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Peptic Ulcer Disease Drugs Usage patterns and its economic burden in a tertiary health institution in Niger Delta, Nigeria

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: Drug utilization evaluation for peptic ulcer disease and its cost implication are rare in Niger Delta. The objective of the study was to evaluate drug usage pattern in peptic ulcer diseases as well as its cost implications.
Methods: The cross sectional drug use evaluation study involving the use of questionnaire and patient case notes was carried out in a tertiary health institution. The validated pretested questionnaire was interviewer administered to 300 patients sampled consecutively followed by a retrospective review of their respective case notes between April to November 2013. Information collected include risk factors, prescribed drugs, *Helicobacter pylori* assay test results among others. Cost of each drug and therapy were then computed appropriately. Data was analyzed using Statistical package for Social Sciences (SPSS) version 20, Microsoft Excel and Graph Pad Prism for windows Instat Version 3.
Results: Out of the 300 patients, *H. pylori* test was conducted in 262 (87.3%) while the presence or absence of the organisms could not be confirmed in the remaining 38 subjects. Out of the 262 patients with *H. pylori* test results, only 166 representing 63.4% were positive. History of non-steroidal anti-inflammatory drugs (NSAID) usage was very high among the subjects (250; 83.3%) and highest for ibuprofen 146 (48.7%). The most prescribed drugs were antacids (268; 89.3%), amoxicillin (165; 55.0%), and a combined formulation of omeprazole, tinidazole, and clarithromycin in 140 (46.7%) subjects, followed by omeprazole alone (125; 41.7%).The national direct cost implication for the estimated 17.6 million is in the range of NGN186,849,000,000.00 ($958,200,000.00), out which NGN109,867,000,000.00 ($563,420,513.00) was for PUD drugs (50.9%) and NGN32,698,575,000.00 ($167,685,000.00) for *H. pylori* tests (17.5%), while the remaining 31.7% valued at NGN59,231,133,000.00 ($303,749,400.00) was for non-ulcer drugs, personnel and transportation.
Conclusion: The pattern of drugs usage is consistent with standard treatment guidelines. Peptic ulcer drugs for the 300 subjects constituted NGN1,618,641 ($8300.72) which represents 73.0% of the total amount spent on drugs. The national direct cost of PUD is close to NGN200 billion ($1.04 billion). Updated information on drug usage and their costs is needed for improved usage and system efficiency.
Keywords: Peptic ulcer, *H. pylori*, Cost of illness, Pharmacoeconomics

INTRODUCTION

Peptic ulcer diseases (PUD) which occur as a result of imbalance between gastric acid pepsin aggression and protective mucosa resistance are of immense public health importance affecting a sizable proportion of the population especially in developing countries. The global annual incidence of PUD has been estimated to be about Four million (Zelickson *et al*, 2011). In Nigeria and many countries of the world, there is a general decrease in prevalence of duodenal ulcer but an increase in prevalence of gastric ulcer and gastro esophageal reflux diseases (GERD) (Nwokediuko *et al*, 2012; Sung *et al*, 2009). The indirect cost of PUD representing work loss in the United States as well as costs of hospitalization and outpatient care (excluding medication costs) has been estimated to be about $5.65 billion per year (Sonnenberg and Everhart, 1997).
The most important etiological factor implicated in PUD is *Helicobacter pylori* infection Marshall *et al*, 1985) which has been reported to infect 60-95% of the populace in Africa and other developing countries, including those with normal endoscopic findings and those without PUD (Tijjani and Umar, 2008; Tanih *et al*, 2010). This is in

sharp contrast to about 35-40% in industrialized world (Moss and Sood, 2003). *H pylori* infection correlates well with socio-economic status and is higher with poor environmental hygiene, crowdedness; low income and low literacy level (Enroth and Engstrand, 2001) as is typical of most developing countries. Out of *H. pylori* infected individuals in developed countries, majority are likely to remain asymptomatic while 10-15% will develop PUD among other conditions (Velin and Michetti, 2006). The use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) which are grossly being abused in many countries is also an important factor (Awofisayo *et al*, 2008). Other predisposing factors are smoking, psychological stress, alcohol, oral bisphosphonates, potassium chloride, immune-suppressant medications and age related reduction in prostaglandin levels (Yuan and Hunt, 2006).

Proper management of PUD includes comprehensive diagnosis, relieve of pain usually with antacids, and eradication of *H. pylori* infection which primarily is a proton pump inhibitor (PPI)-based triple therapy of various combinations (Wong *et al*, 2000; Brian, 2007). These regimens can lead to cure of the infection and subsequent healing in approximately 85-90% of cases, however, re-occurrence is common without successful *H. pylori* eradication (Fischbach *et al*, 2009). Avoidance of NSAIDs, their cautious use, and choice of cyclooxygenase 2 (COX-2) specific NSAIDs, PUD prophylaxis in at-risk patient as well as stoppage of smoking are pertinent to achieve complete healing. The most common complications of poorly managed PUD in Nigeria are obstruction and perforation followed by bleeding (Wang *et al*, 2011).

