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Therapeutic management of dyspepsia in patients with *Helicobacter pylori* at Ahmadu Bello University Teaching Hospital, Zaria.

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Abstract

The aim of this study was to examine the prevalence of *Helicobacter pylori* among dyspeptic patients referred for endoscopy, and to establish guidelines for diagnostic evaluation and therapeutic management of *H. pylori* infection. Fifty (50) consecutive adult dyspeptic patients that attended the gastroenterology unit of the Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria from February through December, 2003 were evaluated. A diagnostic oesophago-gastro-duodenoscopy (EGD) was performed at which antral mucosal biopsies were taken to determine the presence of *H. pylori*. The success of *H. pylori* eradication with a triple regimen was prospectively studied. The main endoscopic findings showed duodenal ulcer (DU) 52%; gastric ulcer (GU) 16%; gastric/duodenal ulcer (GU/DU) 8%; gastro-oesophageal reflux disease (GERD) 6%; gastric cancer (GC) 8% and non-ulcer dyspepsia (NUD) 10%. Among the thirty patients that took Esomeprazole + Clarithromycin + Amoxycillin (ECA), 70% were cured, 16.7% mildly improved and 13.3% did not improve. On the other hand, 55% were cured, 30% mildly improved and 15% showed no improvement in dyspeptic symptoms among the twenty (20) patients that took Omeprazole + Clarithromycin + Amoxycillin (OCA). Statistical analysis showed that these two regimens (ECA and OCA) did not differ significantly in eradicating *H. pylori* and healing of organic lesions among patients with different types of dyspepsia ($P > 0.05$). *H. pylori* was found to be associated with PUD, GERD, GC and NUD. Proton-pump inhibitor based triple therapy was found to eradicate *H. pylori* and it healed gastrointestinal ulcers among the patients studied.

Key words: Helicobacter pylori, endoscopy, proton-pump inhibitors, triple therapy

Introduction

Dyspepsia is defined as upper abdominal or retrosternal pain, discomfort, heartburn, nausea, vomiting or other symptoms considered being referable to the proximal alimentary tract[(1)]. It is a very common symptom-complex and is the reason for most referrals for oesophago-gastro-duodenoscopy (EGD). Since the discovery of *H. pylori* as an important aetiological agent in gastroduodenal disease, there has been substantial health care cost associated with dyspepsia. The presence of *H. pylori* causes a number of changes to the stomach and duodenum. In particular, it disrupts the protective layer of mucous and causes the release of certain enzymes and toxins that directly or indirectly cause injury to the cells of the stomach or duodenum. These changes make underlying tissues more vulnerable to damage by digestive juices resulting in chronic inflammation in the walls of the stomach or

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duodenum and subsequently, ulceration. Most of the patients with dyspepsia either have no identifiable cause of dyspepsia (functional dyspepsia) or have peptic ulcer disease (PUD), namely: gastric or more commonly, duodenal ulcers. Less common causes of dyspepsia include gastric cancer and pancreatic diseases. Dyspepsia occurs in approximately 25 percent of some populations each year with majority affected persons not seeking medical attention [2, 3]. It has been reported that in about 50-60 percent of dyspeptic patients undergoing investigation, a specific etiology is not identified [4, 5]. Socioeconomic factors however, have made adequate and detailed studies of non-ulcer dyspepsia (NUD) rather difficult particularly in developing countries [6]. The isolation of *H. pylori* brought hopes not only of a new approach to management of peptic ulcers, but also the possibility of an explanation for NUD [7]. Currently, the widely accepted investigation for evaluating dyspeptic patients is fibreoptic upper gastrointestinal endoscopy (Oesophago-gastro-duodenoscopy) [8]. The benefit of treatment to eradicate *H. pylori* in functional dyspepsia remains controversial [9]. To manage uninvestigated dyspepsia in developed countries, some authors recommend screening patients less than 50 years of age without severe symptoms with a noninvasive test for *H. pylori,* and then treat those with positive results with *H. Pylori* eradicating drugs [10]. However, in Africa, disparity exists between the high prevalence of *H. pylori* infection (> 90% in many areas) [11] and the occurrence of clinically important disease[12]. According to Knigge [13], *H. pylori* test-and-treat strategy in a primary care setting in an economically depressed area such as Africa, should be based on data that show an association between dyspepsia and *H. pylori* infection.

