PREVALANCE OF GASTRIC ULCERS AND DUODENAL ULCERS IN A TERTIARY CARE SETTING

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Significance: Peptic ulcer disease is common especially in developing countries. Studies of prevalence of gastric ulcers in the Philippines show varying results. The objective of this study is to determine the prevalence of pepticulcers at a government tertiary care hospital.

Methodology: This study is a retrospective, cross-sectional study. Random sampling of months within the specified time period was done. The minimum sample size required to achieve a confidence interval of 95% is 307 reports. Age, sex, location at time of endoscopy; presence of ulcers, number and location, Forrest classification, endoscopic intervention and presence of Helicobacter pylori infection was recorded. Descriptive statistics such as means and standard deviations, frequency tables and crosstabulations were used. The Chi Square statistic and/or the Cramer's V was used to test for relationship between variables.

Results: A total of 946 endoscopy reports were reviewed. There was equal prevalence of peptic ulcers in inpatients (24.29%) and in outpatients (22.54%), (χ^2 (1) = 0.4248, p = 0.514563). More severe ulcers in terms of Forrest Classification is seen in inpatients compared to outpatients (χ^2 (3)= 45.2902, , p < 0.00001; Φ = 0.33775895). For inpatients, Helicobacter pylori prevalence was similar for those with and without ulcers (χ^2 (1)= 3.0726, p = 0.07962) However, for outpatients Helicobacter pylori prevalence was higher among those with ulcers (, χ^2 (1)= 9.4558, p = 0.002105).

Conclusion: The prevalence of peptic ulcer disease remained high in this institution. However despite the persistent prevalence of the disease, severity, morbidity and mortality from peptic ulcers have all decreased.

Keywords: Peptic ulcer disease, Prevalance, Esophagogastoduodenoscopy, Forrest Classification, Helicobacter pylori

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INTRODUCTION

Peptic ulcers are defects in the stomach or duodenal mucosa caused by the action of gastrointestinal secretions in susceptible mucosa. [1] Peptic ulcer disease is still a common problem around the world, especially in developing countries. Studies are still required to provide insight into the patterns of peptic ulcer disease in different parts of the world [2].

Globally, the incidence of peptic ulcers have been decreasing through time [3-5]. However, within similar time period, the prevalence of peptic ulcers still vary in different areas of the world [2]. Variations also exist between western and eastern populations. [6] This variation is due to the difference in the demographics, and the difference in the prevalence of risk factors for the development of this disease.

Aside from race and geographical region, several factors determine the prevalence and distribution in the gastrointestinal tract, of peptic ulcers. The severity, hospitalization rate and complication rate has been shown to differ according to age and sex as well [7,8]. For example, it has been shown that elderly patients has a higher frequency of bleeding from peptic ulcers compared to young patients. [9]

In terms of sex, both gastric and duodenal ulcers in younger age groups classically occurred more often in men and had a higher chance of bleeding [10]. However, more recent studies have shown that the male to female ratio for the prevalence, hospitalization, and mortality of peptic ulcers is decreasing. This is due to decreasing duodenal ulcer rates in men and increasing gastric ulcer rates in women [11].

Marshal and Warren during the 1980s, discovered that infection with Helicobacter pylori is a major cause of development of peptic ulcer disease [12]. Thus, eradication of these infections can prevent ulcer formation, recurrence and complications from ulcers. [13-15] In fact, This decreasing trend has been shown in different regions of the world. [7, 16,17]

There are many ways to test foe the presence of helicobacter pylori infection. A common practice in most endoscopy units is the use of bedside urease tests wherein mucosal biopsies are taken from different parts of the stomach and are placed in rapid urease kits. Pronto Dry (Medical Instruments Corporation, Solothurn, Switzerland)is a validated test kit with a sensitivity of 98.1% and a specificity of 100%. [18]

However, even if a decline in prevalence of peptic ulcer disease has been seen, the increasing population of elderly, and the increase in use of drugs like NSAIDs and antiplatelets might offset the decrease in helicobacter pylori prevalence. [19-21]

There are several ways to visualize peptic ulcer disease. Radiologic exams carried out by experienced radiologists can detect mucosal defects [22]. However, for chronic ulcers, as much as 50 % of ulcers in the stomach and 40% of ulcers in the duodenum can be missed by radiologic exams alone [23-26]. And almost all acute mucosal lesions can be missed by radiology.

