

CHAPTER 1: INTRODUCTION

1.1 GENERAL INTRODUCTION

There are three major academic hospitals affiliated with the University of the Witwatersrand, namely Chris Hani Baragwanath Academic Hospital (CHBAH); CMJAH and Helen Joseph Hospital (HJH). Each hospital has its own approach in the management of *H.pylori* associated PUD. CHBAH and HJH do not routinely test for the presence of *H.pylori* infection in patients with PUD. On the contrary, CMJAH routinely tests for the presence of *H.pylori* infection in patients with PUD and treat it accordingly. After taking note of the differences in the management approach with regards to *H.pylori* infection in patients with PUD among these hospitals, a need arose to try and standardize this approach to patient management in Johannesburg. The focus of this research was centred on CMJAH which was the only hospital out of the three, which still confirmed the presence of *H.pylori* infection prior to treatment in patients with PUD. The study was aimed at determining if empiric eradication therapy for *H.pylori* (i.e. eradication without confirming the presence of infection through diagnostic tests) was justified in patients with PUD at CMJAH.

1.2 LITERATURE REVIEW

1.2.1 Peptic Ulcer Disease

Peptic ulcers are defects in the mucosa of the gastro-intestinal tract. By definition they extend through the muscularis mucosae. Typically they develop in the stomach (i.e. gastric ulcers) and in the proximal duodenum (i.e. duodenal ulcers) (1). PUD is estimated to affect 4 million people worldwide annually; with an incidence rate of 1.5 – 3%. They may be complicated or uncomplicated. The three major complications include bleeding, perforation and obstruction.

These present as acute surgical emergencies. Ten to twenty percent of patients with PUD will have complications; of these 2-14% will be perforated ulcers (2, 3).

The uncomplicated PUs present with pain typically in the epigastrium which is often relieved by meals or alkali. The symptoms are usually periodic i.e. they occur, wane and recur (3, 4). The incidence rate (IR) of uncomplicated PUD was found to be in the order of one case per 1000 person-years in the general population, based on a systematic review of studies published over the last three decades (5). Direct epidemiologic comparisons between developed and developing countries are difficult, due to the differences that exist in the availability and accessibility of the diagnostic tests (6).

PUD develops when there is an imbalance between the mucosal defence barriers i.e. mucous and bicarbonate secretion and the damaging effects of gastric acid and pepsin. The protective barriers become overwhelmed by the toxic effects of gastric acid and pepsin (2, 7). The major risk factors for PUD include *H.pylori* infection; NSAIDs; smoking; corticosteroids, previous history of PUD and physiological stress. Other risk factors include excessive alcohol intake and excessive acid secretion by a gastrin secreting tumour i.e. gastrinoma in Zollinger-Ellison Syndrome (2, 28).

1.2.2 *Helicobacter pylori* infection

1.2.2.1 History of *H. pylori* organism

Helicobacter pylori is a gram-negative, microaerophilic curved bacillus. It was first reported in 1875 by Bottcher and Letulle when they observed it in the margins of peptic ulcers. However it was not reproducible in vitro and this accidental discovery did not receive much attention. Then in the 1980s, more information about this organism was discovered. It was successfully cultured in Perth Australia in 1982. A pathologist by the name of Robin Warren and his colleague Barry Marshall isolated *H.pylori* from human gastric mucosal biopsy

specimens of patients with histologic gastritis and were able to culture it in artificial nutrient media. Initially it was named *Campylobacter pylori* (*C.pylori*). However due to its unique characteristics e.g. its potent urease activity, it was later re-named *H.pylori*. The urease is a cell-surface nickel-containing enzyme that catalyzes the hydrolysis of urea to ammonia and carbon dioxide. The ammonia neutralizes the gastric acid, making it an optimum environment for the *H.pylori* organism to survive and infect the gastric mucosa. Therefore this *H.pylori* associated urease activity has significant pathogenic implications and most *H.pylori* diagnostic tests are based on it (8, 9).

Warren and Marshall further suggested that most GUs and gastritis could be associated with this organism. To support this ground breaking discovery, in 1983 Marshall demonstrated the role of *H.pylori* infection in the pathogenesis of GIT diseases, particularly antral gastritis by drinking a culture of the bacterium. Subsequently he developed *H.pylori* associated antral gastritis. Since then, *H.pylori* has been the focus of much research. Further developments demonstrated its role in the pathogenesis of DUs and duodenitis. In 2005, Warren and Marshall were acknowledged for the discovery of *H.pylori* pathogenicity by being awarded the Nobel Prize in Physiology or Medicine (9).

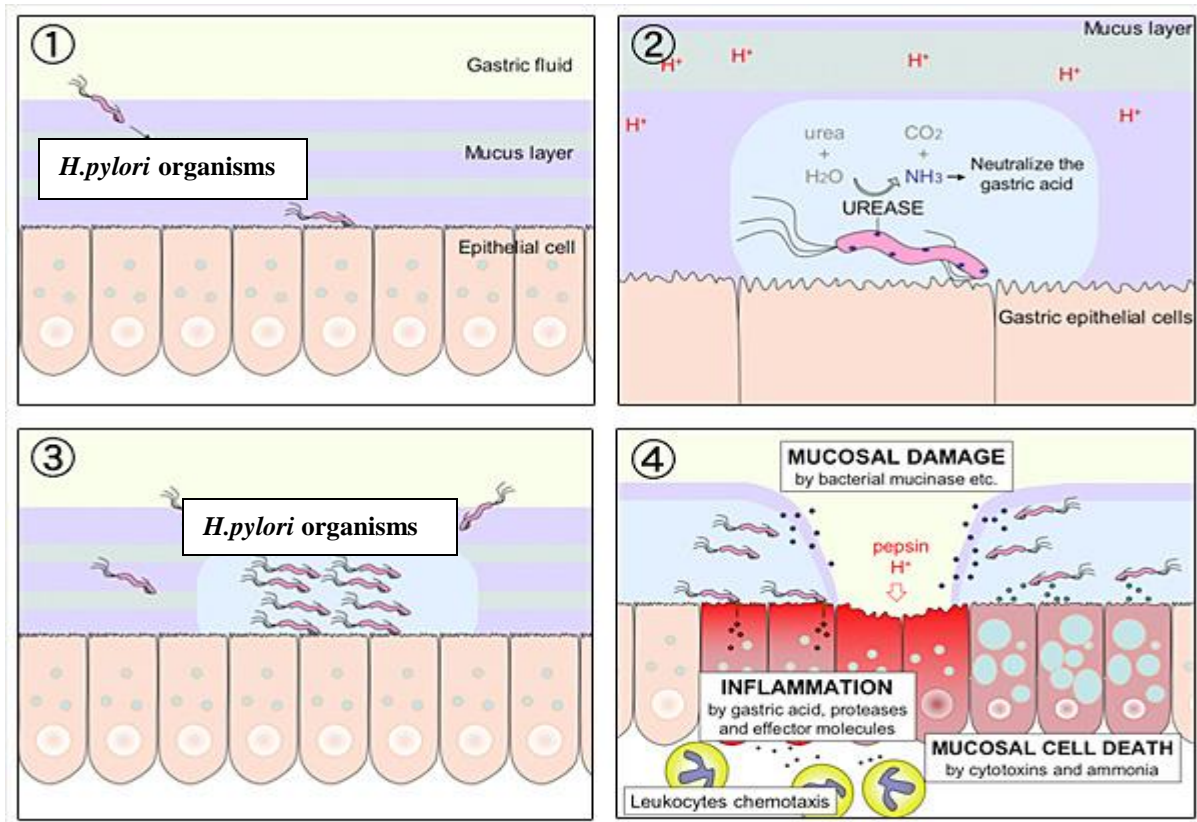


Figure 1.1: *Helicobacter pylori* pathogenesis overview.

Adapted from:

(https://www.google.co.za/search?q=Helicobacter+pylori+pathogenesis+overview&dcr=0&source=lnms&tbn=isch&sa=X&ved=0ahUKEwjolZuDvPrXAhWnIMAKHXO7CWsQ_AUICigB&biw=1264&bih=635#imgrc=cEgrUDL9sq3aSM:&spf=1512737958608);

Accessed on 08/12/2017

1.2.2.2 Epidemiology of *H.pylori* infection

H.pylori infection is found in approximately 50% of the world's population (9). It affects more than 4 billion people in the world (10). Its prevalence varies in relation to geography, socioeconomic status, age, and gender. It is generally higher in developing countries, with the prevalence ranging between 70 to 90% and lower in developed countries with a prevalence of 35 to 40%. The colonization of gastric mucosa by *H.pylori* occurs early in life, usually before the age of 10 years and will persist for life in the absence of antibiotics. This is usually the case, particularly in developing countries. Generally, its seropositivity rates increase progressively with age worldwide (6,8,9).

The transmission of *H.pylori* is thought to be from person-person, largely via the oral-oral or faecal-oral routes. Factors such as poor hygiene, inadequate sanitation, lack of safe drinking water, inappropriate diets and overcrowding, allow its prevalence to vary within areas of different countries, particularly between the affluent urban and rural populations. In terms of gender, there have been reported low occurrences of *H.pylori* infection among females in developing countries that is thought to be due to the frequent use of antibiotics by this group for gynaecological conditions. Thus far, race has not been proven to influence infection by *H.pylori* (6,8,11).

