg tds 5 days | NC               | C                   |
| A9         | Urinary incontinence | 3(30.0)                       | 1                                | Amoxicillin 500mg tds 5 days             | Ciprofloxacin 500mg PO 12 hourly                          | C                | C                   |
| A10        | HIV and hypertension | 2(8.3)                        | 1                                | Ciprofloxacin 500mg PO 12 hourly         | Amoxicillin 500mg tds 5 days                              | C                | C                   |
| A11        | Urine catheter       | 7(29.2)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly         | Amoxicillin 500mg tds 5 days                              | C                | C                   |
| A12        | Diabetes             | 3(23.1)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly         | Amoxicillin/clavulanic acid 1g bd 5 days                  | C                | C                   |
| A13        | HIV                  | 3(14.3)                       | 2                                | Fosfomycin 3g single dose                | Amoxicillin/clavulanic acid 1g bd 5 days                  | NC               | C                   |

| Patient ID | Risk factors         | Frequency of risk factors (%) | Number of reoccurring infections | Treatment provided                           |                                                                             | According to STG | According to SAAGAR |
|------------|----------------------|-------------------------------|----------------------------------|----------------------------------------------|-----------------------------------------------------------------------------|------------------|---------------------|
|            |                      |                               |                                  | Current treatment                            | Previous treatment                                                          |                  |                     |
| A14        | Diabetes             | 4(30.8)                       | 1                                | Amoxicillin/clavulanic acid 1 bd 5 days      | Ciprofloxacin 500mg PO 12 hourly                                            | NC               | C                   |
| A15        | Use of spermicide    | 1(20.0)                       | 1                                | Amoxicillin/clavulanic acid 375mg tds 5 days | Amoxicillin/clavulanic acid 1g tds 5 days                                   | NC               | C                   |
| A16        | Diabetes             | 3(23.1)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly             | Amoxicillin/clavulanic acid 1g bd 5 days                                    | C                | C                   |
| A17        | Urinary incontinence | 5(50.0)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly             | Amoxicillin 500mg tds 5 days                                                | C                | C                   |
| A18        | HIV                  | 3(14.4)                       | 1                                | Fosfomycin 3g single dose                    | Amoxicillin/clavulanic acid 375mg tds 5 days                                | NC               | C                   |
| A19        | Urine catheter       | 8(33.3)                       | 2                                | Amoxicillin/clavulanic acid 1 bd 5 days      | Ciprofloxacin 500mg PO 12 hourly<br>Amoxicillin/clavulanic acid 1 bd 5 days | NC               | C                   |



| Patient ID | Risk factors                       | Frequency of risk factors (%) | Number of reoccurring infections | Treatment provided                      |                                              | According to STG | According to SAAGAR |
|------------|------------------------------------|-------------------------------|----------------------------------|-----------------------------------------|----------------------------------------------|------------------|---------------------|
|            |                                    |                               |                                  | Current treatment                       | Previous treatment                           |                  |                     |
| A20        | HIV                                | 3(14.3)                       | 1                                | Fosfomycin 3g single dose               | Amoxicillin/clavulanic acid 375mg tds 5 days | C                | C                   |
| A21        | No risk factors                    | 27(27.0)                      | 1                                | Ciprofloxacin 500mg PO 12 hourly        | Amoxicillin 500mg tds 5 days                 | C                | C                   |
| A22        | Urinary incontinence               | 2(20.0)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly        | Amoxicillin 500mg tds 5 days                 | C                | C                   |
| A23        | Hypertension and use of spermicide | 2(22.2)                       | 1                                | Ciprofloxacin 500mg PO 12 hourly 3 days | Amoxicillin/clavulanic acid 1g bd 5 days     | C                | C                   |

**Key:** bd: twice daily, tds: three times daily, PO: take orally, -: not applicable; (C) refers to compliant and (NC) to non-compliant (NC).

At study hospital, most patients either had a chronic condition or were immunocompromised. Amongst the 100 patients, over half (52.25%) of the treatment prescribed complied with the STG/EML. Although amoxicillin and ciprofloxacin is available on the EML, there could be multiple reasons for non-compliance such as unavailability of the drug or poor training on the EML (Barry *et al.*, 2017). Amoxicillin/clavulanic acid is only recommended in children under 35 kg (National Department of Health, 2018). The South African Expert Advisory Group on Antimicrobial resistance (SAAGAR) recommends amoxicillin/clavulanic acid, ciprofloxacin, nitrofurantoin, cephalexin and trimethoprim for the treatment of uncomplicated UTIs (Dolinsky *et al.*, 2017). Therefore, there was 100% compliance with SAGAAR in the treatment of UTIs at the study hospital. In South Africa, nitrofurantoin is used for prophylaxis as it reduces the risk of reoccurring UTIs in women (Lewis *et al.*, 2013). Continuous prophylaxis with nitrofurantoin is effective in the management of reoccurring uncomplicated UTIs and can only be initiated after the eradication of a previous UTI (Lewis *et al.*, 2013). In uncomplicated UTIs, 21% of patients were HIV positive. As confirmed by observational studies, the incidence of various bacterial infections in HIV infected patients, including urinary tract infections, is inversely correlated with lymphocyte CD4+ count (Foxman, 2003; Skrzat-klapaczy *et al.*, 2018). Therefore, in order to decrease UTI reoccurrences, the CD4+ count should be managed and monitored as that may be the cause of UTIs in the study hospital. The incidence of UTIs in the HIV population is clearly related to infection and immune function, determined by lymphocytes CD4+ cells count (Skrzat-klapaczy *et al.*, 2018).

One recent study of women experiencing a first-time UTI found that the use of a condom within the previous two weeks was associated with a 43% increase in the odds of a UTI compared with women using oral contraceptives or no method of birth control (Dolinsky *et al.*, 2017). Spermicide use increases the risk of UTIs. Spermicide users, even those with no history of UTI, typically have higher levels of introital and peri-urethral colonization with uropathogenic organisms than do women using other means of contraception (Kubone *et al.*, 2020).

The results of this study indicate that UTIs amongst Type 2 diabetics occur commonly due to the glucose present in the urine and also are often caused by resistant pathogens (Chazan, 2015). Diabetic patients are more prone to getting UTIs due to frequent urination, high blood and urine glucose levels (Kubone *et al.*, 2020). High blood sugar levels give a favourable growth environment to the pathogens (Vasudevan, 2014). To combat the increased glucose in the urine amongst diabetics, treatments such as diabetic sodium glucose cotransporter 2 inhibitors for example glibenclamide reduce the risk of symptomatic UTIs by preventing glucose accumulation in the urine (Chazan, 2015). If high blood sugar levels increase the chances of getting UTIs, it is important for the sugar levels to be managed as that will reduce UTI reoccurrences. Unfinished voiding signifies the primary risk factor for UTIs related to conditions such as urinary incontinence (Kubone *et al.*, 2020). Correcting the presence of excess urine remains the most effective prophylaxis in the patients with urinary incontinence. Bladder function changes throughout life and may be particularly profound in clinical populations at high risk of UTIs (Grabe *et al.*, 2015).

#### **4.3.2. Complicated UTIs: Patient file review**

A total of 100 uncomplicated UTIs were diagnosed at the study hospital. Pregnant patients are classified as complicated as they cannot use some antibiotics for example ciprofloxacin or trimethoprim-sulfamethoxazole even though some have different categories and may be safe to use in different stages of pregnancy. The number of reoccurring infections was noted together with the risk factors that each patient has for complicated UTIs (Appendix F). The treatment profiles for reoccurring infections were noted and the resistant patterns of the antibiotics was analysed based on the antimicrobial susceptibility patterns that were described in Chapter 3. Table 4.2 shows the risk factors, number of infections and treatment outcomes in uncomplicated UTIs.

**Table 4. 2:** Risk factors, number of infections and treatment outcomes in complicated UTIs

| Patient ID | Risk factors                           | Frequency of risk factors n (%) | Number of reoccurring infections | Treatment provided                           |                                             | According to STG | According to SAAGAR |
|------------|----------------------------------------|---------------------------------|----------------------------------|----------------------------------------------|---------------------------------------------|------------------|---------------------|
|            |                                        |                                 |                                  | Current treatment                            | Previous treatment                          |                  |                     |
| B1         | Urine catheter                         | 2 (14.3)                        | 0                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | -                                           | NC               | C                   |
| B2         | Diabetes                               | 3 (14.3)                        | 1                                | Amoxicillin/clavulanic acid 1g bd 5days      | Amoxicillin 500mg tds 5 days                | NC               | C                   |
| B3         | Hypertension and urine catheterisation | 1 (4.8)                         | 2                                | Amoxicillin/clavulanic acid 375mg tds 5 days | Amoxicillin 500mg tds 5 days                | NC               | C                   |
|            |                                        |                                 |                                  |                                              | Amoxicillin/clavulanic acid 375mg bd 5 days | NC               | C                   |
| B4         | HIV                                    | 3 (27.3)                        | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | Amoxicillin 500mg tds 5 days                | NC               | C                   |
| B5         | HIV and hypertension                   | 1 (5.6)                         | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | Amoxicillin/clavulanic acid 375mg bd 5 days | NC               | C                   |
| B6         | Urinary incontinence                   | 2 (100)                         | 0                                | Amoxicillin 500mg tds 5 days                 | -                                           | C                | C                   |

| Patient ID | Risk factors              | Frequency of risk factors n (%) | Number of reoccurring infections | Treatment provided                           |                                              | According to STG | According to SAAGAR |
|------------|---------------------------|---------------------------------|----------------------------------|----------------------------------------------|----------------------------------------------|------------------|---------------------|
|            |                           |                                 |                                  | Current treatment                            | Previous treatment                           |                  |                     |
| B7         | Diabetes                  | 5 (23.8)                        | 1                                | Amoxicillin/clavulanic acid 375mg bd 5 days  | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| B8         | Urine catheter            | 3 (21.4)                        | 1                                | Amoxicillin/clavulanic acid 375mg tds 5 days | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| B9         | Hypertension and diabetes | 2 (6.9)                         | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| B10        | Diabetes                  | 3 (14.3)                        | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | Amoxicillin/clavulanic acid 375mg tds 5 days | NC               | C                   |
| B11        | Diabetes                  | 2 (9.5)                         | 1                                | Amoxicillin/clavulanic acid 375mg bd 5 days  | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| B12        | HIV                       | 3 (27.3)                        | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days  | Amoxicillin 500mg tds 5 days                 | NC               | C                   |
| B13        | Diabetes                  | 3 (14.3)                        | 1                                | Amoxicillin/clavulanic acid 625mg tds 5 days | Amoxicillin 500mg tds 5 days                 | NC               | C                   |

| Patient ID | Risk factors                  | Frequency of risk factors n (%) | Number of reoccurring infections | Treatment provided                          |                                             | According to STG | According to SAAGAR |
|------------|-------------------------------|---------------------------------|----------------------------------|---------------------------------------------|---------------------------------------------|------------------|---------------------|
|            |                               |                                 |                                  | Current treatment                           | Previous treatment                          |                  |                     |
| B14        | Urine catheter                | 4 (28.6)                        | 1                                | Amoxicillin/clavulanic acid 625mg bd 5 days | Amoxicillin/clavulanic acid 375mg bd 5 days | NC               | C                   |
| B15        | Diabetes and hypertension     | 3 (10.3)                        | 1                                | Amoxicillin 1g tds 5 days                   | Amoxicillin 500mg tds 5 days                | C                | C                   |
| B16        | HIV and urine catheterisation | 4 (16.0)                        | 1                                | Amoxicillin 500mg tds 5 days                | Amoxicillin/clavulanic acid 625mg bd 5 days | C                | C                   |

**Key:** bd: twice daily, tds: three times daily, PO: take orally, -: not applicable, (C) refers to compliant and (NC) to non-compliant (NC).

Amongst the 100 complicated patients in the study, 18.8% of the treatment complied with the STG/EML and 81.3% did not comply because amoxicillin/clavulanic acid is being used more in uncomplicated UTIs than the recommended nitrofurantoin by the EML (National Department of Health, 2018). SAAGAR recommends amoxicillin/clavulanic acid, cephalexin, trimethoprim and nitrofurantoin for the treatment of UTIs in uncomplicated UTIs (Dolinsky *et al.*, 2017). There was 100% compliance according to SAGAAR in the management of complicated UTIs at the study hospital. The incidence of complicated UTI are common in individuals with underlying conditions such as pregnancy and diabetes (Lee *et al.*, 2018). In pregnant women, it is important to obtain culture and sensitivities for all pregnant women (even if asymptomatic) so that they are given the correct regimen and dosage as that will help in avoiding reoccurrences. Diabetic women should have their sugar levels managed as that will also help in lowering reoccurrences and reduce chances of becoming resistant to antibiotics. The incidence of various bacterial infections in HIV-infected patients, including UTIs, is inversely correlated with lymphocyte CD4+ count suggesting that HIV patients who have a lowered immunity are more likely to present with UTIs (Foxman, 2003). In HIV patients, it is important to boost the immune system by checking the CD4+ count. In this study, overall prevalence of UTI in diabetic pregnant women in South Africa was 21%, which is in line with the prevalence rates reported in diabetic and non-diabetic pregnant women. Various impairments in the immune system, poor metabolic control, and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of UTIs (Chazan, 2015). Patients with neurogenic bladder will highly likely have other evolving medical issues which increase the risk of UTIs (Storme *et al.*, 2019b). Therefore, it is important to treat the risk factor for a strong immune system as that will reduce the incidence of UTIs in pregnant women. More forceful antimicrobial prophylactic strategies may be appropriate in these patients (Storme *et al.*, 2019b). According to another study, drug susceptibilities of *E. coli* to nitrofurantoin (83.8%) showed high sensitivities hence it can be a good alternative to use in treating UTIs in public hospitals (Odoki *et al.*, 2019).

#### 4.3.3. Analysis of risk factors in complicated and uncomplicated UTIs

The risk factors were recorded when patient files were reviewed. Table 4.3 shows the age adjusted risk factors of the enrolled participants.