Drug utilization research defined by World Health Organization (WHO) as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (WHO, 2003) can be used to evaluate the health care delivery system for efficiency, particularly with respect to adherence to standard treatment guidelines. Cost implications of therapy would reveal the economic burden of diseases and can strengthen measures at stemming the astronomical increase in disease prevalence rate. There is paucity of information on the usage pattern of PUD drugs in Niger Delta region, more so, research on cost implications of therapy are scarce to non-existence which are invaluable in decisions and policy formulations. This study was therefore designed to evaluate drug usage pattern in PUD as well as its cost implications.

MATERIALS AND METHODS

The study was carried out in the General Outpatient Department of a tertiary health institution in Bayelsa State, south-south Nigeria. The 252 bed hospital serves as a referral center to other hospitals in the State and has a patient turnover of over 5000 per month.

The population for the study includes 1190 peptic ulcer patients (487 males and 713 females) who attend the General Outpatient Department of the hospital. Inclusion criteria were adult patients, readiness to participate by giving informed consent, diagnosed cases of PUD who were placed on anti-peptic ulcer therapy and had visited the hospital at least twice prior to this study. Exclusion criteria include In-patients PUD, non-consenting, those who were too ill to participate and those with less than two visits to the hospital. Representative sample size of 291 was determined based on the average annual total PUD population of 1190 who visited the hospital in the preceding three years using a sample size calculator with a 95% confidence level at 5% confidence interval (TCRS, 1982).

Following ethical approval, the cross sectional drug use evaluation study was carried out between April and November 2013. Prospective interaction with the 300 consented patients using pretested questionnaire was carried out followed by retrospective review of their respective case notes.

The questionnaire for this study was developed, validated and pretested. The developed questionnaire was validated for content of standard variables and its relationships with established facts about PUD. Face, content and construct validity were ensured. The pretesting involved administration and analysis of initial questionnaire to 20 participants similar to the sampled population but excluded from the main study. Appropriate corrections were made after the pretesting. Information requested and collected include patients demographics, remarkable risk factors in lifestyle, awareness concerning the use of ulcer restricted drugs, history and type of NSAIDs usage, diagnostic test to confirm *Helicobacter pylori*, concurrent illnesses, knowledge of drug being used and common causes of non-adherence among others.

The questionnaires were interviewer administered to consecutively sampled patients on Tuesdays which were the hospital gastrointestinal tract (GIT) clinic days. In the interviewed subjects case notes, collected pieces of information include prescribed drugs with doses, *Helicobacter pylori assay* test results conducted for each patient (if any), and any other information that could not be provided by the patient that is required in the study and is contained in the case note. Appropriate data collection form for objective parameters and other information from the patient case notes was included as an extension and the final section of the questionnaire. The pieces of information were filled after prospective interaction with the respective patients on each day of interview.

Cost information on therapy was the hospital value which include consultation fees (in lieu of personnel cost), drug costs, diagnostic/monitoring test costs. Transportation cost was calculated using the fees paid for *to and fro* movement from the longest distance within the state capital metropolis where the hospital was located. One diagnostic test and one test of cure test were considered.

Defined daily dose (DDD) of each drug as prescribed and therapy duration which conforms to standard treatment guidelines were taken into consideration in drug cost computation (WHO, 2011). The calculated drug cost was predominantly for 14 days duration (about 70.0% of patients) meant to eradicate *H. pylori* while others lasted for four weeks as reflected in prescriptions and appointment duration. Non-ulcer drugs as well were estimated using the same duration as reflected on the respective prescriptions. Only direct medical cost was included in cost of therapy computation with a societal perspective. Discounting of appropriate cost was at a 3.0% (Suleiman and Tayo, 2010) rate over two years (2013 to 2015).

Statistical package for Social Sciences (SPSS) version 20, Microsoft Excel and Graph Pad Prism for Windows Instat Version 3 (Graph Pad Software, San Diego, CA, USA) were used for analysis of data. Descriptive statistics were used in result presentation. A $p = 0.05$ at two-tailed test was considered significant using Chi squared test or Fisher exact as appropriate.