On the contrary, a local study done in 2008 in the Eastern Cape (one of the rural areas in SA) revealed a different observation with regards to race and gender. They found a higher prevalence of *H.pylori* infection among the coloured population (68.4%), followed by blacks (65.8%) and then the white population (59.5%). With regards to gender, the females had a higher prevalence of *H.pylori* infection (69.5%) compared to the 60.0% found in males. However the female: male ratio in this study favoured the females with 1.8:1. In addition all these results that associated *H.pylori* infection with the demographic features i.e. race and gender, were not statistically significant ($p>0.05$) (12).

1.2.2.3 Diseases associated with *H.pylori* infection

There are multiple strains of *H.pylori* which differ in terms of their virulence. This together with the interaction, with the host and environmental factors, lead to different disease patterns caused by this organism. These include chronic gastritis, which can be atrophic or non-atrophic, PUD, *H. pylori* associated dyspepsia, gastric cancer and gastric MALToma (4, 9, 13). Despite its UGIT disease manifestations most of the people infected are asymptomatic carriers, only a minority of the people are symptomatic (6, 4, 9, 10, 13, 14, 15).

- ***Helicobacter pylori* associated dyspepsia and gastritis**

According to the Rome III consensus, the definition of functional dyspepsia include the presence of chronic dyspeptic symptoms such as postprandial fullness, early satiety, epigastric burning sensation or pain, in the absence of any structural abnormality i.e. normal investigations. Furthermore there is a subset of patients with dyspepsia who will respond to *H.pylori* eradication therapy and are able to sustain the relief of symptoms for six to twelve months. The recent Kyoto consensus meeting has labelled these patients as having organic dyspepsia secondary to *H.pylori* gastritis. This allows for *H.pylori* associated dyspepsia to be considered as a separate clinical entity. Furthermore, the Kyoto consensus proposed for the classification of gastritis to be based on its aetiology and concluded that *H.pylori* associated gastritis is an infectious disease that can have serious sequelae such as PUD and/or gastric cancer if left untreated (13).

- ***Helicobacter pylori* associated PUD and gastric cancer**

H.pylori tends to reside primarily in the portion of the gastric mucosa which has the highest pH. Under normal circumstances, its survival is virtually impossible in the body of the stomach. This is the area where the parietal cells secrete hydrochloric acid for transport into the lumen of the stomach. The pH in this area is less than 1. Therefore *H.pylori* infection

tends to be high in the portion of the stomach which does not secrete hydrochloric acid i.e. the antrum. It makes sense then that *H.pylori* associated gastritis is most severe in the antrum. It then progresses proximally into the portion of the stomach which secretes hydrochloric acid i.e. the body (4).

This progression marks the advancement of the transitional zone of the atrophic gastritis which forms a border to the normal epithelium of the body of the stomach. GUs tend to develop at this progressive atrophic area. Therefore, the site of the *H.pylori* associated GU gives information with regards to the extent and severity of the gastritis i.e. for GUs in the body of the stomach, there has to be associated gastritis in the body of the stomach as well (4).

On the contrary, DUs are associated with non-atrophic gastritis in the body of the stomach, with normal to high hydrochloric acid secretion. The same applies to Pre-pyloric ulcers. Under normal circumstances *H.pylori* is inhibited by bile. It therefore cannot cause infections in the duodenum. Low pH causes precipitation of glycine conjugated bile acids. When the acid secretion is adequate to lower the pH in the proximal duodenum, it results in metaplastic changes in the duodenum to gastric mucosa, allowing *H.pylori* to infect the duodenum causing inflammation and ulceration. Therefore the portion of the stomach which secretes hydrochloric acid i.e. the body should be normal or near normal in order for the DUs to develop. With regards to Gastric cancer, it is usually associated with pangastritis. The extent and severity of the gastritis increases the likelihood of developing gastric cancer (4).

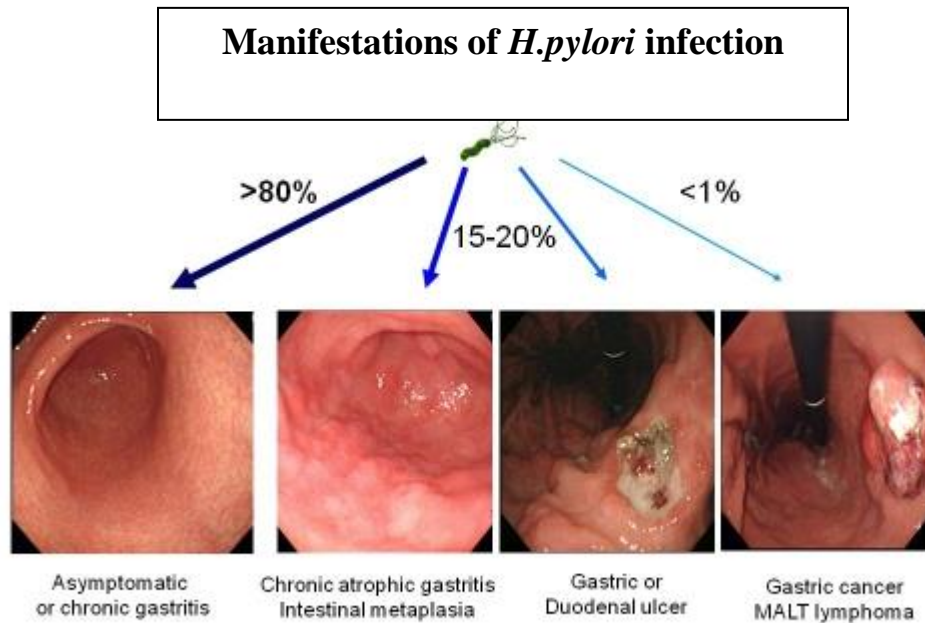


Figure 1.2: UGIT diseases associated with *H.pylori* infection

Adapted from:

(https://www.google.co.za/search?q=clinical+outcomes+of+helicobacter+pylori+infection&dcr=0&source=lnms&tbn=isch&sa=X&ved=0ahUKEwj9wOWku_rXAhUIJcAKHRs_qC4YQ_AUICigB&biw=1264&bih=635#imgrc=_35OpXd6655tM:&spf=1512737768358); Accessed on 08/12/201

1.2.2.4 Diagnostic tests for *H.pylori* infection

H.pylori infection can be detected by using non-invasive methods and invasive methods i.e. endoscopic biopsy of gastric mucosa. The two recommended non-invasive tests in clinical practice are the urea breath test (UBT) and the stool antigen test (SAT). The serological tests are also considered to be part of the non-invasive tests. However both the UBT and SAT are more accurate than the serological tests. The major downfall of serology with detection of

H.pylori antibodies is that it cannot differentiate between active infection and previous *H.pylori* exposure. There is an increased likelihood of false positive results with serological *H.pylori* antibody testing, because they can remain positive for a while after successful eradication of the organism. Therefore it is not recommended for routine clinical use (10).

The UBT is the best accepted non-invasive testing method for the diagnosis of *H.pylori* infection (10). It relies on the potent *H.pylori* urease activity in the stomach. It is based on the detection of C13/C14 labelled CO₂ in expired air as a result of the *H.pylori* urease activity (16). Its sensitivity and specificity rates are 94.7% and 95.7% respectively (16, 17). The SAT or stool antigen assay is an enzymatic immunoassay which detects *H.pylori* antigen in the stool specimen (16). The sensitivity of the SAT ranges from 89% to 98%, with a specificity of over 90% (18). It is imperative that therapy with PPIs and bismuth compounds/antibiotics be discontinued 2 weeks and 4 weeks respectively, before testing for *H.pylori* using the UBT and SAT. This is done to avoid false-negative results (10).

The invasive *H.pylori* tests include the rapid urease test (RUT), histology and culture. They all require endoscopic derived gastric mucosal biopsy specimen. Therefore in order for them to be performed, endoscopy should be indicated and there should be no contraindication for a biopsy to be performed. The RUT is the first-line diagnostic test in this category. It uses the urease activity of *H.pylori* to confirm its presence. The biopsy sample is tested for the increased pH using phenol red, which is found in *H.pylori* positive patients as a result of the urease activity of the bacteria. The sensitivity and specificity of the test ranges between 90-100%. It is recommended to take two biopsies when performing this test, one from the antrum and another one from the corpus of the stomach (10, 19).

Histology detects the presence of *H.pylori* infection through histochemical staining. There are a number of different histochemical stains that can be used e.g. Haematoxylin and Eosin (H and E) stain, Giemsa stain etc. The modified Giemsa stain has a sensitivity of 85% and

specificity of 89%. The detection of *H.pylori* organism on histology depends on its morphology. It is either identified or not identified on the surface epithelium (10, 20). When there is a low density of the bacteria, immunohistochemical staining e.g. using Immunoperoxidase stain, for *H.pylori* can be done to improve the histological assessment yield. This is expected in cases of chronic gastritis and atrophic gastritis or during follow-up after eradication therapy. This is supported by the European guidelines (10).

