Post caesarean section wound infections at Rahima Moosa Mother and Child Hospital

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DECLARATION:

I, Adebowale Victor Temenu, hereby declare that this research report/dissertation is the outcome of my original work, except where acknowledgement shows otherwise, and that this work, neither as a whole, nor in part has been or is being submitted for another degree at this university or any other institution.

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Signature

September 2019.

DEDICATION:

I dedicate this work to the memory of my late father, Chief R.I.O. Temenu, for the painful sacrifices he made for my life, upbringing and education: and my uncle, Mr M O Temenu, for his financial support and help that saw me through undergraduate medical education.

ABSTRACT

Introduction

Caesarean section is a surgical intervention commonly performed as part of obstetric care services globally. It is a life-saving procedure for either a pregnant woman or her baby or both. The World Health Organisation recommends that C/S should be perform when it is medically necessary. Caesarean section is associated with a myriad of maternal morbidities and mortality, including and not limited to postoperative wound infections. The Rahima Moosa Mother and Child Hospital alone had a high caesarean section rate of over 40% in 2017.

Objectives

To determine the in-hospital admission (readmission) rate for post caesarean section wound infections, to characterise the risk factors for post caesarean sections wound infections, and to describe the morbidities, microbiology pattern, preoperative and postoperative antibiotic usage in post caesarean section wound infections at Rahima Moosa Mother and Child Hospital.

Methods

This was a retrospective descriptive study. Medical records, labour ward records, caesarean section theatre records, admission ward records and outpatient ward records of all patients, age 18 and above, who had caesarean sections from 01 Jan 2017 to 30 June 2017, and present with post caesarean section wound infections were reviewed. Data extracted were uploaded unto the Redcap data online platform. The data were statistically analysed.

Results

Two thousand seven hundred and forty-six caesarean sections were performed in the first half of 2017, representing a caesarean section rate of 41.9%, a post caesarean section wound infection rate of 2.91%, and an in-hospital admission (re-admission) rate of 1.31%. The study population were largely healthy, as 83% had no known comorbidity. Black Africans disproportionately suffer more from post-Caesarean wound infection: prolonged labour, higher number of vaginal examinations, having an emergency caesarean section and the skill of surgeons may have played a role in the post caesarean section wound infections in this study. The morbidities associated with post caesarean section wound

infections were not life threatening, as more than half the patients were managed as outpatients. Among the readmitted patients, 50% had superficial wound sepsis. The incidence of deep tissue/organ involvement were very low: acute severe maternal morbidity occurred in 7.2% of cases, comprising of one patient requiring a subtotal abdominal hysterectomy with repair of bladder injury and another patient requiring a total abdominal hysterectomy with left salpingo-oophorectomy who later required ICU admission and dialysis for acute kidney injury. In addition, here was one High Care Area admission for management of severe preeclampsia, while no mortality occurred.
The microbes identified were skin and vaginal flora and the most common isolated organism was Staphylococcus aureus. Empirical broad-spectrum antibiotics: a triple regimen of ampicillin, gentamycin and metronidazole, and a co-amoxiclav based antibiotics regimen that cover Gram-positive, Gram-negative and anaerobes were found to be largely effective in the management of post caesarean section wound infections.

Conclusion

Although the caesarean section rate is high in this study setting, the in-hospital admission rate for post caesarean section wound infection is very low. Intrapartum events play a role in the post caesarean wound infections. The morbidities associated with post caesarean section were not life threating as more than half were managed as outpatients and the majority of the admitted patients had superficial wound sepsis. The study further indicates that Staphylococcus aureus is the most preponderant microbe isolated, and that empirical broad-spectrum antibiotics are effective in managing post caesarean section wound infection.

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Finally, I would like to acknowledge the Rahima Moosa Mother and Child Hospital and the University of the Witwatersrand for giving me the opportunity to do this research.

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LIST OF ABBREVATIONS

AKI - Acute Kidney Injury
ARVs – Anti-Retroviral drugs
ASA – American Society of Anaesthesiology
BMI – Body Mass Index
CD4 – Cluster of Differentiation 4 T-lymphocyte count
CBD – Central Business District
CEASAR – Caesarean Section Surgical Technique Trials
CEO – Chief Executive Office
CI – Confidence Interval
C/S – Caesarean Section
DM – Diabetes Mellitus
DVT– Deep Vein Thrombosis
E. coli – Escherichia coli
FDC– Fixed Dose Combination
HAART – Highly active retroviral therapy
HbA1c - Glycosylated Haemoglobin level
HIF-1 - alpha – Hypoxia inducible factor 1 alpha
HIV – Human Immunodeficiency Virus
HR – Hazard Ratio
IV - Intravenous
LMIC – Low and Middle-Income Countries
LMWH – Low Molecular Weight Heparin
MRSA – Methicillin Resistance Staphylococcus aureus
MSSA – Methicillin Sensitive Staphylococcus Aureus
NICU – Neonatal Intensive Care Unit
NNS – Neonatal Sepsis
NS – Nylon sutures
OR – Odds Ratio
PE – Pulmonary Embolism
PGA – Polyglycolic Acid

RCT – Randomized Control Trials

PPROM – Prolonged Pre-labour Rupture of Membrane

PROM – Pre-labour Rupture of Membrane

RMMCH – Rahima Moosa Mother and Child Hospital

ROM – Rupture of Membranes

RR – Risk Ratio

SD – Standard Deviation

SS – Skin staples

SSI – Surgical Site Infection

USA – United States of America

UTI – Urinary tract Infection

VBAC – Vaginal Birth after Caesarean section

VEGF – Vascular Endothelial Growth Factor

VL – Viral load

VTED – Venous thrombo-embolic disease

WHO – World Health Organisation

WITS – University of the Witwatersrand

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1. INTRODUCTION

Caesarean section (C/S) is the most common surgical procedure performed in maternity care services (1). Caesarean section makes up 15% of all deliveries globally (1). However, different C/S rates have been reported across different regions of the world, from 16% in Haiti, to 40% in Chile (2), while North American statistics have shown 28% in Canada in 2011 (3, 4), and the US reported 32.8% (5). The Kenyan demographic and health survey reported a C/S rate of 6% in 2009. The C/S rate in Tanzania lies between 21.4% and 31.8% (6, 7), and that of South African private practice was reported to be 60.4% in 2009 (8), while lower rates were observed in the public sector with a national average of 23.1%, and regional hospital C/S ranged from 32% to 46% from 2014 to 2017 (9).

In 1985, the World Health Organisation's (WHO) group of experts in Fortaleza, Brazil came to a conclusion that "there is no justification for any region of the world to have a C/S rate higher than 10-15%" (10). In the last three decades, this conclusion generated intense debates, criticisms, controversies and divided opinions, while the rate of the caesarean mode of delivery has been on the increase. This trend has generated global concern because of the short term and long-term risks associated with C/S, which may affect future pregnancies and quality of life. While C/S can be life saving for mother and child when obstetrically indicated, there is no evidence that it is beneficial to the women and their infants when not medically indicated. Of greater concern is the fact that the causes of increases in the C/S rate are multifactorial and not well understood (11-15). To address these issues, the WHO met in Geneva, Switzerland in October 2014, and released a statement, which summarized results of systematic reviews, and ecological analysis conducted at population level. The WHO stated that a C/S rate higher than 10% - 15% is not associated with a reduction in maternal and perinatal mortality rates (16, 17). The WHO further stated that C/S might be associated with short and long-term complications including permanent disability and death in a setting where facilities and capacity are lacking to conduct safe surgery and manage surgical complications, and C/S only be performed when it is medically indicated. They concluded that the non-availability of a timeously conducted C/S might lead to severe birth asphyxia, stillbirth, obstructed labour, ruptured uterus, peripartum hysterectomy and significant intrapartum haemorrhage (18). The WHO stated that a C/S should be performed when indicated, rather than to achieve a specific rate, to all women who is in need, as determined by health care givers, on a case

by case basis (19). This current study aims to evaluate one of the short-term morbidities associated with C/S, namely wound sepsis.

Wound sepsis as a post-operative complication is a cause of serious morbidity and mortality in the postpartum period (20). Postoperative wound infection, regarded as a surgical site infection (SSI), is define as an infection of the surgical site occurring within 30 days of surgery, affecting either the incision site, superficial or deep tissues or extending to organs and body cavities (21). Postoperative wound infection was regarded as the most common nosocomial infection in surgical patients worldwide and could be community acquired (22). The incidence of SSI after C/S varies and is reported to range from 2 - 20% across the US (23). Varied SSI rates are also reported across Africa, with 24% in Tanzania (24), 5% - 25% in Nigeria depending on the area of practice (25) and 19% in Nairobi, Kenya (26). The current SSI rate in South Africa is unknown, however, Johnson and Buchmann in a descriptive study at Chris Hani Baragwanath Academic Hospital in 2012, reported an incidence of possible mild wound infection of 11% (27).

Surgical site infection poses significant morbidity to the patients, such as impaired wound healing, wound break down, need for further surgery, an increased risk of adhesions, ectopic pregnancy, chronic pelvic pain, infertility and intestinal obstruction (28). Consequently, this leads to a prolonged hospital stay, and exerts pressure on hospital resources, facilities and finances (28).

Despite the importance of SSI, only a few studies have been done on the magnitude of SSI in third world countries, more specifically: few studies have been done to establish the rate of SSI in South Africa.

2. LITERATURE BACKGROUND

Early history from 10 200 BC to 200 AD confirmed that surgeries were carried out in an unsterilized environment, and equipment, and postoperative mortality was high due to overwhelming sepsis (29). Ignac Semmelweis of Vienna in 1847, recorded a 20% maternal mortality in his hospital due to post-partum streptococcal sepsis, and against his expectation, found that maternal death at home delivery was 1%. He inferred that health care workers were transmitting infections from one patient to another. He introduced chlorine hand washing and subsequently sepsis dropped to 1%. His colleagues were outraged by his findings that doctors were killing their patients, and he was dismissed from medical practice (30).

After the Crimean War in 1856, Florence Nightingale drastically reduced mortality by introducing ventilation and antisepsis (31). Louis Pasteur already showed in 1862 that the germs causing fermentation and putrification, are killed by heat and this lead to the publication of his work on the first germ (bug) theory (32). Five years later, Joseph Lister successfully used carbolic acid as antiseptic to prevent putrification in compound fractures: this antiseptic technique later used in surgical operations lead to a reduction in mortality from amputation from 45% to 15% (33, 34). Ernest Bergmann introduced heat sterilisation of surgical equipment in 1891 (35). The discovery of Penicillin by Alexander Flemings in 1928 significantly improved the prognosis of postoperative sepsis (36). In 2006, Peter Pronovost, a doctor at John Hopkins Hospital, proposed a five-point checklist protocol for critical care that greatly diminished infection from 11% to zero during insertion of a central venous pressure (CVP) line (37).

2.1 Caesarean section

Caesarean birth is performed either as elective or emergency procedure, depending on the indications for delivery and the urgency to prevent morbidity and mortality in the mother and the fetus. Importantly, over the last decade, health policy makers and clinicians have raised concerns over the increasing caesarean birth rate and the potential unpleasant impact on maternal and infant health (27, 28, 38).

2.2 Post-operative wound infections

Infective morbidity after C/S remains a major cause of concern in the health sector (28). Its presentation varies widely ranging from, fever malodourous lochia, endometritis, to cervical necrosis, pelvic collection, necrotising fasciitis, overwhelming sepsis and endotoxic shock. In the majority of cases, post C/S wound infections are not life threatening, but it negatively impacts on these women in terms of increasing the period of hospital stay, higher medical costs, loss of economically proactive hours and constraints in social function (39).

Caesarean birth is the single most important factor associated with puerperal sepsis. The risk of infection is increased five to 20-fold, relative to vaginal delivery (39). The incidence of post C/S wound infections, varies geographically and it is influenced by population demographics, difference in obstetric protocols and individual patient risks (39).

Post C/S wound infection incidence ranges from 5% to 25% depending on the nature and area of practice. More specifically, Buchmann *et al*. reported a 1.5% puerperal sepsis and a possible mild wound infection of 11% in a study of 272 C/S wounds in 2010, at Chris Hani Baragwanath Academic Hospital in Soweto (27).

2.3 Risk factors for post caesarean section wound infection:

2.3.1. Patient related factors:

A review of several studies has considered patient related factors such as obesity, diabetes mellitus (DM), immune status, chronic illness, cigarette smoking and low haemoglobin levels which all impair wound healing (40).

2.3.1.1 Obesity

Obesity was strongly associated with development of post C/S infection, with the risk increasing as the Body Mass Index (BMI) increases. In 2012, a multicentre cohort study in the UK, investigated risk factors for surgical site infections (SSI) (41). This study found that compared with patients with a normal BMI (18.5 – 25.0 kg/m^2), overweight women (BMI 25.1-29.9 kg/m^2) had an Odds Ratio (OR) of 1.6 for post C/S wound infections, and

obese women (BMI >30.0 kg/m^2) had an OR of 2.4 for SSI (41). The study further showed that raised BMI was significantly associated with the development of either superficial or deep incision or organ/space infection (41). However, a Brazilian case-control study, involving 79 cases and 79 controls, found that post C/S wound sepsis associated with obesity was 45.8% versus 35.7% in the control group, but this difference of 10.1% was not statistically significant (42).