**Table 4.3:** Age adjusted risk factors in complicated and uncomplicated UTIs.

| Variable                 | Uncomplicated UTI (n=100) | Complicated UTI (n=100) | p-Value |
|--------------------------|---------------------------|-------------------------|---------|
| Age (years)              | 33.3 ( $\pm$ 23.5)        | 33.3 ( $\pm$ 26.3)      | 0.703   |
| HIV/AIDS (%)             | 21 (27.3)                 | 11 (14.7)               | 0.017   |
| Diabetes mellitus (%)    | 13 (16.9)                 | 21 (28.0)               | 0.534   |
| Urine catheter (%)       | 24 (31.2)                 | 14 (18.9)               | 0.004   |
| Use of spermicide (%)    | 5 (6.5)                   | -                       | 0.052   |
| Urinary incontinence (%) | 10 (13.0)                 | 2 (2.7)                 | 0.018   |
| Blood pressure (%)       | 4 (5.2)                   | 7 (9.3)                 | 0.306   |

**Key:** The study population was divided into 2 groups, that is, complicated and uncomplicated UTIs. Data was presented as number (percentage) or as mean  $\pm$  SD; SD = standard deviation. -: not applicable due to pregnancy.

The study also noted that women experiencing UTIs are not a heterogeneous group and that the factors associated with reoccurrence may differ by age and other population characteristics. In younger women, the behavioural factors implicated in sporadic UTIs are likely to continue to predominate (Kubone *et al.*, 2020). In older populations, the role of sexual and contraceptive practices may be diminished, and other factors (for example, non-secretor status) may become relatively more important (Ghaima *et al.*, 2018). Diabetes patients have a greater likelihood for reinfection and



a higher incidence of treatment failure. Concomitant use of ciprofloxacin and sulfonyleureas or oral hypoglycaemic agents may result in hypoglycaemia or hyperglycaemia (Vasudevan, 2014).

#### 4.4. Selection of antibiotics according to classifications

Antibiotics were selected by considering the patient file review, antimicrobial susceptibility results and identification of the pathogen. In the study, most patients were given ciprofloxacin which is becoming resistant. Co-trimoxazole is also prescribed for patients, and is also becoming highly resistant.

##### 4.4.1. Uncomplicated UTI: Antibigram

An antibiogram for uncomplicated UTIs, complicated UTIs as the infections are treated differently and were classified based on resistance patterns. Table 4.4 shows the antibiogram for uncomplicated UTIs.

**Table 4.4:** Antibigram for uncomplicated UTIs

| Bacteria                     | Total number of isolates (n) | Percentage number of isolates susceptible to each antibiotic (%) |       |        |      |      | Recommended for treatment |
|------------------------------|------------------------------|------------------------------------------------------------------|-------|--------|------|------|---------------------------|
|                              |                              | Cip                                                              | Fos   | Amoxil | Ceph | TSX  |                           |
| <i>Klebsiella pneumoniae</i> | 22                           | 0                                                                | 100   | 0      | 0    | 0    | Fosfomycin                |
| <i>Enterobacter spp</i>      | 19                           | 0                                                                | 100   | 0      | 0    | 0    | Fosfomycin                |
| <i>Enterococcus faecalis</i> | 27                           | 7.41                                                             | 51.85 | 44.44  | 0    | 3.70 | Fosfomycin, amoxicillin   |
| <i>Enterococcus faecium</i>  | 4                            | 100                                                              | 50    | 0      | 0    | 0    | Ciprofloxacin             |
| <i>Escherichia coli</i>      | 41                           | 2.44                                                             | 97.56 | 7.31   | 2.44 | 4.88 | Fosfomycin                |
| <i>Staphylococcus aureus</i> | 7                            | 0                                                                | 100   | 0      | 0    | 0    | Fosfomycin                |

| Bacteria                            | Total number of isolates (n) | Percentage number of isolates susceptible to each antibiotic (%) |     |        |      |     | Recommended for treatment |
|-------------------------------------|------------------------------|------------------------------------------------------------------|-----|--------|------|-----|---------------------------|
|                                     |                              | Cip                                                              | Fos | Amoxil | Ceph | TSX |                           |
| <i>Staphylococcus epidermidis</i>   | 35                           | 0                                                                | 100 | 0      | 0    | 0   | Fosfomycin                |
| <i>Staphylococcus haemolyticus</i>  | 4                            | 0                                                                | 100 | 100    | 0    | 0   | Fosfomycin, amoxicillin   |
| <i>Staphylococcus lugdunensis</i>   | 6                            | 0                                                                | 100 | 100    | 0    | 0   | Fosfomycin, amoxicillin   |
| <i>Staphylococcus saprophyticus</i> | 73                           | 0                                                                | 100 | 0      | 0    | 0   | Fosfomycin                |

**Key:** Cip- Ciprofloxacin, Fos – Fosfomycin, Amoxil – Amoxicillin, Ceph – Cephalexin, TSX – Co-trimoxazole

Standard treatment guidelines of South Africa identified that second-line options for empiric treatment of uncomplicated UTIs were ciprofloxacin 500 mg twice daily, orally for three days or levofloxacin 500 mg once daily, orally for three days which is inconsistent with this research. These agents were considered alternative options due to the propensity for adverse side-effects and the critical utilization for more serious infections other than cystitis (Kubone *et al.*, 2020). The use of short-term fosfomycin for the treatment of UTIs is encouraged as there are less resistance rates compared to other antimicrobial agents and this is consistent with the current research as fosfomycin had the least resistant rates (Wagenlehner *et al.*, 2011; Lewis *et al.*, 2013). Fosfomycin is also useful as it is short-term and is preferred by patients who cannot adhere to five to seven day regimens (Wagenlehner *et al.*, 2011). When the effects of antibiotics after one treatment session, short-term treatment lasting three to six days, and long-term treatment lasting 7 to 14 days were compared in older adults (aged over 60 years) with uncomplicated cystitis, there were no differences in therapeutic effects between the short-term and long-term treatments (Kang *et al.*, 2018). The study highlighted that for uncomplicated UTIs, fosfomycin is only recommended for the treatment of urinary tract infections caused by *K. pneumoniae*, *Enterobacter* spp, *E. coli*, *S. aureus* and *S. saprophyticus*. Ciprofloxacin or fosfomycin are recommended in

treating urinary tract infections caused by *E. faecium*. Amoxicillin or fosfomycin are recommended in treating infections caused by *E. faecalis*, *S. haemolyticus* and *S. lugdunensis*.

#### 4.4.2. Complicated UTI: Antibigram

In complicated UTIs, the Antibigram and recommended treatment are show in table 4.5.

**Table 4.5:** Antibigram for complicated UTIs

| Bacteria                           | Total number of isolates (n) | Percentage number of isolates susceptible to each antibiotic (%) |     |        |      |     |       | Recommend for treatment                              |
|------------------------------------|------------------------------|------------------------------------------------------------------|-----|--------|------|-----|-------|------------------------------------------------------|
|                                    |                              | Cip                                                              | Fos | Amoxil | Ceph | TSX | Aug   |                                                      |
| <i>Enterococcus faecalis</i>       | 91                           | 0                                                                | 100 | 0      | 0    | 0   | 13.19 | Fosfomycin                                           |
| <i>Escherichia coli</i>            | 43                           | 0                                                                | 100 | 13.95  | 0    | 0   | 13.95 | Fosfomycin                                           |
| <i>Staphylococcus epidermidis</i>  | 4                            | 0                                                                | 100 | 14.29  | 0    | 0   | 14.29 | Fosfomycin                                           |
| <i>Staphylococcus haemolyticus</i> | 7                            | 0                                                                | 100 | 100    | 0    | 0   | 100   | Fosfomycin, amoxicillin, amoxicillin/clavulanic acid |
| <i>Staphylococcus aureus</i>       | 49                           | 2.04                                                             | 100 | 0      | 0    | 0   | 73.47 | Fosfomycin, amoxicillin/clavulanic acid              |

**Key:** Cip- Ciprofloxacin, Fos – Fosfomycin, Amoxil– Amoxicillin, Ceph – Cephalexin, TSX – Co-trimoxazole, Aug- Amoxicillin/clavulanic acid.

The findings of this study noted that amoxicillin-clavulanic acid or oral cephalosporins should only be used when other options are not available (Bhattacharya *et al.*, 2013). Also, due to increased resistance and lower efficacy, the use of co-trimoxazole alone should be avoided as an empirical option (Kubone *et al.*, 2020). Diabetic pregnant

women are predisposed to an increased risk of developing UTIs because of increased chances of getting glycosuria, adherence of bacteria to the uroepithelium and dysfunction of the immune system (Bash *et al.*, 2016). The study noted that in complicated UTIs, fosfomycin is recommended in treating urinary tract infection caused by *E. faecalis*, *E. coli* and *S. epidermidis*. Amoxicillin, amoxicillin/clavulanic acid or fosfomycin are recommended when treating urinary tract infections caused by *S. haemolyticus*. Urinary tract infections caused by *S. aureus* can be treated with amoxicillin/clavulanic or fosfomycin.

#### **4.5. Guidelines for the Management of UTIs**

The purpose of this guideline is to provide multidisciplinary recommendations for the management of women with complicated and uncomplicated UTIs (Appendix G). These guidelines are intended for healthcare professionals in public hospitals. They are designed to guide clinical judgment but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the patient. Choosing the right antimicrobial is an essential part of managing pregnant patients with urinary tract infections. It is not only important to choose the right medication, but also consideration should be given to selecting the right dose and treatment duration.

By effectively treating urinary tract infections it is hoped to reduce resistance rates by identifying the causative micro-organism and giving the right antimicrobial agent. Consideration should also be given to potential teratogenicity when choosing an antimicrobial in pregnant patients. This may be more difficult in the setting of penicillin allergy but the risks and benefits should be explained to the patient. It is also important that antimicrobials are used correctly to minimise risk of antimicrobial resistance emerging in the population.

Hospitals should have an antimicrobial stewardship team who can support the correct use of antimicrobials in UTI cases. All hospitals must have one or more clinical pharmacists with responsibility for antimicrobial use in the hospital. Patients should be

informed of the rationale for prescribing antimicrobials, and informed of any associated risks or adverse effects. Laboratories should observe antimicrobial resistance, including annual review of antibiograms as appropriate. Susceptibility results should be released in a restrictive manner where possible. All hospitals should have local or regional antimicrobial prescribing guidelines based where possible on local antimicrobial resistance data.

In uncomplicated UTIs, fosfomycin, amoxicillin, ciprofloxacin and cephalexin are the drug choices. Amoxicillin, fosfomycin and amoxicillin/clavulanic acid are used to treat UTIs in complicated UTIs as they have low resistance patterns and adverse effects. Co-trimoxazole should not be prescribed for pregnant women with established folate deficiency or women taking folate antagonists. When choosing an antimicrobial regimen for pregnant patients it is important to consider issues of teratogenicity and absorption. It is important to always review the antimicrobial choice by referring to antimicrobial susceptibility results from previous samples and from current tests.

Antimicrobial prophylaxis should be considered in pregnant women and in reoccurring UTIs. The use of antimicrobial prophylaxis for recurrent UTIs is difficult as there is no clear evidence based indications at present. Nitrofurantoin can be used for prophylaxis but should be avoided near term in pregnant patients because of the risk of neonatal haemolysis. The use of broad spectrum antimicrobials such as amoxicillin/clavulanic acid and cephalexin should be done following assessment of the benefits of prophylaxis against the risk of generating antimicrobial resistance in the patient leading to more limited treatment options at a later stage.

Fosfomycin, a natural product antibiotic has been in use for 20 years in Spain, Germany, France, Japan, Brazil and South Africa for UTIs (Silver, 2017). Initial tests indicated that fosfomycin was efficacious against specific isolates of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. vulgaris* and *S. aureus* (Silver, 2017). Fosfomycin is promptly excreted in urine and very low levels are found in tissues, making it an excellent choice for the treatment of UTIs (Tan and Chlebicki, 2016). Fosfomycin has activity against most Enterobacteriaceae spp. and *Enterococcus* spp. Given the high

*E. coli* susceptibility rates and its low potential for collateral damage, fosfomycin is one of the agents recommended for uncomplicated UTIs (Sofia *et al.*, 2019).

Initially it was estimated that co-trimoxazole was the most cost effective treatment for UTIs. However, the study noted that antimicrobial resistance of co-trimoxazole increased to 100% making it less cost effective. Fosfomycin with lower resistance, taken once became the most cost effective choice to treat UTIs.

#### **4.7. Summary**

- Amoxicillin, ciprofloxacin, nitrofurantoin and amoxicillin/clavulanic acid are being used to treat UTIs even though resistance is increasing.
- Ciprofloxacin is the most frequently given antibiotic at the study hospital.
- Fosfomycin is recommended according to the treatment protocol in the management of UTIs in public hospitals.
- Majority of the patients had urine catheters or had diabetes mellitus.
- Pregnant patients should have their urine samples cultured before antimicrobial therapy.

# CHAPTER 5

## CONCLUSION

---

### 5.1. Overview of the study

The study subject of antimicrobial resistance patterns of UTIs in a selected public hospital has been explored. Urinary tract infections mainly caused by *E. coli* are increasingly becoming resistant to antimicrobials proving the need for more research in UTIs. This study comprehensively examined antimicrobial resistance patterns in the selected public sector hospital by focusing on both complicated and uncomplicated UTIs. The research also identified the treatment profiles at the public sector hospital, compared them to the susceptibility testing results, identifying the causative micro-organism and suggested guidelines for the treatment of UTIs.

The findings of the study are addressed in this chapter based on the study aims and objectives. The main findings of the study are reviewed in the first part against each aim of the study. The strengths together with the limitations are outlined and discussed further. The contributions of the study are also discussed and lastly, a summary of the recommendations in clinical practice are outlined.

### 5.2. Achieved study aims

The general aim of this study was to contribute to knowledge about antimicrobial resistance patterns in UTIs in South Africa. Identified gaps from the review of literature in Chapter 1, noted that each aim was addressed in the Chapters of the study.

#### 5.2.1. Objective 1: To determine the antimicrobial resistance patterns of confirmed UTI infections within identified patients seeking treatment at the study hospital.

The average age of participant ( $\pm$ SD) was 33,  $33 \pm 23$ , 5 years in uncomplicated UTIs and 33,  $33 \pm 26$ , 3 years in complicated UTIs. In both complicated and uncomplicated

UTIs, 75% of the patients had pre-existing conditions which are considered as risk factors for UTI development. In uncomplicated UTIs, 16.9% of the patients had diabetes but in complicated UTIs, 27.3% of the patients had diabetes. The majority of the patients had leucocytes (100%), followed by nitrites (93%) and in complicated UTIs, all the patients had leucocytes in their urine, 96% of the patients had nitrites.