Culturing *H.pylori* organism is not that useful in the diagnosis of *H.pylori* infection in clinical practice. This is because of its prolonged incubation period which can take up to 2 weeks. Its role is in identifying potential antibiotic resistance and to identify an alternative treatment regimen after two failed eradication therapy attempts. This is done through antibiotic sensitivity testing for the antibiotics which are commonly used in the treatment of *H.pylori* infection. Another role in testing for the presence of *H.pylori* infection through culture is for the research purposes (10, 19).

1.2.3 Treatment of *Helicobacter pylori* infection

1.2.3.1 *H.pylori* eradication therapy

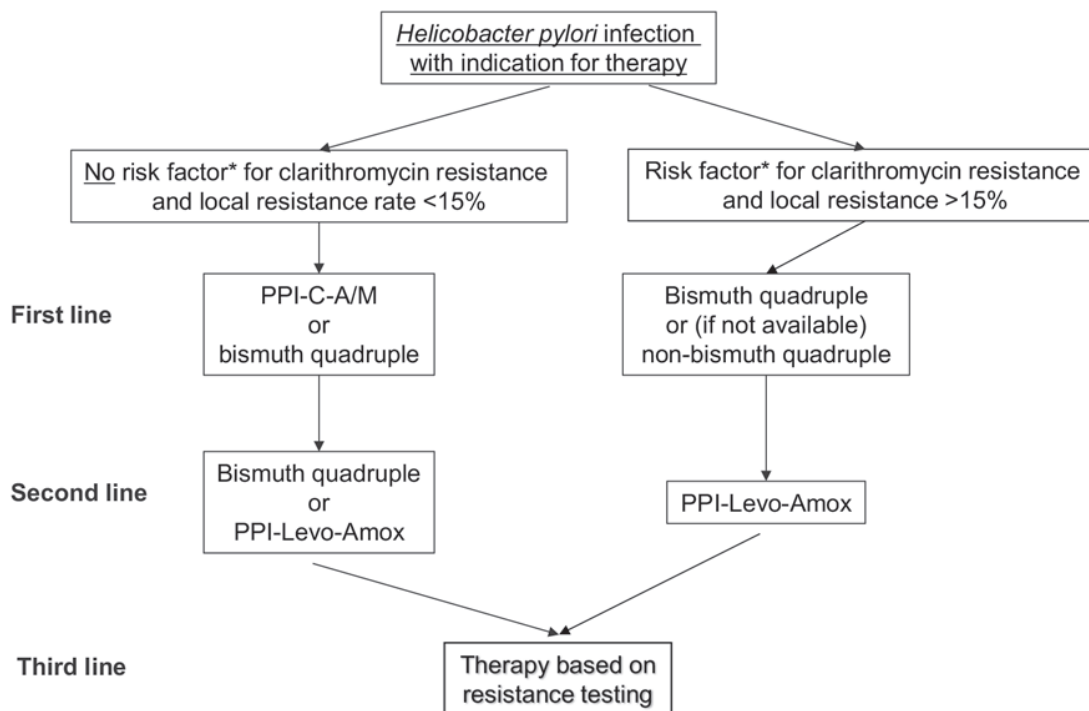


Figure 1.3: *H.pylori* treatment algorithm (10)

PPI-C-A/M: PPI: Proton Pump Inhibitor – C: Clarithromycin A:Amoxicillin/M:Metronidazole

PPI-Levo-Amox: PPI: Proton Pump Inhibitor - Levo: Levofloxacin - Amox: Amoxicillin

The aim of treating *H. pylori* infection is to eradicate the bacteria. The advantages of eradicating *H.pylori* are the prevention of the diseases associated it, potentially curing PUD and reducing the lifetime risk of gastric cancer, as well as decreasing its transmission rates. To achieve this, the ideal therapeutic regimen for *H.pylori* infection should reach eradication rates of equal to or above 80%. The choice of the therapeutic regimen is guided by the local antibiotic resistance rates to *H.pylori* (15, 21).

The 1st line therapy as decided upon by several consensus conferences include the triple therapy which consists of a proton pump inhibitor (PPI) and two antibiotics, amoxicillin and clarithromycin for 7 to 14 days. This therapeutic regimen can achieve eradication rates which range between 70% and 85%. The side effect profile associated with it includes GIT upset and diarrhoea. In addition clarithromycin causes an altered taste and amoxicillin is associated with headaches. Furthermore, there have been reports of an increase in gastro-oesophageal reflux disease (GORD) following *H.pylori* eradication therapy. However such reports have been disputed by the World Gastroenterology Organisation (WGO) Global Guidelines and the Maastricht III Consensus, which both state that “eradication therapy for *H.pylori* does not cause GORD” (6, 21, 22, 23).

The alternative 1st line therapy to triple therapy in areas with a high prevalence of clarithromycin resistance (>15%) is quadruple therapy, which consists of a PPI, bismuth, metronidazole and tetracycline for 10 to 14 days. This has been recommended by the Maastricht III and Maastricht IV consensus. Its eradication rates range between 75% and 90%. The side effects of this regimen are associated with the individual drugs; metronidazole causes a metallic taste in the mouth, dyspepsia and a disulfiram-like reaction with alcohol consumption. Tetracycline causes GI upset and photosensitivity. Bismuth compounds cause GI upset, nausea as well as darkening of the tongue and stools. Failure of this treatment regimen is usually attributed to the development of metronidazole resistance (21).

If the 1st line triple therapy fails in areas with a low prevalence of clarithromycin resistance, then the 2nd line therapy as recommended by the Maastricht IV consensus should include either a bismuth-containing quadruple therapy or a levofloxacin-containing triple therapy. There is level I evidence to suggest that the levofloxacin-based triple therapy is superior to bismuth-containing quadruple therapy as the second-line treatment. Furthermore it has fewer side effects and is better tolerated than the quadruple therapy regimen. In areas with a high prevalence of clarithromycin resistance, the levofloxacin-containing therapy is still

recommended as the 2nd line therapy in case of failure of the bismuth-containing quadruple therapy. Failure of the 2nd line therapy should prompt culture of *H.pylori* and performing antibiotic susceptibility testing (21).

1.2.3.2 Indications for *H.pylori* eradication therapy

H.pylori eradication therapy is indicated in cases of *H.pylori* associated gastritis. This was the recommendation at the Kyoto global consensus in 2015, which recognized *H.pylori* gastritis as an infectious disease. The rationale behind treating *H.pylori* gastritis was the fact that the clinical course of *H.pylori* infection is unpredictable. It can be uncomplicated and asymptomatic or symptomatic with severe complications such as gastric cancer. In addition if left untreated, there is a high risk of transmission to other individuals, increasing the prevalence of the infection as well as the costs incurred in treating *H.pylori* associated complications. Eradication of *H.pylori* is therefore indicated in the following conditions (10);

- GU/DU, whether it is active or not and includes complicated PUD.
- Atrophic gastritis
- After the resection of gastric cancer
- First-degree relatives of patients with gastric cancer
- Gastric MALToma and diffuse large B-cell lymphoma
- Lymphocytic gastritis
- *H.pylori* test and treat in case of unconfirmed dyspepsia
- *H.pylori* test and treat in case of unexplained iron deficiency anaemia
- *H.pylori* test and treat in case of idiopathic thrombocytopenic purpura
- Before long-term use of aspirin and non-steroidal anti-inflammatory drugs in patients with ulcer history.

1.2.3.3 Approach to *H.pylori* eradication therapy

The efficacy of *H.pylori* eradication therapy has been proven. The controversy is whether or not should its presence be confirmed through diagnostic tests prior to eradicating it. In uninvestigated dyspepsia, the guidelines suggests that the test and treat strategy should be employed. However in PUD, there is no consensus between confirming the presence of *H.pylori* infection prior to eradicating it or treating it empirically. Empiric eradication therapy is defined as administering triple therapy or quadruple therapy without confirming the presence of *H.pylori* infection through diagnostic tests. In one study, its cost-effectiveness was compared to the performance of *H.pylori* diagnostic tests prior to treatment, in patients with a previously diagnosed uncomplicated DU. The empiric eradication therapy was subsequently found to be more cost-effective (13, 22, 24).

Likewise, another study looked at the cost-effectiveness of this empiric *H.pylori* eradication in a group of asymptomatic patients known with PUD, currently on maintenance anti-secretory treatment. They found that immediate empiric eradication therapy with cessation of anti-secretory treatment resulted in fewer ulcers and less ulcer symptoms at a lower cost, as opposed to reserving it only for symptom relapse while still continuing with anti-secretory treatment (25).

Furthermore, it has been suggested that empiric eradication therapy for *H.pylori* may be acceptable if there is a high prevalence of this infection in the area and if DUs are invariably associated with *H.pylori* infection. This is due to the fact that the diagnostic tests done for confirming *H.pylori* infection are not without shortcomings. They may be falsely negative and result in untreated chronic *H.pylori* infection. Also, there is an inverse relationship between the prevalence of *H.pylori* infection in patients with DUs and the negative predictive value of a negative diagnostic result, even in tests with up to 95% sensitivity and specificity (26).