RESULTS AND DISCUSSION

Results

Two hundred and thirteen (213; 71.0%) of the participants were females, 87(29.0%) were males. Eighty percent (240) of the subjects were below 50 years of age with a modal group being those below 30 years. Majority (about 75.0%) were gainfully employed leaving about 25.0% as unemployed, or retired. Ninety one percent (272) had at least secondary education with a tertiary proportion of (80) 26.7%. About half (149; 49.7%) were married and most of them (250; 83.4%) are of blood group O. (Table 1)

Table 1: Socio-Demographic Data of Respondents

	FEMALE	MALE	Total	P value
Age (Years)				
<30	92 (30.7)	35(11.7)	127(42.4)	0.0800
31-50	76 (25.3)	37(12.3)	113 (37.6)	
51-60	23(7.7)	13 (4.3)	36 (12.0)	
>60	22(7.3)	2 (0.7)	24 (8.0)	
	213 (71.0)	87 (29.0)	300 (100.0)	
Occupation	68 (22.7)	3(1.0)	71(23.7)	0.0001
Business/trading	23 (7.7)	48(16.0)	71 (23.7)	
Civil servant	48 (16.0)	0 (0.0)	48 (16.0)	
Housewife	4 (1.4))	11 (3.7)	15 (4.34)	
Retiree	12 (4.0)	2 (0.7)	14 (4.7)	
Unemployed	58 (19.3)	23 (7.7)	81 (27.0)	
Others	213 (71.0)	87 (29.0)	300 (100.0)	
Education status	1 (0.3)	1 (0.3)	2 (0.7)	0.0001
None	19 (6.3)	7 (2.3)	26 (8.7)	
Primary	148 (49.3)	44 (14.7)	192 (64.0)	
Secondary	45 (15.0)	35 (11.7)	80 (26.7)	
Tertiary	213 (71.0)	87 (29.0)	300 (100.0)	
Marital status	81(27.0)	33 (11.0)	114 (38.0)	0.0029
Single	99 (16.7)	50 (16.7)	149 (49.7)	
Married	5 (1.3)	4 (1.3)	9 (3.0)	
Divorced	28 (9.3)	0 (0.0)	28 (9.3)	
Widow	213 (71.0)	87 (29.0)	300 (100.0)	
Blood Group	11 (3.7)	2 (0.7)	13 (4.3)	0.1802
A	3 (1.0)	0 (0.0)	3(1.0)	
B	20 (6.7)	14 (4.7)	34 (11.3)	
AB	179 (59.7)	71 (23.7)	250 (83.4)	
O	213 (71.0)	87 (29.0)	300 (100.0)	

Of the 300 respondents, *H. pylori* test was conducted in 262 (87.3%), out of which 166 (63.4%, n=262) were confirmed positive, while 96 (36.7%, n=262) were negative. About sixty nine percent (206; 68.6%) confirmed their peptic ulcer disease status less than a year indicating new episodes, while in about one-third (61;

30.4%) the duration was between one to two years. The most common concurrent illnesses were hypertension and diabetes, both occurred in 110 (36.6%) of the participants. The most important cause of non- adherence to therapy was high cost in 172 (56.7%), followed by forgetfulness in 152 (50.6%) of the subjects. Remarkable life styles among the participants include smoking (n=41; 7.0%), alcohol (112; 37.3%), and fasting of varying frequencies in (75; 25.0%).

Out of 134 (44.7%) who correctly identified their medication, only six subjects (2.0%) were aware of ulcer restricted drugs such as NSAIDs. Proportion of the participants on herbal medicines was about one-fifth (66; 22.0%). Respective history of NSAIDs usage reported was 146 (48.7%) for ibuprofen, 60 (20.0%) for diclofenac, 25 (8.3%) for aspirin and 19 (6.3%) for others. (Table 2)

A total number of 1754 drugs were prescribed giving an average number of drugs per patient to be 5.86, counting the combination formulation as one drug. The most frequently prescribed drugs for the PUD management were antacids (268; 89.3%), amoxicillin (165; 55.0%), a co-formulated triple combination of omeprazole (20mg), tinidazole (500mg), and clarithromycin (250mg) in 140 (46.7%) subjects followed by omeprazole alone (125; 41.7%) and cimetidine (109; 36.3%).