The source plate (sampling from patient) was examined to identify the number types of single colonies. These were colonies which have significantly different macro morphology traits, that is, size, colour shape, elevation and margin. Cultures were then isolated into single colonies amounting to 238 single colonies identified in uncomplicated UTIs and 194 single colonies identified in the complicated UTIs. Forty bacterial isolates were selected for identification based on the grouped macro morphology results. *Escherichia coli* had the highest prevalence followed by *E. faecalis* in uncomplicated UTIs. In complicated UTIs, *E. coli* and *S. aureus* were highly prevalent followed by *E. faecalis*. In the study, co-trimoxazole had the highest resistance patterns followed by ciprofloxacin in uncomplicated UTIs and co-trimoxazole, ciprofloxacin in complicated UTIs. The treatment of UTI cases is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens (Van Schoor, 2015).

#### **5.2.2. Objective 2: To determine the prevalence of past urinary tract Infection and past treatment practices in the management of these infections.**

In developing treatment guidelines, retrospectively reviewing data of bacterial susceptibility patterns over time is useful to produce accurate information (Ghaima *et al.*, 2018). In uncomplicated UTIs, 21% of participants were HIV positive, hence were immunocompromised, 31% had catheter associated UTIs and 17% of the patients had diabetes. In complicated UTIs, 15% of the participants were HIV positive, 19% had catheter associated UTIs and 27% had diabetes. This high correlation to immune suppression and UTI development indicates that they may have a bearing on risk of reoccurrences because an overactive immune response appears to increase risk of developing UTIs.



In the 100 uncomplicated UTIs, 216 antibiotics were prescribed in the same year meaning one patient had at least two UTI episodes in the same year. Ciprofloxacin was highly prescribed followed by trimethoprim-sulfamethoxazole. In complicated patients, 195 antibiotics were prescribed in the same year hence showing that most patients had reoccurrences. Amoxicillin was highly prescribed followed by nitrofurantoin.

### **5.2.3. Objective 3: To suggest a treatment policy and infection management protocols for UTIs.**

An antibiogram was recommended based on the susceptibility results as well as the bacteria identification results determined in Chapter 3. From these findings, it was determined that fosfomycin was highly effective followed by ciprofloxacin, cephalixin, amoxicillin and lastly, trimethoprim-sulfamethoxazole. The antibiogram together with the susceptibilities and patient file review data was used to develop a treatment policy for the management of UTIs.

The selected public sector hospital prescribes ciprofloxacin and trimethoprim-sulfamethoxazole mostly, despite the increasing level of resistance of the identified bacterial isolates to these treatments. Fosfomycin is highly effective and less prescribed at the selected public sector hospital as this item has not been selected as an essential medicine for public sector treatment of UTIs. This is due to fosfomycin's treatment expense, however, the efficacy of the product may reduce the rate of reoccurrences that are currently being experienced at public hospital settings, as shown in the patient file review presented in Chapter 4. Fluoroquinolone antimicrobials are effective, but should be reserved for women who are unable to tolerate first line agents or who experience reoccurrences of UTIs with resistant organisms while receiving first line regimens (Bezuidenhout, 2017).

## **5.4. Study limitations**

This research incorporates obtainable data while focusing on the methodologies, sample culturing and identification of the causative micro-organism. The study

evaluated the data base at the study hospital in terms of previous UTIs and past treatment practices. Using secondary data for health research has advantages, but a common limitation these data files is incompleteness of data for research. Lack of patient records was also a limiting factor as that meant that the exact pathogen causing the previous UTI cannot be compared to the latest results. When selecting patients, those who had taken antibiotics two weeks before consultation were excluded as the antibiotics would be found concentrated in urine as compared to those who had not taken antibiotics. Another common problem, is the missing information in patient files on potential risk factors for the development of UTIs (Sofia *et al.*, 2019).

Potential selection bias was another limitation during the research. The literature review in Chapter One states that the majority of patients with UTIs are treated with antibiotics, pending results of the urine sample submitted to NHLS for processing. Therefore, there is a potential to skew data to more resistant cases or falsely elevating the prevalence of resistance in this thesis if data is evaluated based on randomly selecting patient samples.

For Chapter three, the procedure used in the microbiology laboratory involved culturing the urine sample, performing antimicrobial susceptibility testing and the identification of the micro-organisms. A sample size of 40 isolates were identified instead of the total 432 samples. While the culture samples for identification were carefully selected, there is always the possibility that some isolates may have been grouped (macro morphological identification) incorrectly. Unfortunately, restricted funding did not allow for the full identification of all 432 samples.

An increasing resistance trend to trimethoprim-sulfamethoxazole and cephalexin were clearly identified in Chapter three, stimulating the need for extra effort to further prevent the spread of resistance to the listed antibiotics. Amoxicillin/clavulanic acid was not tested in uncomplicated UTIs as it is not recommended but it is interesting in future studies to compare between complicated and uncomplicated UTIs.

## 5.5. Contribution to the knowledge of UTIs

The undertaken research has not only contributed to new knowledge, but also confirmed existing evidence about antimicrobial resistance of UTIs in a hospital setting. The two main contributions to knowledge from the research undertaken are:

- 1) The confirmation of the increase in resistance of *E. coli* and *S. aureus* to antimicrobial agents.
- 2) Policy development using the results from antimicrobial susceptibility testing and antibiogram.

The increasing resistance in UTIs identified in the study hospital has effects on the treatment regimens of UTIs. Ciprofloxacin is considered the antimicrobial agent for use in severe life threatening infections, therefore it is important to monitor resistance patterns of such antimicrobial agents (Morley and Wacogne, 2018). This knowledge contribution is significant in South Africa because the study can inform as to which antimicrobial agents must be monitored closely. The research findings suggest the need for continuous monitoring of resistance patterns as it helps to control antimicrobial resistance. Data obtained helps to provide information on emerging resistance patterns to identify antimicrobials that need specific antibiotics and therefore prevent further increases in resistance.

Identification of previously unknown patient groups at high risk of antimicrobial resistance is a major contribution, in this case through antimicrobial susceptibility testing and reviewing patient files. It has been established that analysing susceptibility test results can help to identify high risk groups as the resistance patterns are noted for the tested antimicrobial agent. Patient file reviews helped to provide information on patient demographics, past infections as proof shows that certain risk factors such as presence of comorbidities and age may be associated with a greater risk of resistance (Sofia *et al.*, 2019). The identification of patients attending the selected public sector hospital are possibly at a greater risk of acquiring a resistant UTI, which demonstrates the importance of improving the treatment protocols annually as significant findings such as these can be detected soon after patient data is collected. The insight on patient risk factors will help to sufficiently manage resistance, as well as assist in

creating a treatment policy to control additional development resistance micro-organisms.

## **5.6. Summary and conclusion**

The findings of this research have contributed to the insight of new knowledge to improved understanding of antimicrobial resistance patterns of UTIs in South Africa. The recommendations made as a result of this thesis are established through evidence that can help to maintain the usefulness of the available antimicrobials. Antimicrobial resistance patterns of micro-organisms are changing constantly, therefore regular investigation needs to continue. Antibiotic usage has proven to be beneficial in counteracting the infection, though the bacteria can become resistant. Periodic surveillance of antimicrobial resistance of uropathogens, re-evaluation of empirical therapy, pre-therapy counselling for delayed antibiotic initiation and short-course antibiotic therapy with sensitive antibiotics are vital in an era of emerging antimicrobial resistance.

In conclusion, the highlights of the study show the urgency for clinicians, academic institutions, public sector healthcare services and the general public to work together towards confronting the matter of antibiotic resistance. Resistance may continue to rise without further efforts to curb the increasing prevalence of antibiotic resistance.

Furthermore, this study provides evidence for an updated treatment protocol, hence, providing valuable tools for antimicrobial stewardship in South Africa.

## REFERENCES

---

- Ahmed S. Shariq., S. Alsallloom., A. Babikir A. Alhomoud I. and Badr N. (2019) Uropathogens and their antimicrobial resistance patterns: Relationship with urinary tract infections. *International Journal of Health Sciences*, **13**: 48-54.
- Aiyegoro O. A., Odjajare E., Igbinosa E. and Okoh A. (2015) Incidence of urinary tract infections (UTI) among children and adolescents in Ile-Ife, Nigeria, *African Journal of Microbiology Research*, **2**: 6-8.
- Alkhyat S. H. and Al-Maqtari M. A. (2014) Prevalence of microorganisms isolates from urinary tract infections at some hospitals in Sana'a city, Yemen., *International Journal of Current Microbiology and Applied Sciences*, **3**: 876–885.
- Barber A. E., Norton J., Spivak A. and Mulvey M.A. (2013) Urinary tract infections: Current and emerging management strategies, *Clinical Infectious Diseases*, **5**: 719–724.
- Barry, M. S. Diallo B., Kanté D. and Diallo I.S. (2017) Antimicrobial susceptibility profile of community-acquired urinary tract infection in adults: A seven months prospective cross-sectional study in Dakar Town, Senegal, *African Journal of Urology*. Pan African Urological Surgeons' Association, **23**, 166–171.
- Bash M. R., Mathew M., Kharusi L. and Heija A.T. (2016) Symptomatic Urinary Tract Infection in Diabetic Pregnant Women , Effect of the Type of Diabetes and Glycemic Control Statistical analysis, **12**, 104–107.
- Bates J., Thomas-Jones E P., Timothy K., Nigel G., Micaela B., Emily H., Kerenza F., Nicolas L., Paul M., Michael R., Kate L., Carlos B., Curt V., Theo C., David W., Mandy H., Robin B. and Christopher C. (2014) Point of care testing for urinary tract infection in primary care, *BMC Family Practice*, **15**, 1–9.
- Bezuidenhout, S. (2017) Antimicrobial prescribing practices in patients admitted with community and hospital acquired urinary tract infections at a private hospital in Pretoria , Gauteng Province., *International Journal of Antimicrobial Agents*, **22**, 61–64.
- Beyene G. and Tsegaye W. (2011) Bacterial Uropathogens in Urinary Tract Infection

and Antibiotic Susceptibility Pattern in Jimma University Specialized Hospital, Southwest Ethiopia, *Ethiopian Journal of Health Sciences*, **21**, 141–146.

Bhattacharya D., Bhattacharya T., Sayi H., Muruganandam D.S., Roy N, Sugunan S. and Purushothaman A. (2013) Emergence of New Delhi metallo-beta-lactamase 1 (NDM-1) producing and multidrug resistant uropathogens causing urinary tract infections in Andaman Islands, India, *Microbial Drug Resistance*, **19**, 457–462.

Chazan, B. (2015) Urinary tract infections in patients with type 2 diabetes mellitus : review of prevalence , diagnosis , and management, *Dove Press Journal*, **8**, 129–136.

CLSI (2020) European Committee on Antimicrobial Susceptibility Testing Breakpoint tables for interpretation of MICs and zone diameters, *European Committee on Antimicrobial Susceptibility Testing*, **7**, 1-91.

Cristina, D., Urinario FA., Gestantes T., Riesgo E.N., Urinário D., Gestantes T., Risco E. and Baixo D (2009) Urinary tract infections in low-risk pregnant women, **17**, 507–513.

Currie, M. L., Raasch M.L., Greenbaum C.S. and Larry A. (2017) Follow-up urine cultures and fever in children with urinary tract infection, *Archives of Pediatrics and Adolescent Medicine*, **12**, 1237–1240.

Dadzie, I., Dakorah Q.E., Abiade M.P., Victoria T., Adusei E. and Richmond A (2019) The Effectiveness of Dipstick for the Detection of Urinary Tract Infection, *Dove Press Journal*, **4**, 5-9.

Demarsh, M. Bookstaver P., Gordon B., Lim C., Grif J., Bookstaver N., Ann N.K. and Kohn J., (2020) Prediction of trimethoprim / sulfamethoxazole resistance in community-onset urinary tract infections , *Journal of Global Antimicrobial Resistance* **21**, 218–222.

Demilie T., Beyene, Melaku G., Tsegaye S. and Wondewosen T (2014) Diagnostic accuracy of rapid urine dipstick test to predict urinary tract infection among pregnant women in Felege Hiwot Referral Hospital , Bahir, *Clinical Infectious Diseases*, **7**, 1–5.

Dolinsky, A. L., Ohiro R., Fan K., Xiao W. and Fusheng C. (2017) National Committee for Clinical Laboratory Standards. 2000. Performance standard for antimicrobial susceptibility testing., *Journal of International Medical Research*, **46**, 18.

Flores-Mireles, A. L., Walker, J. N., Caparon, M., & Hultgren, S. J. (2015). Urinary tract

infections: Epidemiology, mechanisms of infection and treatment options. *Nature Reviews Microbiology*, **13**, 269–284.

George, C., Ramana N., Mukherjee G. and Tata D. (2015) Treatment of uncomplicated symptomatic urinary tract infections: Resistance patterns and misuse of antibiotics, *Journal of Family Medicine and Primary Care*. Medknow, **4**, 416.

Ghaima, K. K., Abdulhassan K., Salman A.Z. and Yahya N. (2018) Prevalence and antibiotic resistance of bacteria isolated from urinary tract infections of pregnant women in Baghdad hospitals, *Biomedical and Pharmacology Journal*, **11**, 1989–1994.

Grabe, M., Bartoletti R, Cai T, Koves T, Naber B, Pickard P, Tenke P, Wagenlehner P. and Wullt B. (2015) Guidelines on Urological Infections, *European Association of Urology*, **6**, 33–40.

Haslund J., Dinesen R, Nielsen M, Brit A. and Carl B. (2013) Different recommendations for empiric first-choice antibiotic treatment of uncomplicated urinary tract infections in Europe, *Scandinavian Journal of Primary Health Care*, **31**, 235–240.

Henn, E. W. (2010) Menopause and its effect on the female lower urinary tract, *South African Family Practice*, **5**, 405–408.

Hickling D. R., Sun T.-T. and Wu X.R. (2015) Anatomy and Physiology of the Urinary Tract: Relation to Host Defense and Microbial Infection, *Microbiology Spectrum*, **3**, 1–29.

Iskander, M. (2018) Microbiological analysis of urinary tract infections in North West England and the impact of fluid intake on the incidence of urinary tract infection, *Journal of Microbiology Research*, **9**, 123–127.

Jafri, S. A. (2014) Antibiotic resistance of E. coli isolates from urine samples of Urinary Tract Infection (UTI) patients in Pakistan, *Bioinformation*, **10**, pp. 419–422.

Kang, C., Park J.K., Kim D., Yeo S., Min J., Lee S., Wie H. and Heon S. (2018) Clinical Practice Guidelines for the Antibiotic Treatment of Community-Acquired Urinary Tract Infections, *Journal of Clinical Practice* **50**, 67–100.