Therefore, the question arises as to whether or not empiric eradication therapy for *H.pylori* associated PUD is applicable in Africa? *H.pylori* infection has been found to be the most common bacterial infection in the African continent, with a prevalence of up to 88% (27). It is documented that in Africa, *H.pylori* infection is the main cause of at least 90% of DUs and 70% of GUs (12). A study done in the United States of America immigrants from East Africa found the prevalence of *H.pylori* infection to be 93% (95% CI = 86%-100%). The empiric eradication therapy in symptomatic patients showed a lower cost per patient, compared to testing and treating only confirmed cases (29). Based on this, empiric eradication therapy for *H.pylori* associated PUD should be justified in Africa.

However there is the concept of the African Enigma, which “postulated that in Africa *H.pylori* was common but it was rarely associated with PUD or gastric cancer” (4). There have been many theories to explain why the concept of the African Enigma existed. One of which has been attributed to insufficient data due to lack of availability and accessibility of resources that existed in Africa at the time, which under-estimated the prevalence of *H.pylori* associated UGIT diseases. Nonetheless, subsequent studies contradicted the concept of the African Enigma by showing a high prevalence of UGI diseases in Africa. Hence, this concept has subsequently been rejected (30).

In South Africa (SA), Tanih et al (12) found an overall *H.pylori* prevalence of 66% when looking at the prevalence of *H.pylori* infection in dyspeptic patients in Port Elizabeth, Eastern Cape. Louw et al (27), found an overall incidence of *H.pylori* infection to be 88% in patients with GUs and 98% in patients with DUs in Cape Town. In addition, Pelsler et al (31), demonstrated that most of the *H.pylori* infection is acquired early in life, with a prevalence of 48.5% by the age of 5 years. They went on to show a steady increase in the prevalence of *H.pylori* infection with age, with the highest prevalence of the infection, 84.2% (95% CI 77 – 91.3%) found in the 10 to 15years age group.

We can therefore extrapolate from the evidence provided by these previous studies, that the prevalence of *H.pylori* infection is high in SA, *H.pylori* infection is acquired early in life with an increase in prevalence into adolescence and adulthood, and most PUD are *H.pylori* associated.

1.3 MOTIVATION FOR THE STUDY

There is currently no recent data on the prevalence of *H.pylori* infection in Johannesburg, Gauteng. As noted at the beginning of this Chapter, the treatment approach to *H.pylori* infection in PUD is currently not standardized among the hospitals affiliated with the University of the Witwatersrand. This led to the need to conduct this study aimed at determining whether or not empiric eradication therapy for *H.pylori* is justified in patients with PUD at CMJAH.

CHAPTER 2: METHODOLOGY

This chapter describes the methods and materials used in collecting the data necessary to answer the study objectives and ultimately the research question.

2.1 AIM OF THE STUDY

To determine if empiric eradication therapy for *H.pylori* is justified in patients with PUD at CMJAH.

2.2 STUDY OBJECTIVES

- 2.2.1** To determine the prevalence of PUD and the commonest site of PUs in patients undergoing OGD at CMJAH.
- 2.2.2** To determine the prevalence of *H. pylori* infection in all patients undergoing OGD and in patients with PUD at CMJAH.
- 2.2.3** To determine the association between *H.pylori* infection and the site of PUs, as well as patient demographics at CMJAH.
- 2.2.4** To estimate the costs incurred through testing for *H.pylori* at CMJAH.

2.3 STUDY HYPOTHESIS

There is a high prevalence of *H.pylori* infection in patients with PUD at CMJAH. Routine testing for *H.pylori* infection is not without major health care costs. Therefore, empiric *H.pylori* eradication therapy is justified in patients with PUD at CMJAH.

2.4 SETTING AND SCOPE OF THE STUDY

The study was conducted in Johannesburg in the Gauteng province of South Africa, at one of the academic hospitals affiliated with the University of the Witwatersrand, CMJAH. The specific site of the study was the GES. It was conducted over a period of three months, between the 1st of October and the 31st of December of 2012. It was a retrospective record review of prospectively collected data on the endoscopy reports of the patients who had OGD for UGIT symptoms done at the time of the study. In addition we reviewed the histology results of the gastric mucosal biopsy specimens which were taken at the time of OGD for histological assessment and to test for *H.pylori* infection.

2.5 SELECTION OF STUDY SUBJECTS

The study included all the surgical patients who had their OGDs done at CMJAH, at the time of the study. This included patients who had their OGDs done in Theatre, Intensive Care Units (ICUs) and at the GES. We used convenience sampling to select the sub-group of patients who had their OGDs done at the GES as the study sample. It was a more controlled environment, the procedures were supervised by either a Gastroenterology fellow or specialist. All the patients were haemodynamically stable with UGIT symptoms, referred for OGD from either the surgical outpatients' department, the emergency department or admitted in the surgical wards. Testing for *H. pylori* was done when there was an abnormal or positive finding on OGD e.g. gastritis. Furthermore, there was an established system in place for data capturing of the OGD reports and gastric mucosal biopsy specimens.

Our exclusion criteria was patients with a previous history of gastric surgery; where there was distortion of the anatomy that could influence the OGD findings e.g. a Billroth I/II procedure; patients with confirmed or suspicion of malignancy (both oesophageal and gastric); patients where the procedure had to be abandoned or was incomplete and/or inadequate due to various reasons e.g. patient not fully prepared for the investigation; as well as patients with only oesophageal pathology.

2.6 SAMPLE SIZE

Prior to conducting the study, a formula-based sample size of **443** was calculated using the formula for the percentage estimation in the population (i.e. $n=15.5 * p * q / d^2$; where p =expected % according to previous studies, d =difference between expected and observed %, for $\alpha=0.05$ and $q=1-p$). The percentage estimation for the prevalence of *H.pylori* infection in the study population was used to calculate this sample size, since it was the main outcome variable required to answer the research question. An estimation of 85% was used as the observed % in this study population to give a value of $d=0.055$. However due to unforeseen circumstances which will be discussed in Chapter 4 of this research report, a sample size (n) of 196 was obtained, following the screening of all the potential study subjects and after excluding those ineligible to participate in the study.

2.7 DATA COLLECTION

Briefly, the process of performing the OGDs was as follows; the clinician managing the inpatients (i.e. from emergency department or surgical wards) would first discuss the indication for requesting the investigation with the endoscopist; who would then triage the patients and give appointments for OGDs accordingly. The outpatients referred from SOPD were booked by the administrator at the GES and given dates according to their requesting forms from their clinicians and availability.

2.7.1 OGD procedure and biopsy sampling

The OGD procedure was performed using Xylocaine local anaesthetic with sedation using intravenous Midazolam. During the procedure whenever there was an abnormal finding seen, particularly in the stomach, pylorus or duodenum (e.g. inflammation or ulceration), biopsies were taken to confirm the diagnosis initially made by the endoscopist, through histological assessment and to test for *H.pylori*.

2.7.2 Testing for *Helicobacter pylori*

A rapid urease test (RUT) was initially done to test for *H.pylori* and another specimen was submitted to the National Health Laboratory Service (NHLS) for histological confirmation of *H.pylori* using routine stains e.g. haematoxylin and eosin (H&E) stain. In cases with low densities of *H.pylori* infection and/or where there was diagnostic uncertainty, immunohistochemistry using special stains e.g. Immunoperoxidase was performed.

2.7.3 Data recording

Once the procedure was completed, the endoscopist would record the patient's demographics (i.e. age and gender), the indication for the OGD, the findings and indicate whether or not biopsy sampling was done in a formal OGD report with two copies attached to it. In cases where the biopsy sampling was done, the RUT was initially done and attached to the second copy of the OGD report that went with the patient's file for interpretation of results by clinicians. The biopsy specimens were then preserved in formalin and submitted to NHLS for histological assessment. The sticker with the bar code to trace the histology results was attached to all the three copies of the OGD reports. The remaining two copies were filed in the GES for data capturing. We reviewed one set of these copies retrospectively in this study. A data collection sheet was used as a tool to collect the data required for the study. It included the following variables: (*appendix 1*)

- The patient's demographics: age and gender.
- The endoscopist's findings on OGD.
- The site of PU where ulceration was present.
- Whether or not *H.pylori* testing was done: yes or no.
- *H.pylori* results, where applicable: positive or negative.

We obtained the *H.pylori* results by tracing the histological assessment results of the biopsy specimens, which were submitted to NHLS. From these we also collected the pathological diagnosis and added it as a separate variable.

2.8 DATA ANALYSIS

The data collected was computerized using Microsoft Excel program. It was then analyzed using Strata version 13.1. Categorical variables were described using frequencies and percentages, whilst the mean and standard deviation were used to summarize numerical variables. The study variables were compared to the main outcome variable i.e. the *H.pylori* status of the study participants. The Chi square and Fisher exact tests were performed to determine if there were any statistically significant associations between the variables. We accepted a p-value of <0.05 as being statistically significant. Tables and illustrations were used to display the study findings.

