Prevalence Of *Helicobacter pylori* And Its Association With Abo Blood Group In Asymptomatic, Ulcer Students Of Western Delta University, Oghara, Nigeria

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Abstract: This study aims to determine the involvement of *Helicobacter. pylori* as a cause of abdominal discomfort and peptic ulcer, and also to determine if there is any correlation with ABO blood group in asymptomatic individuals. Blood samples were collected from (fifty) healthy individuals, consisting of 8 males and 42 females aged between 17-30 years (mean 23.5 years). This was accompanied with a questionnaire for demographic data. *H. pylori* one step test kit was used. ABO blood group and rhesus factors were determined by slide agglutination using serum that was serially diluted. Results showed that $64^0/_0$ were sero-positive for *H pylori*. Of the seropositive subjects, $62.5^0/_0$ (n=5/8) were male and 35.7% (n=15/42) were females. The frequency of the ABO and rhesus positive (Rh+) blood groups among seropositive subject was (A=6%, B=8%, AB=4% with rhesus positive 58% and rhesus negative 6%) and among seronegative subjects it was (A=8%, B=0%, AB=0%, 0=28% with rhesus positive 34% and rhesus negative 2%). The results of this study, showed that ABO blood group and rhesus compatibility greatly influenced the seropositivity for *H pylori* infection. Further dilution of the blood samples showed a clear significant rise in titer up to 1:160. The prevalence of cases after the dilution dropped in the following manner (1:20=26%, 1:40=12%, 1:80=8%, and 1:160=2%) the seronegative cases increased during the dilution as (1: 20=74%, 1:40=92%, and 1:160=98%). Prevalence of *H. pylori* infection still remains high after serial dilution. Conclusion: The detection of high prevalence of H. *pylori* infection among asymptomatic individuals and the involvement of ABO blood groups necessitates blood screening for every individual especially those that possess the blood groups that are at most risk of infection.

Key words: Seroprevalence; Asymptomatic individuals; ABO blood group; Helicobacter pylori; Infection.

Introduction

Warren and Marshall, in 1983 discovered *Helicobacter pylori (H. pylori)* and this became an important discovery for the management of all forms of abdominal discomfort (Talley et al., 2005). Numerous studies have reported a high prevalence of *H. pylori* infection among healthy and non-healthy persons in different places (Durazzo et al., 2004; Seyda et al., 2007; Rodrigues et al., 2005). *H. pylori* has been rated as a 'Class One' carcinogen by the World Health Organization (Peterson et al., 2000; Aguemon et al., 2005) It is to peptic ulcer, as cigarette smoking is to lung cancer. Globally, it remains one of the most common infections and it is estimated that 50% of the world's populations are carriers of the bacterium (Goodman et al., 2008).

Helicobacter pylori is a microaerophilic, Gram negative, motile, curved rod and flagellated bacterium with a capability for abundant urease production which has been implicated in several upper gastrointestinal diseases that present as dyspepsia (Suerbaum et al,. 2002; Oluwasola et al,. 2002). It has

been suggested that up to 95% of duodenal and 70% of gastric ulcers are attributable to *H. pylori* infection, and most cases occur in middle aged individuals, the highly productive age groups in societies (Rothenbacher 2007). The organism is usually found under the mucus layer in the gastric pit in close opposition to gastric epithelial cells where it causes damages to the cells (Malfertheiner et al, 2007). *H. pylori* infection is recognized as the major cause of chronic gastritis and a factor in the pathogenesis of peptic ulcer disease (Lyra et al,. 2003) and gastric adenocarcinoma (Windsor et al,. 2005). *H. pylori* infects a large portion of the world population (Windsor et al., 2005), but there are large differences in the prevalence of infection among ethnic groups (Santos et al., 2005; Pillary et al., 2007). Infection occurs early (Santos et al., 2005) and *H. pylori* sero-positivity increased with age (Robertson et al., 2003; Naja et al.. 2007). Lower socioeconomic status (crowded living conditions) is associated with high infection rates (Seyda et al., 2007; Naja et al., 2007). The pylori infection may, in some instances, originate

as a zoonosis (Dore et al., 1999). Once *H. pylori* infection is acquired, it persists probably for life in untreated persons (Pillay et al., 2007). A high level of education was associated with negative *H. pylori* status (Shi et al., 2008). The ABO blood groups have been associated with some infectious and non-infectious diseases (Jaff MS 2011). Previous serological studies have related a higher prevalence of antibodies against *H. pylori* in some professions (abattoir workers, shepherds and veterinary workers) to direct contact with *H. pylori* infected animals (Papiez et al., 2003). Also, *H. pylori* has been isolated from the intestinal tract of dogs, cats and sheep (Dore et al., 2001). Research has also demonstrated that *H. pylori* can live for several days in milk and water in its infectious bacillary form and in river water for several months in a non-culturable but viable form (Braganca et al., 2007). *Helicobacter pylori* was identified as the main etiology of peptic ulcers, chronic gastritis, and a variety of gastrointestinal symptoms. Many epidemiologic studies had found that non secretors of ABO blood group antigens and individuals of blood group O were overrepresented among patients with peptic ulcers, (Rosenstock et al., 1997). These studies encouraged many researches to investigate the relationship between ABO blood groups and their secretor status with peptic ulcer. Many authors reported an association between blood group O and *H. pylori* infection (Kanbay et al., 2005), while others failed to find such an association. (Niv et al., 1996). Peptic ulcer disease is now viewed as an infectious disease since eradication of *H. pylori* leads to its cure. (Malfertheiner et al.,2007). The paucity of information in Nigeria as regards the relationship of ABO blood group and rhesus compatibility to *Helicobacter pylori* prevalence and the need to screen for *H. pylori* antigen in blood samples of asymptomatic individuals necessitated this study.

Materials And Methods

This study which was prospective and cross-sectional was conducted in Western Delta University, Oghara, Delta State. A total of fifty volunteers were recruited for the studyand this consists of eight (8) males and fourty two (42) females. Demographic data was obtained by means of standard questionnaire. A questionnaire is a good tool that is employed in various aspects of epidemiological studies to gather information. In this study, a questionnaire was administered to the subjects in order to obtain their socio-demographic and economic data. Data such as age, sex, socio economic status, history of any peptic ulcer disease, and drug taken. Blood samples were collected in duplicate from each voluntary participant using 5mls syringes. 2.5mls each was dispensed into a sterile anti-coagulated bottle containing Ethylene

Diamine Tetra-acetic acid (EDTA). The other 2.5mls was dispensed into a sterile coagulated bottle containing coated beads which is the clothing factor. This was spun using the centrifuge and serum was separated into a sterile plane bottle and this was stored in the fridge at 2-8oC. Based on the presence of the antigen in the blood samples, the samples were further serially diluted in a four-fold dilution. The other part of the samples was used to carry out ABO blood group or Landsteiner group. Sterile anti-coagulated Ethylene Diamine Tetra acetic acid (EDTA) bottles, sterile coagulated bottle, syringes, cotton wool, 70% alcohol, *H. pylori* global test kit, pipettes, hand gloves, Face mask, test-tubes, test-tube rack, autoclave, aluminum foil paper, normal saline, blood samples, thermo-cool refrigerator. All test-tube and beakers used in this study were thoroughly washed with detergent and jik then rinsed in clean water to ensure that they were grease-free and were covered with cotton wool and aluminum in an autoclave at $121^{O}C$ for 15 min. at 15 pound/pressure.

Selection Of Subjects

In selecting these subjects, the aim of this study was explained to them and they conceded to continuing with the test. Samples were collected from eligible members based on the questionnaire data. Those with history of peptic ulcer and those currently using anti-ulcer medications were excluded from the study. Subjects' participation in this study was voluntary. Information collected from participant was kept confidential.

Detection Of *Helicobacter Pylori* Antibodies Using Blood Serum On Global Kit

The *H. pylori* one step test device utilizes a combination of *H. pylori* antigen coated particles and anti-human IgG to qualitatively and selectively detect *H.pylori* antibodies in serum just within ten minutes. The blood samples were allowed to cloth thereafter, they were spun using the bucket centrifuge at 4000 revolution per minute (RPM) for five (5) minutes. The global kit was removed from the foil pouch and placed on a sterile laboratory bench. Using the disposable specimen dropper, three drops (apporximatelly 100nl) of the serum was dispensed on the specimen well labeled **(S)** on the test kit. This was allowed to flow and result was read after 10 miuntes. Interpretation of results was based on the position and number of line appearing on the test kit. Positive results were read as having two distinct red lines, one red line on the control region (C) and another line in the test region (T). On the other hand the negative result was read as having one red line only on the control region (C) and no apparent red line in the test region (T).