Kidwai, S., Ghaznavi N., Bashir F. and Jamal F (2017) Antibiotic susceptibility in commonly isolated pathogens from urinary tract infection in a cohort of subjects from low socioeconomic strata, *Biomedical and Pharmacology Journal* **33** 2-9.

- Konar, J., Bhattacharyya S., Sipra P. and Dipankar M.S. (2014) Nitrofurantoin in Urinary Tract Infection : Old is Gold, *Clinical Infectious Diseases*, **10**, 1456-1476.
- Kubone, P. Z., Mlisana, K. P., Govinden, U., Abia, A. L. K., and Essack, S. Y. (2020). Antibiotic Susceptibility and Molecular Characterization of Uropathogenic *Escherichia coli* Associated with Community-Acquired Urinary Tract Infections in Urban and Rural Settings in South Africa. *Tropical Medicine and Infectious Disease*, **5**, 176.
- Lee, D. S. (2018) Community-acquired urinary tract infection by *Escherichia coli* in the era of antibiotic resistance, *BioMed Research International*, **10**, 23-45.
- Leekha, S., Terrell, C. L. and Edson, R. S. (2011), General principles of antimicrobial therapy, *Mayo Clinic Proceedings*, **86**, 156–167.
- Lewis, D. A., Gumede, L. Y.E. Van der Hoven, L. A. De Gita, G. D. De Kock, E. J.E. De Lange, T. Maseko, V. Kekana, V. Smuts. and Perovic F, (2013) Antimicrobial susceptibility of organisms causing community-acquired urinary tract infections in Gauteng Province, South Africa, *South African Medical Journal*, **103**, 377–381.
- Lichtenberger, P. and Hooton, T. M. (2011) Antimicrobial prophylaxis in women with recurrent urinary tract infections, *International Journal of Antimicrobial Agents*. **38**, 36–41.
- Lin, Y. (2016) Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials, *World Journal of Urology*, **34**, 1207–1219.
- Lin, H. A., Yang, Y. S., Wang, J. X., Lin, H. C., Lin, D. Y., Chiu, C. H., Yeh, K. M., Lin, J. C., & Chang, F. Y. (2016). Comparison of the effectiveness and antibiotic cost among ceftriaxone, ertapenem, and levofloxacin in treatment of community-acquired complicated urinary tract infections. *Journal of Microbiology, Immunology and Infection*, **2**, 237–242.
- Linhares, I. (2013) Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: A ten-year surveillance study (2000-2009), *BMC Infectious Diseases*, **13**, 13-19.
- Liu, L. (2011) Phosphodiesterase-5 inhibitors for lower urinary tract symptoms secondary to benign prostatic hyperplasia: A systematic review and meta-analysis, *Urology*., **77**, 123–129.



Mambatta A. K., Jayarajan R.J., Vinitha L .H., Sanchitha M., Sujaya K. and Jayachandran K (2015) Reliability of dipstick assay in predicting urinary tract infection, *Journal of Clinical Pharmacy* **4**, 265–268.

Manikandan S.(2011) Antimicrobial Susceptibility Pattern of Urinary Tract Infection Causing Human Pathogenic Bacteria, *Asian Journal of Medical Sciences*, **3**,56–60.

Mitchell B. G., Ferguson J., Anderson K.,Sear M. and Barnett J, (2016) Length of stay and mortality associated with healthcare-associated urinary tract infections: A multi-state model, *Journal of Hospital Infection.*, **93**, 92–99.

Morley, G. L. and Wacogne, I. D. (2018) UK recommendations for combating antimicrobial resistance: a review of antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NICE guideline NG15, 2015) and related guidance, *Archives of disease in childhood - Education & practice edition*, **103**, 46–49.

Moyo, S. J., Kasubi A., Mabula M. and Samuel Y. (2010) Bacterial isolates and drug susceptibility patterns of urinary tract infection among pregnant women at muhimili national hospital in Tanzania, *Tanzania Journal of Health Research*, **12**, 236–240.

National Department of Health (2018) Standard Treatment Guidelines And Essential Medicines List for South Africa: Hospital Level 2018 Edition, 3.1-3.11.

Odoki, M., Aliero A, Tibyangye A., Maniga J.A., Wampande J.,Kato E.,Agwu C.A. and Ezera J.B (2019) Prevalence of Bacterial Urinary Tract Infections and Associated Factors among Patients Attending Hospitals in Bushenyi District, Uganda, *International Journal of Microbiology*, **12**, 345-350.

Odongo, C. O.. (2013) Antibigrams from community-acquired uropathogens in Gulu, northern Uganda - a cross-sectional study, *BMC Infectious Diseases*, **13**, 1-14

Reis, A. C. C., da Silva de Souza S.,Saldanha S.C., Pitanga M.G.,Oliveira T.N. and Riccio R. (2016) Ciprofloxacin resistance pattern among bacteria isolated from patients with community-acquired urinary tract infection, *Revista do Instituto de Medicina Tropical de Sao Paulo*, **58**, 1–6.

Rezaee, M. A. and Abdinia, B. (2015) Etiology and Antimicrobial Susceptibility Pattern of Pathogenic Bacteria in Children Subjected to UTI A Referral Hospital-Based Study in Northwest of Iran, *International Journal of Antimicrobial Agents* **94**, pp. 1–4.

- Riley, M. A. (2012) Resistance is futile: The bacteriocin model for addressing the antibiotic resistance challenge, *Biochemical Society Transactions*, **40**,1438–1442.
- Sadler, S., Holmes, M., Ren, S., Holden, S., Jha, S., & Thokala, P. (2017). Cost-effectiveness of antibiotic treatment of uncomplicated urinary tract infection in women: A comparison of four antibiotics. *BJGP Open*, **3**, 190-197.
- Saeed, A. (2017) Elevated antibiotic resistance of sudanese urinary tract infection bacteria, *EXCLI Journal*, **16**, 1073–1080.
- Schmiemann, G., Gebhardt K.E.,Matejczyk K., Martha M., Hummers P. and Eva P. (2010) Diagnose des harnwegsinfekts: Eine systematische übersicht, *Deutsches Arzteblatt*, **107**, 361–367.
- Setu, S. K., Sattar, Saleh A., Roy A.A, Chandan K.,Muhammadullah M. and Humayun S.K. (2017) Study of Bacterial pathogens in Urinary Tract Infection and their antibiotic resistance profile in a tertiary care hospital of Bangladesh, *Bangladesh Journal of Medical Microbiology*, **10**, 22–26.
- Sheerin, N. S. and Glover, E. K. (2019) Urinary tract infection, *Medicine (United Kingdom)*, **47**, 546–550.
- Silver, L. L. (2017) Fosfomycin : Mechanism and Resistance, *Cold Spring Harbor Perspective in Medicine*, **7**, pp. 1–11.
- Singh ., B. (2014) Urinary tract infection and its risk factors in women: An appraisal, *Journal of Pure and Applied Microbiology*, **8**, 4155–4162.
- Skrzat-klapaczy, A. (2018) Factors associated with urinary tract infections among HIV-1 infected patients, *Deutsches Arzteblatt*, **3**,1–10.
- Sofia E., Petra D., Uga G.,Hermes K.,Kling J. and Maria A. (2019) Antimicrobial resistance of Escherichia coli isolates from outpatient urinary tract infections in women in six European countries including Russia, *Journal of Global Antimicrobial Resistance*, **17**, 25–34.
- Sraboni, A. S., Program, M. and Sciences, N. (2018) Bacteriological profile and its antibiotic susceptibility in patients with Urinary Tract Infection in a diagnostic center in Dhaka, *Journal of Clinical Pharmacy*, **7**, 56-78.
- Stewardson, A. J. (2015) Collateral damage from oral ciprofloxacin versus

nitrofurantoin in outpatients with urinary tract infections: A culture-free analysis of gut microbiota, *Clinical Microbiology and Infection*., **21**, 344-348.

Storme, O. (2019) Risk factors and predisposing conditions for urinary tract infection, *Clinical Microbiology and infection*, **4**, 19–28.

Tai, D. S. (2013) Low rates of short-and long-term graft loss after kidney-pancreas transplant from a single center, *JAMA Surgery*, **148**, 368–373.

Tan, C. W. and Chlebicki, M. P. (2016) Urinary tract infections in adults, *Singapore Medical Journal*, **57**, 485–490.

Tessema, N. N., Ali, M. M., & Zenebe, M. H. (2020). Bacterial associated urinary tract infection, risk factors, and drug susceptibility profile among adult people living with HIV at Hawassa University Comprehensive Specialized Hospital, Hawassa, Southern Ethiopia. *Scientific Reports*, **1**, 1–9.

Van Schoor, J. (2015). Urinary tract infections in women. *SA Pharmaceutical Journal*, **7**, 29–32.

Vasudevan, R. (2014) Urinary tract infection: An overview of the infection and the associated risk factors,” *Journal of Microbiology & Experimentation*, **1**, 42–54.

Wagenlehner, F. M. E.. (2011) Unkomplizierte harnwegsinfektionen, *Deutsches Arzteblatt*, **108**, 415–423.

World Health Organization (WHO) (2017) Antimicrobial resistance Accessed March 5th, 2020.

# APPENDIX A

## A1: Human Research Ethics Committee (MEDICAL)

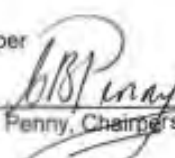


R14/49 Ms B Jaji

### HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL) CLEARANCE CERTIFICATE NO. M180645

**NAME:** Ms B Jaji  
**(Principal Investigator)**  
**DEPARTMENT:** School of Therapeutic Sciences  
Department of Pharmacy and Pharmacology  
Medical School  
University  
**PROJECT TITLE:** Antimicrobial resistance patterns of urinary tract infections (UTI) in a South African public hospital

**DATE CONSIDERED:** 29/06/2018  
**DECISION:** Approved unconditionally  
**CONDITIONS:**

**SUPERVISOR:** Ms S de Rapper  
**APPROVED BY:**   
Professor CB Penny, Chairperson, HREC (Medical)  
**DATE OF APPROVAL:** 27/08/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

#### DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Philip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.  
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. I agree to submit a yearly progress report. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initiated on June and will therefore be due in the month of June each year. Unreported changes to the application will be referred back to the HREC (Medical).

  
Principal Investigator Signature

27.08.2018  
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

## APPENDIX B

---



### B.1: The participant informed consent form

#### PARTICIPANT INFORMED CONSENT FORM

**Research Project entitled:** Antimicrobial resistance patterns of Urinary Tract Infections (UTIs) in a South African public hospital.

I hereby confirm that I have accurately read and understood the information sheet provided by the researcher, and I understand that the following will be done:

1. I will provide my urine sample and the specimen will be collected aseptically for culture sensitivity
  2. I will need to provide fresh urine
  3. The urine will be cultured and the bacteria causing the infection will be identified
  4. Glucose measurements will be done on me
  5. Pregnancy tests will be done
- I confirm that that I was given an opportunity to ask questions about the study, and all the questions asked have been answered to my satisfaction.
  - I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily, and that I may withdraw at any time during the study.
  - I hereby agree that I understand the requirements of this project and am willing to participate and provide feedback for research purposes.

Sign: \_\_\_\_\_ Date: \_\_\_\_\_

## APPENDIX C

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD  | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape            | Margin           | Elevation | Group ID |
|------------|--------|----|------|----|-----|-----|-----|----|-----|----|-----|----|-------|--------|------------------|------------------|-----------|----------|
| A061 1     | 0      | 0  | 0    | 0  | 2   | 1   | 25  | 1  | 0   | 0  | 0   | 0  | Large | Cream  | Spreading colony | Entire           | Flat      | 1        |
|            |        |    |      |    |     |     |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A053 4     | 6      | 1  | 8    | 1  | 9   | 1   | 24  | 0  | 0   | 0  | 0   | 0  | Large | Cream  | Spreading colony | Spreading colony | Convex    | 2        |
|            |        |    |      |    |     |     |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A023 1     | 13     | 1  | 8    | 0  | 26  | 1   | 24  | 1  | 14  | 1  | 0   | 0  | Large | Cream  | Irregular        | Lobate           | Convex    | 3        |
| A036 2     | 13     | 0  | 8    | 1  | 25  | 0,9 | 24  | 1  | 14  | 1  | 0   | 0  | Large | Cream  | Irregular        | Lobate           | Convex    |          |
|            |        |    |      |    |     |     |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A045 3     | 0      | 0  | 2    | 0  | 9   | 0   | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Spreading colony | Convex    | 4        |
| A069 1     | 0      | 0  | 2    | 1  | 9   | 1   | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Spreading colony | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape     | Margin           | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-----------|------------------|-----------|----------|
| A042 1     | 0      | 0  | 2    | 0  | 9   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Spreading colony | Convex    |          |
| A046 1     | 0      | 0  | 2    | 1  | 9   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Spreading colony | Convex    |          |
| A057 1     | 0      | 0  | 2    | 1  | 9   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Spreading colony | Convex    |          |
| A059 1     | 0      | 0  | 2    | 1  | 9   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Spreading colony | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |           |                  |           |          |
| A032 1     | 0      | 0  | 2    | 1  | 9   | 1  | 24  | 1  | 3   | 0  | 0   | 0  | Large | Grey   | Irregular | Entire           | Flat      | 5        |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |           |                  |           |          |
| A068 1     | 0      | 0  | 3    | 0  | 10  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    | 6        |
| A084 2     | 0      | 0  | 3    | 1  | 10  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    |          |
| A008 2     | 0      | 0  | 3    | 1  | 10  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    |          |
| A002 3     | 0      | 0  | 3    | 1  | 10  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    |          |
| A026 1     | 0      | 0  | 3    | 1  | 10  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    |          |
| A027 1     | 0      | 0  | 3    | 1  | 10  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round     | Entire           | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin     | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|------------|-----------|----------|
| A034 1     | 0      | 0  | 3    | 1  | 10  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round | Entire     | Convex    |          |
| A038 1     | 0      | 0  | 3    | 1  | 10  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round | Entire     | Convex    |          |
| A047 1     | 0      | 0  | 3    | 1  | 10  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round | Entire     | Convex    |          |
| A054 1     | 0      | 0  | 3    | 0  | 10  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Large | Grey   | Round | Entire     | Convex    |          |
| A003 3     | 0      | 0  | 3    | 1  | 10  | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Large | Grey   | Round | Entire     | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |            |           |          |
| A007 1     | 18     | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 2   | 1  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      | 7        |
| A017 1     | 18     | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 2   | 0  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      |          |
| A028 2     | 18     | 1  | 6    | 1  | 4   | 1  | 9   | 0  | 2   | 1  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      |          |
| A029 4     | 18     | 0  | 6    | 1  | 4   | 0  | 9   | 1  | 2   | 0  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      |          |
| A077 4     | 18     | 1  | 6    | 1  | 4   | 1  | 9   | 0  | 2   | 1  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      |          |
| A071 1     | 18     | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 2   | 1  | 0   | 0  | Small | Grey   | Round | Not smooth | Flat      |          |