2.9 ETHICS

The permission to conduct the study was granted by the University of the Witwatersrand's Human Research Ethics Committee (HREC) on the 28th of June 2013 (see clearance certificate with number M130668 in *appendix 2*). The clinical executive officer (CEO) at CMJAH also gave us the permission to conduct the study on the 25th of July 2013 (see the letter of approval by the CEO of CMJAH in *appendix 3*). The Head of Department (HOD) at the GES (Area 554), which was the site of the study, gave us the permission to conduct the study in his unit (*appendix 4*). Once the approval to conduct the study had been received from all parties, we commenced with the study.

2.10 FUNDING

Only administrative costs such as printing of histology results and data collection sheets as well as photocopying were incurred during this study. These were covered by the principal researcher.

CHAPTER 3: RESULTS

The research question that led us to conduct this study was whether empiric eradication therapy for *H.pylori* in patients with PUD was justified at CMJAH. To be able to answer this question we had to determine the overall prevalence of *H.pylori* infection in patients who presented with UGIT symptoms and particularly in patients with PUD, who underwent OGD at CMJAH at the time of the study. This was based on the previous literature which had shown that empiric *H.pylori* eradication may be acceptable if there is a high prevalence of *H.pylori* infection in the area, and if DUs are invariably associated with *H.pylori* infection (26).

We screened a total of 311 OGD reports of patients who presented with UGIT symptoms and had undergone OGD at the GES, at CMJAH at the time of the study. Of these 285 (91.6%) were diagnostic OGDs, whilst 26 (8.4%) were interventional e.g. insertion of PEG. The interventional OGDs were not considered for this study. Of the 285 diagnostic OGDs, 89 (31.2%) were excluded as they met the exclusion criteria of the study. In this group there were patients with a history of previous gastric surgery, patients suspected or confirmed to have a malignancy, patients where the OGD could not be completed due to various reasons and lastly a subgroup of patients who only had oesophageal pathology on OGD. Ultimately a total of 196 cases (68.7%) were included in the study and statistical analysis was performed.

3.1 DEMOGRAPHIC CHARACTERISTICS

3.1.1 Age

The mean age of the study participants was 52.5+/-16 years. Only one patient was over 60 years of age. The age group with the highest number of patients (55; 29.1%) was below 20 years (Figure 3.1.1).

3.1.2 Sex

The majority of the study subjects were females (59.7%) (Figure 3.1.2).

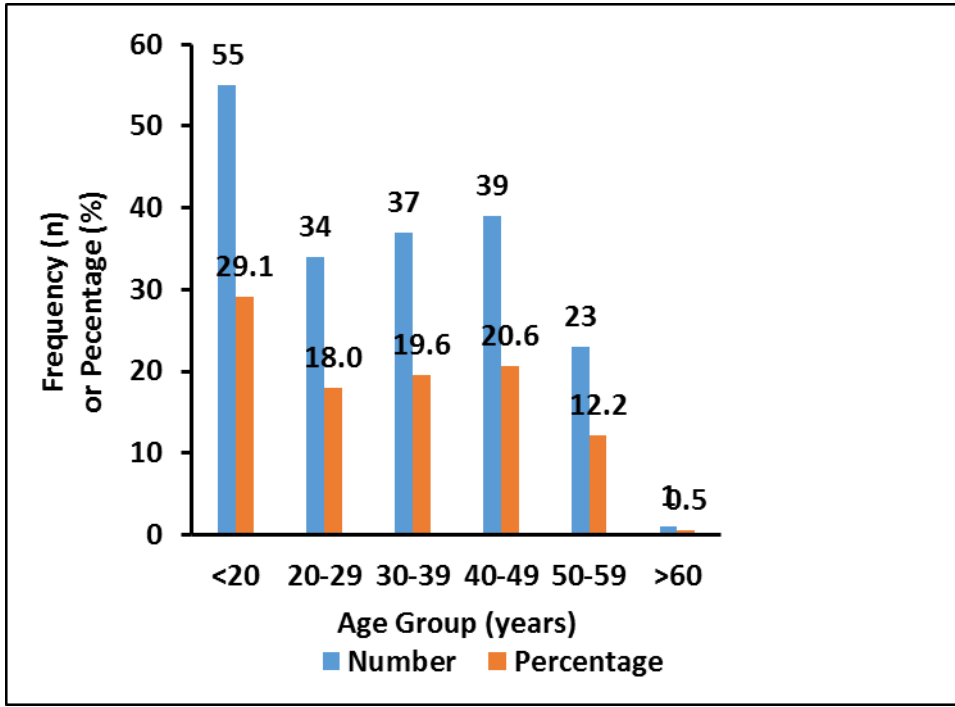


Figure 3.1.1 Age group categories of study participants (n=189). Age was not recorded in 7 patients.

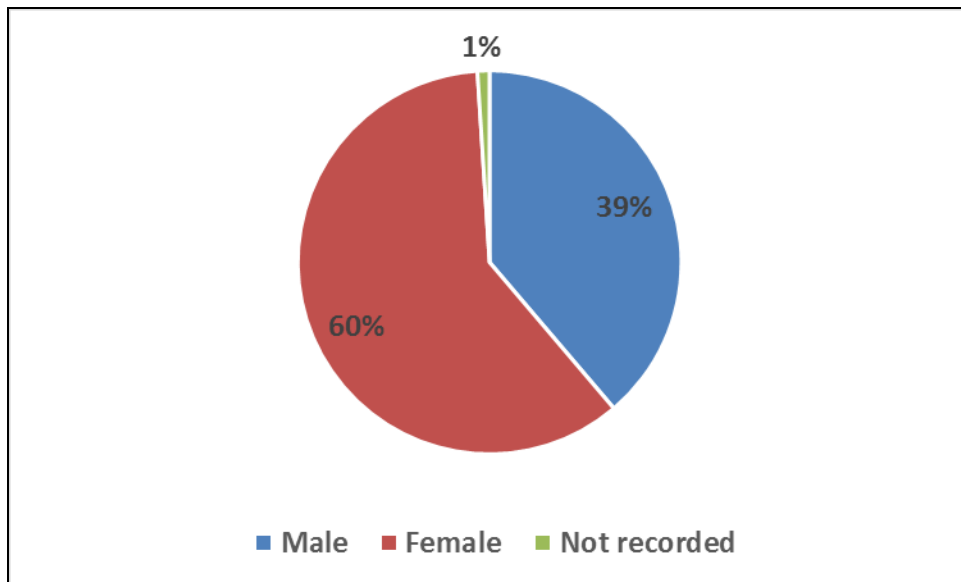


Figure 3.1.2 Distribution of study participants by sex

3.2 ENDOSCOPIC FINDINGS

Among the 196 study participants, 28 (14.3%) were normal; 69 (35.2%) had gastritis on OGD; 58 (29.6%) had ulceration, whilst 31 (15.8%) had multiple positive endoscopic findings. Of the 58 study participants with ulceration, a differentiation was made between two sub-groups i.e. those with simple peptic ulcers (i.e. ulcers only) and those with complex peptic ulcers (i.e. ulcers mixed with other pathology e.g. gastritis). The simple peptic ulcers accounted for 32 cases, whilst the complex peptic ulcers made up the remaining 26 cases. Therefore the prevalence of PUD (i.e. ulcers only and those mixed with other pathology) in our study participants was 29.6%. The majority of the study participants (138; 70.4%) had no ulceration (Figure 3.2).

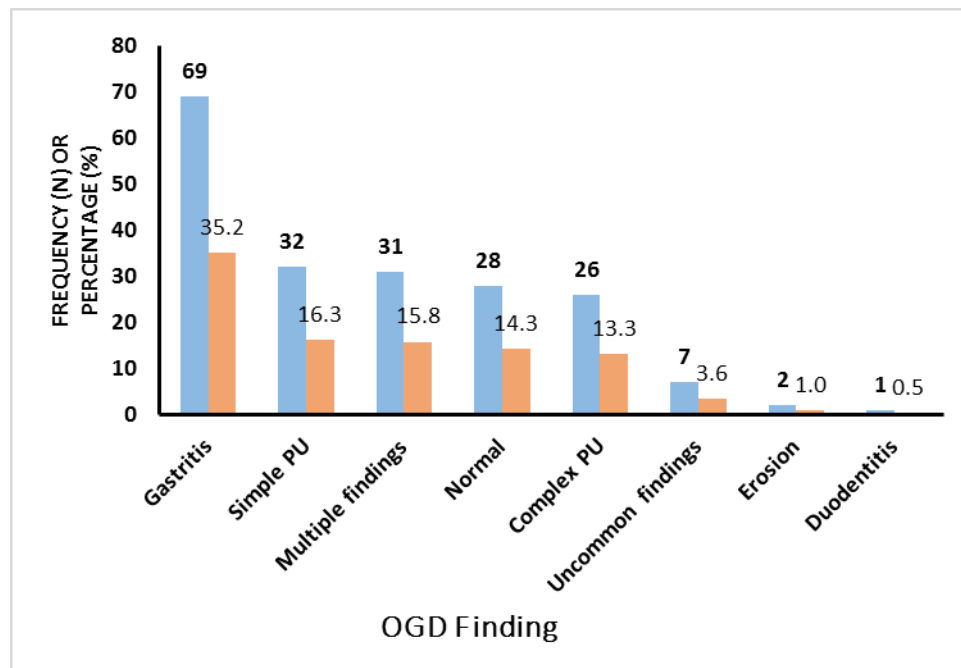


Figure 3.2 Endoscopic findings of the study participants

3.3 SITES OF PEPTIC ULCERS

The most common site of these PUs was found to be the stomach, with 18 (31.0%) cases of gastric ulcers and 14 (24.1%) of pre-pyloric ulcers. Duodenal ulcers accounted for 15 (25.9%) cases (Figure 3.3).