Patients and methods

From February to December 2003, fifty (50) consecutive adult dyspeptic patients that attended the gastroenterology unit of the Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria were prospectively studied with their consents. Pregnant women, patients with clinical evidence of an organic disease known to cause dyspepsia, patients that tested *H. pylori* negative during the endoscopic procedure, and those that have a socio-economic factor (to be included in the study) were excluded. Personal interviews using the study questionnaire were conducted individually with the 50 patients. The socio-demographic profile of each patient (age, sex, educational background, occupation, marital status, family size and income, use of alcohol and smoking behaviour), symptoms, aggravating and relieving factors and history of antibiotic use (within the previous months) were obtained. Each patient also had abdominal ultrasound examination to further help exclude organic diseases like pancreatic and hepatobiliary disease. In addition, stool microscopy was done on every study subject to exclude parasitic infections like ascariasis and strongyloidosis as these may also cause dyspepsia.

Endoscopy was performed by standard procedures after an overnight fast, using a forward viewing Olympus upper gastrointestinal endoscope. Two antral biopsy specimens were taken from each subject and were used for the rapid urease test and culture in order to confirm the presence of *H. pylori.*

Those patients that were *H. pylori* negative were given antacids and were not enrolled for the study. Twenty that were positive on rapid urease or culture test for *H. pylori* were given combination of Omeprazole (20 mg), Clarithromycin (500 mg) and Amoxycillin (1000 mg) twelve hourly with or without meals for one week, then 20 mg of Omeprazole twelve hourly

before food with half glass of water for three weeks (OCA). The remaining 30 patients were given Esomeprazole (20 mg), Clarithromycin (500 mg) and Amoxycillin (1000 mg) orally twelve hourly after meals with half glass of water for one week (ECA). These regimens are amongst those approved by United Stated Food and Drug Administration for the treatment of *H. pylori* infection. Also, abuse of these drugs has not been documented in the study environment. The patients were followed up at two weekly intervals for four weeks and endoscopy was repeated eight weeks after treatment to confirm *H. pylori* eradication and ulcer healing.

Statistical analyses

The data was analyzed using statistical analysis software (SAS) system. Fisher's Exact test was used to determine significance of association between categorical variables. P values equal to or less than 0.05 were considered significant, less than 0.01 very significant and less than 0.001 as highly significant.

Results

The main endoscopic findings were duodenal ulcer (DU) 52%; gastric ulcer (GU) 16%; non-ulcer dyspepsia (NUD) 10%; gastric/duodenal ulcer (GU/DU) 8%; gastric cancer(GC) 8%; and gastro-oesophageal reflux disease (GERD) 6% (Table I).

Table I: Distribution of gastrointestinal diseases among subjects studied

S/No	Endoscopic Diagnosis	Number of patients	Percentage number of patient
I	Non ulcer dyspepsia (NUD)	5	10%
II	Duodenal ulcer (DU)	26	52%
III	Gastric ulcer (GU)	8	16%
IV	Gastric/Duodenal ulcer (GU/DU)	4	8%
V	Gastric cancer (GC)	4	8%
VI	Gastro-oesophageal reflux disease (GERD)	3	6%
	TOTAL	50	100%

Twenty-three (46%) of the studied population were males and 27 (54%) were females, with a mean age of 43.7± 17.42 and 33.6±14.79 years respectively. There was statistically significant difference between the mean ages for males and females (confidence interval (C.I), 1.2 to 19 years; $P<0.05$. On bivariate analysis, smoking, alcoholic use, non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotic misuse were not statistically significantly ($P > 0.05$) associated with *H. pylori* infection among the various gastrointestinal diseases (Table II).