**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape     | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-----------|--------|-----------|----------|
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |           |        |           |          |
| A041 1     | 0      | 0  | 14   | 1  | 9   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Large | Cream  | Irregular | Lobate | Convex    | 8        |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |           |        |           |          |
| A015 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    | 9        |
| A043 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A051 1     | 0      | 0  | 0    | 0  | 2   | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A020 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A022 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A024 2     | 0      | 0  | 0    | 0  | 2   | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A025 3     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A031 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A033 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A034 3     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A048 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A050 1     | 0      | 0  | 0    | 0  | 2   | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |
| A058 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round     | Entire | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape            | Margin           | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|------------------|------------------|-----------|----------|
| A067 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Convex    |          |
| A073 1     | 0      | 0  | 0    | 0  | 2   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Convex    |          |
| A080 1     | 0      | 0  | 0    | 0  | 2   | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A005 1     | 0      | 0  | 0    | 0  | 0   | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round            | Entire           | Umbonate  | 10       |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A073 2     | 9      | 1  | 8    | 1  | 9   | 1  | 3   | 1  | 0   | 0  | 0   | 0  | Large | White  | Round            | Entire           | Flat      | 11       |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A072 1     | 10     | 1  | 7    | 1  | 16  | 1  | 0   | 0  | 12  | 1  | 0   | 0  | Small | Grey   | Spreading colony | Entire           | Flat      | 12       |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |          |
| A089 2     | 2      | 1  | 6    | 1  | 15  | 1  | 9   | 1  | 6   | 1  | 0   | 0  | Small | White  | Spreading colony | Spreading colony | Flat      | 13       |
| A099 2     | 2      | 0  | 6    | 1  | 15  | 0  | 9   | 1  | 6   | 1  | 0   | 0  | Small | White  | Spreading colony | Spreading colony | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A002 2     | 5      | 1  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 14       |
| A007 3     | 5      | 0  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A040 2     | 5      | 1  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A071 3     | 5      | 1  | 2    | 1  | 8   | 0  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A076 2     | 5      | 1  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A077 3     | 5      | 0  | 2    | 1  | 8   | 0  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A083 2     | 5      | 1  | 2    | 0  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A085 2     | 5      | 1  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A091 1     | 5      | 0  | 2    | 1  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A092 2     | 5      | 1  | 2    | 0  | 8   | 1  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A089 5     | 5      | 1  | 2    | 1  | 8   | 0  | 0   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A038 2     | 3      | 0  | 4    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 15       |
| A049 1     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A096 1     | 3      | 1  | 4    | 1  | 4   | 0  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A006 2     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A008 3     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A040 4     | 3      | 1  | 4    | 0  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A066 4     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A076 3     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A093 3     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A034 4     | 3      | 1  | 4    | 0  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A052 2     | 3      | 1  | 4    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A054 3     | 3      | 0  | 4    | 0  | 4   | 0  | 6   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A009 1     | 0      | 0  | 2    | 0  | 15  | 1  | 2   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Convex    | 16       |
| A070 1     | 0      | 0  | 2    | 1  | 15  | 1  | 2   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A066 3     | 19     | 0  | 6    | 1  | 10  | 1  | 12  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Convex    | 17       |
| A075 1     | 19     | 1  | 6    | 1  | 10  | 0  | 12  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Convex    |          |
| A087 2     | 19     | 1  | 6    | 1  | 10  | 1  | 12  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Convex    |          |
| A090 1     | 19     | 1  | 6    | 1  | 10  | 1  | 12  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A003 2     | 6      | 1  | 0    | 0  | 3   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 18       |
| A045 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A053 1     | 6      | 0  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A065 1     | 6      | 1  | 0    | 0  | 2   | 0  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A077 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A078 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A082 1     | 6      | 0  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A084 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A086 1     | 6      | 0  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A097 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A008 1     | 6      | 0  | 0    | 0  | 2   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A025 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A028 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A029 2     | 6      | 0  | 0    | 0  | 2   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A030 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A036 1     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A044 1     | 6      | 0  | 0    | 0  | 2   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A062 2     | 6      | 1  | 0    | 0  | 2   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A079 1     | 6      | 0  | 0    | 0  | 2   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A093 2     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 19       |
| A096 3     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A098 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A001 3     | 2      | 0  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A005 2     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A012 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A014 3     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A018 3     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A026 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A027 2     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A032 3     | 2      | 0  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A035 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A037 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A040 3     | 2      | 0  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A043 2     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A047 3     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A071 3     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A052 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A075 3     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A084 4     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A087 4     | 2      | 0  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A088 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A091 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A100 3     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A091 3     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A053 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A054 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A064 4     | 2      | 0  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A087 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A089 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A001 2     | 2      | 0  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A002 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A003 1     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A006 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A007 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A010 1     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A012 1     | 2      | 0  | 5    | 1  | 5   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A014 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A016 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A017 2     | 2      | 0  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A018 2     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A019 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A024 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |



**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A028 3     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A029 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A032 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A034 2     | 2      | 0  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A035 3     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A036 4     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A037 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A039 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A040 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A041 2     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A044 4     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A047 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A049 2     | 2      | 0  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A055 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A062 1     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A063 1     | 2      | 0  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A064 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A065 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A066 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A074 1     | 2      | 1  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A075 4     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A077 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A078 2     | 2      | 0  | 5    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A079 2     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A081 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A083 1     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A085 1     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A086 2     | 2      | 1  | 5    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A088 1     | 2      | 1  | 5    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A089 4     | 2      | 1  | 5    | 0  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| A087 3     | 2      | 1  | 4    | 0  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 20       |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A018 1     | 2      | 0  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A023 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A035 2     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A044 2     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A049 3     | 2      | 1  | 4    | 0  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A056 1     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A064 1     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A066 1     | 2      | 0  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A075 2     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A078 3     | 2      | 1  | 4    | 0  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A090 3     | 2      | 0  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A091 4     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A009 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A012 3     | 2      | 0  | 4    | 1  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A018 4     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A023 4     | 2      | 1  | 4    | 0  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A026 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A032 4     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A037 2     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A038 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A041 3     | 2      | 1  | 4    | 0  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A049 4     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A060 3     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A062 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A072 3     | 2      | 0  | 4    | 0  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A074 2     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A083 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A085 3     | 2      | 0  | 4    | 1  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A088 3     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A089 3     | 2      | 1  | 4    | 0  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A094 2     | 2      | 0  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| A096 4     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size           | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|----------------|--------|-------|--------|-----------|----------|
| A056 2     | 2      | 1  | 4    | 1  | 9   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small          | White  | Round | Entire | Flat      |          |
| A060 2     | 2      | 1  | 4    | 1  | 9   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small          | White  | Round | Entire | Flat      |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |                |        |       |        |           |          |
| A009 2     | 3      | 1  | 0    | 0  | 15  | 1  | 4   | 1  | 0   | 0  | 0   | 0  | Small          | White  | Round | Entire | Convex    | 21       |
| A070 2     | 3      | 0  | 0    | 0  | 15  | 0  | 4   | 1  | 0   | 0  | 0   | 0  | Small          | White  | Round | Entire | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |                |        |       |        |           |          |
| A082 2     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    | 22       |
| A081 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 0  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    |          |
| A004 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    |          |
| A011 1     | 0      | 0  | 8    | 0  | 9   | 1  | 24  | 0  | 7   | 1  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    |          |
| A013 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 0  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    |          |
| A081 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulate<br>d | Cream  | Round | Entire | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size       | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|------------|--------|-------|--------|-----------|----------|
| A004 1     | 0      | 0  | 8    | 1  | 9   | 0  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A013 3     | 0      | 0  | 8    | 0  | 9   | 0  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A015 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 0  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A056 3     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 0  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A090 2     | 0      | 0  | 8    | 0  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A092 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 0  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A093 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A094 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A095 1     | 0      | 0  | 8    | 0  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size       | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|------------|--------|-------|--------|-----------|----------|
| A096 2     | 0      | 0  | 8    | 1  | 9   | 0  | 24  | 1  | 7   | 0  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A097 2     | 0      | 0  | 8    | 1  | 9   | 0  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A098 1     | 0      | 0  | 8    | 0  | 9   | 1  | 24  | 0  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A099 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 0  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A100 1     | 0      | 0  | 8    | 1  | 9   | 0  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A060 1     | 0      | 0  | 8    | 1  | 9   | 1  | 24  | 1  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
| A068 2     | 0      | 0  | 8    | 0  | 9   | 1  | 24  | 0  | 7   | 1  | 0   | 0  | Granulated | Cream  | Round | Entire | Convex    |          |
|            |        |    |      |    |     |    |     |    |     |    |     |    |            |        |       |        |           |          |
| A023 2     | 6      | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 4   | 0  | 0   | 0  | Small      | Yellow | Round | Entire | Flat      | 23       |
| A001 1     | 6      | 0  | 2    | 0  | 5   | 0  | 9   | 1  | 4   | 0  | 0   | 0  | Small      | Yellow | Round | Entire | Flat      |          |
| A071 2     | 6      | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 4   | 1  | 0   | 0  | Small      | Yellow | Round | Entire | Flat      |          |

**Table C1:** Morphological characteristics and antimicrobial susceptibility patterns in uncomplicated UTIs.

| Patient ID | Amoxil | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|--------|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| A092 3     | 6      | 1  | 2    | 1  | 5   | 1  | 9   | 0  | 4   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| A021 1     | 6      | 1  | 2    | 1  | 5   | 1  | 9   | 0  | 4   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| A054 4     | 6      | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 4   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| A100 2     | 6      | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 4   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
|            | 0      |    | 0    |    | 0   |    | 0   |    | 0   |    | 0   | 0  |       |        |       |        |           |          |