2.3.1.2. Diabetes

Poorly controlled diabetes mellitus (DM) is associated with an altered inflammatory response and depressed immunity. A multicentre cohort study in England, considering post C/S wound infection, found that 218 (5.6%) out of 3 917 women were diabetic, of which 160 (4.1%) had gestational diabetes and 41 (1.0%) had pre-existing diabetes (41). The risk of post C/S infection for diabetic women was 15.6% (95% CI 11 - 21.1%) compared to 9.6% (95% CI 8.7 – 10.6%) for non-diabetic women (OR 1.8, 95% CI 1.2-2.6) (41). The guidelines for maternity care in South Africa recognise diabetes as a risk factor for puerperal sepsis (43).

In an American study, where the impact of glycosylated haemoglobin and DM in wound healing complications and infections after foot and ankle surgery investigation, enrolled 322 diabetic patients. The study found that HbA1c levels, and existence of at least one other comorbidity was associated with surgical site infections (44). After adjustment for this coexisting morbidity, the only significant factor was HbA1c levels, such that a 1% increase in HbA1c increased the odds of infection by a factor of 1.59 (44). The study also found that BMI, having at least one comorbidity and HbA1c are significant factors for non-infective wound healing complications (44). However, in a prospective observational-blinded study, consisting of 115 diabetic participants, in which the relationship of glycaemic control to the outcome of dental extractions were investigated (45), 78 out of the 115 patients were followed up for two weeks. On the rate of postoperative epithelisation, there was no statistically significant difference between the diabetic- and non-diabetic patients based on preoperative glycaemic levels, HbA1c levels, or patient history (45). The study concluded that glucose levels had no influence on post-dental extraction healing in patients diagnosed with diabetes (45).

2.3.1.3. HIV infections and immuno-compromised state

In a retrospective study in North California, surgical outcomes of HIV-infected patients in the era of highly active retroviral therapy, were compared and matched with non-HIV infected patients (46). Surgical patients were enrolled in the study after appendectomy, bowel resection, arthrotomy or arthroscopy, cardiothoracic procedures, hernia repairs, hysterectomies, hip or knee replacements, laparoscopy or laparotomy and mammoplasty. Patients were followed up for one-year for postoperative complications (46). Each HIV positive patient was paired with an HIV negative patient for follow up. These pairs had similar comorbidities, length of hospital stay and number of postoperative surgical visits ($p > 0.5$ for all variables) (46). Among the HIV patients, the year median of infection was 8.4, the median CD4 count was 379, and 61.5% of patients had viral loads of less than 500 copies/ml, while 68% were receiving highly active antiretroviral therapy (46). Various complications were no more frequent in HIV positive than in the HIV negative patients (11.1% versus 10.2%), except for pneumonia ($p = 0.04$). Importantly, there were more deaths amongst the HIV positive patients within the 12 month follow up period (10/332 versus 2/332; $p = 0.02$) (46). In this study, the investigators found that there were increased complications among patients with viral loads of 30 000 and more, but that CD4 counts of less than 200 was not associated with poorer outcomes (46).

A 2016 systematic review on fracture management in HIV positive individuals showed that individual risk of early wound infection in operatively managed closed fractures, were not influenced by HIV positivity (47). The review further found that the rate of pin track infections in open injuries managed with external fixators was low (47). However, in open injuries managed with internal fixations, the review indicated that the rate of early wound infection was higher in the HIV positive population compared to that in HIV negative patients (47).

In South Africa, HIV infection complicated by tuberculosis and Pneumocystis jeroveci pneumonia is one of the leading causes of maternal mortality (48). The Sixth Confidential Enquiry into Maternal Deaths Report showed that 65% of the women who died were HIV positive, and that almost 90% of women who died of non-pregnancy related infections were HIV positive, while 55% were on HAART. It is unknown whether these women were not virally supressed or if there was a compliance problem (48).

In the 7th Saving Mothers Report 2014-2016, it was reported that maternal deaths due to HIV has dropped by 52% from 2011 to 2016. These deaths were unrelated to post C/S wound infections but attributed to respiratory failure, immune system failure, and septic shock (49).

2.3.1.4 Maternal lifestyle

The impact of maternal lifestyle choices such as alcohol consumption and cigarette smoking, as risk factors for post C/S wound infection is conflicting. Many studies have shown that smoking and alcohol does not significantly increase the risk of post C/S wound infection (6, 42, 50-52). However, a 2012 systematic review and meta-analysis, involving 140 cohort studies (479 150 participants) and four randomized controlled trials (RCTs) (477 participants) had different findings (53). In the RCTs, it was found that smoking cessation significantly lowered the postoperative wound infections, but not other wound complications (53). The cohort studies showed that, smokers have a relatively significant increased risk of wound necrosis and tissue flap damage (nine studies), wound dehiscence and delayed healing (12 studies), postoperative wound infections (32 studies), unspecified wound complications (17 studies), hernia (seven studies) and in bone non-union (four studies) (53). In this review, researchers found that, for all healing complications combined, former smokers have a higher risk of postoperative complications than non-smokers, but a lower risk than current smokers, and concluded that across all surgical specialities, smokers have a higher incidence of infectious and non-infectious healing complications after surgery, compared to non-smokers (53). Former smokers have a higher risk of healing complications during their lifetime compared to never smokers, and smoking cessation for a period of four weeks prior to surgery reduced surgical site infections but no other healing complications (53).

Available evidence and animal studies have revealed that alcohol consumption impedes wound healing and predisposes to an increased risk of infections (54). A recent review showed that alcohol changes the host's defence after traumatic injury (55). Acute alcohol intoxication induced a suppression of pro-inflammatory mediator release during the inflammatory process (55). The review further found that decreased polymorph mobilisation and phagocytosis, which are hallmarks of acute alcohol consumption, correlates with higher incidence of post-trauma infections (55).

Alcohol exposure impaired the proliferative phase of wound healing. In animal experiments, a serum alcohol level of 100mg/dl caused disturbances in re-epithelisation, blood-vessel formation, fibroblastic activity of laying down collagen, and wound closure (56, 57, 58). After the first intake of ethanol, blood vessel formation within the wound decreased by about 61%. This decrease resulted from reduced expression of VEGF receptors and decreased expression of HIF-1 alpha in the nucleus of the endothelial cells of the blood vessels (57). Abnormal angiogenesis leads to poor wound perfusion, poor oxygenation, tissue hypoxia and oxidative stress, decreased collagen production and altered protease enzyme balance at injury sites (56, 57).

A 2012 Swedish study on 16 alcoholics investigated wound healing in alcohol abuse and after withdrawal (59). Nine patients abstained from alcohol for a period of 8 weeks, and were re-tested. The participants showed no evidence of liver or kidney injury or failure (59). Two polytetrafluoroethylene tubes implanted into the subcutaneous tissue of the granulating wounds to collect deposited proline and hydroxyproline, which was used to estimate the amount of collagen and total protein accumulation in the granulating tissue (59). It was found that proline and total protein increased significantly after alcohol abstinence for 8 weeks with a median of 81.3 nmol/mm (interquartile range 77.7-92.9 nmol/mm) versus 69.3 nmol/mm (68.5-76.3 nmol/mm), $p < 0.05$, and 632 nmol/mm (505-1127 nmol/mm) versus 571 nmol/mm (544-831 nmol/mm), $p < 0.05$ respectively (59). However, the change in hydroxyproline was not significant. It was concluded from the study that there was an adverse protein content change during wound healing in alcoholics, which appeared to reverse with alcohol withdrawal (59).

2.3.2. Pregnancy and labour related factors

Complicated pregnancy and labour shown to increase the risk of post C/S wound sepsis. Studies have reported on some of these factors, which include prolonged pre-labour rupture of membrane (PPROM), prolonged labour, number of vaginal examinations, chorioamnionitis, gestational age, interval between rupture of membrane and delivery, hospitalisation before C/S (risk for nosocomial infection), emergency versus elective C/S, previous C/S and postpartum haemorrhage (42).

A case control study by Farret *et al.* of risk factors for post C/S wound infection in a Brazilian hospital over a four-year period, showed a total of 8 180 women had C/S performed with only a 1.44% wound infection rate (42). In the univariate analysis,

prolonged labour and prolonged PPROM found not to show any statistically significant difference compared to the control group, whereas the number of vaginal examinations, interval between rupture of membrane and delivery, and emergency C/S showed statistically significant differences in comparison to the control group (42). Multivariate analysis was done to identify independent risk factors for post C/S wound infection and it was found that the duration of ruptured membranes is the only independent risk factor for C/S wound sepsis (42).

A Nepalese study which involved 648 C/S patients found that emergency C/S and prolonged rupture of membrane before C/S were statistically significant for increased risk of post C/S wound infection, with emergency C/S (90.2 versus 9.8%) compared to elective C/S ($p = 0.0004$) (60).

A Tanzanian study involving 345 C/S patients, indicated that wound sepsis occurred significantly often in women with three or more vaginal examinations (HR 3.3 95% C1 1.7-6.5 $p = 0.001$). The study also found that ruptured membranes for 8 hours or more before C/S (HR 2.7 95% C1 1.3 – 5.8 p-value 0.011) and hypertension/preeclampsia eclampsia (HR 2.2 95% CI 1.1- 4.7 p-value = 0.031) significantly increase risk of wound sepsis. Higher American Society of Anaesthesiology (ASA) status (HR 2.7 95% C1=1.3-5.5 p-value = 0.005) and surgery time of more than 1 hour (HR 2.4, 95% C1 1.1 -5.6 p-value = 0.020) (24) were also found to increase risk of wound infections.

The Tanzanian study also revealed that 92% of the C/S, were emergency C/S and that all the postoperative wound sepsis occurred in this group (24). However, length of stay of preoperative admission, gestational age at delivery, anaemia, parity, maternal age and intraoperative blood loss did not significantly increase the risk of postoperative-wound sepsis (24). It also found that nosocomial infection slightly increased the risk for post C/S wound infection (24). However, a South African study found rupture of membranes ≥ 18hrs did not significantly increase the risk of puerperal infection (27).

2.3.3. Microbial factors

In an English cohort study, 394 post C/S wound infections were identified from 4 107 C/S, accounting for a 9.6% infection rate (41). However, causative microorganisms were not reported for about 60% of the cases. Of the reported cases, 24.2% were poly-microbial. Staphylococcus aureus was the commonest organism at 40.4%, of which 17% were

methicillin resistant (MRSA) (41). Anaerobes were the second most common at 31% (Anaerobic bacilli 13, Peptostreptococcus three, anaerobic cocci 47), Enterobacteriaceae at 13.3% (Escherichia coli six, Enterobacter one, Klebsiella one, Proteus two, other coliforms 17), Streptococcus species 7.4% (Strep agalactiae group B ten, strep pyogenes group A one, strep other anaerobic species four), Enterococcus species 3.9%, Pseudomonas 2%, and other bacteria 2% (41).

A study done in Tanzania by Mpogoro *et al*. found a similar microbiology pattern (24). In a study of 345 C/S cases, the wound infection rate was 10.9, pus swab culture taken from 25 (73.5%) of suspected cases isolated 18 positive cultures and four significant polymicrobial infections (24).

Among the microbial agents cultured 14 (63.3%) cases was of Gram-negative bacilli. Of the Staphylococcus aureus cultures, five (83.3%) were MSSA and one (16.7%) was MRSA. Other isolates include Klebsiella species (five, 22.7%), E.coli (three 13.6%) Acinetobacter species (two 9.1%) Proteus (one, 4.5%), Enterobacter species (one, 4.5%) Micrococcus species (one, 4.5%) and coagulase negative Staph species (one, 4. 5%) (24).

In a study done in Nigeria by Osakwe *et al*, they looked into all the surgical procedures, and found a slightly different microbiology pattern (61). Out of 31 culture positive wounds, Staph aureus was isolated in 19 cases (61.3%) Klebsiella and Pseudomonas aeruginosa occur more frequently than Strep pyogenes with 16.1 % and 12.9% respectively and Strep pyogenes occur least with 9.7% (61).

Onoh *et al.*, in Abakaliki Nigeria found, in a study of 1301 deliveries out of which 399 (30.7%) had C/S, a post C/S wound infection rate of 7% = 28 cases (28). Twenty-five of 28 infected wounds were cultured. Microbes isolated showed equal preponderance of Staph aureus and Citrobacter species, with each occurring at 27.8% (28). This represents a complete deviation from the microbiology pattern shown in other studies (61). Onoh *et al*. also found an equal incidence of Enterobacter species, Klebsiella species and Proteus mirabilis, each at 11.1%, while E. coli and Pseudomonas aeruginosa occur least with each 5.6% (28).

Johnson and Buchmann studied puerperal infection at Chris Hani Baragwanath Academic Hospital but unfortunately, the study did not include the microbiology pattern (27). The

paucity of data on the microbiology pattern for post C/S wound infection in SA is one of the compelling reasons that necessitated this study.