Table II: Distribution of social and drug history among *H. pylori* positive dyspeptic patients with various gastrointestinal diseases at ABUTH, Zaria (Feb. to Dec., 2003)

S/No	Social and Drug History	Types of Dyspepsia						
		DU	GU	NUD	GU/DU	GERD	GC	P value
I	Smoking	10(38.5%)	5(62.5%)	-	1(25%)	2(66.7%)	1(25%)	0.242
II	Alcohol use	9(34.6%)	6(75%)	1(20%)	1(25%)	1(33.3%)	1(25%)	0.338
III	NSAIDs misuse	24(92.3%)	8(100%)	3(60%)	4(100%)	2(66.7%)	4(100%)	0.244
IV	Antibiotic misuse	15(57.7%)	7(87.5%)	3(60%)	3(75%)	2(66.7%)	4(100%)	0.484

(DU = Duodenal ulcer, GU = Gastric ulcer, NUD = non-ulcer dyspepsia, GU/DU = Gastric/duodenal ulcer, GERD = Gastro-esophageal reflux disease, GC = gastric cancer, NSAIDs = Non - steroidal anti-inflammatory drugs)

Weight loss ($P < 0.05$), anorexia ($P < 0.05$), melaena ($P < 0.01$). dysphagia ($P<0.001$), and haematemesis ($P < 0.05$) were significantly associated with various gastrointestinal diseases observed in this study. Nocturnal pains, vomiting and postprandial fullness did not show a statistically significant association ($P > 0.05$) with the presence of *H. Pylori* among various gastrointestinal diseases (Table III).

Table III: Distribution of the different clinical features amongst *H .pylori* positive dyspeptic patients at ABUTH, Zaria (Feb. to Dec., 2003).

S/No	Clinical feature	Types of Dyspepsia						
		DU	GU	NUD	GU/DU	GERD	GC	P value
I	Nocturnal	21(80.8%)	4(50%)	2(40%)	4(100%)	2(66.7%)	3(75%)	0.176
II	Pains	4(15.4%)	1(12.5%)	1(20%)	-	-	4(100%)	0.00953**
III	Weight loss	16(61.5%)	4(50%)	3(60%)	3(75%)	3(100%)	4(100%)	0.516
IV	Vomiting	7(26.9%)	1(12.5%)	2(40%)	1(25%)	-	4(100%)	0.036*
V	Anorexia	14(53.9%)	2(25%)	2(40%)	1(25%)	1(33.3%)	4(100%)	0.189
VI	Postprandial	1(3.9%)	3(37.5%)	-	-	-	3(75%)	0.00464**
VII	Fullness	1(3.9%)	1(12.5%)	1(20%)	-	3(100%)	3(75%)	0.000192***
VIII	Melaena Dysphagia Haematemesis	2(7.7%)	3(37.5%)	-	1(25%)	-	3(75%)	0.015*

*; represents significant P value ($P<0.05$)
**; represents very significant P value ($P<0.01$)
***; represents highly significant P value ($P<0.001$)
(DU = Duodenal Ulcer, GU = Gastric Ulcer, NUD = Non-ulcer dyspepsia, GU/DU = Gastric/Duodenal ulcer, GERD = gastro-esophageal reflux disease, GC = Gastric cancer)

There was also no statistically significant ($P > 0.05$) association between duration of dyspeptic symptoms prior to study with various endoscopic findings (Table IV).

Table IV: Distributi on of duration of dyspepsia among the 50 dyspeptic patients with *H. pylori* at ABUTH, Zaria (Feb. to Dec., 2003).