## APPENDIX D

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size       | Colour | Shape | Margin           | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|------------|--------|-------|------------------|-----------|----------|
| B040 1     | 0  | 0   | 0  | 7    | 1  | 11  | 0  | 12  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Convex    | 1        |
| B020 2     | 1  | 0   | 0  | 7    | 1  | 11  | 1  | 12  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Convex    |          |
| B093 1     | 1  | 0   | 0  | 7    | 0  | 11  | 1  | 12  | 0  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Convex    |          |
| B099 1     | 1  | 0   | 0  | 7    | 1  | 11  | 1  | 12  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Convex    |          |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |            |        |       |                  |           |          |
| B047 1     | 1  | 8   | 1  | 8    | 0  | 11  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    | 2        |
| B069 1     | 0  | 8   | 0  | 8    | 1  | 11  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |          |
| B080 1     | 1  | 8   | 1  | 8    | 1  | 11  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |          |
| B081 2     | 1  | 8   | 1  | 8    | 1  | 11  | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size       | Colour | Shape | Margin           | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|------------|--------|-------|------------------|-----------|-----------|
| B082 1     | 0  | 8   | 1  | 8    | 0  | 11  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |           |
| B084 1     | 1  | 8   | 1  | 8    | 1  | 11  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |           |
| B074 1     | 1  | 8   | 1  | 8    | 1  | 11  | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |           |
| B086 1     | 1  | 8   | 0  | 8    | 1  | 11  | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |           |
| B027 2     | 0  | 8   | 1  | 8    | 1  | 11  | 0  | 24  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Spreading colony | Convex    |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |            |        |       |                  |           |           |
| B009 1     | 1  | 16  | 1  | 7    | 1  | 9   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      | 3         |
| B006 1     | 1  | 16  | 0  | 7    | 0  | 9   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      |           |
| B050 1     | 0  | 16  | 1  | 7    | 1  | 9   | 0  | 26  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      |           |
| B071 1     | 1  | 16  | 1  | 7    | 1  | 9   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      |           |
| B083 1     | 1  | 16  | 1  | 7    | 1  | 9   | 1  | 26  | 0  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      |           |
| B096 2     | 1  | 16  | 1  | 7    | 0  | 9   | 1  | 26  | 1  | 0   | 0  | 0   | 0  | Granulated | Grey   | Round | Entire           | Flat      |           |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| B011 1     | 1  | 8   | 1  | 7    | 0  | 5   | 1  | 24  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Irregular | 4        |
| B061 2     | 0  | 8   | 1  | 7    | 1  | 5   | 1  | 24  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Irregular |          |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| B001 2     | 1  | 11  | 0  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      | 5        |
| B003 1     | 1  | 11  | 1  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B017 2     | 0  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B018 3     | 1  | 11  | 1  | 9    | 0  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B020 1     | 0  | 11  | 0  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B025 1     | 1  | 11  | 1  | 9    | 1  | 5   | 0  | 25  | 0  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B026 2     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B028 2     | 1  | 11  | 0  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B014 1     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B035 1     | 0  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B023 1     | 1  | 11  | 1  | 9    | 0  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B037 2     | 0  | 11  | 0  | 9    | 1  | 5   | 1  | 25  | 0  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B042 1     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B048 2     | 1  | 11  | 1  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B050 1     | 1  | 11  | 0  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B054 2     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B055 2     | 0  | 11  | 1  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B060 2     | 1  | 11  | 1  | 9    | 0  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B063 2     | 0  | 11  | 0  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B065 2     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B066 1     | 1  | 11  | 1  | 9    | 1  | 5   | 0  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B067 1     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B073 1     | 0  | 11  | 0  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B076 1     | 1  | 11  | 1  | 9    | 0  | 5   | 1  | 25  | 0  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
| B083 2     | 1  | 11  | 1  | 9    | 1  | 5   | 1  | 25  | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Flat      |          |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| B036 1     | 0  | 9   | 1  | 4    | 1  | 4   | 1  | 8   | 0  | 2   | 0  | 0   | 0  | Large | Grey   | Round | Entire | Flat      | 6        |
| B075 1     | 1  | 9   | 1  | 4    | 0  | 4   | 1  | 8   | 1  | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD  | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|-----|-----|----|-----|----|-------|--------|-------|--------|-----------|-----------|
| B080 2     | 1  | 9   | 1  | 4    | 1  | 4   | 0  | 8   | 0   | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
| B081 1     | 0  | 9   | 1  | 4    | 1  | 4   | 1  | 8   | 0,6 | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
| B086 2     | 1  | 9   | 1  | 4    | 1  | 4   | 1  | 8   | 1   | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
| B089 2     | 1  | 9   | 0  | 4    | 1  | 4   | 1  | 8   | 1   | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
| B090 1     | 1  | 9   | 1  | 4    | 1  | 4   | 0  | 8   | 1   | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
| B059 1     | 1  | 9   | 1  | 4    | 0  | 4   | 1  | 8   | 1   | 2   | 1  | 0   | 0  | Large | Grey   | Round | Entire | Flat      |           |
|            |    |     |    |      |    |     |    |     |     |     |    |     |    |       |        |       |        |           |           |
| B016 2     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      | 7         |
| B021 1     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B034 1     | 1  | 18  | 0  | 2    | 1  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B042 3     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B044 2     | 1  | 18  | 1  | 2    | 0  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B105 1     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B106 1     | 1  | 18  | 0  | 2    | 1  | 5   | 1  | 9   | 0   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B002 1     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |
| B007 1     | 1  | 18  | 0  | 2    | 1  | 5   | 1  | 9   | 1   | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |           |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B011 2     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B021 3     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B024 1     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B029 2     | 1  | 18  | 0  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B053 1     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B070 1     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B025 3     | 1  | 18  | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B100 1     | 0  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B007 3     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B010 2     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B011 3     | 1  | 18  | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | flat      |          |
| B028 3     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B042 2     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B048 3     | 1  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
| B103 1     | 0  | 18  | 0  | 2    | 1  | 5   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | Cream  | Round | Entire | Flat      |          |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B057 2     | 1  | 9   | 1  | 6    | 1  | 10  | 1  | 10  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      | 8        |
| B032 1     | 0  | 9   | 1  | 6    | 1  | 10  | 0  | 10  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B045 1     | 1  | 9   | 1  | 6    | 0  | 10  | 1  | 10  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B056 1     | 1  | 9   | 0  | 6    | 1  | 10  | 0  | 10  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B058 1     | 1  | 9   | 1  | 6    | 0  | 10  | 1  | 10  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B072 1     | 1  | 9   | 1  | 6    | 1  | 10  | 1  | 10  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B079 1     | 1  | 9   | 1  | 6    | 1  | 10  | 0  | 10  | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B088 1     | 1  | 9   | 1  | 6    | 1  | 10  | 1  | 10  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B098 1     | 0  | 9   | 1  | 6    | 0  | 10  | 1  | 10  | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |          |
| B101 1     | 0  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      | 9        |
| B102 1     | 1  | 13  | 1  | 7    | 1  | 4   | 0  | 6   | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B104 1     | 1  | 13  | 1  | 7    | 0  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B107 1     | 1  | 13  | 0  | 7    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B012 1     | 1  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |
| B013 1     | 1  | 13  | 1  | 7    | 1  | 4   | 0  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape            | Margin           | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|------------------|------------------|-----------|-----------|
| B022 1     | 1  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
| B055 1     | 1  | 13  | 0  | 7    | 0  | 4   | 0  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
| B065 1     | 1  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
| B089 1     | 1  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 0  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
| B094 1     | 1  | 13  | 1  | 7    | 1  | 4   | 1  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
| B097 1     | 0  | 13  | 0  | 7    | 1  | 4   | 0  | 6   | 1  | 0   | 0  | 0   | 0  | Small | Grey   | Round            | Entire           | Flat      |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |           |
| B064 3     | 1  | 19  | 1  | 10   | 0  | 6   | 1  | 10  | 1  | 8   | 1  | 0   | 0  | Small | White  | Spreading colony | Spreading colony | Convex    | 10        |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |                  |                  |           |           |
| B015 2     | 1  | 18  | 1  | 7    | 0  | 11  | 1  | 12  | 0  | 8   | 1  | 0   | 0  | Small | White  | Round            | Entire           | Convex    | 11        |
| B036 2     | 1  | 18  | 1  | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 0  | 0   | 0  | Small | White  | Round            | Entire           | Convex    |           |
| B016 1     | 1  | 18  | 1  | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 1  | 0   | 0  | Small | White  | Round            | Entire           | Convex    |           |
| B015 1     | 0  | 18  | 0  | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 1  | 0   | 0  | Small | White  | Round            | Entire           | Convex    |           |
| B004 1     | 1  | 18  | 1  | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 1  | 0   | 0  | Small | White  | Round            | Entire           | Convex    |           |



**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|-----------|
| B004 2     | 1  | 18  | 1  | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 1  | 0   | 0  | Small | White  | Round | Entire | Convex    |           |
| B063 1     | 1  | 18  | 14 | 7    | 1  | 11  | 1  | 12  | 1  | 8   | 0  | 0   | 14 | Small | White  | Round | Entire | Convex    |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |           |
| B074 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      | 12        |
| B039 1     | 0  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B085 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B091 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B092 1     | 1  | 7   | 1  | 6    | 0  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B004 3     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B001 1     | 0  | 7   | 0  | 6    | 0  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B002 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |
| B003 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |
| B005 3     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B007 2     | 0  | 7   | 0  | 6    | 0  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |
| B008 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |
| B010 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B017 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |          |
| B018 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B021 2     | 0  | 7   | 0  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B026 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B027 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B028 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B029 1     | 0  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B030 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B031 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B043 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B035 2     | 1  | 7   | 1  | 6    | 0  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B037 1     | 0  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B038 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B038 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B039 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B041 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B044 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B046 1     | 1  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B047 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B048 1     | 0  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B051 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B052 1     | 1  | 7   | 0  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B054 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B057 1     | 0  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B060 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B061 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B062 1     | 1  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B064 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B068 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B071 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B073 3     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B077 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Group ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|----------|
| B078 1     | 0  | 7   | 0  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B087 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B095 1     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B096 1     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B103 2     | 0  | 7   | 0  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B005 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |          |
| B062 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B068 1     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B078 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B036 3     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B041 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B047 3     | 1  | 7   | 0  | 6    | 0  | 4   | 0  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B059 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B066 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B067 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |
| B071 3     | 0  | 7   | 0  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |          |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size  | Colour | Shape | Margin | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|-------|--------|-------|--------|-----------|-----------|
| B073 2     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B087 2     | 1  | 7   | 1  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B090 2     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B105 2     | 0  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B002 3     | 1  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | flat      |           |
| B003 3     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B031 2     | 1  | 7   | 1  | 6    | 0  | 4   | 1  | 9   | 0  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B100 2     | 1  | 7   | 1  | 6    | 1  | 4   | 0  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
| B106 2     | 0  | 7   | 0  | 6    | 1  | 4   | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | White  | Round | Entire | Flat      |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |           |
| B005 2     | 1  | 9   | 1  | 3    | 0  | 15  | 1  | 9   | 1  | 0   | 0  | 0   | 0  | Small | Yellow | Round | Entire | Convex    | 13        |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |       |        |       |        |           |           |
| B008 2     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Convex    | 14        |
| B009 2     | 1  | 18  | 0  | 2    | 1  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Convex    |           |
| B018 1     | 0  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 0  | 7   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Convex    |           |
| B019 1     | 1  | 18  | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small | Yellow | Round | Entire | Convex    |           |

**Table D1:** Morphological characteristics and antimicrobial susceptibility patterns in complicated UTIs.

| Patient ID | SD | Aug | SD | Ceph | SD | Cip | SD | Fos | SD | TSX | SD | Nys | SD | Size       | Colour | Shape            | Margin           | Elevation | Gro up ID |
|------------|----|-----|----|------|----|-----|----|-----|----|-----|----|-----|----|------------|--------|------------------|------------------|-----------|-----------|
| B025 2     | 0  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 0  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B029 3     | 1  | 18  | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B052 2     | 0  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B054 3     | 1  | 18  | 0  | 2    | 1  | 5   | 0  | 9   | 1  | 7   | 0  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B064 1     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B066 3     | 0  | 18  | 1  | 2    | 1  | 5   | 0  | 9   | 1  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B070 2     | 1  | 18  | 1  | 2    | 1  | 5   | 1  | 9   | 0  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
| B075 2     | 0  | 18  | 0  | 2    | 0  | 5   | 1  | 9   | 1  | 7   | 1  | 0   | 0  | Small      | Yellow | Round            | Entire           | Convex    |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |            |        |                  |                  |           |           |
| B032 2     | 0  | 10  | 1  | 4    | 1  | 9   | 1  | 10  | 0  | 6   | 0  | 0   | 0  | Small      | White  | Round            | Entire           | Flat      | 15        |
| B033 2     | 0  | 10  | 0  | 4    | 1  | 9   | 1  | 10  | 1  | 6   | 1  | 0   | 0  | Small      | White  | Round            | Entire           | Flat      |           |
| B0361      | 0  | 10  | 1  | 4    | 1  | 9   | 0  | 10  | 1  | 6   | 1  | 0   | 0  | Small      | White  | Round            | Entire           | Flat      |           |
|            |    |     |    |      |    |     |    |     |    |     |    |     |    |            |        |                  |                  |           |           |
| B049 1     | 1  | 9   | 1  | 6    | 1  | 12  | 1  | 25  | 1  | 4   | 1  | 0   | 0  | Granulated | Grey   | Spreading colony | Spreading colony | Convex    | 16        |

## APPENDIX E

**Table E1:** Risk factors in uncomplicated UTIs.

|                             | HIV positive | Hypertension | Diabetes | Urinary incontinence | Use of spermicide | Total |
|-----------------------------|--------------|--------------|----------|----------------------|-------------------|-------|
| <b>Number of incidences</b> | 21           | 4            | 13       | 10                   | 5                 | 63    |
| <b>Percentage incidence</b> | 33.3         | 6.3          | 20.6     | 23.8                 | 7.9               | 100   |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                    |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|-----------------------------------------|
| A001               | 28 January 2019   | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A001               | 30 December 2018  | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A001               | 29 April 2018     | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                    |                   |                       |                            |                       |                                         |
| A002               | 28 January 2019   | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A002               | 28 September 2018 | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly        |
|                    |                   |                       |                            |                       |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A003                      | 28 January 2019          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A003                      | 25 June 2018             | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A004                      | 30 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A004                      | 22 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A005                      | 30 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A005                      | 05 October 2018          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A006                      | 20 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A006                      | 23 October 2018          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A007                      | 20 February 2019         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |



| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A007                      | 30 August 2018           | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A008                      | 25 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A008                      | 24 April 2018            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A009                      | 25 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A009                      | 04 May 2018              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A010                      | 25 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A010                      | 23 October 2018          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A010                      | 20 May 2018              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A011                      | 25 February 2019         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A011                      | 28 November 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A012                      | 04 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A012                      | 25 May 2018              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A013                      | 04 March 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A013                      | 18 October 2018          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A014                      | 04 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A014                      | 13 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A015                      | 05 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A015                      | 07 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A016                      | 05 March 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A016                      | 12 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A016                      | 10 October 2018          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A017                      | 06 March 2019            | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days          |
| A017                      | 02 November 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A017                      | 30 September 2018        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A018                      | 06 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A018                      | 31 August 2018           | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A019                      | 13 March 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A019                      | 27 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A019                      | 18 March 2018            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A020                      | 14 March 2019            | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days          |
| A020                      | 23 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A020                      | 30 July 2018             | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A021                      | 14 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A021                      | 18 April 2018            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A022                      | 18 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A022                      | 10 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A023                      | 18 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A023                      | 21 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A024                      | 19 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A024                      | 23 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days          |
|                           |                          |                              |                                   |                              |                                         |
| A025                      | 19 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A025                      | 03 January 2019          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A026                      | 19 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A026                      | 07 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A027                      | 19 March 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A027                      | 23 November 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A028                      | 10 April 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A028                      | 14 February 2019         | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
|                           |                          |                              |                                   |                              |                                         |
| A029                      | 10 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg tds 5 days          |
| A029                      | 20 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg bd 3days            |
| A029                      | 12 August 2018           | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
|                           |                          |                              |                                   |                              |                                         |
| A030                      | 15 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
| A030                      | 15 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A030                      | 09 May 2019              | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
|                           |                          |                              |                                   |                              |                                         |
| A031                      | 15 April 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A031                      | 17 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A032                      | 15 April 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A032                      | 10 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days          |
|                           |                          |                              |                                   |                              |                                         |
| A033                      | 15 April 2018            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A033                      | 24 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A034                      | 15 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A034                      | 22 February 2019         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
|                           |                          |                              |                                   |                              |                                         |
| A035                      | 29 April 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A035                      | 06 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A036                      | 24 April 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A036                      | 28 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A037                      | 29 April 2019            | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A037                      | 15 September 2018        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |
| A038                      | 30 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
|                           |                          |                              |                                   |                              |                                         |
| A039                      | 06 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
| A039                      | 30 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |



| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>             |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|-----------------------------------------|
|                           |                          |                              |                                   |                              |                                         |
| A040                      | 06 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A040                      | 23 October 2018          | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
|                           |                          |                              |                                   |                              |                                         |
| A041                      | 06 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly 3 days |
| A041                      | 10 February 2019         | No                           | No                                | Yes                          | Fosfomycin 3g single dose               |
| A041                      | 03 August 2018           | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A042                      | 20 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
|                           |                          |                              |                                   |                              |                                         |
| A043                      | 20 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A043                      | 14 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg bd3 days            |
|                           |                          |                              |                                   |                              |                                         |
| A044                      | 21 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days            |
| A044                      | 03 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly        |
|                           |                          |                              |                                   |                              |                                         |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A045                      | 21 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A045                      | 16 November 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A046                      | 27 May 2019              | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A046                      | 10 February 2019         | No                           | No                                | Yes                          | Amoxicillin 1g bd 5days          |
| A046                      | 10 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A047                      | 28 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A047                      | 23 March 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A048                      | 30 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A048                      | 18 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A049                      | 11 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A049                      | 22 March 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
|                           |                          |                              |                                   |                              |                                  |
| A050                      | 12 June 2019             | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
| A050                      | 21 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A050                      | 28 February 2019         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A051                      | 12 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A051                      | 15 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A052                      | 13 June 2019             | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
| A052                      | 02 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A053                      | 13 June 2019             | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A053                      | 25 April 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed             |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|----------------------------------|
| A054               | 18 June 2019      | No                    | No                         | Yes                   | Ciprofloxacin 375mg tds 5 days   |
| A054               | 15 March 2019     | No                    | No                         | Yes                   | Amoxicillin 1g tds 5 days        |
|                    |                   |                       |                            |                       |                                  |
| A055               | 26 June 2019      | No                    | No                         | Yes                   | Fosfomycin 3g single dose        |
| A055               | 15 February 2019  | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days     |
|                    |                   |                       |                            |                       |                                  |
| A056               | 26 June 2019      | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly |
| A056               | 19 January 2019   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days     |
|                    |                   |                       |                            |                       |                                  |
| A057               | 24 June 2019      | No                    | No                         | Yes                   | Ciprofloxacin 375g tds 5 days    |
| A057               | 12 December 2018  | No                    | No                         | Yes                   | Fosfomycin 3g single dose        |
|                    |                   |                       |                            |                       |                                  |
| A058               | 24 June 2019      | No                    | No                         | Yes                   | Ciprofloxacin 500mg PO 12 hourly |
|                    |                   |                       |                            |                       |                                  |
| A059               | 24 June 2019      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days     |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A059                      | 30 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A060                      | 26 June 2019             | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A060                      | 18 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A060                      | 21 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A061                      | 02 July 2019             | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A061                      | 22 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A062                      | 16 July 2019             | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A062                      | 28 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A063                      | 22 July 2019             | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A063                      | 21 April 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A064                      | 23 July 2019             | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A064                      | 12 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A065                      | 24 July 2019             | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A065                      | 09 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A066                      | 24 July 2019             | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A066                      | 12 October 2018          | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A067                      | 24 July 2019             | No                           | No                                | Yes                          | Nitrofurantoin 100mg tds 5 days  |
| A067                      | 15 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A067                      | 10 March 2019            | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A068                      | 06 August 2019           | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A068                      | 09 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
|                           |                          |                              |                                   |                              |                                  |
| A069                      | 06 August 2019           | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A069                      | 30 June 2019             | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A070                      | 19 August 2019           | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A070                      | 16 April 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A071                      | 02 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A071                      | 11 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A072                      | 03 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A072                      | 19 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A073                      | 05 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A073                      | 15 January 2019          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A074                      | 05 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A074                      | 21 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A075                      | 05 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A075                      | 09 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A076                      | 09 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A076                      | 28 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A077                      | 09 September 2019        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A077                      | 15 April 2019            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |



| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A078                      | 09 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg bd 5 days    |
| A078                      | 12 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A079                      | 09 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A079                      | 21 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A080                      | 09 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg tds 5 days   |
| A080                      | 02 August 2019           | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A081                      | 10 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A081                      | 02 July 2019             | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
| A081                      | 15 March 2019            | No                           | No                                | Yes                          | Amoxicillin 500g tds 5 days      |
|                           |                          |                              |                                   |                              |                                  |
| A082                      | 10 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A082                      | 05 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A083                      | 10 September 2019        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A083                      | 03 August 2019           | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A084                      | 10 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A084                      | 13 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A085                      | 11 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A085                      | 20 July 2019             | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A086                      | 11 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A086                      | 05 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A086                      | 12 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A087                      | 11 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A087                      | 23 May 2019              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A088                      | 11 September 2019        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A088                      | 16 February 2019         | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5days    |
|                           |                          |                              |                                   |                              |                                  |
| A089                      | 12 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A089                      | 05 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A089                      | 28 October 2018          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A090                      | 12 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A090                      | 31 July 2019             | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A091                      | 12 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A091                      | 12 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A091                      | 25 December 2018         | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A092                      | 12 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A092                      | 02 August 2019           | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A093                      | 12 September 2019        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A093                      | 19 January 2019          | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A094                      | 13 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A094                      | 09 June 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
|                           |                          |                              |                                   |                              |                                  |
| A095                      | 13 September 2019        | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A095                      | 23 April 2019            | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |
|                           |                          |                              |                                   |                              |                                  |
| A096                      | 13 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A096                      | 28 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A097                      | 13 September 2019        | No                           | No                                | Yes                          | Fosfomycin 3g single dose        |
| A097                      | 16 June 2019             | No                           | No                                | Yes                          | Nitrofurantoin 50mg tds 5 days   |
| A097                      | 18 December 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
|                           |                          |                              |                                   |                              |                                  |
| A098                      | 13 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A098                      | 23 June 2019             | No                           | No                                | Yes                          | Amoxicillin 1g bd5 days          |
|                           |                          |                              |                                   |                              |                                  |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>      |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------|
| A099                      | 13 September 2019        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A099                      | 19 May 2019              | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
|                           |                          |                              |                                   |                              |                                  |
| A100                      | 13 September 2019        | No                           | No                                | Yes                          | Ciprofloxacin 500mg PO 12 hourly |
| A100                      | 13 July 2019             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days     |
| A100                      | 17 December 2019         | No                           | No                                | Yes                          | Ciprofloxacin 375mg tds 5 days   |

## APPENDIX F

**Table F1:** Risk factors in complicated UTIs.

|                      | HIV positive | Hypertension | Diabetes | Urinary incontinence | Urine catheterisation | Total |
|----------------------|--------------|--------------|----------|----------------------|-----------------------|-------|
| Number of incidences | 11           | 7            | 8        | 2                    | 14                    | 42    |
| Percentage incidence | 26.2         | 16.7         | 19.0     | 4.8                  | 33.3                  | 100   |

**Table F2:** Treatment prescribed in complicated UTIs.

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B001               | 19 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B001               | 02 August 2018    | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                  |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------------------|
| B002                      | 20 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 1 bd 5 days      |
| B002                      | 15 July 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
|                           |                          |                              |                                   |                              |                                              |
| B003                      | 20 September 2018        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
| B003                      | 3 August 2018            | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
|                           |                          |                              |                                   |                              |                                              |
| B004                      | 20 September 2018        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
| B004                      | 28 June 2018             | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                     |
|                           |                          |                              |                                   |                              |                                              |
| B005                      | 20 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg tds 5 days |
| B005                      | 17 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |



| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B006               | 25 September 2019 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B006               | 07 August 2018    | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |
|                    |                   |                       |                            |                       |                                             |
| B007               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
| B007               | 30 June 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B008               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B008               | 23 May 2018       | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B009               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B009               | 04 May 2018       | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B010               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B010               | 05 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
| B010               | 20 May 2018       | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |
|                    |                   |                       |                            |                       |                                             |
| B011               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B011               | 03 June 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B012               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B012               | 25 May 2018       | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B013               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
| B013               | 02 August 2018    | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
|                    |                   |                       |                            |                       |                                             |
| B014               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B014               | 13 May 2018       | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |
|                    |                   |                       |                            |                       |                                             |
| B015               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B015               | 30 April 2018     | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B016               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
| B016               | 20 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg TDS 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B017               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B017               | 04 August 2018    | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                 |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|---------------------------------------------|
| B017                      | 05 June 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B018                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B018                      | 15 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
|                           |                          |                              |                                   |                              |                                             |
| B019                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B019                      | 27 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
| B019                      | 18 March 2018            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
|                           |                          |                              |                                   |                              |                                             |
| B020                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B020                      | 17 June 2018             | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                    |
|                           |                          |                              |                                   |                              |                                             |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B021               | 26 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B021               | 18 April 2018     | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B022               | 26 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 325mg bd 5 days |
| B022               | 28 May 2018       | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |
|                    |                   |                       |                            |                       |                                             |
| B023               | 26 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B023               | 27 April 2018     | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 325mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B024               | 26 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B024               | 19 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                 |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|---------------------------------------------|
| B025                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B025                      | 21 April 2018            | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B026                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B026                      | 07 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
|                           |                          |                              |                                   |                              |                                             |
| B027                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B027                      | 12 April 2019            | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                    |
|                           |                          |                              |                                   |                              |                                             |
| B028                      | 26 September 2018        | No                           | No                                | Yes                          | Amoxicillin 500mg TDS 5 days                |
| B028                      | 14 February 2018         | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                    |
|                           |                          |                              |                                   |                              |                                             |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B029               | 26 September 2019 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 1g bd 5days     |
| B029               | 20 July 2019      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B030               | 26 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B030               | 15 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
| B030               | 09 May 2018       | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B031               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B031               | 01 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B032               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
| B032               | 10 May 2018       | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
|                    |                   |                       |                            |                       |                                             |
| B033               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin 1g tds 5 days                   |
| B033               | 27 August 2018    | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B034               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |
| B035               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B035               | 12 May 2018       | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                    |
|                    |                   |                       |                            |                       |                                             |
| B036               | 29 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B036               | 19 August 2018    | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |
|                    |                   |                       |                            |                       |                                             |



| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                 |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|---------------------------------------------|
| B037                      | 29 October 2018          | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B038                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B039                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B039                      | 24 July 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B040                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
| B040                      | 23 June 2018             | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                    |
|                           |                          |                              |                                   |                              |                                             |
| B041                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                         |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|----------------------------------------------|
| B042               | 31 October 2018   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
| B042               | 12 July 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                              |
| B043               | 31 October 2018   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
| B043               | 14 March 2018     | No                    | No                         | Yes                   | Cephalexin 1g tds 5 days                     |
|                    |                   |                       |                            |                       |                                              |
| B044               | 31 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B044               | 03 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B045               | 31 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B045               | 16 July 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 675mg bd 5 days  |
|                    |                   |                       |                            |                       |                                              |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                 |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|---------------------------------------------|
| B046                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 1g bd 5days     |
| B046                      | 10 July 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5days  |
| B046                      | 30 May 2018              | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
|                           |                          |                              |                                   |                              |                                             |
| B047                      | 31 October 2018          | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
| B047                      | 23 March 2018            | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
|                           |                          |                              |                                   |                              |                                             |
| B048                      | 06 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |
| B049                      | 06 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                |
| B049                      | 22 September 2018        | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                           |                          |                              |                                   |                              |                                             |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                         |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|----------------------------------------------|
| B050               | 07 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg tds 5 days |
| B050               | 21 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
| B050               | 24 July 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days  |
|                    |                   |                       |                            |                       |                                              |
| B051               | 07 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
| B051               | 15 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days  |
|                    |                   |                       |                            |                       |                                              |
| B052               | 07 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                              |
| B053               | 07 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B053               | 25 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                  |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------------------|
| B054                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
| B054                      | 15 July 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B055                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B055                      | 12 June 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B056                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B056                      | 18 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B057                      | 09 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
| B057                      | 13 June 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                  |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------------------|
| B058                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B059                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
|                           |                          |                              |                                   |                              |                                              |
| B060                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 1g bd 5 days     |
| B060                      | 17 August 2018           | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B061                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B061                      | 21 August 2018           | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B062                      | 07 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                  |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------------------|
| B063                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B063                      | 21 June 2018             | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
|                           |                          |                              |                                   |                              |                                              |
| B064                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B064                      | 14 August 2018           | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B065                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B066                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin 50mg tds 5 days                  |
| B066                      | 15 June 2018             | No                           | No                                | Yes                          | Cephalexin 1g tds 5 days                     |
|                           |                          |                              |                                   |                              |                                              |
| B067                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg bd 5 days  |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                            |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|-------------------------------------------------|
| B067               | 13 May 2018       | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                 |
|                    |                   |                       |                            |                       |                                                 |
| B068               | 12 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                 |
|                    |                   |                       |                            |                       |                                                 |
| B069               | 12 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days  |
| B069               | 30 June 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                                 |
| B070               | 12 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days  |
|                    |                   |                       |                            |                       |                                                 |
| B071               | 12 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                 |
| B071               | 11 July 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                                 |



| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                  |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|----------------------------------------------|
| B072                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B072                      | 16 June 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B073                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B074                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B074                      | 24 August 2018           | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                           |                          |                              |                                   |                              |                                              |
| B075                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 1g bd 5 days     |
| B075                      | 18 September 2018        | No                           | No                                | Yes                          | Amoxicillin 500mg tds 5 days                 |
|                           |                          |                              |                                   |                              |                                              |
| B076                      | 12 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic acid 625mg bd 5 days  |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                         |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|----------------------------------------------|
|                    |                   |                       |                            |                       |                                              |
| B077               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B077               | 01 October 2018   | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B078               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 675mg bd 5 days  |
| B078               | 21 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B079               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
| B079               | 03 August 2018    | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                              |
| B080               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B080               | 14 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                            |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|-------------------------------------------------|
|                    |                   |                       |                            |                       |                                                 |
| B081               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                 |
|                    |                   |                       |                            |                       |                                                 |
| B082               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 1g bd 5days      |
| B082               | 14 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                 |
|                    |                   |                       |                            |                       |                                                 |
| B083               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days  |
| B083               | 12 July 2018      | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                                 |
| B084               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days  |
| B084               | 16 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                                 |

| <b>Patient Identifier</b> | <b>Date of infection</b> | <b>Urine sample cultured</b> | <b>Micro-organism identified?</b> | <b>Antibiotic prescribed</b> | <b>Treatment prescribed</b>                    |
|---------------------------|--------------------------|------------------------------|-----------------------------------|------------------------------|------------------------------------------------|
| B085                      | 19 November 2018         | No                           | No                                | Yes                          | Amoxicillin 500mg tds<br>5 days                |
|                           |                          |                              |                                   |                              |                                                |
| B086                      | 19 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |
| B086                      | 14 July 2018             | No                           | No                                | Yes                          | Amoxicillin 500mg<br>tds5 days                 |
|                           |                          |                              |                                   |                              |                                                |
| B087                      | 19 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |
| B087                      | 15 August 2018           | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 375mg bd 5 days |
|                           |                          |                              |                                   |                              |                                                |
| B088                      | 19 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |
| B088                      | 12 July 2019             | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 375mg tds 5days |
|                           |                          |                              |                                   |                              |                                                |
| B089                      | 19 November 2018         | No                           | No                                | Yes                          | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                           |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|------------------------------------------------|
|                    |                   |                       |                            |                       |                                                |
| B090               | 19 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                |
| B090               | 31 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                |
|                    |                   |                       |                            |                       |                                                |
| B091               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 1g bd 5days     |
| B091               | 20 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                |
|                    |                   |                       |                            |                       |                                                |
| B092               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |
| B092               | 30 August 2018    | No                    | No                         | Yes                   | Amoxicillin 500mg tds<br>5 days                |
|                    |                   |                       |                            |                       |                                                |
| B093               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic<br>acid 625mg bd 5 days |
|                    |                   |                       |                            |                       |                                                |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                         |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|----------------------------------------------|
| B094               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin 1g tds 5 days                    |
| B094               | 21 September 2018 | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B095               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B095               | 16 September 2018 | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg tds 5 days |
|                    |                   |                       |                            |                       |                                              |
| B096               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |
| B096               | 21 August 2018    | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B097               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                 |
|                    |                   |                       |                            |                       |                                              |
| B098               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days  |

| Patient Identifier | Date of infection | Urine sample cultured | Micro-organism identified? | Antibiotic prescribed | Treatment prescribed                        |
|--------------------|-------------------|-----------------------|----------------------------|-----------------------|---------------------------------------------|
| B098               | 02 October 2018   | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 375mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B099               | 20 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
|                    |                   |                       |                            |                       |                                             |
| B100               | 21 November 2018  | No                    | No                         | Yes                   | Amoxicillin/clavulanic acid 625mg bd 5 days |
| B100               | 13 July 2018      | No                    | No                         | Yes                   | Amoxicillin 500mg tds 5 days                |

# APPENDIX G

---

## **G1: Guidelines for the management of UTIs.**

### **Purpose and Scope**

The purpose of this guideline is to provide multidisciplinary recommendations for the management of women with complicated and uncomplicated UTIs. These guidelines are intended for healthcare professionals in public hospitals. They are designed to guide clinical judgment but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the patient.