2.3.4. Antibiotic prophylaxis.

To reduce the risk of post-caesarean sepsis, prophylactic antibiotics were administered pre-procedurally, which has been shown to be effective. Indeed, the Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa (Saving Mothers 2011-2013 report) recommended the use of prophylactic antibiotics, namely 2g Cephazolin in every C/S patient whether elective or emergency and to be administered 30-60 minutes preoperatively (48). The report further recommended that, an additional five days of therapeutic antibiotics administered in all the following cases. These cases includes HIV positivity, intra-operative blood transfusion, antepartum/postpartum haemorrhage ≥ 1000mls, late second stage emergency C/S, PPROM (≥ 12 hours), more than five vaginal examinations during labour, when an assistant has to push up the head vaginally to de-impact the fetal head deeply impacted in the pelvis and BMI greater than 40kg/m^2. The prolonged days of antibiotics treatment recommended, was not evidence-based.

In a Cochrane systematic review of 2014, on antibiotic prophylaxis *versus* no prophylaxis for preventing infection after C/S, Sail *et al*. identified 95 studies with over 15 000 participants (62). The systematic review found that the use of prophylactic antibiotics in women undergoing C/S, reduced the incidence of wound infection (RR 0.40, 95% CI 0.35 to 0.46, 82 studies of 14 407 women). The study concluded that prophylactic antibiotics given to all women undergoing elective or emergency C/S is of benefit to the women, but its consequence for the baby remains uncertain (62).

However, Women and New-born Health Service, Perth, Western Australia, recommended administration of antibiotic prophylaxis prior to skin incision for all C/S to prevent wound sepsis and endometritis as studies have shown that such antibiotic prophylaxis significantly reduced the incidence of the infection without compromising the baby (63). Furthermore, the Australian Therapeutic Guidelines Limited 2014, prescribed prophylactic antibiotics for C/S (64), and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (65) recommended the same.

In Mulago Hospital, Uganda, Dlamini *et al*. conducted a randomised control trial evaluating the effect of timing the administration of antibiotic prophylaxis, on incidence of

postoperative infections as primary outcome, and adverse neonatal events as secondary outcome (66). The secondary outcomes studied included Neonatal Intensive Care Unit (NICU) admission, neonatal sepsis (NNS) and severe birth asphyxia. In this Ugandan study, there were safety concerns in respect of occurrence of adverse events, such that a data-safety management board comprising of anaesthesiologists, obstetricians, paediatricians, and pharmacists was constituted to monitor adverse occurrences. It was stated that if adverse neonatal outcomes occurred in more than 15% of the patients, the study would be stopped and the event would be treated in the paediatric unit as per protocol. However, the adverse neonatal outcomes did not exceed the set target and the study continued until the sample size was attained (66).

In this current study, which spanned from January 2014 to March 2014, the C/S rate was 49% (66). Fifty patients did not meet the inclusion criteria and one declined to participate. The remaining 464 participants were randomized into a pre-incision group (A) and post-incision group (B). Thirty-two patients were lost to follow up. The remaining 421 met the sample size for a power of 80% and a 0.05 level of significance. On timing, group A received antibiotics on average at 26.09 minutes prior to skin incision, and group B was given antibiotic prophylaxis on average at about 12.93 minutes after skin incision.

Regarding the primary outcome, the overall infection rate of group A was 65.9% (139/211) while that of group B was 85.1% (188/221), this difference was statistically significant (RR = 0.77, 95% CI 0.62 to 0.97, p-value = 0.022) (66). Group A had a wound infection rate of 57.2% (108/211) while group B had a wound infection rate of 61.5% (136/211). Endometritis was found in 14.7% (31/211) of group A and 23.5% of group B, this difference was statistically significant (RR = 0.62, 95% CI 0.39 to 0.99 p-value = 0.036) (66). The adverse neonatal outcome was 1.4% (3/211) and 0.4% (1/211) of group A and B respectively and the difference between the groups was not statistically significant (66).

The study concluded that the timing of antibiotic prophylaxis did not affect the neonatal outcomes significantly. However, the entire neonatal period could not be evaluated as neonates were followed up to 10 days of life only. Therefore, it remains unknown if there were long term adverse effects (66). The authors acknowledged that it was limited by not using laboratory investigation to confirm diagnosis of infection, and that the study was a single- blind design (66).

In a 2012 systematic review and meta-analysis, Baaqeel *et al*. reviewed studies on timing of prophylaxis antibiotics administration for C/S and its effects on maternal and neonatal infection morbidity. Six studies met the inclusion criteria, totalling 2 313 women and 2 345 neonates (67). The results of this meta-analysis revealed that preoperative administration of prophylactic antibiotics was associated with a significant 41% decrease in the rate of endometritis, relative to intraoperative administration (RR 0.59, 95% CI 0.37 to 0.94). However, in the pre-operative group, there was a decrease in the wound infection rate but this was not statistically significant (RR = 0.71. 95% CI 0.46 - 1.95 I^2 0%) (67). Neonatal adverse outcomes showed no significant reductions in the rate of neonatal sepsis (RR 0.81, 95% CI, 0.47 – 1.41 1^2 0%), neonatal sepsis workup (RR 0.93, 95% CI 0.71-1.21, 1^2 0 %) and Neonatal Intensive Care Unit admission (RR 0.92, 95% CI, 0.65-1.28 1^2 0 %) (60). Further findings include non-significant increase in maternal pyelonephritis (RR 1.09 95% CI 0.49-2.43 1^2 0 %) and in neonatal pneumonia (RR 3.36, 95% CI 0.55-20.4 1^2 0 %) (67). This systematic review and meta-analysis concluded that, preoperative prophylactic antibiotics, when compared with intraoperative use, significantly reduced the rate of endometritis but not wound infection, and that the absence of significant neonatal infectious morbidity should be cautiously interpreted given the limited power of the trials to detect such adverse effect (67).

A study on the effect of maternal obesity on tissue concentrations of prophylactic cefazolin during caesarean delivery, enrolled 29 patients stratified based on their BMI into lean (BMI < 30.0) 10 patients, obese (BMI 30.0 - 39.9) 10 patients and extremely obese (BMI > 40) 9 patients. All these participants received 2g of cefazolin 30 - 60 minutes pre-skin incision, and it the study found that the cefazolin concentrations in the subcutaneous fat during skin incision were inversely proportional to the patients BMI (68). The antibiotic concentration in the adipose tissue in the lean group was 9.4 plus or minus 2.7mcg/g, that of the obese group was 6.4 plus or minus 2.4mcg/g, and the extremely obese group had 4.4 plus or minus 1.2mcg/g. While all groups achieved therapeutic cefazolin concentration for Gram-positive cocci, the obese and extremely obese groups failed to achieve the minimum inhibitory concentration of greater than 4 mcg/g for Gram-negative bacilli in subcutaneous fat. There was no significant difference in antibiotic concentration in mean closure adipose, myometrium and serum samples in all categories. Therefore, it was suggested that the present antibiotic dosing might fail to provide adequate antibiotic coverage for obese patients (68).

In a randomised control trial (RCT) by Valent *et al*, they compared post C/S oral cephalexin and metronidazole with placebo on SSI among obese women (69). In this study, 202 participants received 500mg oral cephalexin, and 500mg oral metronidazole every 8 hours for 48 hours, and 201 controls received placebo. The primary outcomes measured were superficial, deep, and organ/space infections within a month post C/S (69). The study showed an overall wound infection rate 10.9%, with 6.4% in the antibiotic group, and 15.4% in the placebo group. The study concluded that a 48-hour regimen of a combination of oral cephalexin and metronidazole compared to placebo decreased the rate of post C/S wound infections within 30 days after delivery among obese women, and that postoperative prophylactic oral cephalexin and metronidazole may be necessary in this group of patients (69).

In the Wits University Training Circuit, the guidelines for obstetric care in the Department of Obstetrics and Gynaecology recommends a single dose of broad-spectrum antibiotics e.g. 1g cefazolin intravenously one hour before C/S, for both elective and emergency procedures. Postoperative co-amoxiclav 1.2g intravenously eight hourly for women with clinical evidence of chorioamnionitis during labour is prescribed. The guidelines also recommend, in cases of post C/S wound infection, the removal of sutures to open the wound, inspecting the depth of the wound to inspect the intactness of the rectus sheath, drainage of subcutaneous abscess, wound swab for microscopy, culture and sensitivity and the addition of cloxacillin 500mg intravenously six hourly. Wound debridement, secondary closure, laparotomy for severe wound sepsis, metronidazole and gentamycin-soaked packs for open wound dressings and relook were recommended as per departmental management protocol (70).

The South African Antibiotic Stewardship Programme recommended the use of a single dose of 2g cephazolin and 500mg metronidazole intravenously for prophylaxis in abdominal procedures, and a second dose administered if the duration of the procedure is longer than 3 hours (71).

2.3.5. Surgical technique related risk factors.

2.3.5.1 Skin preparations

The Centre for Disease Control and Prevention has stated that, showering with chlorhexidine water before surgical procedures has a significant effect in reducing the

bacterial load on the skin. A study that compared chlorhexidine with povidone-iodine has shown that the bacterial colony count is reduced nine-fold in the chlorhexidine group versus 1.3-fold in the povidone iodine group after a preoperative shower. However, it is unknown if this reduction in bacterial colony count, translate into a decreased risk of postoperative infections, because the studies used different concentrations and varied methods of skin preparations (29). A recent RCT did not show a significant decrease in the rate of postoperative infections with chlorhexidine compared to soap, or no showering (72). Many agents such as chlorhexidine gluconate and povidone iodine were used for preoperative hand antisepsis. In a prospective cohort study of 128 health care providers, the use of alcohol products for preoperative hand cleansing was associated with a lower rate of positive bacterial culture (6.2%) compared to chlorhexidine hand scrubs (47.6% $p < 0.001$) (73).

In a Cochrane review of three randomised controlled trials, shaving of hair was associated with increased wound infection risk post C/S, compared with clipping (74). Shaving is believed to cause micro-abrasions of the skin and create room for bacterial growth. However, in the same review, a separate analysis of six studies did not show a benefit of pre-operative hair removal in any way, compared with no hair removal, indicating that hair removal might not be necessary (74).

2.3.5.2. Surgical techniques

Caesarean section involves abdominal and uterine incisions and closures. Abdominal incisions are either transverse or vertical. Transverse incisions include Pfannenstiel, Kustner, Cherney, Maylard, Mouchel, or Joel-Cohen, while vertical incision could be midline/median or paramedian (75). While transverse incisions produce better cosmetic appearance, they tend to cause increased operation time, more haemorrhage, and limit access to the upper abdominal cavity. Midline incisions allow for better exposure, less blood loss, quicker access into the abdomen and pelvis, but are more frequently associated with wound dehiscence and incisional hernias (76).

In a 2013 Cochrane review of RCTs of abdominal surgical incisions for C/S, four studies involving 666 participants were included: In two of the studies, the Joel-Cohen incision compared to the Pfannenstiel incision showed that there was a 65% reduction in post C/S febrile morbidity with Joel-Cohen incisions (77). One study reported a decreased post C/S analgesic need, operation time, delivery time, total dose of analgesia on the first day post

C/S, estimated blood loss, length of hospital stay post CS and longer time to first dose of analgesia compared to the Pfannenstiel incision group (77). In the other two studies, one study (68 participants) compared the Mouchel incision with Pfannensteil. The fourth study (97 women) compared the Maylard incision with Pfannensteil and found no significant difference in febrile complications, blood loss and need for transfusion, post C/S wound infections, muscle strength test at 12 weeks post C/S, and length of hospital stay after delivery (77). The authors concluded that Joel-Cohen is better than Pfannensteil for the mother in terms of less intraoperative and postoperative morbidities, shorter hospital stay and less analgesic requirement after surgery, which translates into a cost saving for healthcare financing (77).

A 2014 Cochrane review of randomised trials of surgical techniques of uterine incision and uterine closure at the time of C/S included 27 studies involving 17 808 participants. Two trials (300 participants) compared automated suturing devices with the usual uterine incision, and showed no statistically significant difference in febrile complications between the automated closure and the conventional incision group. Five studies (2 141 participants) compared sharp *versus* blunt dissection while performing uterine incision and found no statistically significant difference in febrile morbidity (four studies 1 941 participants). However, average blood loss (two studies 1 145 participants) and the need for blood transfusion post C/S (two studies 1 345 participants) were both significantly decreased in the blunt dissection group (71).

In the review by Mood *et al*. a trial (811 participants) compared transverse with vertical blunt extension of the uterine incision and indicated that although the estimated blood loss was reduced after transverse extension, the volume difference was so small, it is of uncertain clinical importance and was not statistically significant (78). Another trial (9 544 participants) compared closure with chromic catgut with polygactin-910, and found that catgut closure is associated with a significantly lower need for blood transfusion, and complications requiring relook laparotomy. Nineteen studies (14 of which were meta-analysis) totalling 13 980 women, comparing single layer with double layer closure of the uterine incision, found no statistically significant difference in febrile morbidity (78). Although the meta-analysis reported that single layer closure was associated with less blood loss, the heterogeneity was high, and as such, rendered this finding not clinically applicable. There was no significant difference in the need for blood transfusion (78). The authors concluded that the varied surgical approaches to uterine incision are equivalent in

terms of short-term maternal outcomes, but the long-term complications remain unknown. Therefore, surgeons were advised to continue using their preferred techniques, until the long-term effects of C/S on the women are known (78).