Table 2: Disease and Treatment Information

Criteria	Frequency (n)			P value
	Female N (%)	Male N (%)	Total N (%)	
Duration of Peptic Ulcer Disease				
<1 year	148 (49.3)	58 (19.3)	206 (68.6)	0.4630
1-2 years	62 (20.7)	29 (9.7)	91 (30.4)	
3-4 years	3 (1.0)	0 (0.0)	3 (1.0)	
5-6 years	0 (0.0)	0 (0.0)	0 (0.0)	
6-10 years	0 (0.0)	0 (0.0)	0 (0.0)	
>10 years	0 (0.0)	0 (0.0)	0 (0.0)	
	213 (71.0)	87 (29.0)	300 (100.0)	
Appointment to the hospital				
2 weeks	146 (48.7)	61(20.3)	207 (69.0)	0.1348
3-4 weeks	66 (22.0)	24 (8.0)	90 (30.0)	
2-3 months	0 (0.0)	2 (0.7)	2 (0.7)	
>3months	1 (0.3)	0 (0.0)	1 (0.3)	
	213 (71.0)	87 (29.0)	300 (100.0)	
***Concurrent Illness**				
Diabetes	35 (11.7)	14 (4.7)	49 (16.3)	0.4479
Urinary tract infection	2 (0.7)	1 (0.3)	3 (1.0)	
Hypertension	47 (15.6)	14 (4.7)	61 (20.3)	
Others	47 (15.6)	15 (5.0)	62 (20.6)	
	131 (43.7)	44 (14.7)	175 (58.3)	
***Causes of non-adherence**				
High cost of drugs	114(38.0)	56 (18.7)	170(56.7)	0.2841
Adverse drug reaction	25 (8.3)	21 (7.0)	46 (15.3)	
Scarcity of drugs	26 (8.6)	18 (6.0)	44 (14.7)	
Forgetfulness to take drugs	103 (34.3)	49 (16.3)	152 (50.6)	
Lack of understanding	30 (10.0)	19 (6.3)	49 (16.3)	
Others	18 (6.0)	2 (0.6)	20 (6.0)	

*****Multiple responses were recorded for some patients

Combination of glibenclamide and metformin were the most prescribed anti-diabetic agents (40; 13,3%) with insulin in 22 (7.3%) diabetic subjects. Co-amilozide (49; 16.3%) and nifedipine (48; 16.0%) were the most widely utilized antihypertensive, followed by lisinopril (23; 7.7%) in various combinations. Ciprofloxacin at a frequency of 46 (15.3%) was the most prescribed antibacterial agent outside the *H. pyloric* eradication therapy. Other high volume drugs include heamatinics/multivitamins (176;58.7%), analgesics/muscle relaxants (47; 15.7%) and antimalarial (58; 19.3%) (Table 3).

Peptic ulcer drugs constituted NGN1,618,641 ($8300.72) which represents 73.0% of the total amount spent on drugs, out of which the highest amount of NGN594,103.30

($3046.68) was for a co-formulated triple combination of omeprazole (20mg), tinidazole (500mg), and clarithromycin (250mg) in 140 (46.7%) subjects. The proportion of the triple combination therapy was 26.8% of total drug cost and 36.7% of PUD drugs cost with an average amount per patient of NGN4243.60 ($21.76). This was followed by clarithromycin in 62 patients which constituted 12.4% of the total drug cost and 17.0% of PUD drugs cost with a total amount of NGN275, 568.50 ($1413.17) and a slightly higher average per patient of NGN4444.64 ($22.79). These were followed by antacids with highest prescription frequency of 268 (89.3%) and a total cost of NGN247, 040.90 ($1266.88).The antacids with an average cost per patient of NGN921.79 ($4.73) represent 11.2% of total drug cost and 15.3% of PUD drugs cost.

Other antibacterial agents were at a cost of NGN94, 971 which constituted 4.3% of the total cost and an average cost of NGN2190.34 ($11.23). Cardiovascular drugs at a total cost of NGN74, 199.26 ($380.51) and average cost of NGN1606 ($8.24) made up of 3.3% of total drug cost while anti-diabetic drugs cost of NGN143, 344.60 ($735.10) is 6.5% proportion of total cost with insulin representing 5.2% [NGN116, 699 ($598.46)]. Hematinics/multivitamins at a cost of NGN156, 881.60 ($804.52) and an average cost of NGN891.37 ($4.57) represents 7.1% of total drug cost proportion. (Table 4).

The total direct cost of therapy for the entire 300 patients was NGN3, 181,092.60 ($16,313.30) giving an average of NGN10,603.64 ($54.38) per patient. Of this cost, 69.7% valued at NGN2, 215,981.60 ($11,364.02) was total drug cost with a PUD drugs proportion of 50.9% valued at NGN1, 618,641.00 ($8,300.72). The cost proportion of other drugs is 18.8% at NGN597, 340.60 ($3,063.29). *H. pylori* diagnostic test and test of cure cost NGN555, 911.00 ($2,850.83) which is 17.5% of overall direct cost of therapy. The personnel and transportation costs were 3.8% and 9.1% of the therapy cost respectively (Table 5).