### **Introduction**

Urinary tract infections are infectious diseases that commonly occur in communities. They are classified as uncomplicated or complicated according to underlying diseases and anatomical or functional abnormalities of the urinary tract. Having a sufficient understanding of these symptoms and using appropriate antibiotics are crucial for preventing serious complications and antibiotic misuse and for inhibiting the expression of resistant bacteria. The global monitoring report on antibiotic resistance released by the World Health Organization in 2014 reported the increased resistance of major bacteria to cephalosporins and fluoroquinolones to be a serious worldwide health issue (National Department of Health, 2018). Policies to establish and distribute standard guidelines for antibiotic selection for appropriate treatment of UTIs and inhibition of the emergence of antibiotic-resistant bacteria have been in demand. This guideline has been made because of the lack of treatment guidelines for UTIs in South Africa. This guideline is on the use of antibiotics for patients aged 18 years or older. The guideline targets complicated and uncomplicated UTIs.

### **Signs and symptoms**

Symptoms associated with UTIs include nausea, vomiting, a strong urge to urinate, a burning feeling upon urinating, frequent and persistent urinating, red or bright pink



urine discolouration, indicating that there is blood within the urine passed and pelvic pain (Singh *et al.*, 2014). Despite these symptoms associated to UTIs, patients are often diagnosed with asymptomatic presentation (Demilie *et al.*, 2014).

### **General Principles of antimicrobial use**

Choosing the right antimicrobial is an essential part of managing pregnant patients with urinary tract infections. It is not only important to choose the right medication, but also consideration should be given to selecting the right dose and treatment duration. By effectively treating urinary tract infections it is hoped to reduce resistance rates by identifying the causative micro-organism and giving the right antimicrobial agent. Consideration should also be given to potential teratogenicity when choosing an antimicrobial in pregnant patients. This may be more difficult in the setting of penicillin allergy but the risks and benefits should be explained to the patient. It is also important that antimicrobials are used correctly to minimise risk of antimicrobial resistance emerging in the population.

Some of the key recommendations in this document for all acute hospitals are:

- Hospitals should have an antimicrobial stewardship team who can support the correct use of antimicrobials in UTI cases.
- All hospitals must have one or more clinical pharmacists with responsibility for antimicrobial use in the hospital.
- Patients should be informed of the rationale for prescribing antimicrobials, and informed of any associated risks or adverse effects.
- Laboratories should observe antimicrobial resistance, including annual review of antibiograms as appropriate. Susceptibility results should be released in a restrictive manner where possible. All hospitals should have local or regional antimicrobial prescribing guidelines based where possible on local antimicrobial resistance data.

### **Treatment options for uncomplicated UTIs**

**Note:** Always review the antimicrobial choice by referring to antimicrobial susceptibility results from previous samples and from current tests.

### Treatment of uncomplicated UTIs

| Drug          | Dose                         | Notes                                                                                                                                                                                                                                                                                                                                                    |
|---------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Fosfomycin    | 3 g stat PO dose             | -May be very useful in patients with resistant UTIs (for example extended beta-lactamases).<br>-Also useful in patients who are likely to not comply with a seven day treatment course.                                                                                                                                                                  |
| Amoxicillin   | 500 mg tds PO, 7 days        | -Not suitable for patients with penicillin allergy.<br>-Can only be used when susceptibility results are out, with evidence that it is the right choice of treatment; not empirical for empirical treatment.<br>-Good treatment for <i>Enterococcus faecalis</i> and <i>Staphylococcus lugdunensis</i> as it has better absorption than oral penicillin. |
| Ciprofloxacin | 500 mg bd, PO, 5 days        | -First ensure that local resistance rates to ciprofloxacin are at least <10%.<br>-Good treatment for <i>Enterococcus faecium</i> .<br>-Advise women of potential issues if they are breastfeeding.                                                                                                                                                       |
| Cephalexin    | 500 mg bd or tds, PO, 7 days | -It is not suitable for a patient with severe penicillin allergy but is good for a patient with mild penicillin allergy.                                                                                                                                                                                                                                 |

**Key:** bd – twice daily, tds – three times daily, PO – take orally.

### Treatment options for complicated UTIs

**Note:** Always review the antimicrobial choice by referring to antimicrobial susceptibility results from previous samples and from current tests.

### Treatment of complicated UTIs

| Drug        | Dose                   | Notes                                                                                                                                                   |
|-------------|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| Amoxicillin | 500 mg tds, PO, 7 days | -It is not suitable for penicillin allergy.<br>-Should be used when susceptibility results are available as it is not suitable for empirical treatment. |
| Fosfomycin  | 3 g stat, PO dose      | -Very useful in patients with multi-drug resistant micro-organisms.<br>-May be useful in patients who cannot comply with a seven day treatment course.  |

|                             |                           |                                                                                                                                      |
|-----------------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| Amoxicillin/clavulanic acid | 625 mg, tds, PO, 5-7 days | -Not suitable for patients with penicillin allergy.<br>-High risk of necrotising enterocolitis in neonates (Ronald and Ludwig, 2001) |
|-----------------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------|

**Key:** bd – twice daily, tds – three times daily, PO – take orally.

The recommended dosages presume normal renal and hepatic function. If the patient has liver or renal failure, discuss with the general practitioner.

### **Antimicrobial prophylaxis for urinary tract infections**

Antimicrobial prophylaxis should be considered in pregnant women and in reoccurring UTIs. The use of antimicrobial prophylaxis for recurrent UTIs is difficult as there is no clear evidence based indications at present. Nitrofurantoin can be used for prophylaxis but should be avoided near term in pregnant patients because of the risk of neonatal haemolysis. The use of broad-spectrum antimicrobials such as amoxicillin/clavulanic acid and cephalexin should be done following assessment of the benefits of prophylaxis against the risk of generating antimicrobial resistance in the patient leading to more limited treatment options at a later stage. Periodic surveillance of antimicrobial resistance of uropathogens, re-evaluation of empirical therapy, pre-therapy counselling for delayed antibiotic initiation and short-course antibiotic therapy with sensitive antibiotics are vital in an era of emerging antimicrobial resistance.

### **Criteria and recommendations in treating UTIs**

1. Imaging of the renal tract may be warranted where a UTI reoccurs or is slow to respond to treatment.
2. Do not prescribe trimethoprim for pregnant women with established folate deficiency or women taking folate antagonists.
3. Take a single sample for urine culture before empiric treatment is started.
4. Women with symptomatic bacteriuria with systemic signs of infection should be given oral antibiotics pending the result of the urine culture.

**5.** When choosing an antimicrobial regimen for pregnant patients it is important to consider issues of teratogenicity and absorption.

# APPENDIX H



## PARTICIPANT DATA COLLECTION TOOL

Patient number (as per confidentiality key) \_\_\_\_\_

### Patient demographics

Gender: Male ☐ Female ☐

Is the patient over the age of 18 years? Yes ☐ No ☐

### Patient history

Does the patient suffer other medical conditions? Yes ☐ No ☐

If yes, please provide details: \_\_\_\_\_

Is the patient currently taking any medications? Yes ☐ No ☐

If yes, please provide details: \_\_\_\_\_

Has the patient used systemic antibiotics within the last 2 weeks?

Yes ☐ No ☐

Is the patient currently pregnant or breastfeeding? Yes ☐ No ☐

### Examination

Does the patient present with the following symptoms?

|                                |     |                          |    |                          |
|--------------------------------|-----|--------------------------|----|--------------------------|
| Fever                          | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Abdominal pain                 | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Nausea                         | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Vomiting                       | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Strong urge to urinate         | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Burning feeling upon urination | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |

### Point of care screening test results

Does the patient present as diabetic? Yes ☐ No ☐

Glucose measurement result: \_\_\_\_\_

Does the patient present as pregnant? Yes ☐ No ☐

Pregnancy test result: \_\_\_\_\_

Patient number (as per confidentiality key) \_\_\_\_\_

**Urine dipstick results**

Is the following present in the patient's urine?

|              |     |                          |    |                          |
|--------------|-----|--------------------------|----|--------------------------|
| Protein      | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Value: _____ |     |                          |    |                          |
| Blood        | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Value: _____ |     |                          |    |                          |
| Leukocytes   | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Value: _____ |     |                          |    |                          |
| Nitrites     | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> |
| Value: _____ |     |                          |    |                          |

**Patient diagnosis:** Uncomplicated UTI ☐ Complicated UTI ☐

**Patient record review**

Date of infection: \_\_\_\_\_

Urine sample cultured Yes ☐ No ☐

If yes, what was the micro-organism identified? \_\_\_\_\_

Antibiotic prescribed Yes ☐ No ☐

Treatment prescribed: \_\_\_\_\_

Date of infection: \_\_\_\_\_

Urine sample cultured Yes ☐ No ☐

If yes, what was the micro-organism identified? \_\_\_\_\_

Antibiotic prescribed Yes ☐ No ☐

Treatment prescribed: \_\_\_\_\_

Date of infection: \_\_\_\_\_

Urine sample cultured Yes ☐ No ☐

If yes, what was the micro-organism identified? \_\_\_\_\_

Antibiotic prescribed Yes ☐ No ☐

Treatment prescribed: \_\_\_\_\_

Patient number (as per confidentiality key) \_\_\_\_\_

**Urine sample culturing results**

Number of colonies identified: \_\_\_\_\_

Colony description(s): \_\_\_\_\_

Identified micro-organism(s): \_\_\_\_\_

**Antibiotic susceptibility testing results**

| Micro-organism tested | Zone of inhibition for antibiotics tested (mm) |            |             |            |                | Augmentin |
|-----------------------|------------------------------------------------|------------|-------------|------------|----------------|-----------|
|                       | Ciprofloxacin                                  | Fosfomycin | Amoxicillin | Cephalexin | Co-trimoxazole |           |
|                       |                                                |            |             |            |                |           |

# APPENDIX H

---



## ***PARTICIPANT INFORMATION SHEET***

**Research Project entitled:** Antimicrobial resistance patterns of Urinary Tract Infections (UTIs) in a South African public hospital.

**Dear patient,**

### **Introduction**

I, Benhilda Jaji, am doing research on the antimicrobial resistance patterns of urinary tract infections. This study will be done in a South African public hospital aiming to suggest a way forward for protocol development and treatment guidelines.

### **Invitation to participate**

Participation in the study is entirely voluntary. I would like to take this opportunity to invite you to take part in this research study.

### **What is involved in the study?**

#### **Patient Record Review**

Your patient records will be reviewed to determine the likelihood of previous UTI. The review will collect information on date of previous infection, treatment offered and the identified cause.



## Examination

A urine culture is a test used to identify the micro-organisms responsible for infection. You will be responsible for obtaining a sample of your urine using sample collection vials, as indicated in the diagram below. This sample will only be collected once.

### *current procedure of urine sample collection*



**Figure 1:** How to give a urine sample.

A pregnancy test will be performed on you to confirm or deny pregnancy. The pregnancy test will be done by taking some few drops aseptically of urine from the urine than was collected. Dip the absorbent end of the test stick and hold it there for 5 to 10 seconds or the time indicated on the instructions. Wait for the 1 to 5 minutes depending on the instructions given. Once the amount of waiting time written on the instructions has passed, check the test stick for the results and it will indicate whether one is pregnant or not. If it shows that you are pregnant, you will be referred to the clinic doctor for further assessments.

## Blood sampling

Point of care blood glucose tests will be performed to identify if you are diabetic. The procedure for performing the blood glucose test will include the following steps. Wash hands and dry thoroughly. Prepare the lancet device and lancet properly. Remove the

test strip from the foil and insert into the glucometer slot. Clean the tip of finger with a dry swab. Place lancet device flat at the side of the finger and press down firmly. Prick finger with lancet device. Massage the finger to obtain sufficient amount of blood. Place a drop of blood against the tip of the test strip. Use a dry swab to clean the punctured site. Wait for the reading to display on the glucometer and this will be the blood glucose level. If the blood glucose is indicative of diabetes, you will be referred to the clinic doctor.

### **Risks**

The risks associated with the study are small as we will be using single use safety lancets. The risks associated include bruising to your finger and the possibility that you might faint at the sight of your blood. The risk associated with an hCG urine test is getting a false-positive or false-negative.

### **Benefits**

You will be afforded the opportunity to get the right treatment for the UTI by reducing the risk of reoccurrence and the risk of antibiotic resistance in future.

### **Participation is voluntary**

You have the right to refuse participation or withdraw at any time during the study. This will not incur any penalty or loss to you.

**Confidentiality:** When partaking in the study, no identifiable data will be collected by the research group.

### **Who has reviewed and given ethical approval for this study?**

This study protocol has been submitted to the University of the Witwatersrand, Human Research Ethics Committee.

If you have any further queries, or would like to report any problems, please do not hesitate to contact any of the research investigators. Contact details provided below:

Researcher: Benhilda Jaji

Tel: 0730352733

E-mail: 859490.student@wits.ac.za

Researcher: Stephanie de Rapper

Tel: 011 717 2268

E-mail: Stephanie.derapper@wits.ac.za

Researcher: Neelaveni Padayachee

Tel: [011 717 2269](tel:0117172269)

E-mail: [Neelaveni.Padayachee@wits.ac.za](mailto:Neelaveni.Padayachee@wits.ac.za).

Should you require any information regarding your rights as a participant or if you have any complaints regarding this research study, you may contact the Chairperson of the Human Ethics Committee at the University of the Witwatersrand:

Prof. Cleaton Jones: 011 717 2100

**Thank you for taking time to consider participation.**