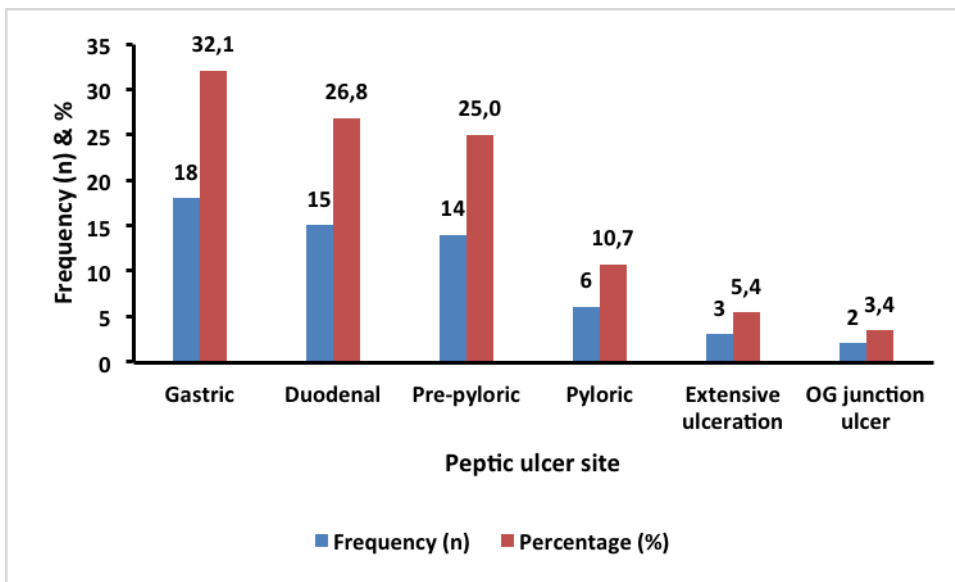


Figure 3.3 Sites of peptic ulcers of the study participants

3.4 PREVALENCE OF *HELICOBACTER PYLORI* INFECTION

The majority of the study participants were tested for *H.pylori*, 137 (69.9%). The prevalence of *H.pylori* infection was found to be 33.6%. Results were not recorded for 3 (2.2%) of patients (figure 3.4).

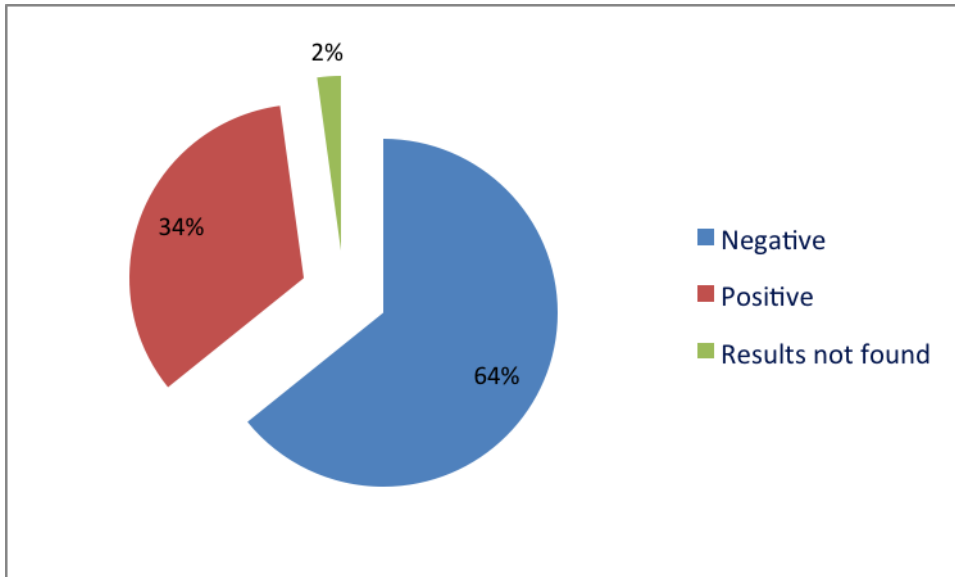


Figure 3.4 *H.pylori* test results of the study participants

3.5 HISTOLOGY FINDINGS

One hundred and thirty seven study participants had biopsies taken for histological assessment of the underlying pathological diagnosis and testing for *H.pylori*. The majority of our cases had gastritis, 116 (84.7%). These cases of gastritis were further classified into active and inactive gastritis. Active gastritis was present in 55 (40.2%) cases and inactive gastritis in 61 (44.5%) cases. 6 cases (4.4%) had ulceration, 5 (3.7%) had multiple findings whilst another 6 cases (4.4%) were normal on histology (Table 1 and Figure 3.5).

Table 3.1: Histology assessment findings of the study participants

	Frequency	Percentage
Active Gastritis	55	40.2
Inactive Gastritis	61	44.5
Ulceration	6	4.4
Erosion	1	0.7
Multiple findings	5	3.7
Oesophagealpathology	1	0.7
Normal	6	4.4
Results not found	2	1.5

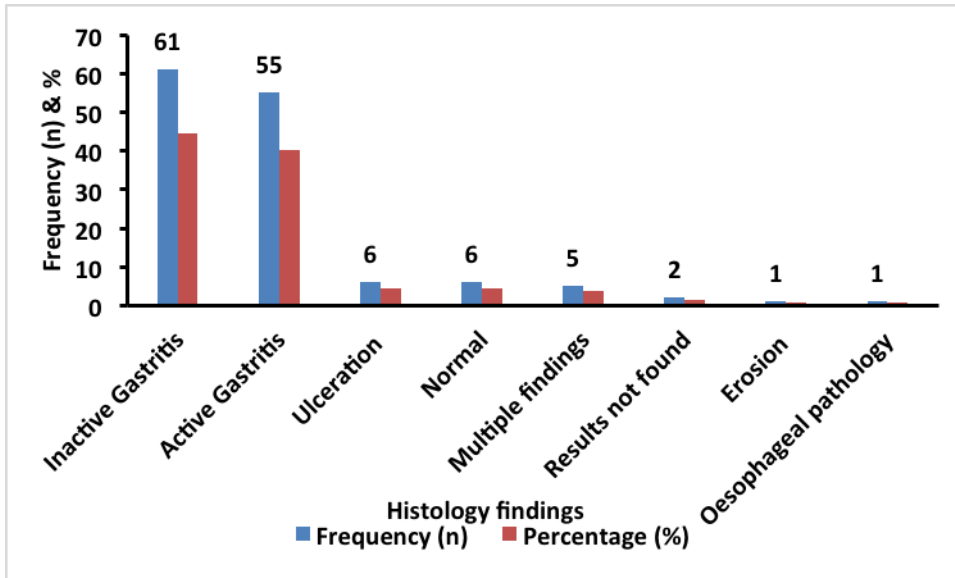


Figure 3.5 Histology assessment findings of the study participants

3.6 COST OF *H.PYLORI* TESTING

Testing for the presence of *H.pylori* organism was done at NHLS. Each gastric biopsy specimen that was submitted to the laboratory was reviewed by a Pathologist, who performed the routine histological assessment using histochemical stains. In cases where there was diagnostic uncertainty, immunohistochemistry was done using special stains e.g. immunoperoxidase. Each bottle of the *H.pylori* test cost the laboratory R1 833. This bottle consisted of a volume of one millilitre that was diluted down to produce approximately 500 tests. Therefore all the 137 *H.pylori* tests that were done in this study were performed using 1 bottle of the *H.pylori* test.

3.7 ASSOCIATIONS BETWEEN *H.PYLORI* RESULTS AND STUDY VARIABLES

The main study outcome variable was the *H.pylori* status of the study participants. This was compared to the other study variables, both categorical and numeric variables. When we tested the statistical significance of our associations against the main study outcome variable

i.e. *H.pylori* status, we found that most of the associations were not statistically significant (Table 2).