Table 3: Drug Utilization Pattern among Peptic Ulcer Disease Patients

Drugs utilized	Prescription frequency		
	Female N (%)	Male N (%)	Total N (%)
Drugs for peptic ulcer			
Cap Omeprazole (20mg)	90 (26.0)	35 (10.0)	125 (41.7)
Tab Cimetidine (400mg)	78 (21.0)	31 (7.7)	109 (36.3)
*Cap Triple drug combination	98 (32.7)	42 (14.0)	140 (46.7)
Tab Ranitidine (20mg)	9 (3.0)	3 (1.0)	12 (4.0)
Tab Misoprostol (200mcg)	19 (6.3)	6 (2.0)	25 (8.3)
Cap Amoxicillin (500mg)	117 (39.0)	48 (16.0)	165 (55.0)
Tab Metronidazole (200mg)	80 (26.7)	30 (10.0)	110 (36.7)
Tab Clarithromycin (500mg)	43 (14.3)	19 (6.3)	62 (20.7)
Tab Famotidine (400mg)	1 (0.3)	0 (0.0)	1 (0.0)
Cap Lansoprasole (20mg)	17 (5.7)	7 (2.3)	24 (8.0)
Tab Hyoscine	38 (12.7)	10 (3.3)	48 (16.0)
Cap Esomeprazole (20mg)	6 (2.0)	4 (1.3)	10 (3.3)
Cap Rabeprazole (20mg)	13 (4.3)	2 (0.7)	15 (5.0)
Antacid preparations	208 (68.3)	44 (4.7)	268 (89.3)
Sub-Total	817 (272.3)	297 (99.0)	1114 (371.3)
Drugs for other infections			
Tab Ciprofloxacin (500mg)	34 (11.3)	12 (4.0)	46 (15.3)
Tab Cefuroxime (250mg)	3(1.0)	1(0.3)	4 (1.3)
Intravenous Ceftriazone	1 (0.3)	1 (0.3)	2 (0.7)
Co amoxiclav tab	13 (4.3)	6 (2.0)	18 (6.0)
Cap Doxycycline	4 (1.3)	0 (0.0)	4 (1.3)
Cap Ampicillin/Cloxacillin	2 (0.7)	0 (0.0)	2 (0.7)
Sub-Total	56 (18.6)	20 (6.7)	76 (25.3)
Cardiovascular drugs			
Tab Nifedipine	37 (12.3)	11 (3.7)	48 (16.0)
Tab Aspirin (75mg)	5 (1.7)	1 (0.3)	6 (2.0)
Tab Co-amilozide	36 (12.0)	13 (4.3)	49 (16.3)
Tab Lisinopril (10mg)	17 (5.7)	6 (2.0)	23 (7.7)
Tab Amlodipine	7 (2.3)	3 (1.0)	10 (3.3)
Tab methyl dopa	20 (6.6)	6 (2.0)	26 (8.6)
Sub-Total	122 (40.7)	40 (13.3)	162 (54.0)
Other classes of drug			
Benzodiazepines	13 (4.3)	3 (1.0)	16 (5.3)
Analgesics/muscle relaxants	31 (10.3)	16 (5.3)	47 (15.7)
Anti-diabetic	82 (27.3)	20 (6.7)	102 (34.0)
Arthemisine antimalarial	48 (16.0)	10 (6.0)	58 (19.3)
Others	3 (1.0)	0 (0.0)	3 (1.0
Sub-Total	291 (97.0)	111(37.0)	402(134.0)

* Triple drug combination= Omeprazole (20mg), Tinidazole (500mg), Clarithromycin (250mg)

National direct cost implication of therapy

There is an estimated population of 185 million in Nigeria (National Bureau of Statistics, 2014) and *H. pylori* infection prevalence estimate of 63.4%, out of which 15.0% (Upper limit of estimate for developed countries (Velin and Michetti, 2006) are likely to develop or have developed PUD. Estimated population with *H. pylori* is 117,475,000 (based on the 63.4% prevalence observed in this study). The 15.0% occurrence proportion of population with *H. pylori* infection and PUD would be about 17,621,250 (17.6 million) representing an assumed national prevalence of 9.5%.

The average total direct cost of therapy per patient for managing PUD (*H. pylori* eradication and relief of symptoms) and co-morbid illnesses is NGN10,603.64 ($54.38) out of which PUD dugs constituted 50.9% valued at NGN5,395.47 ($27.67). The average cost of drugs for co-morbid illnesses is NGN1,991.14 ($10.21) which represented 18.8%, while that of *H. pylori* diagnostic test and test of cure is 17.5% valued at an average of NGN2121.80 ($10.88) per patient.

The national direct cost implication for the estimated 17.6 million is in the range of NGN186,849,000,000.00 ($958,200,000.00), out which NGN109,867,000,000.00 ($563420513.00) was for PUD drugs (50.9%) and NGN32,698,575,000.00 ($167,685,000.00) for *H. pylori* tests (17.5%), while the remaining 31.7% valued at NGN59,231,133,000.00 ($303,749,400.00) was for non-ulcer drugs, personnel and transportation