Preparation Of Slide Agglutination ABO Blood Grouping Landsteiner Blood Group And Rhesus Compactibility

According to the method used by Landsteiner and Wiener, ABO and Rhesus (Rh) blood groups were determined for both sero-positive and sero-negative subjects, using standardized haemaglutination methods that is slide agglutination test. First the blood samples collected in a sterile anti-coagulated ethylene diamine tetra acetic acid (EDTA), a drop of each blood sample, was placed on each part of the rocking tile. Equal drops of anti-sera A, B, and D were placed on each section of the tile. Using sterile glass rods, it was used to mix each and was in turn cleaned. The rocking tile was rocked back and forth for two (2) minutes in other to detect the antibodies. Thereafter the results were interpreted as follows:

- An agglutination in A and O indicates A rhesus "D" positive
- An agglutination in B and O indicates B rhesus "D" positive
- An agglutination in A,B and O indicates AB rhesus "D" positive
- An agglutination in O only indicate O rhesus "D" positive
- An agglutination in A and non in O indicate A rhesus "D" negative
- An agglutination in A, B and non in O indicates AB rhesus "D" negative
- There was no agglutination in all indicates O rhesus "D" negative

The results with the sero-positive and sero-negative were compared with the blood group and Rhesus factor

3.9.0 Four-Fold Serial Dilution For *H. pylori* Antibody Detection

Serial dilution means diluting with a constant factor. Blood samples collected were spun using the bucket centrifuge at 4000 revolution per minute (RPM) for five minutes. Thereafter, the serums were separated using pasture pipettes. They were stored in the fridge at -20^{0}C. During serial dilution, the sera were brought out and allowed to completely thaw to room temperature that is 20^{0}C. The serums were further serially diluted in a four-fold dilution in other to know the highest titre that is highest dilution in which the reaction stopped. First normal saline was prepared by weighing 0.85g of sodium chloride and dissolved into 1000ml of serial water. Six test tubes were arranged on the test tube rack and were labeled one to six respectively. 1ml of the serum was dispensed into first tube this serves as the neat, (1:10 dilution) 0.5ml of normal saline was dispensed into the remaining 5 tubes with 5ml pipettes. Thereafter, using a 1ml pipette, 0.5ml of serum was transferred from tube 1 to tube 2. The content was properly mixed by carefully drawing the liquid up into the pipette and discharging it slowly back down into the tube three

times. This process was repeated serially to tube five by transferring 0.5mls and the last 0.5mls was discarded instead of adding to tube six. Thus tube six has only normal saline which was used as the negative control. The *H. pylori* one step test kit contains H. pylori antigen coated particles and anti-human IgG coated on the membrane. It was allowed to flow and results were interpreted after 10 minutes. For serum which contains *H. pylori* antibodies a red colored line appeared on the test region (T) and also on the control region (C) of the test kit, this was reported as positive. While the serum which does not contain *H. pylori* antibodies, a red colored line appeared only on the control region (C) of the test kit, this was reported as negative. This was based on manufacturer's recommendation. The antibody titer was recorded as 1:20, 1:40, 1:80, 1:160, and 1:320

The results of this study were compared with sero-positive and sero-negative subjects as well as ABO or Landsteiner blood group and rhesus compatibility.

3.10.0 Statistical Analysis

Data generated from this study were analyzed using Statistical Package for Social Sciences (SPSS) Chicago IL. Chi-square test was used to detect statistically significant differences among variables. P values < 0.05 were considered significant. Chi-square test was used for the analysis of the association of *H. pylori* infection according to ABO blood group and rhesus factor. The results were recorded based on percentages.

Results

4.1.0 Prevalence Of *H. pylori* And Its Association With Abo Blood Group And Rhesus Compactability.

Of the 50 blood samples analyzed, it was found that 32 samples were positive and 18 were negative.

Pylori antigen was detected in 32 subjects, yielding an overall prevalence of 64% while the sero positive as compared to other ABO blood types (Tables 2). In the same vain rhesus "D" positive also has the highest *H. pylori* sero positive (3). The prevalence was higher in females than in males. Of the 42 females used during the study, *H. pylori* was detected in 27 (64.3%) as against 5 (62.5%) of 8 males using serum on global test kit (Table 4). There was a reduced detection of *H. pylori* antigen in a four-fold serial dilution amongst the 27 (64.3%) females of 42 females, 11 (26.2%) were positive after serial dilution, whereas amongst the 8 males, only 2 (25%) of the males where positive. It was also observed that H. pylori prevalence is higher amongst blood group O and rhesus "D" positive individuals (Table 2 and 3).

Table 1: Frequency of occurrence of H. pylori antigen detection.

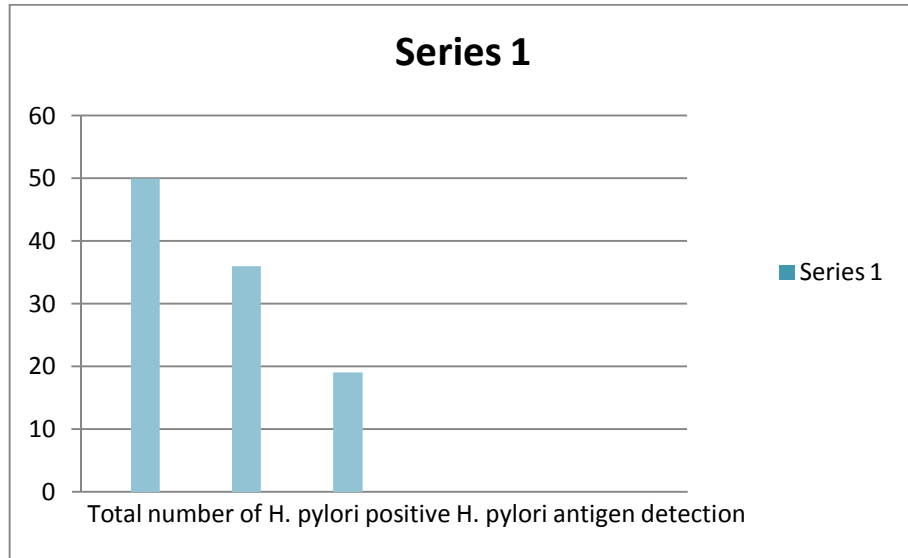| H. pylori samples	Total number (N)	Percentages (%)
H. pylori positive	32	64
H. pylori negative	18	36
Overall total	50	100

Figure 1: frequency of occurrence of H. pylori antigen detection

Table 2: Association between H. pylori and ABO blood group

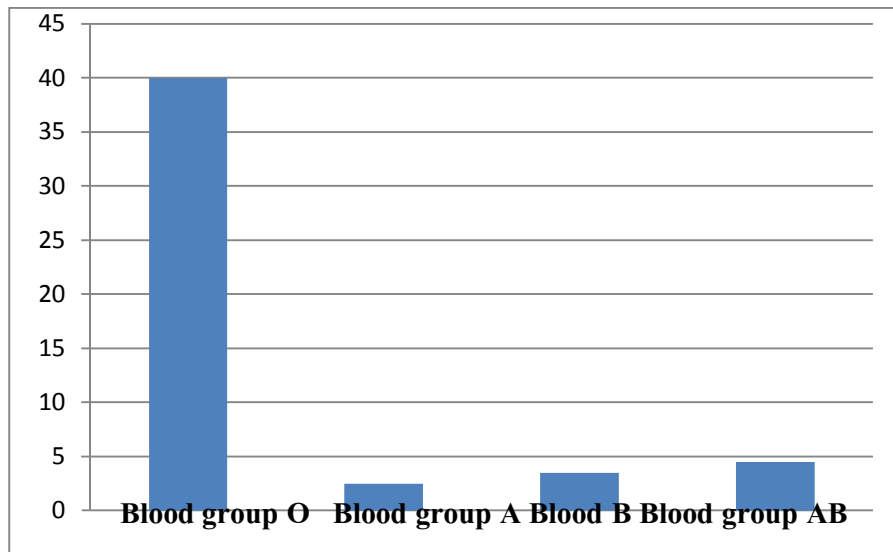| Antigen in Serum	Total number	Percentage occurrence in blood group							
		A		B		AB		O	
		Number	(%)	N	(%)	N	(%)	N	(%)
H. pylori positive	32	3	6	4	8	2	4	23	46
H. pylori negative	18	4	8	0	0	0	0	14	28

Figure 2: Percentage frequency distribution of H. pylori amongst ABO blood group

Table 3: Association between *H. pylori* and Rhesus compactibility

Samples	Total Number (N)	Percentages (%)	Rhesus factor			
			Rhesus "D" positive		Rhesus "D" negative	
			(N)	(%)	(N)	(%)
H. pylori Positive	32	64	29	58	3	6
H. pylori Negative	18	36	17	34	1	2
Overall Total	50	100	46	92	4	8

Table 4: Frequency of occurrence of *H. pylori* amongst typed gender

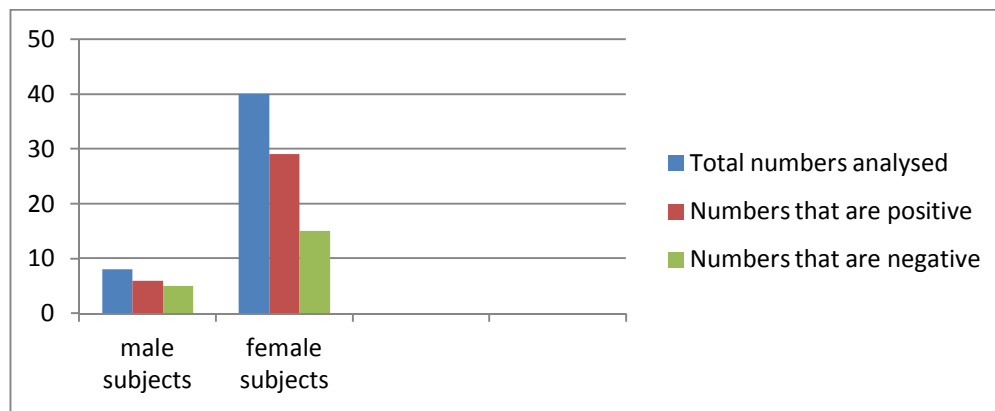| Samples	Males		Females	
	(N)	(%)	(N)	(%)
H. pylori positive	5	62.5	27	64.3
H. pylori negative	3	37.5	15	35.7
Overall total	8	100	42	100