For the C/S surgical technique investigation, a 2 x 2 x 2 factorial randomised controlled trail (CEASER), recruited 3 033 participants, who underwent C/S for their respective deliveries, while certain alternative surgical techniques were carried out and the risk of adverse outcomes were evaluated. Surgical techniques done included: single *versus* double layer closure of uterine incision, closure and non-closure of pelvic peritoneum and routine *versus* restricted use of sub-rectus sheath drains (79). Randomisation of participants was telephonic, and the main outcome measured was maternal infectious morbidity. The study found an overall risk of maternal infectious morbidity to be 17%, and found that for each pair of alternative surgical techniques there was no difference in the primary outcomes: single *versus* double closure of uterine incision, closure or non-closure of pelvic peritoneum, routine *versus* restricted use of sub-rectus sheath drain (79).

Secondary outcome measures included among others: a temperature of 39 degrees centigrade or higher, a temperature of 38 degrees centigrade on day two or later, antibiotics administered for febrile morbidity, known endometritis, wound infections, additional analgesia on day three, blood transfusions, severe maternal morbidity and readmission to hospital within six weeks of C/S. The results showed that there were no differences in these outcomes and no significant adverse effects of any of the techniques performed on the participants (79). The CAESAR trial concluded that, although short term outcomes showed no difference, the potential effects of these alternative surgical approaches on long term, the integrity of the uterine scar in subsequent pregnancies, chronic pelvic pain, infertility, peritoneal adhesions, and bowel obstructions are now being considered important factors in guiding clinical decision making (79).

There have already been three follow up studies after the CAESAR trials, although the sample sizes of these three trials were small. One of the studies compared single *versus* double closure of the uterus, which showed no differences in the interval between pregnancies, length of hospital stay, preterm birth, chorioamnionitis, postpartum endometritis, abruptio placentae, postpartum haemorrhage, wound dehiscence and blood transfusion (80). However, a large observational study associated a single layer closure of uterine incision with an increased risk of rupture (81). Another study, which assessed

follow up on closure versus non-closure of the pelvic peritoneum, found that there, was no difference in adhesions, painful intercourse, constipation, abdominal pain and secondary infertility (82).

2.3.5.3 Skin closure

A 2012 Cochrane review on techniques and materials for skin closure in C/S, identified 18 trials, but only eight contributed to the review. The incidences of wound infection were similar when absorbable subcuticular sutures compared with non-absorbable staples was used (83). The study showed that wound complications were similar for both materials when used for closure of the Pfannensteil incision, and for both outcomes (wound infection and wound complications). Staples had varied effects depending on the type of skin incision namely Pfannensteil or vertical, and non-absorbable staples were associated with increased risk of wound separation and hence the need for re-closure (83). Similarly, a retrospective cohort study done in 2014 by Schrufer-Poland *et al*. involving 186 women compared the incidence of wound complications in C/S skin closure with sutures *versus* traditional (non-absorbable) staples *versus* absorbable subcuticular staples. The authors found that the incidence of wound complications using sutures and subcuticular absorbable staples were not significantly different, but that there were significantly higher complications among patient with non-absorbable staples compared to sutures and absorbable subcuticular staples (84). They concluded that based on the reduction in the incidence of wound complications with subcuticular absorbable staples, it therefore represented a convenient, safe and cost-saving skin closure method during C/S (84).

A RCT investigated glue *versus* subcuticular monofilament sutures for skin closure after C/S. The study included 108 women randomised into a glue group and a suture group. Scar assessment were done after eight weeks. The study was powered at 80%. The participants in both groups were similar in terms of demographic characteristics, clinical background, pre-pregnancy BMI, and subcutaneous thickness. No significant differences were found between the groups regarding wound disruptions, length of hospital stay post-surgery, wound infection, and estimate blood loss (85). Scar assessment scores after eight weeks were similar for both groups. The study concluded that skin closure using glue and subcuticular monofilaments sutures had similar results, and that either may be used based on the surgeon's discretion and the patient's choice (85).

In a study done in 2017 by Choudhury *et al*. compared wound outcomes of Pfannensteil incisions closed in C/S using interrupted mattress *versus* subcuticular sutures. One hundred and four participants recruited were randomised to either the mattress group or subcuticular suture group. Wound outcomes measured included: wound hematoma, wound infection, non-union, and dehiscence, need for re-suturing, pain, and cosmetic appearance were compared between the two groups (86). It was found that participants who had subcuticular sutures had less pain, better wound results, quicker recovery, shorter postoperative hospital stay, and aesthetically superior scars hence better patient satisfaction compared with interrupted mattress sutures. It was concluded that subcuticular skin closure at C/S with absorbable sutures is associated with less wound complications and cosmetically superior scars, though the search for the best materials and methods for skin closure after C/S continues (86).

A 2012 South African RCT study, compared Polyglycolic Acid (PGA) suture, skin staples (SS), and nylon sutures (NS), used for skin closure at C/S. The study randomised 1 100 participants into three groups. The PGA group had 361 participants, while the SS group and the NS group had 373 and 366 participants respectively. Participant's characteristics such as age, gestational age and parity were similar across the three groups. The study found that the overall infection rate was 7%, and that patients in the NS group compared to the PGA group had a 9.5-fold increased risk for wound infection, while the SS group had a 6.93 fold increased risk for wound infection compared to the PGA group (87). The study concluded that use of skin staples for skin closure of C/S is associated with a significantly higher risk of wound infections and thus recommended that skin staples should not be used in C/S in South African district hospitals. However, the study also found other factors such as rupture of membranes after more than 12 hours, increased duration of surgery, and HIV infections added to the increased the risk of wound infections (87).

Recent advances in C/S skin closure involved the use of laser welding and Steri-strip S Surgical Skin Closure (3M, St Paul, MN, USA). In laser welding, two near-infrared radiations (980 and 1064 nm) were combined to achieve skin incision closure and healing without using sutures. While this laser technique is still being investigated for clinical application, the Steri-strip S, which differ significantly from the standard Steri-strips already in use, in terms of its configuration has shown superior scar quality and better patient satisfaction when used for abdominal surgeries (88, 89).

3. PROBLEM STATEMENT, AIM and OBJECTIVES

3.1. Problem statement

The WHO worldwide ecological study found that a substantial part of a crude association between C/S rate and mortality is attributed to socioeconomic factors. However, below a C/S rate of 10%, an increase in C/S rate is associated with a decrease in maternal and perinatal mortality. If the C/S rate is between 10% and 30%, it does not have any effect on mortality. This longitudinal approach of data analysis, using country level data adjusted for socioeconomic index, appeared to overcome limitations of cross-sectional studies in systematic reviews, noting that ecologic association does not imply causality (90).

A systematic review by the WHO, on the causes of maternal mortality worldwide, estimated that 9.7% of maternal deaths in Africa were due to puerperal sepsis, and that C/S remains an important risk factor for post-partum infections (91).

The Sixth Report on the Confidential Enquiries into Maternal Deaths in South Africa (Saving Mothers 2011-2013 Report) stated a national C/S rate of 23.1%. There were 1 243 maternal deaths post C/S compared to 1 471 deaths after vaginal delivery. While HIV, eclampsia, pre-eclampsia and haemorrhage remain the leading causes of direct maternal deaths, pregnancy-related sepsis, and post C/S infection remain significant contributors of maternal mortality as the risk of death from sepsis/infection increases three-fold (48).

According to the Rahima Moosa Mother and Child Hospital (RMMCH) obstetrics statistics for 2016, there were 12 948 deliveries with a 34.2% C/S rate, which is 11.1% above the national average. The maternal mortality ratio for 2016 was 76 per 100 000 live births. The report showed that complicated HIV infection and eclampsia, rank high as contributors to maternal death (92). Data on puerperal sepsis and post C/S wound infections were not collected and therefore the magnitude and impact of post C/S wound infection on maternal health at RMMCH remains unknown. However, post C/S wound infections do indeed impact negatively on patients and the health care system.

3.2. Study justification

Post C/S wound infections come at a cost apart from prolonged hospital stay, and loss of valuable economic hours to the patient and family members, it expends additional financial, material and human resources within the health systems.

Increasing the risk for the patient is the prolonged hospital stay, which predisposes them to developing nosocomial infections. Approximately 1.7 million nosocomial infections occur in the US annually, and postoperative infections account for 20% of the cases (93, 94).

According to the Saving Mothers 2011-2013 Report, Gauteng with 19% is the second largest contributor to maternal deaths in South Africa. Second to KwaZulu-Natal with 22%, Gauteng is ranked first in the total number of deliveries, but second to KwaZulu-Natal in C/S rate (48). The RMMCH is well suited to carry out a study to investigate the pattern and determinants of post-operative infectious morbidity after C/S.

3.3. Aim

The aim of the study was to determine the rate and predictors of post C/S wound infections at the RMMCH from 1st January 2017 to 30th June 2017.

3.4. Objectives

(i) To determine the wound infection in-hospital rate among the C/S patients at RMMCH.

(ii) To characterise the risk factors of post C/S wound infection among these patients.

(iii) To evaluate the morbidity associated with post C/S wound infection among these patients.

(iv) To describe the microbes associated with the wound infection.

(v) To describe the pattern of pre-operative and post-operative antibiotic use in these patients.

4. DESIGN AND METHODOLOGY

4.1 Methodology

The researcher visited the gynaecology wards, and checked the admission/discharge registers as well as the ward round record book, to identify patients seen and admitted for C/S wound infections. Patient files were obtained from the Medical Records Department at RMMCH.

Wound infections can be identified clinically by one or combinations of following features: wound erythema, fluctuant subcutaneous pus collection, offensive purulent wound discharge, wound breakdown, necrosis and dehiscent associated with infection, necrotic and dusky cervix on speculum examinations, sub-involution with uterine tenderness and offensive lochia, and pus collection in the abdomen and pelvis on ultrasound examination.

4.2. Study setting

The study was done at the RMMCH, which forms a complex with Helen Joseph Academic Hospital and is part of the WITS Academic Complex. It serves as a referral centre to many peripheral hospitals/clinics and Maternal Obstetric Units (MOU) in regions B and C encompassing Diepsloot, Fourways, Sunninghill, Florida, Rosebank, Randburg, Bram Fischerville, Thulani, Soweto, Parkwood, Ormonde, Benrose, Kensington, Lenasia, and Eldorado Park.

There is a nine-delivery suite labour ward situated directly opposite the obstetrics admission ward and two C/S theatres in operation from 07:00 to 17:00. There is one theatre operating throughout the night, however, there is an arrangement in place to open a second theatre at night, if the need arises. On the average, about 350 to 380 C/S were performed monthly at RMMCH.

There are two gynaecology wards, a gynaecology emergency/admission ward, and access to a shared emergency theatre. There is also an elective theatre for elective cases and endoscopic surgeries that operate five days a week from Mondays to Fridays, except on public holidays.

At the RMMCH, post C/S wound infection and sepsis are usually managed in the gynaecology wards.

4.3. Study design

This was a retrospective, descriptive, record review study using maternal case records and gynaecology patient files. The post C/S wound in-hospital infection rate obtained in this study was compared to similar rates obtained in similar studies in low resource countries, as a way of assessing this aspect of obstetric care offered at RMMCH, and to identify and address challenges, if, where or when we are underperforming. This rate is compared to similar rates from studies carried out in high resource countries, as this would emphasize the need to improve our standards of care.

The microbiology pattern obtained from this study is compared to that obtained from other studies carried out in sub-Saharan Africa, to establish if there was concurrence or divergence of microbes causing post C/S infection in this region of the world.

4.4 Study population and period

The study included all patients who had a C/S, either as an emergency or as an elective procedure at RMMCH from January 1st 2017 to June 30th 2017, who later presented to RMMCH with wound sepsis.

4.5 Inclusion criteria

All women who had a C/S at the RMMCH within the specified study period and who developed wound infection complications.

4.6 Exclusion criteria

Any patient who may have been recorded in admission/discharge registers or ward round books as having had wound sepsis but for whom no records can be found.

4.7 Data collection and statistical analysis.

A data collection sheet was developed in conjunction with RedCap, for data collection. Antenatal history, past medical history and patient biomedical data were extracted from the patient records (Appendix A).

The data collected was loaded into RedCap, and then exported to Stata version 14 (Stata Corp, USA) statistical software. Categorical variables such as HIV status and booking status were described using frequencies, percentages and appropriate charts. Continuous variables such as gestational age, duration of labour, length of hospital stay was reported as mean and standard deviation (SD) if normally distributed, and if not normally distributed, the median (interquartile range) was reported.

The infection rate is calculated by dividing the number of C/S wound infections by the total number of patients who had C/S, multiplied by 100 and expressed as a percentage.

Categorical variables (risk factors) were presented as percentages.

Normally distributed continuous variables were presented as measures of central tendency.

Non-normally distributed continuous variables were presented as ranges.

Various infectious morbidities found among the participants were presented as frequencies and percentages together with the appropriate charts.

The types of microbes and their respective diagnosis were described as frequencies and percentages.

4.8. Definition of terminology

Total duration of labour defined as the estimated hours from onset of labour to the surgery-end time written in the C/S delivery operation notes, documented in the patient's records.