Discussion

The drug usage pattern among the subjects is consistent with standard treatment guidelines (Brian, 2007; FMOH, 2008; Fashner and Gitu, 2015), however, drugs for co-morbid illnesses and symptomatic relive of pain contributed to high poly pharmacy observed in this study and the cost implications as well. The average cost of treatment ranging from two to four weeks per patient of NGN10,603.64 ($54.38) and estimated national total direct cost of therapy for PUD close to 200 billion naira ($1.04billion) is huge with the dwindling economy. The real amount would be much more due to non-inclusion of cost of managing complications, the usual extended duration in many cases as well as indirect cost due to lost in productivity. The wide use of antibacterial therapy in this study has been demonstrated for decades to be more cost effective relative to long term symptomatic treatment (Sonnenberg and Townsend, 1995; Fendrick *et al* 2005) which is still rampant from personal observations in many developing countries. In the management of gastric ulcer diseases, $3,031 was reported to be the total cost with no treatment, $1,545 with intermittent PPI, $1,459 with maintenance PPI and $1,369; the lowest amount with *H. pylori* eradication (Ford *et al* 2004). Reports of other cost analyses, economic decision models and a randomized controlled trial have all shown that eradicating *H. pylori* from patients with peptic ulcer disease results in decreased health care costs. (Perri et al 2001).

The PUD drug utilization patterns which include cost estimation and probable national cost implications is a major strength and a valuable addition to existing policy related body of knowledge particularly with the dwindling economic conditions across the globe. Some of the weaknesses are relatively small sample size, non-randomization of sampling, the use of one study center and inference estimate of prevalence rate.

The observed highest prevalence of PUD among the youth below 40 years of age is similar to previous report in Nigeria (Tijani and Umar, 2008) and contradicted observations from Europe (Graham, 2003). About a quarter of the subjects are economically disadvantaged which is consistent with cost as the most important causes of non-adherence to therapy among the subjects. The observation of more than eighty percent of respondents to be of blood group O, which is consistent which earlier reports (Alkout, 2000; Jaff, 2011) and suggests why individuals with the blood group need to particularly take extra caution as regards the various risk factors of PUD.

Forgetfulness attitude to medication adherence and knowledge deficit about drugs to be avoided with PUD are big issues as well as wide spread use of NSAIDs in about half of respondents. This calls for urgent educational, managerial and regulatory interventions as applicable, to avoid sky-rocketing prevalence of ulcer and the burden of its attendant cost. About half of the modal age group (<30 years) affected with PUD had taken one NSAID or the other but the highest degree of NSAID usage (100.0%) was recorded for age group of 31-50 years which may due to daily stress or fatigue of work. The working class among others would also benefit from workshops on stress management which can impact PUD as well. NSAID, some of which are marketed as over the counter medications destroys the protective defensive mechanism in the mucosa membrane and it's long known to be the greatest cause of gastric ulcer (Awofisayo, 2011; Chey and Wong, 2007). There have been several reports of NSAIDs induced PUDs (Chey and Wong, 2007). This is why they are contraindicated and should be avoided as much as possible in PUDs or use cautiously. Taking them after meals reduces this impact. If the use of NSAID is inevitable, misoprostol, PPI and double dose of histamine 2 receptor antagonists (H2RAs) are effective in preventing NSAID related PUD (Rostom, 2000; Yeomans, 2002). These modalities are superior to COX-2 specific agents (Brian, 2007). *H. pylori* infection, the most implicated factor in PUD which was confirmed in 63.4% of the subjects, prevalence similar to some earlier reports in Africa (Tanih *et al* 2010) when co-exist with NSAIDs usage constitute independent and synergistic risk factors for un-complicated PUDs (Papatheodoridis *et al* 2006). Testing and eradication of *H. pylori* for some

categories of patients prior to NSAIDs therapy if indicated has thus been recommended (Bazzoli *et al*, 2001)

The consistency of *H. pylori* eradication therapy relative to acceptable standard is an indication that with full cooperation of patients in adherence to both drug and non-drug therapy, optimal level of care is assured.

The most widely utilized regimen to eradicate *H pylori* is a single formulation containing omeprazole, tinidazole and clarithromycin. In this combination amoxicillin was substituted for tinidazole probably due to resistance or allergies associated with the penicillins. Fewer tablets in such combination to be administered can facilitate adherence by patients. Regimens similar to these combinations had been reported to achieve greater than 80.0% *H. pylori* eradication and 94.0% ulcer healing rates in Asia and Africa (Wang, 2011). However, other salvage therapies for persistent *H. pylori* infection not in regular usage in many developing countries which include bismuth quadruple therapy (PPI q.d. tetracycline, Pepto Bismol, metronidazole q.i.d.) and Levofloxacin triple therapy (PPI, amoxicillin 1 g b.i.d., levofloxacin 500 mg q.d.) has been shown to be superior for resistant cases (Isakov et al 2002). Respective eradication rates for levofloxacin-based triple therapy and bismuth-based quadruple therapy of 87% (95% CI 82–92%) and 68% (95% CI 62–74%) have been reported (Saad et al, 2006) while the use of rabeprazole, levofloxacin, and tinidazole in place of amoxicillin yielded an intention to treat eradication rate of 84% (Giannini et al,2006).