Figure 3: frequency of *H. pylori* antigen detection according to gender

Table 5: Association between *H. pylori* and rhesus compactability

Samples	Rhesus "D" positive				Rhesus "D" negative			
	O	A	B	AB	O	A	B	AB
H. Pylori positive	21 (60%)	3 (50%)	4 (100%)	1 (100%)	1 (100%)	0	0	1 (100%)
H. pylori negative	14 (40%)	3 (50%)	0	0	0	1 (100%)	-(0)	0

TABLE 6: Association between *H. pylori* and female ABO blood group with rhesus compactibility

Samples	ABO blood group (%)				Rhesus "D" positive (%)				Rhesus "D" negative (%)			
	A	B	AB	O	A	B	AB	O	A	B	AB	O
H. pylori positive	1(2.4)	4(9.5)	2(4.8)	20(47.7)	1(2.4)	4(9.5)	1(2.4)	18(42.9)	0	0	1(2.4)	2(4.8)
H. pylori negative	2(4.8)	0	0	12(28.6)	2(4.8)	0	0	12(28.0)	1(2.4)	0	0	0

TABLE 7: Association between *H. pylori* and male ABO blood group with rhesus compactability

Samples	ABO blood group				Rhesus "D" positive				Rhesus "D" negative			
	A	B	AB	O	A	B	AB	O	A	B	AB	O
H. pylori positive	2(25)	0	0	3(37.5)	2(25)	0	0	3(37.5)	0	0	0	0
H. pylori negative	1(12.5)	0	0	2(25)	1(12.5)	0	0	2(25)	0	0	0	0

4.2.0 Serial Dilution Of Samples

The blood samples were further diluted and test carried out to detect possible positive blood cases in the same comparative study. The results are as shown in the tables below. It is of interest to note that there were clear significant variations between the undiluted and

diluted blood samples based on the rise in titre. After a four-fold dilution, the titre was still high up to 1:160. As the positive cases kept reducing, the negative cases kept increasing according to the titres (Table 1) while figure 1 shows the variations of titre. Blood group O rhesus "D" still has the highest number of *H. pylori* infection which means that they are more prone to *H. pylori* infection (Table 4 and 5) there was a reduction of antibody titre of males subjects in Table 6 while that of females was still high (Table 7).

TABLE 8: A four-fold serial dilution frequency of occurrence *H. pylori* antigen detection

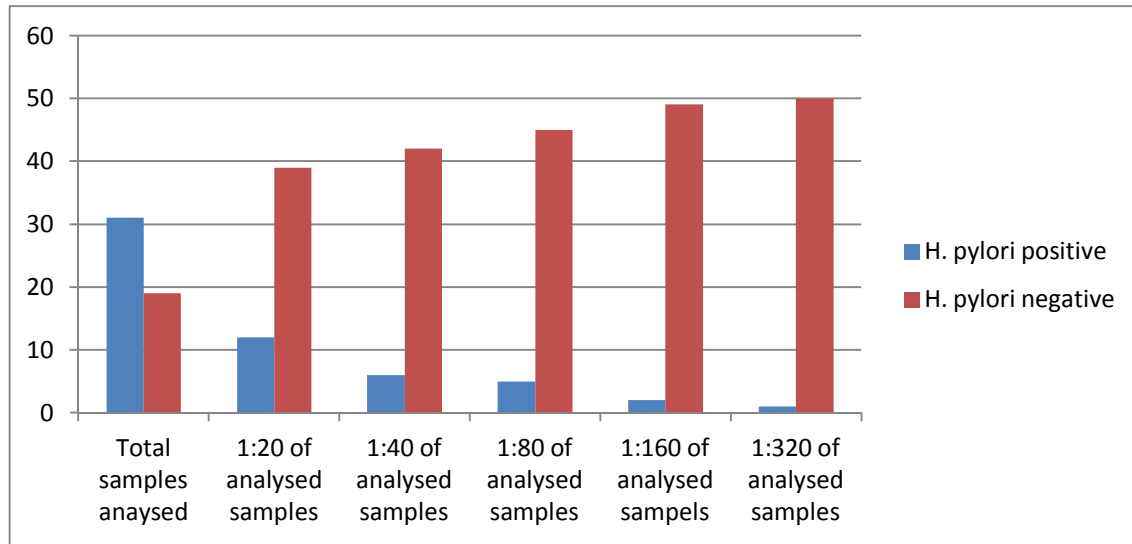| samples	Serum neat	1.20	1.40	1.80	1.160	1.320
H. pylori positive	32	13(26%)	6(12%)	4(8%)	1(2%)	0
H. pylori negative	18	37(74%)	44(88%)	46(92%)	49(98%)	50(100%)
Overall total	50	50 (100%)	50 (100%)	50 (100%)	50 (100%)	50 (100%)

Figure 4: A four-fold serial dilution showing frequency of occurrence of *H. pylori* antigen detection

TABLE 9: *H. pylori* positive antigen detection in relation to ABO blood group after a four-fold serial dilution.

ABO blood group	1:20	1:40	1:80	1:160	1:320
A	2	1			0
B	3	2	1		0
AB	1				0
O	7	3	3	1	0

TABLE 10: *H. pylori* positive antigen detection in relation to rhesus compatibility after a four-fold serial dilution.

	Rhesus	1:20	1:40	1:80	1:160	1:320
Rhesus "D" positive	A	2	1			0
	B	3	2	1		0
	AB	1				0
	O	5	3	3	1	0
Rhesus "D" negative	A					
	B					
	AB					
	O	2				

TABLE 11: A four-fold serial dilution for the detection of *H. pylori* antigen amongst male subjects

Samples	Serum neat	1:20	1:40	1:80	1:160	1:320
H. *Pylori* positive	5	2(25%)	1(12.5%)	0	0	0
H. pylori negative	3	6(75%)	7(87.5%)	8(100%)	8(100%)	8(100%)
Overall total	8	8(100%)	8(100%)	8(100%)	8(100%)	8(100%)

TABLE 12: A four-fold serial dilution for the detection of *H. pylori* antigen amongst male subjects

Samples	Serum neat	1:20	1:40	1:80	1:160	1:320
H. *Pylori* positive	27	11(26.2%)	5(11.9%)	2(4.8%)	1(2.4%)	0
H. pylori negative	15	31(73.8%)	37(88.1%)	40(95.2%)	41(97.6%)	42(100%)
Overall total	42	42(100%)	42(100%)	42(100%)	42(100%)	42(100%)

Chapter five
Discussion Conclusion Recommendations
5.1.0.   Discussion

Helicobacter pylori infection has an important clinical significance because individuals infected with *H. pylori* develop serum antibodies which correlate strongly with histologically confirmed *H. pylori* infection and the testing for *H. pylori* antibodies helps in early detection of "silent" peptic ulcer (Vaira et al., 1994). This study showed that amongst the fifty asymptomatic subjects analyzed, 32(64%) were positive which indicates that these subjects were carriers of the organism (H. pylori) without knowing that they are already infected (silent sufferers) as previously reported by Vaira et al., 1994. Reports have also indicated substantial evidence for the acquisition of H. pylori primary infection at early age, both in developed and developing countries (Ndip et al., 2004; Alborzia et al., 2006; Ahmed et al., 2007). The mode of H. pylori transmission however remains controversial. Results of this study also showed a high percentage association between the O blood group and infection caused by *H. pylori* (percentage = 64%), a finding which is consistent with literature reports (Kanbay et al., 2005, lin et al., 1998). In this study, the prevalence of sero-positive H. pylori infection was 64% (32 of 50) even after serially diluting the blood serum, the titre still remains very high (up to 1:160) in asymptomatic students in Western Delta University, Oghara, Delta State, Nigeria is higher than the average prevalence in the world's population (50%) as reported by Parsonnet 2006. This made the second hypothesis of this study a valid hypothesis. This present study is in view that the higher susceptibility of O blood group individuals to *H. pylori* infection is most probably due to the higher frequency of secretor status in O blood group individuals (Jaff 2010). This view is supported by a previous demonstration, by Alkout et al, (2000) that H antigen represents an important receptor expressed in the gastro-duodenal mucosal cells to which *H. pylori* adheres, (Alkout et al., 2000) which also enhances colonization of *H. pylori* bacteria.

It was also observed from the administered questionnaire that most of the subjects who expressed high pathogenic response were of the blood group O. This observation was previously reported that Blood group O individuals expressed a higher inflammatory response of *H. pylori* with higher levels of lymphocyte infiltration in the gastrointestinal mucusa, (Alkout et al., 2000; Abdulhamid et al., 2000), a lower level of Von Willebrand's factor, (Franchini et al.,2007; Brown et al., 2003) and a higher frequency of secretor status; (Jaff 2010), all these together, in the view of the present author, explain these individuals' increased susceptibility to peptic ulceration.

Regarding rhesus status, this study showed a relative difference between the sero-positive subjects and sero-negative subjects as the rhesus seropositive subjects had a high prevalence than the rhesus seronegative subjects, although this report did not agree with the general population as previously reported by the studies of Petrovic et al., 2011.