S/No	Duration of dyspepsia	Endoscopic finding						
		DU	GU	NUD	GU/DU	GERD	GC	Total
I	<1 year	2(7.7%)	-	1(20%)	-	1(33.3%)	-	4
II	1-5 years	14(53.8%)	4(50%)	3(16%)	2(50%)	1(33.3%)	-	24
III	6-10 years	6(23.1%)	2(25%)	1(20%)	1(25%)	-	-	10
IV	>10 years	4(13.4%)	2(25%)	-	1(25%)	1(33.3%)	4(100%)	12
	TOTAL	**26**	**8**	**5**	**4**	**3**	**4**	**50**

P = 0.204 (Not significant); (< less than, > greater than, DU = Duodenal ulcer, GU = Gastric ulcer, NUD = Non ulcer dyspepsia, GU/DU = Gastric/duodenal ulcer, GERD = Gastro-oesophageal reflux disease, GC= Gastric cancer)

Round pepper significantly ($P < 0.05$) aggravated dyspeptic symptoms to varying degrees ($P < 0.05$). There was no statistically significant ($P > 0.05$) association between other aggravating factors and dyspeptic symptoms among the gastrointestinal diseases studied (Table V).

Table V: Distribution of aggravating factors among *H. pylori* positive dyspeptic patients at ABU TH, Zaria (Feb. to Dec., 2003).

S/No	Aggravating factors	Types of dyspepsia						
		DU	GU	NUD	GU/DU	GERD	GC	P value
I	Hunger(H)	24(92.3%)	7(87.5%)	4(80%)	4(100%)	2(66.7%)	3(75%)	0.390
II	Stress(S)	25(96.2%)	6(75%)	3(60%)	3(75%)	2(66.7%)	4(100%)	0.06
III	Anxiety(A)	8(30.8%)	4(50%)	2(40%)	1(25%)	1(33.3)	-	0.685
IV	Spicy foods(SF)	8(30.8%)	2(25%)	-	-	1(33.3%)	1(25%)	0.695
V	Pepper(P)	7(26.9%)	5(62.5%)	-	1(25%)	3(100%)	1(25%)	0.028*
VI	Meals(M)	1(3.9%)	1(12.5%)	1(20%)	1(25%)	-	-	0.344
VII	Emotional upsets (EU)	3(11.5%)	2(25%)	1(20%)	1(25%)	-	1(25%)	0.706

*; represent a significant P value ($P<0.05$)
(DU = Duodenal Ulcer, GU = Gastric Ulcer, NUD = Non-ulcer dyspepsia, GU/DU = Gastric/Duodenal ulcer, GERD = gastro-esophageal reflux disease, GC = Gastric cancer)

The effects of food and antacids show statistically significant ($P > 0.05$) differences in relieving dyspeptic symptoms among patients with different endoscopic diagnosis ($P < 0.01$) and ($P < 0.05$) (Table VI).

Table VI: Distribution of relieving factors among *H. pylori* positive dyspeptic patients at ABUTH, Zaria (Feb. to Dec., 2003)

S/No	Relieving factors	Types of dyspepsia						
		DU	GU	NUD	GU/DU	GERD	GC	P value
I	Food (F)	24(92.3%)	4(50%)	3(60%)	4(100%)	1(33.3%)	2(50%)	0.00765**
II	Rest (R)	22(84.6%)	7(87.5%)	2(40%)	3(75%)	2(66.7%)	3(75%)	0.262
III	Milk (M)	12(46.2%)	4(50%)	2(40%)	1(25%)	1(33.3%)	1(25%)	0.964
IV	Antacids (A)	26(100%)	7(87.5%)	3(60%)	4(100%)	3(100%)	3(75%)	0.031*
V	Vomiting (V)	7(26.9%)	1(12.5%)	3(60%)	-	2(66.7%)	1(25%)	0.322
VI	H_2 blockers (H_2B)	19(73.1%)	6(75%)	1(20%)	2(50%)	1(33.3%)	2(50%)	0.176
VII	Herbs (H)	5(19.2%)	4(50%)	2(40%)	1(25%)	-	2(50%)	0.332
VIII	PPIs	7(26.9%)	4(50%)	-	-	1(33.3%)	1(25%)	0.369