Direct visualization by Esophagogastroduodenoscopy is the current gold standard for the diagnosis of peptic ulcer disease. On top of confirming the presence and absence of peptic ulcers, Esophagogastroduodenoscopy allows accurate localization and subsequent therapeutic modalities to control bleeding. [27]

Forrest, Finlayson and Shearman published a pivotal study in 1974 that showed outcomes of peptic ulcer bleeding is greatly improved by endoscopic therapies. A standardized classification scheme to describe peptic ulcers was developed. Ulcers are classified as type 1 if with active bleeding (1A squirting blood, 1B oozing blood); type 2 if with signs of recent bleeding (2A non bleeding visible vessel, 2B adherent clot, 2C ulcer with a flat pigmented spot); or type 3 if without sign of bleeding / clean ulcer base. The endoscopic appearance subsequently guides therapeutic modalities that will be used and furthermore, post-endoscopy management and disposition. This classification system reliably stratifies patients and predicts the risk of bleeding and/or death. [27-28]

Studies of prevalence of gastric ulcers in the Philippines show varying results. In a local 1989 study 1,542 endoscopies done over a 6 year period showed that 27.6% of upper endoscopies showed peptic ulcers with gastric ulcers outnumbering duodenal ulcers [29]. In another local study done in 2002 done at a different institution, 16.95% of upper endoscopies showed gastric ulcers while 10.27% had duodenal ulcers [5].

SIGNIFICANCE AND OBJECTIVES

The objective of this study is to determine the prevalence of gastroduodenal ulcers at the Philippine General Hospital, a tertiary care hospital. Furthermore this study investigated the characteristics of ulcers in terms of number and Forest classification

GENERAL OBJECTIVES

1. Determine the prevalence of gastroduodenal ulcers among adult patients at the Philippine General Hospital
2. Determine the prevalence of Helicobacter pylori infection among adult patients at the Philippine General Hospital

SPECIFIC OBJECTIVES

1. Determine the demographics of patients with peptic ulcers
2. Determine the classification of peptic ulcers in terms of forest score
3. Determine the common endoscopic lesions of patients with helicobacter pylori infection

METHODOLOGY

Subjects and setting

This study is a retrospective, cross-sectional study of the electronic endoscopy reports from August 2017 to July 2018 of the Section of Gastroenterology, Department of Medicine, Philippine General Hospital.

Based on a previous prevalence studies, the highest prevalence of peptic ulcers seen on upper endoscopies was 27.6%. Using a finite population correction factor of 1,000,000 and a maximum permissible error of 5%, the minimum sample size required to achieve a confidence interval of 95% is 307 reports, while to achieve a confidence interval of 99.9% the minimum sample size is 865 reports. The sample size was computed using Open Epi sample size calculator (www.openepi.com).

Random sampling of months of endoscopy reports, of adult patients done either as in patient or outpatient, within the specified time period was done. All upper endoscopy reports within the time period of adult patients whether admitted or outpatient was included.

Exclusion criteria are (1) upper gastrointestinal tract endoscopic ultrasound or endoscopic cholangiopancreaticography reports since these diagnostic modalities, although still with endoscopic views, are not used for examination of the mucosa (2) patients with ulcers from caustic ingestion (3) patients with ulcers from trauma or (4) patients with ulcers from post operative changes since these have a different pathophysiology.

Data Collection

Electronic endoscopy reports from August 2017 to July 2018 of the Section of Gastroenterology, Department of Medicine, Philippine General Hospital will be reviewed. Data such as age, sex, location of patient at time of endoscopy, presence or absence of ulcers, number and location of ulcers, forest classification of ulcers,[27,28] and type of endoscopic intervention was recorded.

For Helicobacter pylori infection, this institution uses rapid urease kits particularly Pronto Dry (Medical Instruments Corporation, Solothurn, Switzerland). A positive helicobacter pylori infection is considered when a color change is seen in the bedside kit.