In this study, *H. pylori* colonization was higher in females than in males with seropositive prevalence of females (64:3%) and males (62.5%) as seen in some other studies reported (Kanbay et al., 2005; Lacy et al., 2001). This result is not in support with the finding of previous reports (Ndip et al., 2004), in which a higher prevalence rate was reported in males than in females. Kaltenthaler et al., (1995) reported that H. pylori infection is generally higher in males than in females and suggested that this might relate to young boys having poorer hygiene than young girls because infection is acquired at an early age. While some other studies have not noticed such relations to gender (Petrovic et al., 2011; Seyda et al., 2007; Khan et al., 2007; Alazmi et. el., 2010; Farshad et al., 2010). We therefore think that our divergent observation in this study could be due to the different sample sizes used because more females participated than males.

From various studies (including this one), genetic predisposition, as well as environmental factors, are suggested as important factors influencing *H. pylori* infection, a view supported by the Malaty and colleagues study on twins (Malaty et al., 1998).

Conclusion: The results obtained from this study have revealed a high prevalence of *H. pylori* antigen from blood specimen of asymptomatic individuals and also a correlation between *H. pylori*, peptic ulcer and gastritis. There is need to improve sanitation, socio-economic standard of living and purified water supply. There should be measures to protect those at most risk of infection especially, the blood group O individuals who are more susceptible to the infection.

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The relatively low H. pylori prevalence in developed countries is related to improved standards of living. Although an exact source of H. pylori infection has not yet been found, studies from Latin America have shown that contaminated water might act as a reservoir for the bacterium (Frenck et al., 2003). It is therefore not surprising that the development of modern water-purification systems might be associated with decreased H pylori prevalence. The mode of transmission for H pylori is also not definitively known; however, epidemiologic studies strongly support person-to-person transmission, with fecal-oral or oral-oral

routes being the most likely. (De Schryver et al., 2006). There are prior studies that have also highlighted the presence of H. pylori ranging from highly faecal polluted sewage water to tap water (Fugimura et al., 2004; Queralt et al., 2005; Ahmed et al., 2006; Ahmed et al., 2007; Braganca et al., 2007; Moreno et al., 2007). Despite its clinical significance, there is still lack of consensus on the way this bacterium is transmitted (Konno et al., 2005; Braganca et al., 2007) and the mode of diagnosis still remains an invasive borne technique. There is need for its early detection amongst an asymptomatic population especially amongst students who are target to poor socioeconomic status, precarious amongst others (Ndip et al., 2003).

It is thus hypothesized that:

- **There is a high percentage prevalence of Helicobacter pylori amongst female student' of Western Delta University.**
- **The infection with H. pylori is amongst students' who have a sero-blood type association with blood group homozygous O.**
1) **To ascertain if there is a significant difference in the prevalence of H. pylori among the female and male student' of Western Delta University.**

Group B in particular: This proves that the hypothesis stated in this study to be true and valid, in the same vain a significant difference was seen in rhesus positive and rhesus negative individuals. Also, it can be concluded that females are more prone to *H. pylori* infection than males. It is advice able that individuals should go for H. pylori screening in other for them to be aware and treated early since it takes time to leave the blood because when it stays too long in the body, it becomes difficult to be manage with the first-line treatment except through endoscopy. Since results of this study shows that female subjects have higher percentage of H. pylori, therefore whatever control measures should be based on the female population. In another vain, individuals with blood group O should also be taken into consideration in whatever control measures that will be put in place since they are also more prone to H. pylori infection.

Recommendation

Increasing sample size and probably sampling throughout the year will improve the epidemiological characterization of H. pylori, to attain much more meaningful results, the study of risk factors and mode of transmission of H. pylori should focused from child birth until time of infection since it takes for H. pylori to manifest and become symptomatic. That is cohort study will reveal details of the dynamics of H. pylori in the studied population. (group B in particular) this proves that the hypothesis stated in this study to be

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Appendix One
Questionnaire
The Questions May Be Answered By Ticking In The Appropriate Box Or By Writing In The Space Provided

1. Name:…………………………………………………………………………………

2. Sex: Female ☐   male ☐

3. Age: 16 – 20 ☐   21 – 25 ☐   25 – 30 ☐   above ☐

4. State of Origin:……………………………………………………………………………

5. Local Government of Origin::…………………………………………………………….

6. Place reside after school:………………………………………………………………….

7. Do you eat regularly?: Yes ☐   No ☐

8. Time interval within which you eat:

   1 -2 ☐   2 – 3 ☐   3 -4 ☐   5 and above ☐

9. Type of food taken: ……………………………………………………………………..

10. Do you have any symptom of ulcer?: Yes ☐   No ☐

11. Have you being diagnosed of ulcer before?: Yes ☐   No ☐

12. If yes, was it (please tick the box)

   Gastric ulcer ☐   Peptic ulcer ☐   Duodenal ulcer ☐   others ☐

13. Where you give medication?   Yes ☐   No ☐

14. If yes, please specify the type of medication taken …………………………………………..

15. Are you on medication now?:   Yes ☐   No ☐

16. If yes, please specify the one you are on now:…………………………………………

17. Have you had any course of taking antibiotic for the last three months?

   Yes ☐   No ☐

18. What is your economic status?

   Basic   secondary ☐   territory ☐

APPENDIX B
Details of *H. pylori* test device used
H. pylori test device
Cassette (serum/plasma)
Lot number HP 2120032
Expiring Date November, 2014.

APPENDIX C
Content Of Blood Group Anti Serials Used
Anti A
   Monoclonal (IgM) blood grouping serial for slide and tube test
   Preservation 0.1% sodium chloride 10ml
   Lot number: BGAL 1211
   Production date: November 2012
   Expiring date: October 2014
   Drug code number: GLU-Drug/G/1150
   Aids virus free HBsAg virus free
Anti B
   Monoclonal (IgM) blood grouping serial for slide and tube test
   Preservative 0.1% sodium Azide 10ml
   Lot number: BGBL 1303
   Production date: February 2013
   Expiring date: January 2015
   Drug code number: GLU-Drug/G/1150
   Aids virus free HBsAg virus free
Anti D
   Monoclonal (IgM/IgM) blood grouping serial for slide and tube test
   Preservative 0.1% sodium Azide 10ml
   Lot number: BGDL 1305
   Production date: March 2013
   Expiring date: February 2015
   Drug code number: GUJ-Drug/G/1150
   Aids virus free HBsAg virus free

   CHAPTER TWO
   Literature Review
   2.1.0 Introduction
   Bacterial pathogens are emerging with new forms of virulence and new patterns of resistance to antimicrobial agents of which H. pylori is not an exception. Helicobacter pylori, a cork-screw shaped, micro-aerophilic gram-negative coccobacillus (0.5um wide by 2-4um long), equipped with two to six flagella that are lophotrichously positioned, has chronically infected more than half of the world's population (Owen 1998; Ndip et al., 2004; Ahmed et al., 2007).
   Although most of the people harbouring this organism are asymptomatic (Ndip et al., 2004), subsequent evidence has linked the bacterium in the pathogenesis and development of certain diseases such as gastric ulcers, chronic gastritis and stomach by this organism usually occurs in the early stages of life (Ma

et al., 1998; Bassily et al., 1999), but persists lifelong in the absence of effective treatment. With the progress in research, intrinsic studies have sharpened consciousness in the clinical importance of H. pylori-linked diseases (Astrat et al., 2004; Ndip et al., 2004; Campbell et al., 2005; Farag et al., 2007). Since its discovery, overwhelming evidence has implicated it as an aetiologic agent of a spectrum of gastro intestinal diseases including gastric ulcers, chronic gastritis and stomach cancers (MacKay et al., 2003; Oleastro et al., 2006; Braganca 2007). Whilst a lot of development has been done to address transmission modes of H. pylori, its transmission pathways are still vague (Mackay et al., 2003; Fujimura et al., 2004; Deport and van der Merwe 2007). Elucidation of the paramount role played by household hygiene and environmental factors in the transmission of bacterial pathogens is of great importance as a prophylactic move, both in developed and in developing countries. Several studies have highlighted the transmission incidence risk as ranging from simple to inevitable multifactor modes of transmission (Fugimura et al., 2004; Konno et al., 2004; Perry et al., 2006; Van der Merwe et al., 2007). Highly ostensible promoting features which are mostly associated with developing countries and lower socio-economic groups in the developed world include precarious hygiene standards, crowded households, deficient sanitation and contaminated environment and water sources (Ndip et al., 2004; Ahmed et al., 2007).
   2.2.0 HISTORICAL ORIGIN
   These two landmark Lancet publications appeared almost 100 years after the first report of spiral bacteria in the human stomach and the initial speculation by several researchers that gastric ulceration was an infectious disease. Although more than 100 experimental studies suggesting a microbial cause of gastritis and peptic ulcers had been published in the first half of the 20th century, and several bacterial and viral species had been implicated as etiologic agents. The organism is one of the most genetically diverse of bacterial species. J. Robin Warren, who was a pathologist working at the Royal Perth Hospital in Western Australia, noticed curved rod-shaped bacilli in about half of the routine gastric biopsies he examined over a period of three years and found a direct correlation between the number of organism in the tissue and the severity of gastritis. Convinced of the significance of his observations he enlisted the participation of Barry Marshall, a trainee in Internal Medicine, and a joint effort was launched to isolate the microorganism. Warren had noticed the resemblance of the curved bacilli to Campylobacter, a family of know intestinal pathogens. Using micro-aerophilic conditions that favour the laboratory growth of Campylobacter, they tried, unsuccessfully, to grow