*; represents a significant P value ($P < 0.05$)

**; represents a very significant P value ($P < 0.01$)

PPIs = proton pump inhibitors; DU = duodenal ulcer; GU = gastric ulcer;

NUD = non-ulcer dyspepsia; GU/DU = gastric/duodenal ulcer;

GERD = gastro-oesophageal reflux disease;

GC = gastric cancer

Rest, milk, vomiting, Histamine (H_2) receptor blockers, proton pump inhibitors (PPIs) and herbs showed no significant effect in relieving dyspeptic symptoms among the patients with different gastrointestinal diseases.

At the end of the study, 21 (70%) and 11 (55%) of the patients that took ECA and OCA triple regimen respectively showed good response to therapy, while 5 (16.67%) and 6 (30%) had mild improvement. Four (13.33%) and 3 (15%) patients on ECA and OCA respectively did not show signs of improvement but their symptoms were not worsened (Table VII).

Table VII: Distribution of responses to different types of treatment regimen at the end of the treatment (Feb. to Dec., 2003)

S/No	Response to therapy	Treatment regimen		Total
		ECA	OCA	
I	Good	21(70%)	11(55%)	32
II	Mild improvement	5(16.67%)	6(30%)	11
III	No improvement	4(13.33%)	3(15%)	7
	TOTAL	**30**	**20**	**50**

P = 0.537 (Not significant)

ECA = Esomeprazole + Clarithromycin + Amoxycillin

OCA = Omeprazole + Clarithromycm + Amoxycilim

There were no statistically significant ($P > 0.05$) differences in response to therapy with either the ECA or OCA treatment regimen.

Overall, 32 (64%) of the patients studied with different types of dyspepsia responded well to the triple therapy (good response), 11 (22%) showed mild improvement and 7(14%) did not respond to the triple therapy (Table VIII).

Table VIII: Distributio n of responses to triple therapy among patients with different types of dyspepsia at ABUTH, Zaria (Feb. to Dec., 2003)

Response to therapy	Types of dyspepsia						TOTAL
	NUD	DU	GU	GU/DU	GERD	GC	
Good	2(40%)	21(80.8%)	6(75%)	1(25%)	1(33.3%)	1(25%)	32
Mild improvement	1(20%)	4(15.4%)	1(12.1 %)	2(50%)	1(33.3%)	2(50%)	11
No improvement	2(40%)	1(3.8%)	1(12.5%)	1(25%)	1(33.3%)	1(25%)	7
TOTAL	**5**	**26**	**8**	**4**	**3**	**4**	**50**

P = 0.038* (significant)
(NUD = Non-ulcer dyspepsia; DU = Duodenal ulcer; GU = Gastric ulcer;
GU/DU = Gastric/Duodenal ulcer; GERD = Gastro-oesophageal reflux disease;
GC = Gastric cancer).

However, there was statistically significant difference ($P < 0.05$) in response to triple therapy among patients with different types of dyspepsia (Table VIII). Also, the response of *H. Pylori* eradication in patients with NUD (60%) did not differ significantly ($P > 0.05$) from patients with organic lesions (88.9%) at endoscopy.

Discussion

The study showed that *Helicobacter pylori* was present in several gastrointestinal (GI) diseases (PUD, GC, GERD and NUD). This is consistent with the report by Knigge[13] which showed an association of *H. pylori* with these GI diseases including Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma. However, the result of this study did not agree with the findings of Abahussain and Hassan[14] in which none of the two hundred Kuwaiti patients referred for endoscopy had GU or GC despite the high prevalence of *H. pylori* in this group of patients. Four out of the fifty patients studied had GC. This justifies World Health Organization (WHO)'s report in 1994 that *H. pylori* is a class I carcinogen and many prospective studies in different populations have associated *H. pylori* with GC [15, 16]. Consumption of ill-processed food, uncertified (not registered) food additive, e.g. bromate in bread, environmental pollutants such as pesticides, heavy metals and toxic gases as well as misuse of drugs such as NSAIDs and antibiotics could possibly contribute to GI cancers in these patients [17].