The number of vaginal examinations was the counted number of per-vagina examinations documented in the patient's file, from the onset of labour to the time of C/S.

4.9. Ethics

Approval of the study was obtained from the University of the Witwatersrand Human Research Ethics Committee before commencement of the study. The ethics clearance number is M180112.

The participants in this study remained anonymous. |Although patient names, hospital numbers, identity numbers and residential addresses were recorded (kept separately from the data sheet, in a safe place only assessable to the principal investigator) each participant was only assigned a study number on the data sheet.

Approval to conduct the study was obtained from the Chief Executive Officer (CEO) of the RMMCH by registering the study online on the National Health Research Database. Reg number: GP-201802-012.

5. RESULTS:

5.1 Wound infection rate

In fulfilling objective i): in the period January 1st 2017 to June 30th 2017, there were a total of 6 550 deliveries in the Rahima Moosa Mother and Child Hospital, of which 2 746 patients had Caesarean deliveries, and 80 patients presented with clinical features of post

C/S wound infections. Of the 80 patients with C/S wound infections, 44 were managed on an outpatient basis and 36 were admitted. Table 5.1 gives a summary of the data.

Table 5.1: C/S rate, Post C/S wound infection rate, and In-Hospital admission rate.

	Total	**Percentage**
Caesarean section	2 746	
Total deliveries	6 550	
Caesarean section rate		41.90
Post caesarean section infection rate	80	2.91
In hospital admission rate	36	1.31

5.2 Characteristics of post-caesarean section sepsis patients

As part of objective ii), the characteristics of the risk factors for post C/S wound infection were explored. Table 5.2 tabulates the findings. Six patients were less than 20 years old, 26 were within the 20 -34 years age range, and four, equal to or more than 35 years and thus advanced maternal age. About 92% of the participants either were coloured or black Africans. Twenty five percent (9 out of 36) of the participants were obese, four had grade I obesity (BMI 30.0 - 34.9kg/m^2), three had grade II obesity (BMI 35.0 - 39.9kg/m^2) and two had grade III obesity (BMI ≥ 40.kg/m^2). About one-fifth of the participants were HIV positive and 50% of the HIV positive participants had an HIV-related severe immune-compromised status.

Table 5.2: Objective ii: Clinical characteristics of the study patients.

		Mean (Range)
Age (years) (18 – 40)		26,8 (18 - 40)
		Number (Percentage %)
Gravidity	Primigravida	16 (44,4)

	Multigravida	20 (55,6)
	Races	Number (Percentage %)
Ethnicity	African	26 (72,2)
	Coloured	7 (19,4)
	White	3 (8,3)
	Indian	0 (0,0)
	Asian	0 (0,0)
Booked for antenatal care	Yes	35 (97,2)
	No	1 (2,8)
		Number (Percentage %)
BMI (Mean 27,4 kg/m^2)	Normal	25 (69,4)
	Overweight	2 (5,6)
	Obese	9 (25)
		Number (Percentage %)
HIV status	Positive	8 (22,2)
	Negative	28 (77,8)
		Number (Percentage %)
CD4 count cells/mm^3	≥ 200	4 (50,0)
	< 200	4 (50,0)

Almost 80% of the participants were healthy with no know pre-existing comorbidity: 11% had hypertensive disorders in pregnancy and 22% were HIV positive. Figure 5.1 illustrates the pre-existing medical conditions found in the study population.

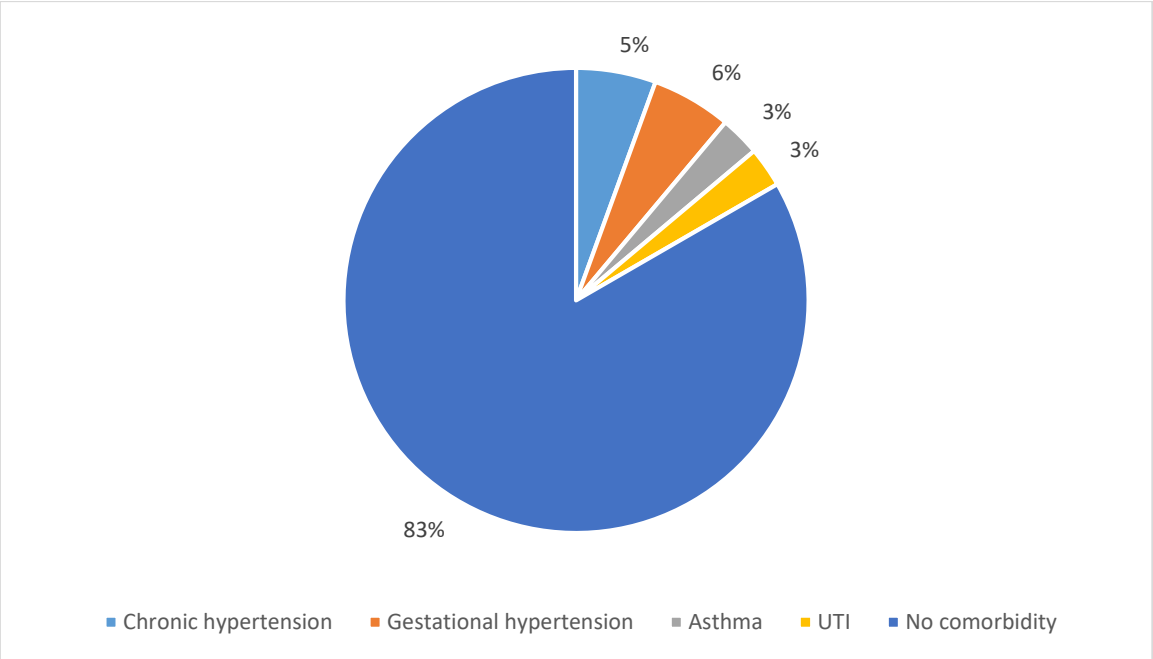

Figure 5.1: Study objective ii, Pie chart showing pre-existing morbidities in the study population.

5.2.1 Incidence of prelabour rupture of membrane and chorioamnionitis

In the study objective ii), prelabour rupture of membrane (PROM) and chorioamnionitis, as a risk factors for post C/S wound infection were studied.

Prelabour rupture of membrane (PROM) was found in 5.6% of the participants, while 91.7% have no features of PROM. However, in 2.8% of the patients, there were no documentation in respect of features of PROM. No clinical features of chorioamnionitis were found in any participant.

As part of objective ii), on characteristics of risk factors, the number of vaginal examinations and prolonged labour was studied. The findings are shown in Table 5.3. There were between two and ten examinations both before delivery and before the C/S, with a mean of seven examinations. This may not be accurate because in clinical practice, midwives and doctors may not document all the per-vagina examinations performed on the patient, including those performed on the operating table in the C/S theatre before the skin incision. The duration of labour was between 18.4 hours and 26 hours, with a mean of 21

hours. Of the 36 women admitted for sepsis seven (19.4%) had an elective C/S and 29 (80.6%) had an emergency C/S.

Table 5.3: The number of vaginal examinations, duration of labour, and type of C/S.

		Mean (Range)
Number of vaginal examinations before giving antibiotics		7 (2 – 10)
Number of vaginal examinations prior to C/S		7 (2 – 10)
		Mean (Range)
Total duration of labour (hours)		21 (18.4 – 26)
		Number (Percentage %)
Type of C/S	Elective	7 (19.4)
	Emergency	29 (80.6)

The majority of the elective C/S patients have had previous uterine surgeries, namely, either one or two previous C/S, or previous myomectomy as shown in Figure 5.2. The other indications shown in Figure 5.2 were a previous hip fracture and surgery with a resultant stiffness, deformation and limited range of movement at the hip joint such that vaginal delivery would be difficult as well as intrauterine fetal death (IUFD) and chronic hypertension as per the notes.

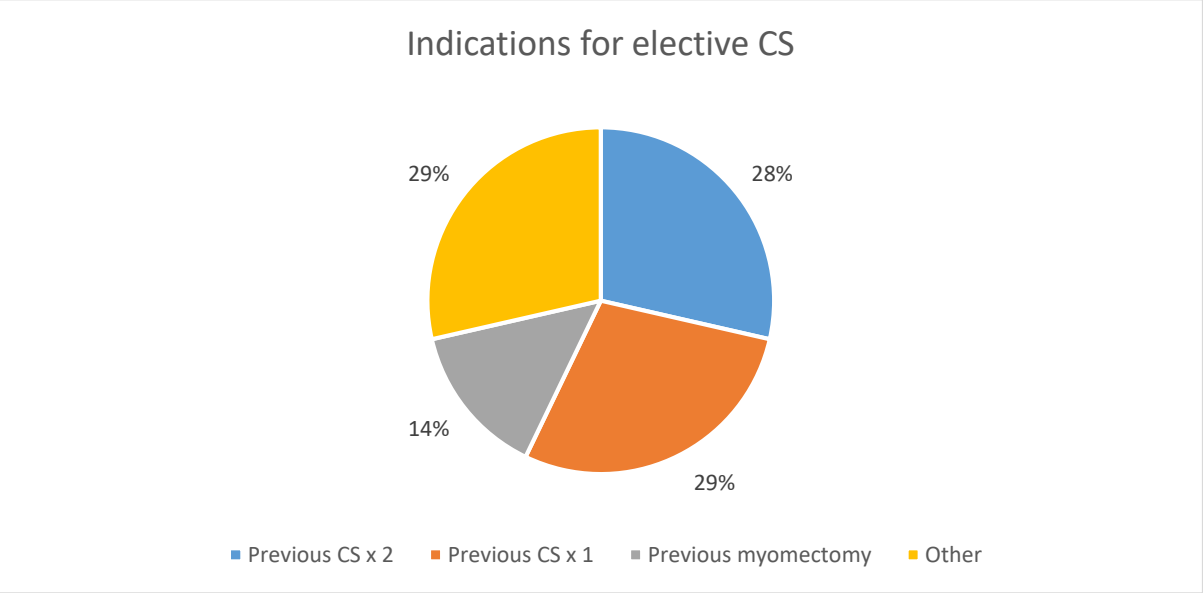

Figure 5.2: Indications for elective Caesarean sections

As part of the characteristics of the risk factors for post C/S wound infections in objective ii), emergency C/S and its indications were studied. Fetal distress is the most common indication for emergency C/S in this study which represented 21.3%, followed by cephalopelvic disproportion and antepartum haemorrhage contributing 12.8% and 8.5% respectively. These findings are shown in Figure 5.3. Severe preeclampsia/eclampsia and prolonged second stage of labour ranked as the next most common reasons for emergency C/S, each contributing 6.4%, followed by failed vacuum/forceps delivery, cardiac disease in pregnancy and poor progress in labour, each contributing 4.3%. The least common indications include: breech in labour, previous C/S, failed augmentation of labour, facial presentation, previous C/S postdate with abnormal fetal heart rate pattern and previous C/S with failed vaginal birth after Caesarean section (VBAC). Other includes abruption of placenta, big baby in labour, failed induction of labour, gestational hypertension with non-reassuring fetal heart rate pattern, gestational hypertension with failed augmentation of labour, antepartum haemorrhage of unknown origin and prolonged labour, which each contributed 2.1%. In our setting, the diagnosis of fetal distress is based on abnormal/pathological cardiotocographic tracing of the fetus and emergency C/S delivery is indicated after failed intrapartum resuscitation. Other risk factors for post C/S wound infection found within the indications for emergency C/S include prolonged labour, second stage C/S indicated by prolonged second stage, and failed vacuum/forceps deliveries.