bacteria from stomach biopsies for more than a year. Serendipity delivered success when abundant bacterial growth was found in cultures that had been inadvertently left in the incubator J. Robin Warren, a pathologist working at the Royal Perth Hospital in Western Australia, noticed curved rod-shaped bacilli in about half of the routing gastric biopsies he examined over a period of three years and found a direct correlation of the number of organism in the tissue and the severity of gastritis. Convinced of the significance of his observations he enlisted the participation of Barry Marshall, a trainee in Internal Medicine, and a joint effort was launched to isolate the microorganism. Warren had noticed the resemblance of the curved bacilli to Campylobacter, a family of known intestinal pathogens. Using microaerophilic conditions that favour the laboratory growth of Campylobacter, they tried, unsuccessfully, to grow bacteria from stomach biopsies for more than a year. Serendipity delivered success when abundant bacterial growth was found in cultures that had been inadvertently left in the incubator unintentionally, extending the incubation period from two to six days. While the isolation of Helicobacter pylori was a breakthrough achievement, it did not establish that the microbe cause gastritis. It was already known from autopsy studies that curved rod-shaped bacilli were present in the stomachs of many individuals who had neither gastritis nor a history of stomach disease. The successful isolation of bacteria from gastric biopsies by Marshall and Warren satisfied the first two of Koch's four postulates, but all four had to be met to indisputably prove that the organism that had been isolated was the cause of the gastritis. In an amazingly daring feat that ultimately fulfilled Koch's postulates, Marshall and another volunteer ingested cultures of the bacteria. Both of them developed acute gastritis proven by endoscopic biopsies from which the suspected pathogen was re-isolated. These results confirmed the link between H. pylori and gastritis, but since neither subject developed an ulcer, that link still remained unproven. Subsequent clinical trials showing that antimicrobial therapy could cure ulcers left no doubt that H. pylori caused gastric and duodenal ulcers. When Warren and Marshall used standard bacteriological tests and electron microscopy to characterize the isolated organism they found that it was not a Campylobacter species, but a newly discovered microbe that was subsequently designated Helicobacter pylori. A high degree of genetic polymorphism in the expression of these virulence factors was observed in different isolates. This phenotypic heterogeneity provided insight into the highly variable host consequences of infection with H. pylori. The entrenched disbelief that microbes could survive in the strongly acidic environment of the gastric mucosa was annulled by the finding that H. pylori produced urease, an enzyme that made it exquisitely suited to survive in an acidic niche. Urea present in gastric secretions is cleaved by the microbial urease to yield ammonia and bicarbonate that create a moat of pH neutrality surrounding the bacterium. Urease activity became the basis of a clinical test that was developed to screen patients for the presence of gastric H. pylori. A major boost was given to the H. pylori field in 1997 when the entire DNA sequence of the bacterial genome was published in Nature (Richard et al., 2005).

2.3.0 Helicobacter pylori

The organism is one of the most genetically diverse of bacterial species. When a new slow-growing Campylobacter-like organism (CLO) was cultured by Marshall in 1982 from mucosal stomach specimens of patients with gastritis, it was classified as Campylobacter pyloridis and shortly after corrected to C. pylori (Marshall et al., 1987). New intestinal CLOs were discovered at the same time, and C. pylori was sometimes referred to as gastric CLO (GCLO) and GCLO-1 when another CLO (GCLO-2, C. jejuni. Subsp doylei) was isolated from the human stomach (kasper et al; 1985; Vandamme et al; 1995). It soon became clear that even though C. pyloric resembles' Campylobacter in many aspects, it differs in important features such as flagellum morphology, fatty acid content, and 16S r RNA sequence (Godwin et al; 1989; Rieggs et al; 1995). C. Pyloric was transferred to a new genus, Helicobacter, and named Helicobacter pylori in 1989, together with Campylobacter fennelliae and Campylobacter cinaedae (Owen 1998) and it belong to the phylum proteobacteria, class Epsilon Proteobacteria, order Campylobacterales and family Halicobacteracae. Currently, this genus Helicobacter consists of over 20 recognized species; H pylori and H. felis are the only species known to infect the human host with many species awaiting formal recognitiob (Fritz et al., 2006; Kusters et al., 2006).

2.4.0 Ecological Niche Of Helicobacter pylori

The bug persists in an acidic gastric environment, typically provided by the corpus and antrum for the lifetime of the host. Also it can tolerate an alkaline environment with pH 9 being the limiting value (Jiang and Doyle 1998). To mimic this environment, microbiologists have come up with marked differences of micro-aerobic atmospheric in a plausible task of culturing this pathogen (Ndip et al., 2003). Gas generation kit, a variable atmospheric incubator or an anaerobic jar refilled with 5-6% O_2, 10% CO_2, 80-85% N_2 gas mixture has been successfully used to mimic the required microaerophilic environment (Ndip et al., 2008). Media such as Columbia Agar Base or Brain Heart Infusion broth supplemented with blood or serum

usually prove adequate for culture (Ndip et al., 2003). Research has also revealed that 99% of H. pylori cell maintain respiratory activity for at least 250 days at 40C as compared to loss of respiratory activity after 24hours at 37oC (Gribbon et al., 1995).

2.5.0. Success Of Helicobacter Pylori In Its Ecological Niche

Controversy still persists on the duration of the relationship between H. pylori and humans considering how this pathogen has adapted in having a complete life in the human stomach. However, co-evolution of H. pylori with humans over thousands of years has effectively refined the interactions that occur between bacteria and host effectors, transmission between hosts, survival during acidic stress within hosts, and avoidance of immune response (Blaser 1997; Scott et al., 2007). Gastric acidity and peristaltic muscle movement of the alimentary canal have the potential to preclude bacterial colonization of the human stomach. However, natural selection has enhanced this organism with some mechanisms to dodge these primary defences thereby initiating an infection (Peek 2005). This organism makes use of a urea splitting enzyme (urease) to neutralize gastric acidity, as it traverse the gastric lumen (Campbell and Thomas 2005) in addition to urea that can be bacterial derived or obtained from the host (Hovey et al., 2007), other enzymes such as catalase and oxidase are produced (Kusters et al., 2006). Locomotion and counteraction of peristalsis, another necessity for persistent infection is aided by the presence of two to six flagella (Brown 2000). Urease activity and flagella secretion are coupled by the gene FlbA (Peek 2005). Adherence is another requirement for prolonged colonization of the stomach by H. pylori (Peek 2005). Inter-species entero- coexistence has been highlighted in several studies, with competitive exclusion failing to take it toll (Gibson et al., 19998; Nagorni 2000; Akada et al., 2003; Fritz et al., 2006; Samie et al., 2007). H. pylori have the capacity for horizontal gene exchange hence enabling genetic variability within the population. In addition, H. pylori show competency in the uptake of DNA from other H. pylori cells (Blaser and Atherton 2004). Diversity of this organism can play an influential role in the survival of the population in its niche. Coexistence is enhanced by failure of competive exclusion by H. pylori strains suggesting that these different strains occupy different gastro-mucosal micro-niches (Akada et al., 2003). Flexibility or adaptability in this population, allows for maximized use of resources in a variety of niches (Blaser and Atherton 2004). The size or availability of these gastro-mucosal micro-niches is affected by host genotype and age or physiology. Inter-specific competition also influences survival of a population in a nich.

2.6.0 Epidemiology Of H. Pylori Infection

Several Studies have highlighted a high prevalence of this organism in the developing world including Africa (Bakka et al., 2002; Delport et al., 2006; Frenck et al., 2006 Fritz et al., 2006; Mbulaiteye et al., 2006; Levin et al., 2007; Ndip et al., 2001: Louw et al., 2001). Dating back as the early 90s, a high prevalence (80%). Careful surveys have also revealed that most persons in the developing world are infected with the bacterium with acquisition commencing at early stages of life. H. pylori infections have been documented in several studies done in developing countries e.g. in Egypt, there was a high prevalence (72.38%) of the infection was noted among school children (Mohammed et al., 2008). In yet another study, H. pylori IgG antibodies were also detected from South Africa African children and their mothers (Mosane et al., 2004).

Recently, in a South African population studied by Fritz et al., (2006). H. pylori prevalence was observed to be 83.3%, which is not significantly different to the 84% noted in another study conducted in Venda region, Polokwane, detection of H. pylori DNA in Faecal samples by PCR revealed a 50.6% prevalence of the organism (Samie et al., 2006). However, on a separate study in Tanzania, seropositivity rose steeply with age from 76% in children aged 0 – 4 years to 99% in adults (Mbulaiteye et al., 2006). Also, a similar trend was noted in Lybia where prevalence rose with age up to about 94% in age above 70 years (Bakka 2002). In Cameroon, a high incidence of H. pylori was recoded among asymptomatic Tunisian children (Maherzi et al., 2003). In Nigerian children, the sero-positivity rate rose from 57 to 82% in children between 5 – 9 years of age (Holcombe et al., 1992).

Also of ambiguity, a serological study in Egypt revealed that increased education was significantly associated with an increased risk of infection among mothers (Bassily et al., 1999). However an improved hygiene-education programme could be necessary to adjust deep-rooted inherent behaviours in a plausible task to reduce microbial infections (Nala et al., 2003).