Occupation, literacy level and marital status did not influence the risk of *H. pylori* infection or the specific type of GI dyspepsia a patient should have. This agrees with most reports in the literature on dyspepsia, which consistently showed that socio-demographic profiles do not reliably predict the disease or differentiate between organic and NUD [19,17].

The symptoms of weight loss ($P < 0.01$), anorexia ($P < 0.05$), melaena ($p < 0.01$), dysphasia ($P < 0.001$), and haematemesis ($P < 0.05$) found to be significantly associated with greater chance of having an organic lesion at endoscopy especially gastric cancer agree with the findings of William *et al*[17].

Round pepper ($P < 0.05$) was found to aggravate dyspeptic symptoms in patients with GUs and GERD much more than other GI diseases. Whereas presence of food in GI lumen ($P <$

0.01) and antacids ($P < 0.05$) relieved dyspeptic symptoms more in duodenal ulcer than other GI diseases. Rest, milk, vomiting, H_2-blockers, PPIs and herbs showed no difference in relieving dyspeptic symptoms among study subjects with either organic or functional dyspepsia. This agrees with the findings of Missalek *et al*[20] that clinical history was not reliable in predicting the chances of having an organic disease at endoscopy.

Proton-pump-inhibitor based triple therapies were chosen because PPIs have direct anti *H. Pylori* activity and it is the better choice when combination therapy includes an antibiotic that has reduced effectiveness in acidic environment (like amoxycillin and clarithromycin) [21]. Esomeprazole and Omeprazole are "pro-drugs" requiring activation in an acid environment of the stomach. The activated forms then bind covalently with the sulfhydryl group of cysteines from the extra-cellular domain of the hydrogen-potassium adenosine triphosphatase (H^+, K^+ ATPase) enzyme, which operates the gut's proton pump. Hydrogen ion is then exchanged for potassium across the micro-villus membrane. Binding to cysteine 813, in particular, is essential for inhibition of acid production, which is irreversible for that pump molecule [22].

Amoxycillin and Clarithromycin augment each other in eradicating *H. pylori* organism. Amoxycillin is broad spectrum penicillin that binds to specific proteins within the bacterial cell walls, leading to direct cell wall lysis (bactericidal effect). Clarithromycin is a macrolide antibiotic that acts by binding selectively to the 50S ribosomal subunit of bacteria thereby inhibiting the processes of translocation, peptide bond formation and release of oligopeptidyl tRNA (bacteriostatic effect). Graham[23] and United States Food and Drug Administration (FDA) approved treatment options for *H. pylori* eradication in which combinations of one anti-secretory drug (PPIs or H_2-receptor antagonist) with 2 effective antimicrobial agents for a period of 7 to 14 days have been clinically evaluated and found to be effective. Similarly Lind *et al*[24] reported that PPI-based triple therapy achieved cure rate of 85% in *H. pylori* infection. However, the cure rates of ECA and OCA regimens fall below the recommended 80% cure rates according to intention-to-treat analysis [25]. The inclusion of patients with NUD, GERD and GC could contribute to the low cure rates obtained from the study since *H. pylori* eradication among these patients still remains a subject of controversy worldwide [9]. Again, these disease conditions are often associated with low level of acid production that might fail to activate PPIs, with consequent decrease in ability to bind to H^+, K^+-ATPase [24]. Tulassay *et al*[26] used same regimen in DU patients and had cure rates of 91% and 92% for ECA and OCA regimens respectively. The low *H. pylori* eradication and ulcer healing rate observed in this study could be as a result of re-infection and antibiotic resistance, since no test was carried out during 2 and 4 weeks followup and sensitivity of *H. pylori* to both amoxycillin and clarithromycin was not assessed before administering the drugs. Although there were statistically significant differences in response to triple therapy among different endoscopic findings ($P < 0.05$), it was observed that patients having PUD did better in terms of improvement in dyspeptic symptoms than those patients having NUD, GERD or GC.