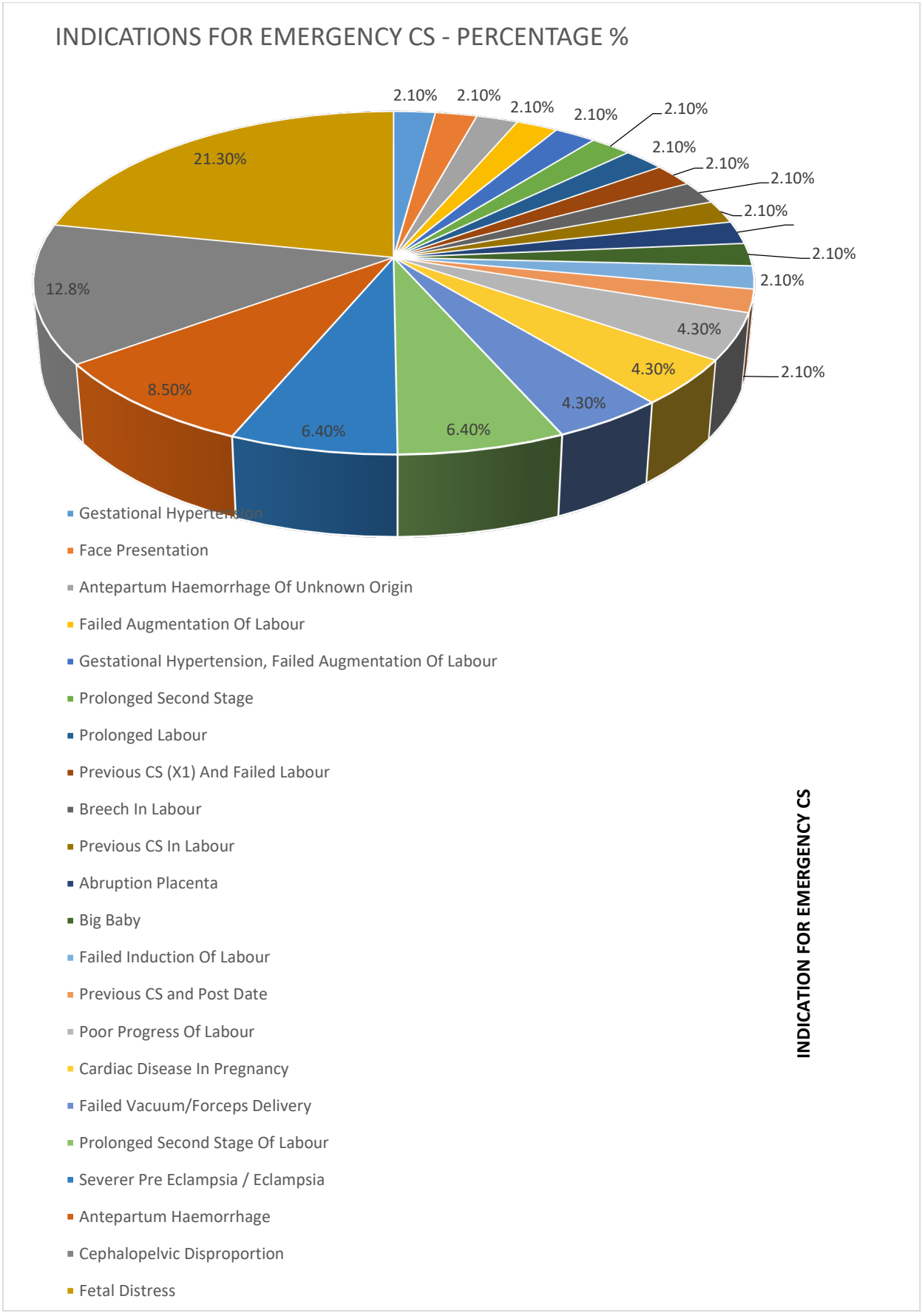

Figure 5.3: Pie chart showing indications for emergency Caesarean section.

As part of study objective ii), Table 5.4 shows surgical details that may be risk factors for post C/S wound infections. The factors considered include the duration of the surgery, administration of prophylactic antibiotics, skin preparations, type of incision on the skin and uterus, skin closure techniques, and the skills of the surgeons. The duration of surgery means the time in minutes from “knife-on-skin” to the last stitch, excluding the anesthetic time, skin preparation time and recovery period. Patients who were found to be allergic to chlorhexidine and betadine received methylated spirit for skin preparation. In terms of the skill of surgeons, all C/S were performed by registrars and medical officers, and none performed by a consultant.

Table 5.4: Surgical details of the caesarean sections

		Mean (Range)
Duration of Surgery (Minutes)		34. (30 – 42)
		Number (Percentage %)
Prophylactic antibiotics usage	Yes	33 (91.7)
	No	0 (0)
	Unknown (Not documented)	3 (8.3)
Specific antibiotic used		Number (Percentage %)
Cefazolin		19 (58)
Co-amoxiclav		14 (42)
		Number (Percentage %)
Skin preparation	Chlorhexidine	11 (30.5)
	Betadine	20(55.5)
	Methylated spirits	4 (11.1)
	Unknown (Not documented)	1 (2.8)
Skin incision	Transverse	28 (77.8)
	Midline sub-umbilical	8(22.2)
Uterine incision	Lower segment transverse	30 (83.3)
	Lower segment vertical	4 (11.1)
	Upper segment vertical	1 (2.8)
	Unknown (Not Documented)	1 (2.8)
Peritoneum closed	Yes	27 (75.0)
	No	8 (22.2)
	Unknown (Not Documented)	1 (2.8)
Skin closure techniques		Number (Percentage %)
-Interrupted Mattress		35 (97.2)
-Unknown (Not Documented)		1 (2.8)
Surgeons		Number (Percentage %)
- Registrars		26 (72.2)
-Medical officers		10 (27.8)

5.3 Morbidity associated with wound sepsis

As part of morbidities post C/S, re-admission to the hospital for in-patient care, and the intervening days from date of C/S delivery to the date of presentation and readmission, the majority, (63.9%), of the patients were re-admitted within the first ten days post C/S as is shown in Table 5.5.

Table 5.5: Number of days from discharge to presentation for re-admission

Number of days	Numbers of Patients	Percentage %
0 – 5	6	16.7
6 – 10	17	47.2
11 – 15	8	22.2
16- 20	2	5.6
>20	3	8.3

Study objective iii) relates to the post C/S wound infections and other morbidities found among the study patients. The findings are shown in Table 5.6. However, there is overlap in the presentations, with 14 patients presenting with more than one clinical entity. While 22 patients had superficial wound sepsis only, four patients had both superficial wound sepsis and deep wound sepsis, with one patient having superficial wound sepsis and a subcutaneous haematoma. Eight patients presented with endometritis, out of which four had endometritis only, the other four had additional presentations, such as hematoma/intra-abdominal bleed, faecal impaction, retained products of conception, and superficial wound sepsis. Two patients had a subcutaneous haematoma only.

Table 5.6: Frequency of wound infection/morbidities post C/S. (Objective iii)

Morbidities	Frequency	Percentage %
Superficial wound sepsis	22	50
Endometritis/Organ-AKI/space infection	8	18.2
Deep wound infections	4	9.1
Wound breakdown	3	6.8
Wound hematoma	2	4.6
Retained products of conceptions	2	4.6
Periumbilical hematoma	1	2.3
Faecal impaction	1	2.3
Paralytic ileus/small bowel obstruction	1	2.3
Septic shock	0	0
Multiple organ dysfunction	0	0
Death	0	0

As part of, study objective iii) Table 5.7 shows surgical management of morbidities associated with post C/S wound infection in this study, 49.1% of patients had superficial wound dressing, and 18.2% had wound debridement and secondary closure. Eleven relook laparotomies were performed on eight patients, thus three patients were relooked twice. The indications for relook laparotomy in the first patient were subcutaneous collection on trans abdominal and transvaginal ultrasound, with queried intra-abdominal collections. It was found intraoperatively that the patient had slough and exudate at the subcutaneous tissue level with no intra-abdominal or pelvic collections and the pelvic organs were healthy. Debridement of slough and washout was done followed by re-suturing. Tissue culture taken at relook laparotomy grew MRSA and Bacillus species. Bacillus species was sensitive to Azithromycin. The indications for relook laparotomy, and operative findings in the second patient is similar to that of the first patient, however, tissue culture was not taken in this patient, and she underwent a secondary wound closure.

The third patient who was relooked twice had abdominal distension with ultrasound findings of dilated loops of bowel there were no intrauterine, intra-abdominal or pelvic collections. The general surgeons reviewed the patient, the CT abdomen with contrast ruled out bowel injury. At first relook, purulent materials was found oozing out of the abdominal incision site, with a septic area in the lower uterine segment, debridement and washout was done and the abdomen was packed, and relooked again after 48 hours for removal of packs, washout and closure of the anterior abdominal wall. Tissue culture samples showed no growth.

The indication for relook laparotomy in the fourth patient was radiological findings of organised intra-abdominal collections anterior to the uterus. Intraoperative findings included a necrotic dusky brown uterus, with bladder injury and leakage of urine into the peritoneal cavity. Subtotal hysterectomy was done for the patients with a repair of bladder injury in a joint procedure with the urology team. She also had a secondary wound closure. Postoperatively the patient had a prolonged catheterisation and was followed up at the urology department after discharge. Tissue culture taken at relook laparotomy showed no growth.

The fifth patient was relooked twice because of a subcutaneous hematoma and intra-abdominal bleed. At first relook, 600mls of clots and hemoperitoneum was evacuated; the left uterine artery was ligated. She developed uterine atony, which failed to respond to

medical management, and a B-Lynch brace suture was applied. She was transfused with four units of blood products. She had a second relook within 24 hours, where a septic and floppy uterus was found, and a total abdominal hysterectomy with left salpingo-oophorectomy was done. Postoperatively she developed severe metabolic acidosis and acute kidney injury. She was admitted to RMMCH High Care Area. On postoperative day two, the patient was transferred to Helen Joseph Hospital Intensive Care Unit for intensive care and renal dialysis, and was discharged home from Intensive Care Unit on postoperative day nine. Tissue culture grew Staphylococcus aureus, which was sensitive to a piperacillin/tazobactam combination.

The sixth patient was relooked twice due to puerperal sepsis. In both instances, no source of sepsis was found and a wash out was done. Tissue culture showed no growth; however, her pus swab grew MRSA and patient received vancomycin for fourteen days, and a secondary wound closure was done.

The seventh patient was relooked because of ultrasound findings of complex fluid collections in the pouch of Douglas, having presented with superficial wound sepsis and endometritis. It was a negative laparotomy. No tissue culture sample was taken.

The last patient that was relooked had a paralytic ileus with features of small bowel obstruction. Abdominal x rays showed multiple air-fluid levels, and CT-abdomen and pelvis findings were not conclusive, the report queried collections in the abdomen and pelvis. At laparotomy, the uterus appeared healthy and well perfused and the adnexal structures looked normal, the loops of bowel were dilated with no evidence of bowel injury. Abdominal fluid taken for culture grew Enterococcal faecalis, Prevotella bivia, Peptostreptococcus and Escherichia coli, which were sensitive to ampicillin, amoxicillin and co-amoxiclav.

Apart from the fifth relook laparotomy patient who was admitted to the High Care Area, one other patient was admitted to the High Care Area post C/S, for blood pressure monitoring and magnesium sulphate administration. Of ten patients who had secondary wound closures, seven presented with superficial wound sepsis, and three were relook laparotomy patients.

Table 5.7: Surgical management of post C/S wound infections

Surgical care	Frequency	Percentage %
Superficial wound dressing	27	49.1
Relook laparotomy	11	20.0
Wound debridement and secondary closure	10	18.2
HCA/ICU admission	2	3.6
Hysterectomy/Oophorectomy	2	3.6
Wound exploration	1	1.8
Wound Hematoma evacuation	1	1.8
Evacuation of uterus	1	1.8
Vacuum dressing	0	0

As part of study objective iii), which relates to the morbidities associated with post C/S wound infections, re-admission to hospital, and length of hospital stay, were studied. The results are shown in Table 5.8. Length of hospital stay on re-admission was calculated by the number of days from date of re-admission to date of discharge from hospital. About 80% of the readmitted patients were re-admitted for a period ranging from one to ten days

Table 5.8: Length of hospital stay in days on readmission

Number of readmission days	Number of Participants	Percentage %
0 – 5	19	52.8
6 – 10	10	27.8
11 – 15	5	13.9
16 – 20	1	2.8
>20	1	2.8

5.4 Microbes associated with wound infection

Objective iv) of the study relates to the microbiology pattern in post C/S wound infection as presented in Table 5.9. In this study, culture samples were taken from 27 out of 36 patients (75%). Some patients had a single culture taken while others had multiple cultures from different anatomical sites.

Pus/wound swabs were taken from 20 patients, nine showed no growth, and one patient showed polymicrobial growth (specific organisms were not identified). Organisms isolated

from pus swabs included, Staphylococcus aureus, Clostridium glycolicum, Streptococcus agalactiae, MRSA, Enterococcal faecalis, Enterobacter cloacae, Pseudomonas, Enterobacter aerogenes and Coagulase negative streptococcus,

Blood cultures were taken from 12 patients, of which ten showed no bacterial growth. Organisms isolated from blood culture were Pseudomonas aeruginosa and Acinetobacter baumannii.

Tissue culture samples were taken in six out of the eight patients who had relook laparotomies, and three samples showed no growth. Organisms found on tissue cultures included, Bacillus species, Streptococcus agalactiae, MRSA, Staphylococcus aureus, Enterococcus faecalis, Prevotella bivia, Peptostreptococcus, and Escherichia coli.

Urine cultures were taken in eight patients, five showed no growth, two showed polymicrobial growth (specific microbes were not identified), and the organism cultured from these urine samples is Escherichia coli.

A high vaginal swab was taken in one patient, with a wet preparation showing Trichomonas vaginalis.

Table 5.9: Microbiological pattern of post C/S wound infections

Microbes	Frequency	Percentage %
Staphylococcus aureus	6	20
Escherichia coli	3	10
Polymicrobial growth	3	10
Enterococcus faecalis	3	10
Streptococcus agalactiae	2	6.7
MRSA	2	6.7
Acinetobacter baumannii	1	3.3
Clostridium glycolicum	1	3.3
Enterobacter cloacae	1	3.3
Enterobacter aerogenes	1	3.3
Pseudomonas aeruginosa	1	3.3
Peptostreptococcus	1	3.3
Prevotella bivia	1	3.3
Gram-positive cocci	1	3.3
Coagulase negative staphylococcus	1	3.3
Bacillus spp	1	3.3
Trichomonas vaginalis No growth - 9 pus swabs, 10 blood cultures, 3 tissue cultures, 5 urine cultures	1	3.3

5.5 Antibiotic use in post C/S wound infection

Objective v) was about antibiotic usage in post C/S wound infection. Thirty of 36 patients were initiated on treatment with empirical broad-spectrum antibiotics. The findings are shown in Table 5.10.