In the Western countries, the pathogen generally affects about 20% of persons below the age of 40 years, 50% of those above 60 years, yet is uncommon in young children. The prevalence H. pylori and the rate of infection are as well inversely related to socioeconomic status and sanitation (Bardhan 1997; Kusters et al., 2006: Ahmed et al. 2007). In certain Western countries, Immigration is responsible for isolated areas in high prevalence (htt:www.helico.com/hepidemiology.html). However, prevalence of the pathogen correlates more with socioeconomic status rather than with ethnicity. In the U.S., the probability of being infected is greater for

older persons (>50 years =>50%), minorities (African Americans 40 – 50%) and Immigrants from developing countries (Latino > 60%, Eastern Europeans > 50%). The infection is less common in more affluent Caucasians (< 40 years = 20%).

2.7.0 Pathogenesis

2.7.1. Attachment in Stomach of Host

Infection by H. pylori is presumed to be from the gastric antrum and then extending down to the corpus after extensive mucosal damage (Akada et al., 2003). Flagella, urease, and adhesins are all essential factors for H. pylori to colonize the gastric mucosa. The curved morphology of H. pylori and the polar motility caused by flagella in one end caused screw-like movements, which may enable the organism to penetrate the mucin layer. Colonization unavoidably stimulates nuclear factor-kappa B (NF_B) activation and interleukin-8 (IL-8) expression in gastric epithelial cells (Kim et al., 2003). Toll-like receptor 2 (TLR2) and 5 (TLR5) recognize H. pylori and initiate signaling pathways that result in enhanced activation of NF_B; IL-8 is secreted by the host cells to attract components of the innate and adaptive immune systems to the site of infection. This polarises the immune response towards a Th1 response, further attracting inflammatory cells and T-lymphocytes. An effective CD4+TR-Cell response is essential to clear H. pylori, however this organism has been shown to inhibit CD4 +t-Cell proliferation and arresting IL-2 cell-cycle progression resulting in avoidance of clearance thereby staging an infection (Gebert et al., 2003: Sundrud et al., 2004). Initial infection by highly pathogenic strains possessing a cluster of genes known as the cag pathogenicity island result in altered expression of several genes associated with glycan biosynthesis especially _3GIeNAc T5, a GIcNAc transferase required for the biosynthesis of Lewis antigens (Marcos et al., 2008). Resultant over expression of _3GIcNAc T5 in human gastric carcinoma cell lines lead to increased sialyl-Lewis x expression, a specific kind of sugar molecule that these cells display on their surface as a flag to attract immune cells to the infection site (Nagorni 2000; Bor-Shyang et al., 2006; Marcos et al., 2008). Among a number of adhesins, this organism uses bacterial adhesion protein called sialic-acid binding adhesion (SabA) to recognize a molecule associated with inflammation and a molecule known as Lewis B antigen binding adhesin (BabA) to adhere to the inflamed cells of the glandular lining (Mahdavi et al., 2002; Bor-Shyang et al., 2006; Baldwin et al., 2007). The ability of H. pylori to adjust its adherence properties to the level of inflammation it causes at the stomach surface could help explain how this bacterium maintains its persistence, decades-long infection in the stomach of millions worldwide.

2.7.2. Avoidance of the Immune response of the Host

Other than inhabiting superficial glycoprotein-rich mucosal niche meant to protect stomach cells from the secreted acids in the stomach cavity, a mirco-distance from inflamed glandular cells (Mahdavi et el., 2002; Delport and Merwe 2007), the organism also avoids recognition by producing specific bacterial factors that stimulate selective expression of host genes and also by inducing an ineffective T-cell response. Genetic diversity of this organism also plays a paramount role in its persistence. While the rocF gene is not essential for the initiation of an infection, it encodes arginase, an enzyme responsible for the hydrolysis of L-arginine to L-ornithine and urea. Reactive nitrogen intermediates are relatively ineffective against H. pylori (Bryk et al., 2000). Unavoidable, arginase allows the bacterium to evade host immune response by competing with macrophage INOS for L-arginine. Due to bacterial cell deficiency in arginine synthesizing enzymes, this organism exploits the host's arginine to maintain the nitrogen balance (Hovey et al., 2007).

2.7.3 Ability to attain a viable but non Culturable State

H. pylori have the ability to remain culturable in natural waters for 2 to 3 days at a low temperature (Gribbon et al., 1995; Adams et al. 2003). In prolonged adverse conditions, the organism can exist in all morphologies in a nonculturable state (Bode et al., 1993; Sorbeg et al., 1996; Atherton 1997; Fujimura et al., 2004). The coccoid form induced by water is capable of colonizing the gastric mucosa and causing gastritis in mice (Cellini et al., 1994; She et al., 2003), but whether H. pylori can revert from its coccoid to its infections form in humans has not yet been determined (Owen 1993). Nevertheless, the persistence of H. pylori cells in the environment in the viable but non-culturable state presents a public health hazard.

2.8.0 Plausible Routes Of Transmission

As one of the medical important bacterial pathogens, H. pylori transmission pathways are still vague (Konno et al., 2005; Braganca et al., 2007) and currently more than 50% of the world's population is infected. The prevalence of H. pylori infection and the rate of infection are inversely related to the standard of living and sanitary practice (Malaty et al., 1998; Ahmed et al., 2007; Dube et al., 2009a). The risks of transmission include precarious hygiene standards crowding, and contaminated environment and water sources (Bunn et al., 2002; Suerbaum and Michetti 2002). The possible routes of transmission include oral-oral and faecal-oral, either with or without transitional transmission steps (Vaira et al., 2001; Ahmed et al., 2006) during episodes of diarrhea or

gastro-oral contact in the event of vomiting (Deport and Merwe 2007). Person to person transmission can be a plausible cause of infection (Brown et al., 2002). Use of contaminated water including municipal tap water has also been suspected to have high impact in the transmission of the organism (Ahmed et al., 2006). However, water purification, improved hygiene, reduced environmental contamination, immunization (vaccination) and antibiotic treatment have played an important role in reducing the morbidity and mortality of bacterial disease especially in the developed world where these are acceptable cultural practices.

2.8.1. H. pylori contaminated water sources

Contaminated of drinking water sources can occur from raw sewage overflow, septic tanks, leaking sewer lines, land application of faeces/sludge, and from partial treated wastewater (Konishi et al., 2007). The use of contaminated drinking water, including municipal tap water, has long been suspected to have a high impact on the transmission of H. pylori (Ahmed et al. 2007; Braganca et al., 2007; Konishi et al., 2007), particularly in areas where the use of untreated water is common. The bacterium has been detected in river, creek, lake and well water (Hulten et al., 1996; Hegarty et al., 1999).

2.8.2 Faecal contamination

In most infected persons, H. pylori can be cultured from the stool, providing evidence that spread by Faecal-oral contact with infected persons is likely (Thomas et al., 1992; Dore et al., 2000). As the organism can survive for several days in water, water contamination with human excrement has the potential for transmission by the Faecal-oral route (Sorbeg et al., 1996; Adams et al., 2003). In natural waters, the microorganism retains its spiral form and shows better culturability than when kept in a nutrient rich environment (Konishi et al., 2007). H. pylori cells remain culturable longer in cooler water (<20oC) than in warmer waters (>20oC) (Gribbon et al., 1995; Adams et al., 2003). Research has also demonstrated that H. pylori can live for several days in milk and tap water in its infectious bacillary form, and in river water for several months in the nonculturable but viable coccoid form (Brown 2005; Dube et al., 2009b). as mentioned before, this form is capable of colonizing gastric mucosa and causing gastritis in mice (She et al., 2003). H. pylori has been positively isolated or tested from faces of adults and children using culture techniques or the H. pylori stool antigen tests (HpSA and HpSTAR kits) (Krausse et al., 2008) and PCR (Klein et al., 1991; Thomas et al., 1992; Mapstone et al., 1993; Lottspeich et al., 2007). In one study, the organism was successfully isolated from fresh stool specimens obtained correlated of infection and faecal pollution has been demonstrated (Queralt et al., 2004). Limited sanitation services in Africa could

unavoidably lead to faecal contamination of the environment and water sources. Hence, playing habits like swimming in river or dam water should have the capacity to accelerate the rate of infection in an African population. If this bug can use water as a vehicle for transmission, then this assumption leaves a lot of questions unanswered pertaining to the prevalence of the organism in rural areas in Africa with poor sources of water.

2.8.3 Water Disinfection

Oxidizing disinfectants like chlorine are most commonly used in drinking water (Margolin 1997). In the viable but non-culturable coccoid form attained due to stressful environments (Cellini et al., 1994; Gribbon et al., 1995; Mouery et al., 2006). H pylori resist the disinfection practices normally used in drinking water treatment (Atherton 1997; Baker et al., 2002; Moreno et al., 2007). In chlorinated water, when compared with E. coil, the survival of H. pylori appears to be linked with superior resistance. Hence, if H. pylori tolerate disinfectants in water distribution systems, then transmission by waterborne route is feasible.

Additionally, microorganisms like Acanthamoeba castellaii have been shown to promote the survival of the pathogen under experimental conditions (Winiecka-Krusnell et al., 2002).

2.9.0 Water Sources In Africa

In Africa, supply of clean water is still a challenge toward the control of microbial infections, hence, focus on how best to improve water quality within 200m radius, a standard required by the World Health Organisation (WHO), will be a step toward controlling the transmission of microorganisms via water. The intervention techniques used to treat water include physical removal of pathogens (for example, filtration, sedimentation, and adsorption), chemical treatment (for example, assisted sedimentation, chemical disinfection, and ion exchange), heat and ultra violet (UV) radiation.