The 80% cure rate according to intention-to-treat analysis obtained in patients with DUs could be due to the higher level of acid production associated with DUs that effectively activated PPIs and thus enhanced activity of amoxycillin and clarithromycin.

Moayyedi *et al*[27] reported that 9% of patients with dyspepsia without ulcer improved from *H. pylori* eradication therapy. Laine *et al*[9] also showed that eradication of *H.*

pylori did not improve the clinical symptoms in patients with NUD. Although often practised, the beneficial effect of eradicating *H. pylori* in NUD is far less than that seen with ulcer related dyspepsia, and could account for the greater improvement in dyspeptic symptoms seen in ulcer related organic dyspepsia as against NUD in the study.

PUD associated with *H. pylori* infection based on this study is shown to be curable with the triple drug regimen containing a PPI with two antibiotics.

It is recommended that more endoscopies be provided in our hospitals and simple (non-invasive) means of detecting *H. pylori* such as urea breath test and *H. Pylori* stool antigen tests be made available for proper evaluation of dyspepsia. Simplified treatment protocol should be worked out based on the experience of clinicians particularly at the primary care level. Such a protocol would reduce the current high cost of treating this very common ailment that cuts across all the socio-economic strata and accounts for considerable loss of man-hours. Finally, clinical pharmacists should also be actively involved in counseling and educating the patients on how and when to use the prescribed medication so as to achieve therapeutic goal.

References

1. Collin-Jones, D. G., Bloom, B., and Bodenar, G. (1988). Management of dyspepsia: report of a working party, *Lancet*, 1(8585): 567-9.
2. Drossman, D. A., Li, Z., Andruzzi, E., Temple, R. D., Talley, N. J., and Thompson, W. G. (1993). U.S. Householder survey of functional gastrointestinal disorders: Prevalence, Socio-demography, and health impact. *Dig Dis Sci*, 38:1569-80.
3. Ofman, J. J., Etchason, J., Fullerton, S., Kahn, K. L., and Soll, A. H. (1997). Management strategies for *Helicobacter pylori* seropositive patients with dyspepsia: Clinical and economic consequences. *Ann Internal Medicine*, 126:280-91.
4. Talley, N. J., Silverstein, M. D., Agreus, L., Nyren, O., Sonnenberg, A., and Holtman, G. (1998). AGA Technical review: evaluation of dyspepsia. *Gastroenterology*, 114:582-95.
5. Richter, J. E. (1991). Dyspepsia: organic causes and differential characteristics from functional dyspepsia. *Scand J. Gastroenterol* (suppl), 182: 11-6.
6. Ayuo, P. O., and Nugent, C. E. (1994). Dyspepsia: Preliminary Experience with upper gastrointestinal fibreoptic endoscopy in Eldoret Kenya E. *Afri. Med. J*, 7(4):261-3.
7. Marshall, B. J. and Warren, J.R. (1984). Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet*, 1:1311-15.
8. Andrew, P. J., Dixon, R. A., Iya, D., and Park, G. T. (1995). Upper Gastrointestinal endoscopy in urban hospital in Northern Nigeria: Association of presenting features with endoscopic findings. *Trop. Doc.*, 25:9-11.
9. Laine, L., Schoenfeld, P., Fennerty, M. B. (2001). Therapy for *Helicobacter pylori* in patients with Non ulcer dyspepsia. A meta analysis of randomized controlled trials. *Ann Intern Med*, 134:361-9.
10. Hunt, R. H., Fallone, C. A., Thomson, A. B. (1999). Canadian *Helicobacter pylori* consensus conference update: infections in adults. *Can J. Gastroenterol*, 13:213-7.
11. Kidd, M., Louw, J. A., Marks, I. N. (1999). *Helicobacter pylori* in Africa: observation on an 'enigma within an enigma'. *J. Gastroenterol Hepatol*, 14:851-8.
12. Shmuely, H., Obure, S., Passaro, D. J., Abuksis, G., Yahav, J., Fraser, G., Pittik, S., and Niv, Y. (2003). Dyspepsia symptoms and *Helicobacter pylori* infection, Nakuru, Kenya. *Emerging Infectious Diseases*, 9(9): 1103-1107.
13. Knigge, K. L. (2001). The role of *Helicobacter pylori* in gastrointestinal disease: a guide to identification and eradication. *Postgrad. Med.*, 110(3):71-82.
14. Abahussian, E. A., and Hassan, F. A. M. (1998). Dyspepsia and *Helicobacter pylori* infection analysis of 200 Kuwait patients referred for endoscopy. *Am Saudi Med*, 18(6):502-505.
15. Forman, D., Newell, D. G., and Fullerton, F. (1991). Association between infection with *Helicobacter*