Proton pump inhibitor being the most important basis of therapy was prescribed to all the patients of which omeprazole was the most widely used in about 90.0% of cases either as part of combination therapy or alone. The prescription of PPI on once daily basis can also be utilized to blunt the ulcer bleeding effect of traditional NSAIDs in patient with history of PUD (Chan, 2002) since NSAID can still cause re-bleeding even in patients in whom *H. pylori* has been eradicated (Gisbert *et al*, 2003). Cardiovascular disease patients on low dose aspirin who can tolerate NSAID such as naproxen are to be placed on PPI as well (Lanza, 2009). Cimetidine, prescribed to about one-third of the subjects was the most prescribed of the H-receptor antagonists (H2RAs) probably due to cost; however, it should be used with caution due to microsomal enzyme inhibition and wide drug interactions, its reversible gynecomastia effects in males, loss of libido and impotence (Chey and Wong, 2007).

Patients for whom interacting drugs such as ciprofloxacin for infection and antacids were prescribed need to be counseled for the dosing to be spaced to avoid chelate complexes which will eventually reduce their respective absorption and subsequent effectiveness. The use of herbal preparation by some subjects needs to be thoroughly examined for possible identification and composition since undesirable interactions can occur which are mostly unpredictable (Ulbricht *et al*, 2008). Useful and evidence based active constituents may equally be obtained from such evaluation.

The average cost of therapy per patient of NGN10603.64 ($54.38) which represents 58.9% of minimum wage for the lowest paid government worker in Nigeria is huge. Most of the expenses are self-funded by patients with poor purchasing power, some of who are living below poverty line earning less than one US dollar per day (UNDP, 2006) or are unemployed. The cost is further complicated with incremental addition for every co-morbid illness in affected patients. For instance, hypertension as a co-morbid illness would lead to 29.8% increment in PUD drugs cost, while co-existing type I and II diabetes mellitus would result in 100.9% and 6.1% incremental costs in PUD drugs cost, respectively. Hence, concerted efforts at preventing non communicable chronic diseases such as PUD particularly as it relate to NSAID usage and *H. pylori* infection should be improved upon. Economic evaluation of available therapeutic options and choice of the most cost effective ones is equally pertinent to optimize the use of limited resources.

Holistic recommendations about PUD management for developing countries were made by Ostrow Brian (2007), some of which include invasive and non-invasive diagnostic modalities such as urea breath test, upper gastrointestinal endoscopy/injection therapy to manage associated hemorrhage, treatment of dyspeptic symptomatic patients who are *H. pylori* positive, testing of all PUD patients for *H. pylori* and treating positive cases, using triple therapy of a PPI, clarithromycin and amoxicillin as first line therapy, assessment of *H. pylori* in non-invasive manner one month post therapy. Others are supervised treatment of persistently *H pylori* patients with second line therapy, avoidance of NSAIDs in PUD patients and encouragement to quit smoking and alcohol as well as avoidance of long term anti-secretory maintenance therapy for uncomplicated *H pylori* cases. Appropriate treatments including surgery for complicated cases such as perforation, gastric outlet obstruction and bleeding were as well recommended.

The results of this study should be generalized with caution since the data is limited to one tertiary hospital. Suggestions for further research include ascertaining the most cost effective agents for treatment with appropriate patient stratification and health related quality of life assessment among PUD patients.