Nineteen of 30 patients received a triple antibiotic regimen (1g ampicillin IV six hourly, 240mg gentamycin IV daily and 500mg metronidazole IV 12 hourly combinations. The mean duration of treatment was 3.5 days, with ranged from one to eight days). Six of 30 patients received co-amoxiclav only, at a dose of 1.2g IV eight hourly, duration of treatment ranged from one to eight days. The remaining five of 30 patients received co-amoxiclav at the same dose and duration stated above, but it was combined with other antibiotics such as, cloxacillin in three patients, with gentamycin and metronidazole in two patients, and with metronidazole alone in one patient. Of the 19 who received the triple antibiotic regimen initially, one got escalated to a combined 1g ceftriaxone IV 12 hourly/600mg clindamycin IV six hourly, as second line empirical antibiotic, when the

patient had two relook laparotomies, and was discharged home on 500mg cloxacillin four times daily for five days. The remaining 18 patients were discharged on varied empirical oral antibiotics, which included amoxicillin, metronidazole, co-amoxiclav, doxycycline, azithromycin and cloxacillin. The duration of take-home antibiotics ranged from three to five days. Of the six patients who were initiated on treatment with co-amoxiclav alone, three were discharged with no take-home antibiotics, while each of the remaining three, received cloxacillin, doxycycline, and amoxicillin with metronidazole, as take-home antibiotics respectively for a duration of three to five days. Of five patients who were initiated on treatment with co-amoxiclav combined with other antibiotics, three were discharged home with no take-home antibiotics, while two went home with empirical cloxacillin at a dose of 500mg four times daily for one week.

The remaining six of the 36 patients received narrow spectrum antibiotics. Two received empirical cloxacillin only at a dose 500mg four times daily for four days. One was treated with targeted vancomycin only at an initial dose of 1g IV 12 hourly for seven days, and later orally at 500mg qid for another seven days. One received empirical azithromycin only at an oral dose of 500mg daily for four days and another received a targeted piperacillin/tazobactam combination at a dose of 4.5g IV six hourly for six days. The last patient was initiated on treatment with empirical cephalexin, but had to be changed to a piperacillin/tazobactam combination after obtaining tissue culture results taken at relook laparotomy, which showed Staphylococcus aureus that was sensitive to a piperacillin/tazobactam combination. She received piperacillin/tazobactam at a dose of 2.25g IV 6 hourly for 12 days. The dosage was adjusted because she had acute kidney injury. She later had renal dialysis.

Table 5.10: Antibiotics used in post C/S wound infections.

Drug	Number treated	Median days	Minimum	Maximum
Ampicillin	19	3.5	1	8
Metronidazole	26	7	2	13
Gentamycin	19	4	1	8
Co-amoxiclav	18	7	1	11
Cloxacillin	10	6	5	7
Amoxicillin	3	4	3	5
Doxycycline	3	5	5	5
Azithromycin	2	4.5	4	5
Piperacillin/Tazobactam	2	9	6	12
Clindamycin	1	7	7	7
Ceftriaxone	1	7	7	7
Vancomycin	1	14	14	14
Cephalexin	1	4	4	4

6. DISCUSSION

6.1. Objective i - Incidence of post C/S wound infection and in-hospital admission.

This study shows a C/S rate of 41.9%, which is higher than the national average of 23.1%, but fall within the C/S rate found in regionals hospital across South Africa stated to be 32-46% (9). While this rate is higher than in high-income countries, it is similar to rates found in low- and medium-income countries like Chile (2, 3, 4, 5). The post C/S wound infection rate was 2.91%, which is lower to the 11.0% reported by Buchmann and Johnson in a 2010 study at Chris Hani Baragwanath Academic Hospital, Soweto (27). This lower rate is possibly attributable to the fact that a number of our C/S patients may have presented to one of the peripheral clinics for post C/S wound infections, or may have embarked on cross-province travel to their homeland in other provinces, to seek help with the care of the new baby. Clouse *et al*. found that 44% of pregnant women in the Johannesburg area do embarked on cross-province or cross-border travel after delivery (95), the duration of such travel in the immediate postpartum period could be from seven to sixty days, with a mean duration of 30 days (95). These mothers travel to 8 other South African provinces, and four other countries (95), thus they may have presented to clinics and hospitals in their provinces, and countries with features of post C/S wound infections. Statistics from RMMCH show that foreign nationals constitute 45.8 to 46.2% of maternity patients, mostly from Southern African countries (92). As such, data of these internal and international migrant mothers who travelled out of Johannesburg could not be captured and therefore are not included in this study. Studies from London, UK, Abakaliki, Nigeria, and Mwanza, Tanzania found post C/S wound infection rates of 3.2%, 7.0%, and 10.9% (41, 28, 24) respectively, which is higher than the rate found in this current study.

The in-hospital admission rate (readmission post C/S) in this study is 1.31%. None of the studies reviewed as part of the literature calculate the in–hospital admission (readmission) rate.

6.2. Objective ii - Characteristics of the factors associated with wound infections.

6.2.1. Demography and pre-existing comorbidities

Considering the demographic factors, the mean age of patients in this current study is 26.8 years, (Range 18 - 40) which is close to the age range of 16 – 43 years quoted in a similar study in Cape Town South Africa (96). On parity, 55.6% were multiparous while 44.4% are primiparous, however, this study did not set to determine if parity is a risk factor for post C/S wound infection. A study from Nnewi, Nigeria compared nulliparity versus grandmultiparity as a risk factor for C/S wound infection and found no statistically significant difference in wound infection rates among the two groups (97). On ethnicity, 72.2% of the patients were Black Africans, 19.4% were Coloured and 8.3% were Whites. This may be a reflection of the demographics of the population of the catchment areas covered by the referral system because RMMCH catchment area is predominantly Black and Coloured dominated areas with few Whites. The mean BMI in this study is 27.4kg/m^2. Of the 36 patients, 69.4% have a normal BMI (18.5 - 24.9kg/m^2) while 5.6% were overweight (BMI 25.0 – 29.9kg/m^2) and 25% of the patients were obese (BMI ≥ 30kg/m^2). This differed from a similar study done in Cape Town, South Africa where the mean BMI was 31.2 kg/m^2, 45.8% were obese and 11.9% were morbidly obese (96). In the 2012 study by Buchmann *et al*. at Chris Hani Baragwanath Academic Hospital on puerperal sepsis, data on BMI were not recorded, but data on mid upper arm circumference less than 23cm was collected and it was found that 15% had possible puerperal sepsis or mild wound infections (28). Obesity has been shown to be associated with an increased risk for postoperative wound infections (41). In this current study, 22.2% of the patients were HIV positive while 77.8% were HIV negative. The HIV sero-prevalence rate agrees with the quoted rated of one-fifth, for women of the reproductive age group by Statistics South Africa in its 2018 mid-year population estimates (98). Dr Bera of the RMMCH, found a HIV sero-prevalence of 18.6% among our pregnant patients (92). Other studies however, found varied rates, while a study from Cape Town, South Africa found a HIV prevalence of 24.5% (96), and a study from Zimbabwe found a lower prevalence of 9.3% (99). Half of the HIV positive patients had a CD4 count of > 200 cells/mm3, while the other half had a CD4 count of < 200 cells/mm3. This study did not include wound infection rates versus CD4 count, or viral loads, which is a weakness of the study. However, it has been shown that high viral loads of 30 000 copies/mL and more, rather than a CD4 count of less than

200 cells/mm3 were associated with an increased risk for wound postoperative complications and poor outcomes (46).

We showed that 83% of the study patients had no known pre-existing medical comorbidity. However, 11% had hypertensive disorders in pregnancy, and 3% (one patient) each, had urinary tract infections and asthma. Annual statistics of 2017 at RMMCH shows that 5.8% of the maternity patients have medical conditions and hypertensive disorders of pregnancy (92). While hypertensive disorders in pregnancy are known to be associated with an increased risk of maternal morbidity and mortality (48), it has been shown to be an independent risk factor for post C/S wound infections (24).

6.2.2. Labour-related factors.

In the current study, 80.6% of the patients had been in labour before C/S, hence had emergency C/S, similarly to a Cape Town study that also found that 80.6% cases to be emergency C/S (96). Studies have shown that emergency C/S, opposed to elective, is associated with an increased risk for post C/S wound infections (60, 99). Prelabour rupture of membrane (PROM) was defined by 24 hours, while 5.6% of the patient has rupture of membranes for a period greater than 24 hours and 91.7% did not meet the criteria for PROM. While a study from Cape Town, South Africa reported a higher value of 32.7% for PROM (96), a Nnewi, Nigerian study reported nine out of 60 patients (15%) had PROM, and also found that PROM significantly increased the risk for post C/S wound infections (97). While a study from sub-Saharan Africa found that PROM significantly increased the risk of post C/S wound sepsis (100), a case – control study from Brazil found that PROM did not significantly increase the risk of post C/S wound infection (42).

Clinical chorioamnionitis was not found among the 36 participants in this study, although there may have been cases of subclinical chorioamnionitis. In Cape Town, South Africa, chorioamnionitis was found in 16.3% of patients (96). Studies have shown that chorioamnionitis is associated with increased risk of postoperative wound infection (101). While the mean number of vaginal examinations in this study was found to be seven (Range 2-10), the Cape Town, South African study reported a lower value of five (96). Studies from Brazil, Nepal and Nnewi, Nigeria did not find that the number of vaginal examinations have an impact on the risk of post C/S wound infections (42, 60, 97). The mean duration of labour in this study was 21 hours (range 18.4 – 26), two Nigerian studies

from Nnewi and Kano respectively have shown that duration of labour greater than 12 hours is associated with an increased risk of post C/S wound infections (97, 102).

6.2.3 Surgical related factors.

In this study, different agents were used for skin preparations. In the majority of the patients (55.5%), Betadine was used, followed by chlorhexidine in 30.5%, while methylated spirit was used in 11.1% of the patients. There is conflicting evidence about the superiority of one agent over the other in reducing the risk of postoperative wound infections. A 2018 Cochrane review (103), assessed skin preparations for C/S. The review compared drape to no drape, one-minute alcohol scrub with iodophor drape *versus* five–minute iodophor scrub without drape, parachlorometaxylenol with iodine *versus* iodine alone, chlorhexidine gluconate *versus* povidone iodine, chlorhexidine 0.5% *versus* 70% alcohol plus drape. This review concluded that evidence is insufficient to fully assess different agents and skin preparation methods for prevention of post C/S wound infections. As such, the most effective agents for skin preparations to prevent postoperative infectious morbidity remain unknown (103).

In this study, 77.8% of the patients had transverse abdominal incisions not differentiated into Pfannensteil or Joel-Cohen, and the other patients had midline subumbilical incisions. A Cape Town study included Pfannensteil in 92.9% of cases (96). Available evidence showed better outcomes with the Joel-Cohen incision (77). About 75% of the participants had closure of the parietal peritoneum, the even though parietal peritoneum closure has been shown to increase operation time and need for postoperative analgesia (104). The majority of patients in this study, which is similar to that of Cape Town, had interrupted mattress skin closure, which is associated with less patient satisfaction (86). On the skill of the surgeons, 72.2% of the surgery were performed by registrars while 27.8% were done by medical officers, but in a Cape Town study, C/S were divided equally between registrars and senior medical officers (96). A study from India compared the grade of surgeons at C/S versus the risk of postoperative infections, compared registrars to consultants and found that C/S performed by consultants is associated with reduced risk of wound infections (105). However, when junior registrars were compared to senior registrars, no difference in risk for post C/S wound infections was found (105). A similar trend in the skill of surgeons and postoperative wound infection was found in a Tanzanian study (24).

6.3. Morbidities associated with post C/S wound infections – Objective iii

In this study, the results show that there are varied morbidities associated with post C/S infections, but they are largely not life threatening. Although the post C/S wound infection rate was 2.91%, only 1.31%, required re-admission, implying that more than half of the patients who presented with postoperative wound infections were managed as out patients. The most common morbidity is superficial wound sepsis, which represent 50%, of cases. This is lower, compared to the 91.8% reported in a 2014 sub-Saharan Africa multi-country study by Médecins Sans Frontiers (100). A similar trend was also reported in a UK study, where an 88.3% of the patients had superficial wound sepsis (41). Being minor cases, superficial wound sepsis was managed with wound dressings and antibiotic therapy.

There are fewer cases of deep wound and organ/space infections found in this study, which is similar to findings in studies from Tanzania, UK and in sub-Sahara African countries (24, 41, 100). These patients required surgical interventions, eight had relook laparotomies, out of which one had a subtotal hysterectomy with repair of bladder injury and prolonged catheterisation, and one had a total abdominal hysterectomy with left salpingo-oophorectomy for uterine atony after medical management and effort to conserve the uterus failed, and later require ICU admission and renal dialysis for acute kidney injury.