The very high prevalence of H. pylori in Africa may be linked to water sources (Ndip et al., 2004). In this part of the world, domestic water sources ranges from indoor tap water to the most ancient forms, such as direct dam or river water (Thomas et al., 1992; Carbone et al., 2005) from which the presence of the antigen cannot be ruled out (Brown 2000; Braganca et al., 2007). Bacteriological water quality relies primarily on the type of disinfectants used and the ability to sustain enough residual concentrations, meaning the concentration of biodegradable compounds in water as well as the prevailing water temperature and the piping material used (Baker et al., 2002). Protected wells, groundwater, and rain water are other forms of domestic water. Whereas containers can be provided to store clean water for drinking and

domestic use, this method is linked with risks of contamination, for example, during transportation, storage, and during domestic use (Figueiredo et al., 2002: Mouery et al., 2006). Several studies have highlighted the presence of the microorganism or their DNA in water (Hulten et al., 1998; Queralt et al., 2004; Hegarty et al., 1999; Braganca et al., 2007; Ahmed et al., 2007; Konishi et al., 2007; Nayak and Rose 2007).

A Council for Scientific and Industrial Research (CSIR) report estimated that only 21% of South African households have access to piped water within their homes. Additionally, 43.3% and 30% of the population in Mangwe and Beitbridge in Zimbabwe were found to be using unprotected water (Baker et al., 2002). Furthermore, a shortage of funds in African countries has an impact on the operation of sewage systems, which are below standard with rural populations using latrines, thereby unavoidably increasing chances of faecal contamination of water sources (Margolin 1997). Because faecally contaminated water has the potential for transmission via the faecal-oral route (Sorbet et al., 1996), most Africans might be at risk of becoming infected with the organism due to the primitive water sources that are still the main water sources in some communities. Use of boiled or filtered water would be an exploitative idea as it has been shown to reduce infection (Figueiredo et al., 2002).

Although tangible evidence of his mode of transmission is lacking, water as a vehicle for the transmission of H. pylori, cannot be ruled out (Dube et al. 2009c). Interestingly, a serological study in Egypt revealed that increased education was significantly associated with an increased risk of infection among mothers (Bassily et al., 1999). Hence, much attention is still necessary to gather more facts on this proposed route of transmission.

2.10.0 Household Hygiene

In preventing waterborne diseases, hygiene is the starting point. High standards of hygiene can be maintained only if a steady supply of clean water and proper sanitation system are available. Several studies have been conducted to relate H. pylori prevalence with household hygiene (Malaty et al., 1998; Perry et al., 2006; Ahmed et al., 2007). Prevalence was observed to be higher within families using non-flush toilets, outdoor toilets, outdoor water taps, and use of river water (Ahmed et al., 2007). Most of the findings show that poor hygiene has a positive correlation with increased prevalence of the micro-organism. Intraspecific transmission from mother to child has been linked to premastication of food (Megraud et al., 1995). In addition, use of common spoons, licking pacifiers or teats of feeding bottles by other subjects may result in the transmission of the organism

(Rothenbacher et al., 1999). Also a strong evidence for a transmission pathway from family members to children was recently observed (Ceylan et al., 2007). Safe disposal of human excreta is the first step in preventing faecal-oral and other routes of disease transmission. Improved sanitation standards reduced contamination of the environment. Poor sanitation, like the lack of sanitary services at home, is believed to be an important risk factor for H. pylori infection (Mendall et al. 1992; Malaty et al., 1998). Impaired hygiene during childhood especially in developing countries seems to be associated with a higher prevalence of the organism. Sharing cups, premastication of food for young children, sharing water for bathing and washing hands and limited sanitary facilities have been shown to be having a positive correlation with increased prevalence of H. pylori (Ahmed et al., 2007).

Several studies have proposed that most people acquire H. pylori infection during childhood (Goodman and Correa 1995; Malaty et al., 1998; Rowland 2000). However, controversy still exists regarding the role of the oral cavity as a route of transmission. The oral-oral route, the transmission of H. pylori could probably take place through the consumption of contaminated food.

2.11.0 Association Between H. Pylori And Blood Group O

Many studies have shown adherence of the H. pylori to blood group O and le b antigen sector in gastric mucosa and babA on the outer membrane of H. pylori mediates adherence of H. pylori to le b antigen expressed on mucosa (Rotherbacher et al., 2004; Backstrom et al., 2004; Magalhaes et al., 2010). In colonizing the human host H. pylori binds to gastric mucins, rather than directly to mucosal epithelium, to protect itself from luminal acidity and shedding (Azevedo et al., 2008). The most efficient binding occurs on mucin Lewis (b) antigens, with some secondary binding to H type 1 antigens (Alkout et al., 1997). Both antigens contain the terminal Fuca 1, 2 residue on which binding occurs. Blood group A and B antigen determinants (GalNaca1,3 and Gala 1,3, respectively) are attached at the third position of the penultimate GalB1,3 moiety, immediately adjacent to the Lewis (b) Fuca 1,2 at the second position, and interact sterically with the Fuca 1,2 residue (Aspholm-Hurtig et al., 2004). For example, some strains of H pylori that bind to the Lewis (b) antigen do not bind to A-Lewis (b) (Aspholm-Hurtig et al., 2004).

H. pylori has several lipopolysaccharides such as O antigen on its outer membrane expressing the membrane of the H. pylori for antigenic mimicry may create persistent colonization and surviving of bacteria in the stomach mucosa. In addition, expression of le b antigen in the gastric mucosa may play as a receptor to

the bacterial adhesion. It seem blood group antigen b-binding adhesion (babA) on the outer membrane of the H. pylori has a major role in persistent colonization of the bacteria with attachment to le b antigen of the gastric mucosa (Rothenbacher et al., 2004; Montecucco et al., 2001). Some heterogenicity has been characterized in expression of the outer membrane protein, especially babA, that describe various comrexteis of different H. pylori for adhesion to le b antigen on the gastric mucosa, a factor determining some difference in clinical outcomes of the infection (Henning et al., 2004; Ishijima et al., 2011). Binding of the H. pylori to H (blood group O) and le antigens in gastric mucosa probably describe higher incidence of chronic gastritis and adenocarcinoma in O blood group phenotype.

2.12.0 Association Between H. Pylori In Water And Clinical Infection

Although H. pylori infection is ubiquitous, its mode of transmission remains an enigma. H. pylori have being presumed to be transmitted orally. One way that H. pylori could be transmitted orally is by means of faecal matter through the ingestion of waste tainted food or water. In addition, the organism could be transmitted from the stomach to the mouth through gastro-oesophagal reflux (in which a small amount of the stomach's contents is involuntarily forced up the oesophagus) or belching, common symptoms of gastritis. The bacterium could then be transmitted through oral contact. Among those having a history of drinking well water, H. pylori serological prevalence in residents who were at least 10 years of age (85.3%) was significantly higher than in those under 10 years of age (25%) or in those with no history of drinking well water (6.3%). In a continuation of the same study, H. pylori DNA was detected in well water obtained from all five wells from which the five sero-positive members had drunk (Egwari and Aboaba 2002).

Many North American arctic communities are characterized by risk markers associated with H. pylori infection, including inadequate water supply and sanitation systems. The prevalence of H. pylori infection was measured in two traditional communities in the central Canadian arctic using PCR to test for the presence of the bacteria in local water supplies (McKeown et al., 1999). Of the 256 | subjects from the two communities, one hundred and thirty (50.8%) were positive for H. pylori IgG antibodies. Compared with sero-negative individuals, the sero-positive subjects were more likely to be male (p - 0.01). Antibody status did not differ with respect to age, community, alcohol or cigarette use, number of persons per household, gastrointestinal complaints or previous investigations, medications, or presence of blood group.O, Lewis a-b+.

2.13.0 Clinical Manifestation

The organism is a major cause of upper gastrointestinal diseases such as gastritis, peptic ulcer and gastric cancer (Ahmed et al., 2007; Tanih et al., 2009). The primary disarray that follows initial colonization of the host is chronic active gastritis (Kusters et al., 2006). It has been suggested that up to .95% of duodenal and 70% of gastric ulcers are attributable to this infection and most cases occur in middle aged subjects (Rothenbacher 2007). In the US, nearly all persons with duodenal ulcer are infected, and that persons without the infection will ever develop duodenal ulcer is highly unlikely. Although gastric ulcer is usually caused by these bacteria, about 30% of gastric ulcers in the US occur in persons without H. pylori and could be related to non-steroidal anti-inflammatory drugs. Most gastric adenocarcinomas and lymphomas occur in persons with current or past infection with H. pylori. The clinical outcome of long-term infection is variable and is considered to relate both to bacterial virulence factors (Gatta et al., 2003; Wang et at, 2003; Monica et al., 2006) and host genotype. The vacuolating cytotoxin VacA (Ye et al., 2000) and the cag pathogenicity island (Atherton 1997, Bravo et al., 2002) are two identified virulence factors that are considered to have an important role in the pathogenesis of H. pylori infection. VacA gene comprises two variable regions, the s region which exists as an s1a, s1b, s1c, or s2 allele, and the m region, which occurs as an m1, m2a, or m2b allele (Figueiredo et al., 2000). H. pylori VacA types 1 strains appear to be more virulent than type s2 strains and are associated with higher risks for peptic ulcer disease, gastric atrophy, and gatric carcinoma (Figueiredo et al., 2000). The VacA types 1 strains appear to be more virulent than type s2 strains and are associated with higher risks for peptic ulcer disease, gastric atrophy, and gastric carcinoma (Figueiredo et al., 2000). The VacA s1 and VacA m1 strains are also strongly associated with a higher degree of inflammation and epithelial damage in the gastric mucosa. The intragastric distribution and severity of the chronic inflammatory process depends on a variety of factors, such as characteristics of the colonizing strains, host genetics and immune response, diet, and the level of acid production (Kusters et al., 2006). Although the relation between H. pylori infection and gastric cancer has been well-established, some studies have shown a negative correlation of H. pylori infection and the development of gastric cancer in Africa. The high prevalence of infections, contrary with low rate of development into gastric cancer, well expressed as "African enigma", is an ambiguity because the headway to atrophic gastritis in the African population does not differ from that reported

in other regions (Segal et al., 2001). The variants of the interferon-c gene (IFNGRI), which are more prevalent in Africans appear to play a significant role in the infection of human host contributing to a high prevalence even-though there is relatively low pathogenesis of infection in Africa (Thye et al., 2003; Ndip et al., 2004).