Table 4: Cost of drugs used by peptic ulcer disease patients

Drugs utilized	Frequency N (%)	Cost of drugs NGN($)			Percent (%)
		Median	Total	Average per patient	
Drugs for peptic ulcer					
Omeprazole	125 (41.7)	779.76 (4.00)	150456.7 (771.57)	1203.66 (6.17)	6.79
Cimetidine	109 (36.3)	259.92 (1.33)	50626.08 (259.62)	464.44 (2.38)	2.28
*Triple drug combination	140 (46.7)	2121.80 (10.88)	594103.30 (3046.68)	4243.60 (21.76)	26.81
Ranitidine	13 (4.0)	1591.35 (8.16)	41375.05 (212.18)	3182.70 (16.32)	1.87
Misoprostol	25 (8.3)	445.58 (2.29)	22278.87 (114.25)	891.16 (4.57)	1.01
Amoxicillin	165 (55.0)	270.53 (1.39)	81710.42 (419.03)	495.21 (2.54)	3.69
Metronidazole	110 (36.7)	265.22 (1.36)	41979.76 (215.28)	381.63 (1.96)	1.89
Clarithromycin	62 (20.7)	1989.19 (10.20)	275568.50 (1413.17)	4444.64 (22.79)	12.44
Lansoprazole	24 (8.0)	1014.75 (5.20)	46537.38 (238.65)	1939.05 (9.94)	2.1
Hyoscine	48 (16.0)	424.36 (2.18)	12306.42 (63.11)	256.38 (1.31)	0.56
Esomeprazole	10 (3.3)	1188.21 (6.09)	20708.74 (106.20)	2070.88 (10.62)	0.93
Rabeprazole	15 (5.0)	1188.21 (6.09)	33948.76 (174.10)	2263.24 (11.61)	1.53
Antacid preparations	268 (89.3)	424.36 (2.18)	247040.9 (1266.88)	921.79 (4.73)	11.15
Sub-Total	1114 (371.1)	NA	1618641 (8300.72)	5724.05 (29.35)	73.04
Drugs for other infections					
Ciprofloxacin	46 (15.3)	318.27 (1.63)	27371.18 (140.37)	595.02 (3.05)	1.24
Co-amoxiclav	18 (6.0)	1670.92 (8.57)	57606.80 (295.42)	3200.37 (16.41)	2.6
Others	12 (4.0)	441.60 (2.26)	9993.66 (51.25)	822.81 (4.27)	0.45
Sub-Total	76 (25.3)	NA		2190.34 (11.23)	4.28
Cardiovascular drugs					
Nifedipine	48 (16.0)	159.13 (0.82)	13728.04 (70.40)	286.00 (1.47)	0.62
Aspirin (75mg)	6 (2.0)	159.13 (0.82)	954.81 (4.90)	159.14 (0.82)	0.04
Co-amilozide	49 (16.3)	119.35 (0.61)	11245.53 (57.67)	229.49 (1.18)	0.51
Lisinopril	23 (7.7)	185.66 (0.95)	7108.022 (36.45)	309.04 (1.58)	0.32
Amlodipine	10 (3.3)	254.62 (1.31)	4752.827 (24.37)	475.28 (2.44)	0.21
Methyl dopa	26 (8.7)	445.58 (2.29)	36410.05 (186.72)	1400.39 (7.18)	1.64
Sub-Total	162 (54.0)	NA	74199.26 (380.51)	1606.49 (8.24)	**3.34**
Other classes of drug					
Benzodiazepines	16 (5.3)	23.87 (0.12)	954.81 (4.90)	59.69 (0.31)	0.04
Analgesics/muscle relaxants	47 (15.7)	159.13 (0.82)	18565.75 (95.21)	395.02 (2.03)	0.84
Oral Anti-diabetic	80 (26.7)	148.53 (0.76)	26645.56 (136.64)	333.04 (1.71)	1.2
Insulin	22 (7.3)	2652.25 (13.60)	116699 (598.46)	5304.50 (27.20)	5.27
Heamatinic/Vitamins	176 (58.7)	233.40 (1.20)	156881.60 (804.52)	891.37 (4.57)	7.08
Arthemisine antimalarial	58 (19.3)	795.67 (4.08)	104710.80 (536.98)	1805.36 (9.26)	4.73
Others	3 (1.0	583.49 (2.99)	3713.15 (19.04)	1237.71 (6.35)	0.17
Sub-Total	402 (134.0)	NA	428169.70 (2195.74)	454245.10 (2329.46)	**19.32**
Grand Total	1754 (584.6)		2,215,981.60 (11,364.02)	7836.46 (40.19)	100

NA= Not applicable, *Triple drug combination = Omeprazole (20mg),Tinidazole (500mg), Clarithromycin(250mg),

Table 5: Cost of Therapy for Peptic Ulcer Diseases

Cost component	No of patient	Total Amount NGN ($)	Cost Proportion (%)	Average cost per patient NGN ($)
Peptic Ulcer Drugs	300	1,618,641.00 (8,300.72)	50.9	5395.47 (27.67)
Other drugs	300	597,340.60 (3,063.29)	18.8	1991.14 (10.21)
H. pylori diagnostic Test	262	555,911.00 (2,850.83)	17.5	2121.80 (10.88)
Personnel	300	120,000.00 (615.38)	3.8	400.00 (2.05)
Transportation	300	289,200.00 (1,483.08)	9.1	964.00 (4.94)
Total		3,181,092.60 (16,313.30)	100.00	10603.64 (54.38)

NGN- Nigerian Naira

CONCLUSION

The pattern of drugs usage is consistent with standard treatment guidelines. Peptic ulcer drugs constituted NGN1,618,641 ($8300.72) which represents 73.0% of the total amount spent on drugs by the 300 patients, out of which the highest amount of NGN594,103.30 ($3046.68) was for a co-formulated triple combination of omeprazole (20mg), tinidazole (500mg), and clarithromycin (250mg) in 140 (46.7%) subjects. The national direct cost of PUD is close to NGN 200 billion ($1.04 billion). Updated information on drug usage pattern and their costs is recommended to be provided on epidemiological scale at regular interval to evaluate the system for efficiency and appropriate recommendations.

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