Table 3.2: Associations between *H.pylori* results and the study variables

SEX	<i>H-pylori</i> negative	<i>H-pylori</i> positive	p-value
Female	50 (56.8)	31 (67.4)	0.24
Male	38 (43.2)	15 (32.6)	
AGE GROUPS	<i>H-pylori</i> negative	<i>H-pylori</i> positive	p-value
< 20	20 (50.1)	17 (45.0)	0.55
20 – 29	16 (6.7)	8 (33.3)	
30 – 39	21 (72.4)	8 (27.6)	
40 – 49	19 (73.1)	7 (26.9)	
50 – 59	10 (66.7)	5 (33.3)	
60 – 69	1 (100.0)	0 (0.0)	
ENDOSCOPIC DIAGNOSIS	<i>H-pylori</i> negative	<i>H-pylori</i> positive	p-value
Gastritis	29 (56.9)	22 (43.1)	0.05
Simple PU	12 (60.0)	8 (40.0)	
Erosion	1 (50.0)	1 (50.0)	
Multiple findings	20 (87.0)	3 (13.0)	
Uncommon findings	6 (100.0)	0 (0.0)	
Normal	7 (77.8)	2 (22.2)	
Complex PU	13 (56.5)	10 (43.4)	

PEPTIC ULCERS	<i>H-pylori</i> negative	<i>H-pylori</i> positive	p-value
Simple PU	12 (60.0)	8 (40.0)	0.82
Complex PU	13 (56.5)	10 (43.5)	
PEPTIC ULCER SITES	<i>H-pylori</i> negative	<i>H-pylori</i> positive	p-value
Duodenal	6 (50.0)	6 (50.0)	0.76
Gastric	9 (52.9)	8 (47.1)	
OG junction	2 (100.0)	0 (0.0)	
Extensive Ulceration	2 (66.7)	1 (33.3)	
Pre-pyloric	5 (71.4)	2 (28.6)	
Pyloric	1 (50.0)	1 (50.0)	

SUMMARY OF THE CHAPTER

In summary, we included 196 patients in our study. Most of which were females, with a female: male ratio of 1.5. Their mean age was 52.5+/-16 years. The prevalence of PUD in our study was found to be 29.6%, comprising of simple ulcers which were the only pathology found on endoscopy and complex ulcers which were associated with other pathologies e.g. gastritis. The commonest site of these peptic ulcers was the stomach. Seventy percent of all the study participants were tested for *H. pylori*, of which 74.0% were patients with PUD. The overall testing for *H.pylori* consumed one bottle of *H.pylori* test which cost NHLS R 1 833.

The prevalence of *H.pylori* infection was found to be 33.6%. The percentage of patients who were found to be infected was similar in both simple and complex ulcers; it ranged from 40.0% to 43.5%. Fifty percent of the DUs were found to be *H.pylori* positive, with 47.1% of gastric ulcers and 28.6% of pre-pyloric ulcers. However these associations were not statistically significant.

CHAPTER 4: DISCUSSION

4.1 *Helicobacter pylori* infection

4.1.1 Overall prevalence of *Helicobacter pylori* infection

The ground breaking discovery of *Helicobacter pylori* organism in 1982 in Australia was one of the important discoveries in the history of medicine. Before then very little attention had been paid to organisms cultured in biopsy specimens of human gastric mucosa. However, after the identification of the causal relationship between *H.pylori* infection and gastro-duodenal disease, this gram-negative microaerophilic curved bacillus became the subject of much research (8).

Many studies looking at different aspects of *H.pylori* have been done worldwide. The ones of particular interest to our research are epidemiological studies. Globally the prevalence of *H.pylori* infection was found to be approximately 50%, with an estimated prevalence of between 70 to 90% found in developing countries. According to the World Gastroenterology Organisation (WGO) 2010 global guidelines, the adult prevalence of *H.pylori* infection in developed countries like the USA and Canada was 30%, whilst developing African countries like Ethiopia and Nigeria, had a prevalence of >95% and 70-90% respectively (6, 8, 9).

In our study we found an overall prevalence of *H.pylori* infection in patients presenting with UGIT symptoms at CMJAH to be 33.6%. This is much lower than what we had hypothesized and compared to the previous similar studies that were done in the past, in SA. One of these studies was done by Tanih et al (12) who looked into the prevalence of *H.pylori* in dyspeptic patients in the Eastern Cape (Port Elizabeth) and found an overall prevalence of 66.1% (12). Similarly, O’Keefe et al (32) reported an overall *H.pylori* prevalence of 80% in the Eastern Cape (East London). The possible explanations for these major differences in the prevalence of *H.pylori* infection among these similar studies could be the following factors:

- 1) Tanih et al (12) excluded patients who had received broad-spectrum antibiotic therapy, PPIs and NSAIDS three months prior to the study. In the present retrospective study we did not have a study questionnaire and excluded cases on the basis of the OGD report as recorded by the endoscopist. Therefore the antibiotic use for various reasons e.g. urogenitaldisease, which is very common in our study population, may have unintentionally eradicated *H.pylori* and contributed to the lower than expected prevalence rate (12).

- 2) Our study was conducted in Gauteng province, which is more urban, compared to the Eastern Cape, with many rural areas. Chemically treated tap water is more readily available in the former than the latter. The transmission of *H.pylori* is mainly by oral-oral or faecal-oral routes. Therefore conditions such as lack of proper sanitation, safe and accessible drinking water, poor diets and overcrowding all favour an increased prevalence of *H.pylori* infection. Since the factors driving the increased prevalence of *H.pylori* are governed by the socio-economic status of the population, there are bound to be variations within different areas of the same country (6). That would explain the higher prevalences found by Tanih et al (12) and O’Keefe et al (32) in their studies conducted in the Eastern Cape Province.

- 3) There has been a decreasing trend in *H.pylori* infection rates in Africa, in the recent years. Kibru et al (33) demonstrated this by finding an overall prevalence of *H.pylori* infection to be 52.4% in Ethiopia in 2014, when looking into *H.pylori* infection and its association with anaemia among adult dyspeptic patients (33). This is a huge drop compared to the >95% prevalence of *H.pylori* infection in Ethiopia, previously reported by the WGO, in its 2010 global guidelines (6). Similarly in SA, over the years the previous studies have demonstrated a decline in the prevalence of *H.pylori* infection. Louw et al (27) reported a prevalence of *H.pylori* infection of 80% and 95% in GUs and DUs respectively in 1993. In 2000, O’Keefe et al (32) reported an overall prevalence of *H.pylori* infection of 80% and 81% in PUs. Then 10 years later (2010), Tanih et al (12) showed a significant decrease in the prevalence of *H.pylori* infection in SA, by reporting an overall prevalence of 66.1% and 70.8% in GUs and 65% in DUs.

This could be due to the increased awareness of *H.pylori* infection and its associated diseases that now exist in Africa. This has been brought about by the attention and research that has been done studying the pathogenicity of *H.pylori* infection and the rejection of the previous African Enigma concept. The other possible explanations include the increased use of *H.pylori* eradication therapy and antibiotic therapy for other conditions with unintentional eradication of *H.pylori* (36).

4.1.2 *Helicobacter pylori* and patient demographics

When we compared *H.pylori* infection rates to patient demographics we obtained the following:

4.1.2.1 Gender

Females had a higher prevalence of *H.pylori* infection than males, 67.4% and 32.6% respectively, with a female:male ratio of 1.5:1. These findings were supported by Tanih et al (12) who found 69.5% *H.pylori* positive females and 60.0% *H.pylori* positive males. They had enrolled more female participants than males in their study, with a female:male ratio of 1.8:1. However in both studies, the association between *H.pylori* and gender was not statistically significant (12).

In contrast Shrestha et al (34), who conducted a similar study in Nepal in 2014, aimed at determining the prevalence of *H.pylori* based on histological assessment and to assess its association with endoscopic and histopathological diagnosis, found the opposite. Their overall prevalence of *H.pylori* infection was slightly higher in males (69.6%) than in females (66.7%). The difference between the two genders favouring males, was more pronounced in the >70 years age group, with the prevalence of 77.8% in males and 28.6% in females (p=0.049). The possible explanation for this observation could be the fact that female patients who are 70 years of age and above, have probably used broad-spectrum antibiotics for other conditions e.g. gynaecological conditions, more than younger females. This could have resulted in

unintentional eradication of *H.pylori*, as described above. However, the sample size in this age group was small (n=16; 9 males and 7 females) (34).

4.1.2.2 Age

In the present study, the highest prevalence of *H.pylori* infection (45.0%) was found to be in the youngest age group i.e.<20 years of age. This is in agreement with the WGO 2010 global guidelines, which state that *H.pylori* infection is much more prevalent in the younger population group than the adults in developing countries (6). It was further supported by Pelsler et al (31), who found a prevalence of 84% (95% CI of 77 - 91.3%) in children between the age group of 10-15 years in Bloemfontein, SA(31). Similarly, Sathar et al (35) found more than 80% of the children to be infected with *H.pylori* by the time they reach 10 years of age (35).

4.2 Endoscopic findings

When analyzing the endoscopic findings in our study, we found a prevalence of PUD of 29.6%. Most the patients (35.2%) had gastritis. Therefore 70.4% of all the study participants who were symptomatic enough to warrant an endoscopic evaluation had no ulceration. Tanih et al (12) also found that the majority of their study population had non-ulcer dyspepsia (33.4%). Shrestha et al (34) further supported this, by finding gastritis as the most common endoscopic finding in 63.2% of their study population (34).