In this study, the incidence of acute severe maternal morbidity (hysterectomy and oophorectomy, septic shock, multiple organ dysfunction and ICU/HCA admission) is moderate at 7.2%, which is lower compared to 12.2% of incidence of severe maternal morbidity found in a similar study in Cape Town, South Africa (96). There were no maternal mortalities due to post C/S wound infection in this study. However, in the 2011-2013 Saving Mothers Report of the National Committee for Confidential Enquiries into Maternal Deaths, C/S-related maternal deaths were evaluated, and post C/S sepsis was recognised as a contributor to maternal deaths. Other contributors include C/S-related haemorrhage, anaesthetic death, death due to hypertensive disorders, and acute collapse and embolism post C/S (48). In the 2014-2016 triennial report, 201 deaths were attributed to pregnancy related sepsis, out of which 85 (42.2%) resulted from post C/S sepsis and the post C/S deaths make out 9.52% of the total mortality (49).

6.4. Microbial pattern in this study- Objective IV

The microbial isolates found in this study are diverse and reflect organisms that are part of skin and vaginal flora. Isolated organisms include Gram-positive bacteria, like Staphylococcus aureus, Streptococcus agalactiae, Methicillin Resistance Staphylococcus aureus (MRSA), and coagulase negative staphylococcus aureus. Gram-negative bacteria include Enterobacter species, Enterococcus faecalis, Pseudomonas aeruginosa, Acinetobacter baumannii, Escherichia coli, and others like Bacillus spp and Trichomonas vaginalis. Studies from Tanzania, UK and Nigeria reflect a similar pattern of microbiology (24, 41, and 102). However, while almost all these studies isolated Klebsiella, and Proteus, these two organisms were not found in this study, but rather found Prevotella bivia and Peptostreptococcus, that were not found in other studies. The predominant organism is Staphylococcus aureus, (MSSA) representing 20%. This correlate with several other studies where Staphylococcus aureus is the most commonly isolated organism with percentages ranging from 31.8% in Kano, Nigeria (101), 33.4% in England, UK, (41) to 40% in Cape Town, South Africa (96).

The next most prevalent group of organisms isolated in this study were Escherichia coli and Enterococci faecalis, each representing 10%, followed by Streptococcus agalactiae (Group B streptococcus) and MRSA and Enterobacter species, which each account for 6.7%. The South African study from Cape Town and a Tanzanian study both reported a higher percentage of 12.1%, and 16.7% respectively for MRSA (96, 24). The MRSA was sensitive to vancomycin. While a study from Abakaliki, Nigeria reported 11.1% for Enterococcus spp, which is very close to the finding in this study (28), a Tanzanian study found a lower incidence of 4.5% for Enterobacter species (24). A higher incidence of 13.6% was found for Escherichia coli in Kano, Nigeria (102) and by Mpogoro *et al*. in Mwanza, Tanzania (24).

The least prevalent organisms in this study were Acinetobacter baumanni, Clostridium species, and coagulase negative Staphylococcus aureus, Bacillus species, Pseudomonas aeruginosa, Prevotella bivia, Peptostreptococcus and Trichomonas vaginalis, each representing 3.3%. A Tanzanian study found a higher incidence of 9.1% for Acinetobacter species (24). A polymicrobial isolate was found in 10% of the cultures in this study, however a higher percentage of 16.7% was found for polymicrobial isolates in Cape Town, South Africa (96). The specific organisms found in the polymicrobial isolates in this study

were not identified on the National Health Laboratory Service website; it was simply described as mixed growth. Similarly, the Cape Town, South African study (96), did not specify the organisms found in the polymicrobial isolates, it was simply described as multiple organisms.

The numbers however are small making it difficult to comment on the dominant cause of sepsis. Suffice to say that there is a wide range of potential pathogens involved in sepsis.

6.5. Antibiotic usage – Objective v

In this study, 91.7% of the participants received prophylactic antibiotics approximately one hour before skin incision. The records of prophylactic antibiotic use in the other 8.3% of patients could not be found due to poor documentation. Among those who received prophylactic antibiotics, 58% got 2g cefazolin IV, and 42% received 1.2g amoxicillin-clavullanic acid combination IV. The decision on which antibiotic to give was made by the anaesthetic team. Evidence shows that outcomes in using either antibiotic is similar, as shown in a 2014 Cochrane review, which investigated different classes of antibiotics routinely given to women for preventing infections at C/S (106). It reviewed evidence and compared cephalosporins with penicillin in terms of maternal sepsis, maternal endometritis, maternal wound infections, maternal urinary tract infection, and maternal composite adverse effect, and found that there is no overall difference between these classes of antibiotics in reducing maternal infections after C/S (106).

The use of antibiotics for post C/S wound infections in this study follows the recommendations of Wits University Guidelines for Obstetrics Care 2017 (70), which recommends initiation of therapy with an empirical broad-spectrum antibiotics. The guideline recommends that antibiotics should be given within one hour of presentation, after taking blood for culture, and a triple regimen of ampicillin 1-2g IV six hourly, gentamycin 240mg IV daily and metronidazole 400mg orally eight hourly or broad-spectrum alternatives are prescribed (70). The guidelines further recommend for antibiotic therapy to be changed later in accordance with the microbiology sensitivity pattern. However, in this study, culture samples were only taken in 75% of the participants, and the one-hour timeline was not strictly adhered to. Thirty participants received empirical broad-

spectrum antibiotics (19 on triple antibiotic regimen and 11 on co-amoxiclav-based broad-spectrum antibiotics) and six participants received a narrow spectrum antibiotic.

All 30 patient on broad spectrum antibiotics responded well and had no change of antibiotics, except for one whose antibiotics was escalated to ceftriaxone and clindamycin, as second line empirical antibiotics when the patient had two relook laparotomies in consideration of the extensive nature of her surgery. All 30 patients were discharged home on oral empirical antibiotics.

Six patients had narrow spectrum antibiotics out of which, three were empirical, this included cloxacillin for two participants with superficial wound sepsis, and azithromycin for a patient who had a history of penicillin allergy. Two participants received targeted antibiotics, and only one participant had to change antibiotics from cephalexin to a piperacillin/tazobactam combination due to culture and sensitivity results and poor clinical response.

The use of antibiotics in this study also complies with the principles for rational antibiotic prescription as recommended by the South African Antibiotic Stewardship Programme (SAASP) (71). South African Antibiotic Stewardship Programme recommend appropriate empiric antibiotics that will target the most likely pathogens. For skin and soft tissue and intra-abdominal site of infections, it recommends that antibiotic choices must cover for Gram-positive, Gram-negative and anaerobes (71). In this study, ampicillin, a beta-lactam (b-lactam) antibiotic, gentamycin, an aminoglycoside, metronidazole, an imidazole, and co-amoxiclav-based broad-spectrum antibiotics, effectively combined, provided coverage for Gram-positive, Gram-negative and anaerobic organisms. The spectrum of microbes covered by this triple regimen is broad, as it covers for almost all microbes isolated in this study, except in six patients who received narrow spectrum antibiotics, either empirically or by targeted therapy.

The SAASP recommends that the likelihood of antibiotic resistance is to be assessed (71). The combinations of empirical ampicillin/gentamycin and metronidazole, or co-amoxiclav based combination therapy, proved largely effective in this study. We had a change of antibiotics in one participant only, from triple regimen to empirical ceftriaxone and clindamycin as in patients who had two relooks laparotomies, considering the extensive nature of the surgery. Among the six patients on narrow spectrum antibiotics, there was only one antibiotic change from cephalexin to piperacillin/tazobactam due to culture and

sensitivity results. There are other possible choices of broad-spectrum antibiotics, which include b-lactam/b-lactamase combinations, like piperacillin-tazobactam, quinolones, carbapenems and 3rd generation cephalosporin in severely ill patients (107). These have been shown to be equally effective, but are more likely to lead to selection of resistant organisms, including mycotic organisms. Cephalosporin and quinolones have a high propensity to cause emergence of clostridium difficile compared to other narrow spectrum antibiotics. (107). A 2011 Indian study on antibiotic sensitivity profiles of bacterial pathogens in postoperative wound infections, also found an undesirable trend of microbial resistance to antibiotic classes such as cephalosporin, fluroquinolones, carbapenems and extended spectrum beta lactamase inhibitors (108). Similarly, a 2011 American study that investigated antibiotics for Gram-positive bacterial infections concluded that Gram-positive bacteria have shown a tendency to develop resistance to all available antibiotics in use, and that superiority data of one agent over the other is lacking except for linezolid when used in the treatment of MRSA infection (109). However, determining the microbial resistance to antibiotics was not part of the study objective.

According to the SAASP principle of rational antibiotic prescription, the choice of antibiotics must show adequate target tissue penetration (71). Ampicillin/penicillin is shown to have good soft tissue perfusion while gentamycin has good genito-urinary tissue penetration only if the glomerular filtration rate is normal (71).

On the antibiotic side effects profile, the participants in this study were not monitored for side effects, however, known side effects of penicillin such as anaphylactic reactions, and that of aminoglycosides such as ototoxicity and nephrotoxicity were not documented in participant's records.

Antibiotic use in this study is guided by Wits University Obstetric Care Protocol and complies with the SAASP guidelines (70, 71).

7. CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS.

7.1. Conclusions.

During the period covered in of this retrospective study, 2 745 C/S were performed, 80 represented with features of wound infections, of which 36 were readmitted. Of the admitted cases, 50% had superficial wound sepsis while 7.2% suffered acute severe maternal morbidity, which included hysterectomy and oophorectomy, HCA/ICU admissions and renal dialysis for acute kidney disease. One of the patients, who had a hysterectomy, also had a repair of a bladder injury. She had a bladder injury that was not noticed during C/S. There were no maternal mortalities in this study. The length of hospital stay on readmission ranged from one to 22 days, with 29 out of 36 patients only staying for a period of one to ten days.

In this study, intrapartum events like prolonged labour and the number of vaginal examinations played a role in post C/S wound infections. Staphylococcus aureus was the most common microbial isolate. Empirical broad-spectrum antibiotics is shown to be an effective approach in the management of post C/S wound infections, however there is a global emerging trend of microbial resistance to antibiotics.

Strategies for prevention for post C/S wound infection must include focus on intrapartum events, labour monitoring, accurate documentation of the timeline of progress of labour, and training to enhance the skills of the surgeons.

7.2. Limitations.

The limitations of the study are the following:

- This study is greatly limited by poor record filing since many files cannot be found and some patients left the hospital with their files, some returning to neighbouring countries. This challenge can be overcome by keeping records electronically.
- Cases of post C/S wound sepsis were not compared to controls, which would have effectively established associations between each risk factor and its contribution to the postoperative infectious morbidity. This would have produced data, which will be of value in determining relevant clinical interventions.
- The number of participants is small and the study is only retrospective.

- There is the possibility of observer's bias when identifying post C/S wound infections, as these cases may be underreported, making these findings less accurate.
- There is a possibility that some/many post C/S wound infections may have presented elsewhere, i.e. other than at RMMCH and as such, they could not be added into this study.

7.3. Recommendations for further studies

A well designed, high powered, multicentre prospective study is be needed, where cases will be matched with control, and univariate and multivariate analysis will be done to determine the association between the risk factors and the development of post C/S wound infections. Further studies are needed to determine the emerging pattern of microbial resistance to antibiotics.

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APPENDIX

CEO Letter

Ethics signed letter

Anti-plagiarism certificate

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

R14/49 Dr AV Temenu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180112

NAME: (Principal Investigator)	Dr AV Temenu
DEPARTMENT:	School of Clinical Medicine Department of Obstetrics and Gynaecology Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	Post caesarean section wound infections at Rahima Moosa Mother and Child Hospital
DATE CONSIDERED:	26/01/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr AJ Wise
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	14/03/2018

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, Phillip 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 initially reviewed in **January** and will therefore be due in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr AV Temenu
School of Clinical Medicine
Department of Obstetrics and Gynaecology
Rahima Moosa Mother and Child Hospital

E-mail: debotemenu@yahoo.com

CC: Supervisor: Dr AJ Wise <amyjulietwise@yahoo.co.uk>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 14/03/2018

REF: *R14/49*

PROTOCOL NO: **M180112** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Post caesarean section wound infections at Rahima Moosa Mother and Child Hospital*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

Enquiries : Karen Marshall
Tel : (011) 470 9284
Fax : 086 553 4623
Email : Karen.Marshall@wits.ac.za

Department of Obstetrics and Gynaecology
University of the Witwatersrand

Dear Dr. Temenu,

RE: POST CAESAREAN SECTION WOUND INFECTIONS AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

Permission is granted for you to conduct the research as indicated in the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you have signed. Failure to comply with these conditions will result in the withdrawal of such permission.

It is crucial for you to inform the Research Coordinator, Karen Marshall of the actual start and end dates of your study. This could be done by e-mail.

Should the study commence more than 12 months after receipt of this approval letter you will have to go through the process of applying again.

You are strongly advised to keep a signed copy of the declaration form so as to ensure that the terms of this agreement are complied with at all times.

Yours sincerely,

DR F BENSON
CLINICAL EXECUTIVE
2018:02:20

ADDRESS: Cnr. FUEL & OUDSTHOORN STREET CORONATIONVILLE 2093 / PRIVATE BAG X20 NEWCLARE 2112 JHB

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