2.14.0 Laboratory Diagnosis Of H. Pylori Infection

Since the discovery of the organism in the early 80s, different techniques have been developed for diagnosing H. pylori in clinical specimen. These tests may be invasive or non-invasive (Shephered et al., 2000; Tanih et al., 2008). Endoscopy backed by gastric mucosal biopsy methods, histology, culture, or urease tests are forms of invasive test that could be used (Stromar et al., 2008). Non-invasive tests include the Urea Breath Test (UBT), Enzyme Immunosorbent Assay (ELISA), H. pylori Stool Antigen Test (HpSA), Rapid H.pylori Antigen Test (HpSTAR) and latex agglutination tests (Ndip et al., 2004; Krogfelt et al., 2005; Dube et al., 2009b).

Culture

The culturing technique has been mostly challenged by the inability of the organism to remain viable for a longer period outside its host. In an unfavorable environment the organism turns into a coccoid form which is viable but non-culturable. However successful cultures of H. pylori have been grown from biopsies, string samples and stool specimen (Thomas et al., 1992; Parsonnet et al., 1999; Dore et al., 2000; Velapatino et al., 2006). After collection, a biopsy sample is homogenized in 0.9% saline solution prior to inoculation (Ndip et al., 2003); for the string sample, homogenizing by vortexing in transport medium containing brain heart infusion (BHI) broth, 20% glycerol and 1% Skirrow supplement is adequate before inoculation (Velapatino et al., 2006). Several agar recipes for isolating and culturing H. pylori are available. BHI agar containing Skirrow supplement (Oxoid), Columbia colistin-nalidixic acid agar with Dent supplement (Oxoid), Skirrow Campylobacter medium, Columbia agar, Chocolate agar, Marshall brain heart infusion (BHI) medium, Mueller-Hinton and Wilkins-Chalgren agar with horse blood and Belo Horizonte medium supplemented with 2, 3, 5 – triphenyltetrazolium chloride are other culture mediums that have been successfully utilized in culturing H. pylori (Velapatino et al., 2006). However, Oxoid BHI agar supplemented with 5% horse blood, 1% IsoVitalex (BBL, Microbiology systems, Becton Dickenson, Cowley) with and without anitbiotics according to either the Skirrow's medium or to the Dent and McNulty medium has been recommended for general use (Owen 1995; Dent and McNulty 1998). As cited in

Ndip et al., (2003), Morgan and co-workers stated that the agar based culturing medium can be substituted by selected enrichment medium that bears Brucella broth (Difco) supplemented with 10% foetal calf serum, 1% (v/v) Iso-Vitalex, polymyxin B sulphate (1000 units/mL), vancomycin (10ug/mL) and amphotericin B (2ug/mL).

Incubation

H. pylori is microaerophilic, therefore, other than using an incubation temperature of 370C, microaerobic conditions should exist for its growth. Outside the human host, atmospheric composition ranging from 5-6% O_2, 7-12% CO_2, 0-85% H_2 are conducive for H. pylori growth (Ndip et al., 2003; Velapatino et al., 2006; Ndip et al., 2007a: Ndip et al., 2007b). incubation periods of up to 10 days are satisfactory to maximize growth particularly if a biopsy sample is taken after an antibiotic treatment.

Urease Test

This test makes use of the ability of the organism to produce urease. When H. pylori infected biopsy sample is added to urea containing medium, ammonia a byproduct. Influence a pH-driven colour change that forms the basis of this diagnostic test (Midolo et al., 2000; Levin et al., 2007). The CLO test and rapid urease tests (RUT-homemade) are of similar sensitivity and specificity i.e. 90% and 100% respectively (Logan and Walker 2001; Levin et al., 2007). False-negative results may be obtained, current reports like these circumstances to the use of suppression medication especially PPIs and other antibiotics.

Non-invasive tests

Urea Breath Test (UBT)

This test is non-quantitative and it determines current infection as it relies on urease activity produced by the bacteria. False negative can arise if there are too few bacteria in the stomach of infected host to produce detectable urease especially during or after a treatment regiment, also in the case of infection with different bacteria that also produce urease. Generally, either 13C or 14C is used. The labeled urea is hydrolysed by the urease enzyme in the stomach of an infected host, and the resulting CO_2 is absorbed across the gastric mucosa into the blood circulatory system, and then excreted through the lungs as expired air.

Serology

This is a useful tool for detecting H. pylori in either fresh or stored serum. Serological tests are non-quantitative and detect immunoglobulin (IgG) or IgA or IgM antibodies to H. pylori infection (Bassily et al., 1999; Brown et al., 2000; Mbulaiteye et al., 2006). The circulating anitbodies to H. pylori can be detected by enzyme linked immunosorbent assay (ELISA) or latex agglutination tests. The resultant colour change

due to the formation of an antigen-antibody detection can be ideal and has been widely in Africa (Bassily et al., 1999; Aoki et al., 2004; Longo-Mbenza et al., 2006; Mohammad et al., 2007), it does not offer direct evidence of current infection resulting in failure to confirm the presence of the antigen. This is critical, especially with infants borne from H. pylori positive mothers where there is a high chance of trans-placental transfer of the IgG (Bassily et al., 1999). It also makes it difficult to differentiate between passively acquired and actively produced antibodies to the organism. In addition, no single antigen is recognized by sera from all subjects, this implies that the precision of serological tests relies on antigens used; hence local validation of the test becomes a requirement.

Stool antigen tests

A simple sandwich-type enzyme immunoassay amplification technology is used to analyze stool samples as per the manufacturer's instructions. It uses monoclonal antibodies specific for H. pylori antigens. To avoid the problem of strain variation, an H. pylori strain found in different geographical regions and dietary groups is selected to produce bacterial sonicates (Larka et al., 1999). The main advantages of this technology are that it detects the present infection and it can be easily employed for large scale epidemiological studies of acquisition of H. pylori in all population groups. In addition, the colour change can be assessed visually in the mirco-plate (HpSA test) or strip (HpSTAR test). These tests have been used successfully worldwide with high sensitivity, specificity and accuracy (Frenck et al., 2006; Lottspeich et al., 2007; Krause et al., 2008; Dube et al., 2009c). its disadvantages include limited use with patients on medication containing antimicrobial agents, proton pump inhibitors and bismuth preparations due to suppressed growth of the organism thereby leading to false negative results. Also there is a possibility of detecting live and dead cells by this method or partially digested cells. The newly introduced Rapid H. pylori Antigen Test (HpSTAR), is fast and results may be obtained within 20 minutes. However this test has shown an acceptable sensitivity of 77% while its specificity and accuracy is over 80% in an adult population (Krausse et al., 2008). However, sensitivity of 96.1% and specificity of 98.5% along with positive (PPV) and negative predictive values (NPV) of 96.1% and 98.5%

respectively have been recorded (Sykora et al., 2003). In a recent study involving Egyptian children, the HpSTAR test had a sensitivity of 93%, specificity of 88% and NPV of 93% (Frenck et al., 2006). In the same study involving Egyptian children, the HpSA test had a sensitivity of 71%, specificity of 76%, PPV of 73 and NPV of 74%. In addition, the major advantage of HpSTAR over the HpSA test is that easy to perform. However, HpSTAR is only qualitative while HpSA test with the combination of the microplate reader is quantitative.

2.15.0 Validation of diagnostic tests

Validation of test is important as a determinant of suitable methods to be employed for improve quality of research .The factors that may affect test validity include patient age, gender and geographic location (Frenck et al., 2006).the gold standers for validating some of the diagnostic test for H. pylori infection are still a challenge. Other than being invasive, biopsy-based techniques mainly used as a gold standard, do not cater for the possibility of patchy distribution of the organism in the human stomach (Brown 2000). To reduce this uncertainly, multiple biopsies can be taken from the antrum and corpus (Krogfelt et al., 2005). Also, high standard disinfection practices need to be exercised to avoid latrogenic transmission of the bug during sampling.

Table 5: Association between H.pylori and rhesus compatability

Samples			Rhesus "D" positive			
O	A	B	AB	O	A	
	B	AB				
H. Pylori positive	21 (60%)	3 (50%)	4 (100%)	1 (100%)	1 (100%)	0	0	1 (100%)
H. Pylori negative	14 (40%)	3 (50%)	0 (100%)	0 -(0)	0	0	1

CHAPTER THR