4.2.1 Endoscopic findings and *Helicobacter pylori* infection

However, the prevalence of *H.pylori* infection in the common endoscopic findings (i.e. gastritis, peptic ulcers and multiple findings) in our study was lower than expected. It was found in 43.1% of the patients with gastritis and 40.0-43.5% of the patients with PUD (p=0.05). This observation contradicts what the previous literature had shown. Shrestha et al

(34) found a higher prevalence of *H.pylori* infection in patients with gastritis (61.8%); GU (84.0%) and DU (85.7%) ($p=0.046$)(34).

In SA, Tanih et al (12) also supported the notion that the most common endoscopic findings are *H.pylori* associated by finding high prevalences of *H.pylori* infection in patients with gastritis (75.0%), GU (70.8%) and DU (65.0%). A few other studies conducted in SA were consistent with these findings (12). Louw et al (27) showed an overall incidence of *H.pylori* infection to be 80% in GUs and 95% in DUs. Similarly O’Keefe et al (32) showed an overall prevalence of *H.pylori* infection to be 80%, with 81% found in PUs.

The possible explanation for the unexpectedly low prevalences of *H.pylori* infection in the common endoscopic findings in our study may have been the following;

1) Gastritis:

Our study was relatively smaller in terms of its sample size compared to the other similar studies. We included 196 study subjects whilst Shrestha et al (34) and Tanih et al (12) included 228 and 254 patients respectively. We had fewer cases of gastritis (35.2%) compared to Shrestha et al (34) (63.2%), that might explain their overall higher prevalence of *H.pylori* associated gastritis of 61.8% compared to ours of 43% (12, 34).

2) PUD:

The low prevalences of *H.pylori* associated PUs found in our study, compared to other previous similar studies could be attributed to the fact that we had a much lower overall prevalence of *H.pylori* infection (33.6%) compared to them. Shrestha et al (34) found an overall *H.pylori* prevalence of 68% with 84.0% of GUs and 85.7% of DUs being *H.pylori* associated. Similarly Tanih et al (12) found an overall prevalence of *H.pylori* to be 66%, with 70.8% and 65.0% of GUs and DUs being *H.pylori* associated respectively (12, 34).

4.3 *H.pylori* testing

In our study we used histology as a form of testing for the presence of *H.pylori* infection. The patients who were tested for *H.pylori* infection had the RUT performed and the biopsy specimen submitted for histological testing. The OGD report with the RUT result was attached to the patient's file for interpretation by the treating clinician. We could not get hold of these reports when conducting our study since they were not registered at the site of the study.

The RUT has a sensitivity of approximately 90% and the specificity which ranges between 95% and 100%. It is therefore very unusual to get a false positive result when using the RUT. As a result it is recommended as the first-line diagnostic test by the Maastricht V guidelines, in patients with an indication for endoscopy and in whom there is no contraindication for biopsy sampling. However false negative results can occur in certain conditions e.g. in patients who had a recent GI bleeding; in patients who are currently using PPIs, antibiotics or bismuth-containing compounds and in patients with marked atrophy and intestinal metaplasia. Therefore patients should discontinue the use of antibiotics or bismuth compounds four weeks and PPIs two weeks prior to performing the RUT (37).

Meanwhile routine histological stains e.g. H&E has been reported to have a sensitivity of 42-99% and a specificity of 100%. The false negative results when using H&E stains are usually in those cases with a low density of *H.pylori* infection. These include patients with chronic gastritis (active or inactive), atrophic gastritis and marked intestinal metaplasia. Patients on PPIs have a high tendency of having false negative results because they may have a low density of *H.pylori* infection or a patchy distribution or the organism may appear in other forms e.g. coccoid form. In such cases Immunohistochemical stains should be used to overcome such challenges. They have a sensitivity of 90% and 100% when compared to

H&E stains. Their use extend to follow-up biopsies after eradication of *H.pylori* when there are low densities of the organism that could be detected by routine histological stains (37).

It is therefore evident that the RUT is the most accurate form of testing for the presence of *H.pylori* infection with its better sensitivity rates (i.e less false negative results) when compared to histochemical stains. In our study we used histochemical stains. One may argue that we may have under reported the prevalence of *H.pylori* infection. However, the cases which were equivocal on histochemical stains were subsequently confirmed with immunohistochemistry to avoid false negative results.

4.4 Study limitations

4.4.1 Time period of the study

We initially planned to conduct the study over a 12 months period (i.e. from January to December 2012). However, we were able to retrieve the reports of the OGDs which were performed between the 1st of October and 31st of December 2012 i.e. over a 3 months period. Most of the reports of the OGDs performed before this time were apparently lost during the relocation of the GES. It was initially located in the surgical department, Area 397. It then moved to area 554.

4.4.2 Sample size

In our protocol we had planned to include a sample size of 443 patients. However in the actual study this sample size was reduced by 56% after following the study's exclusion criteria. This was due to the fact that we used a shorter time period for the study i.e. 3 months, instead of 12 months, as described above. In addition, we had to expand on our exclusion criteria. This was not considered when we formulated the study protocol. The expansion was based on the findings after screening all the reports of the OGDs which were done at the time of the study. This included cases where the procedure was suboptimal, incomplete or

abandoned and where the OGD finding was only oesophageal pathology. These factors were not initially applied in the exclusion criteria of the protocol of the study. Hence the sample size was significantly reduced.

4.4.3 *H.pylori* RUT results

During the OGDs the initial *H.pylori* test which was performed, was the RUT. This was recorded in one of the OGD reports. Subsequently, the biopsy samples were submitted to the laboratory for histological assessment and testing for the presence of *H.pylori* infection. The OGD reports with the RUT were attached to the patients' files for the reading of the results by the referring clinicians so that treatment could be administered immediately. Meanwhile the other OGD reports with the laboratory sticker to trace the histology results were filed at the GES. We could not get access to the RUT results for our study participants as they were not filed in the GES. We could only trace and use the histological assessment results.

4.5 Potential bias

The potential source of bias in our study was the fact that since this was a retrospective study of the data already collected, we could not exclude certain confounding factors that could have influenced our results. These include patients on PPIs, patients who had recently received antibiotic therapy and patients with other risk factors for PUD such as NSAID use, smoking etc.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

In conclusion, the prevalence of PUD in symptomatic patients at CMJAH is 29.6%, with gastric ulcers being the most common site of PUs. The overall prevalence of *H.pylori* infection in patients presenting with UGIT symptoms is 33.6%, in keeping with the downward trend in the prevalence of *H.pylori* infection in the recent years in Africa and SA. We found *H.pylori* to be associated with 40-43.5% of PUs in general and 50.0% of DUs. However this association was not statistically significant. Our study found no association between *H.pylori* infection and the patient demographics i.e. age & sex.

With the prevalence of *H.pylori* infection in patients with PUD at CMJAH being less than or equal to 50% and the fact that testing for *H.pylori* is cost-effective, our study favours confirming the presence of *H.pylori* infection through diagnostic tests prior to commencing eradication therapy in patients with PUD at CMJAH. However, we recommend larger future studies and prospective studies, excluding confounding factors in the prevalence of *H.pylori* infection such as the recent use of PPIs and antibiotic therapy, as well as other risk factors for PUD e.g. NSAIDs. We also recommend the use of RUT as a form of testing for the presence of *H.pylori* infection, since it is more sensitive than histochemical staining and is the recommended first line diagnostic test in patients requiring OGD. A study comparing the cost of over-treating with empiric *H.pylori* eradication versus the cost of testing for the presence of *H.pylori* infection prior to treatment in patients with PUD is highly recommended.

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R14/49 Dr Nosisa Thabile Sishuba and Prof TE Luvhengo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130668

NAME: Dr Nosisa Thabile Sishuba and Prof TE Luvhengo
(Principal Investigator)

DEPARTMENT: Surgery
Charlotte Maxeke Johannesburg Academic
Hospital


PROJECT TITLE: Does a High Prevalence of Helicobacter Pylori
in Patients with Peptic Ulcer Disease at
Charlotte Maxeke Johannesburg Academic
Hospital, Justify Empiric H Pylori Eradication

DATE CONSIDERED: 28/06/2013

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Prof TE Luvhengo

APPROVED BY: 

Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 31/07/2013

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 Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized 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 the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature _____

Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Office of the Chief Executive Officer
Tell: 011 488 3792
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Date: 25 July 2013

Dr. N. T. Sishuba
Registrar Department of General Surgery
University of the Witwatersrand

Dear Nosisa

RE: "Permission to conduct a study on: Does a high prevalence of Helicobacter pylori in patients with Peptic ulcer disease at Charlotte Maxeke Johannesburg Academic Hospital justify empiric H. pylori eradication?"

Please note that permission to conduct the above mentioned study is provisionally approved. Your study can only commence once ethics approval is obtained. Please forward a copy of your ethics clearance certificate as soon as the study is approved by the ethics committee for the CEO's office to give you the final approval to conduct the study.

Ms. G. Bogoshi

Chief Executive Officer

Date: 25/07/2013

Appendix 4

To whom it may concern

I hereby give permission to Dr N Sishuba to conduct research on H Pylori in the files of the patients attending CMJAH gastroenterology unit.

Dr AD Mahomed

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Principal Physician Consultant, Gastroenterologist

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