pylori and risk of gastric cancer: evidence from a prospective investigation. *BMJ*, 302:1302-5.

16. Asaka, M., Takeda, H., and Sugiyama, T. (1997). What role do *Helicobacter pylori* play in gastric cancer? *Gastroenterology*, 113 (6 suppl): 556-60.
17. Williams, B., Lukas, M., Ellingham, J. H. M., Dain, A., and Wicks, A. C. B. (1988). Do young patients with dyspepsia need investigation? *Lancet*, 2:1349-51.
18. Anuka, J. A. (2002). The Role of Sex Hormones in Sexual Differentiation of the Brain. *West Afr. J. Pharmacol. Drug. Res.* 18(1&2):1-5.
19. Christic, J., Shepherd, N. A., Codling, B. W., and Valori, R. M. (1997). Gastric cancer below the age of 55: implications for screening patients with uncomplicated dyspepsia. *Gut*, 41:513-7.
20. Missalek, W., Jone, F., Mmuna, K. and Cutinha, P. (1991). P-value of fibre optic oesophago-gastro-duodones copy; experience with 4000 procedures at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. Trop. Doct., 21 : 165-168.
21. Hunt, R.H. (1996). Eradication of *Helicobacter Pylori* infection. *Am J med*, 100 (5A): 42-50S.
22. Hoogerwerf, A.W. and Pasricha, P.J. (2001). Agents used for control of gastric acidity and treatment of peptic ulcers and GERD. In: Goodman and Gilman. The Pharmacological basis of therapeutics, PP. 1005-1020, McGraw-Hill companies, Inc. U.S.A.
23. Graham, D.Y. (2000). Therapy of *Helicobacter pylori*: Current Status and Issues. Gastroenterology, 118 : S2-S8.
24. Lind, T., Megraud, F., and Unge, P. (1999). The MACH-2 study: role of omeprazole in eradication of *Helicobacter pylori* with 1-week triple therapies. *Gastroenterology*, 116:248-53.
25. Suerbaum, S., and Michetti, P. (2002). *H. pylori* infection. *N Engl J med.*, 347 (15): 1175-1186.
26. Tulassay, Z., Kryszewski, A., Dite, P., Kleezkowski, D., Rudzinski, J., Bartuzi, Z., Hasselgren, G., Larko, A., and Wrangstadh, M. (2001). One week of treatment with esomeprazole based triple therapy eradicates *Helicobacter pylori* and heals patient with duodenal ulcer disease. *Eur J. Gastroenterol Hepatol*, 13(12): 1457-65.
27. Moayyedi, P., Bardhan, C., Young, L., Dixon, M.F., Brown, L. and Axon, A.T. (2001). *H. pylori* eradication does not exacerbate reflux symptoms in GERD. Gastroenterology, 121 : 1120-1126.