Ethics

All information was handled with strict confidentiality. Names of patients were not collected and only initials were used as identifiers. There are minimal perceived risks nor direct benefits to the patients whom the medical records were reviewed. Patients did not receive any form of compensations or reimbursements. The population studied is not deemed as a vulnerable risk group.

Statistical analysis

Collected data was encoded in Microsoft Excel. Descriptive statistics such as means and standard deviations as well as frequency tables and crosstabulations will be used to describe the statistics. The Chi Square statistic and/or the Cramer's V was used to test for relationship between variables.

RESULTS

For the chi square statistics, an alpha level of 0.05 was used for all tests. Chi square statistic was computed using an online calculator (https://www.socscistatistics.com/tests/chisquare2/Default2.aspx). Formula for Cramer's V taken from the world wide web (https://peterstatistics.com)

Table 1. Prevalence of peptic ulcers in upper endoscopies done the Philippine General Hospital

	Inpatient	Outpatient	Overall
Total Endoscopies	489	457	946
With ulcer n (%)	119 (24.29)	103 (22.54)	222 (23.44)
both gastric and duodenal ulcer	22 (4.49)	12 (2.63)	34 (3.59)
gastric ulcer only	59 (12.06)	64 (14.00)	123 (13.00)
duodenal ulcer only	38 (7.77)	27 (5.91)	65 (6.87)
Without ulcer n (%)	370 (75.66)	354 (77.46)	724 (76.53)

A chi square test of independence was calculated comparing the frequency peptic ulcer disease in outpatients and inpatients. A non significant interaction was found, χ^2 (1) = 0.4248, p = 0.514563. There was equal prevalence of peptic ulcers in inpatients (24.29%) and in outpatients (22.54%)

Table 2. Characteristics of Patients with Peptic Ulcers who underwent upper endoscopies done the Philippine General Hospital

	Inpatient n = 119	Outpatient n = 103	Overall n = 222
Age mean + sd	53.35 ± 15.82	54.97 ± 12.05	54.10 + 14.19
Sex			
Male n, (%)	76 (63.87)	65 (63.11)	141 (63.51)
Female n, (%)	43 (36.13)	38 (36.89)	81 (36.48)
Distribution of peptic ulcers	n, (%)	n, (%)	n, (%)
With Both Gastric and Duodenal ulcer	22 (18.49)	12 (11.65)	34 (15.32)
Gastric ulcer only	59 (49.58)	64 (62.13)	123 (55.41)
Duodenal ulcer only	38 (31.93)	27 (26.21)	65 (29.27)
Number of Gastric Ulcer per patient n (% of patients with gastric ulcer)			
Multiple Gastric	37 (45.68)	34 (44.74)	72 (45.22)
Solitary Gastric	44 (54.32)	42 (52.26)	86 (54.78)
Number of Duodenal Ulcer per patient n (% of patients with duodenal ulcer)			
Multiple Duodenal	21 (35)	17 (43.59)	37 (38.38)
Solitary Duodenal	39 (65)	22 (56.41)	61 (61.61)

A test of independence was calculated comparing the distribution of peptic ulcers (whether gastric and duodenal vs gastric only vs duodenal only) in inpatients and outpatients. A non-significant interaction was found using Pearson's Chi square (χ^2 (2)= 3.8729, p = 0.144213) and a weak association was found using Cramer's V (Φ =0.132081) . The proportion of patients having both gastric and duodenal ulcers, gastric ulcers only, and duodenal

ulcers only is the same for both inpatient and outpatient. For both inpatient and outpatient endoscopies, stomach affectation is more common than duodenal affectation and having both gastric and duodenal ulcers are less common than with gastric or duodenal ulcers.

A chi square test of independence was also calculated comparing the frequency of having multiple versus solitary ulcers (in either the stomach or duodenum) in inpatient and outpatient endoscopies. For both Gastric ulcers, (χ^2 (1)=0.0141, p = 0.905643) and duodenal ulcers (χ^2 (1)= 0.7374, p = 0.390498) a non significant interaction was found. The prevalence of having either multiple or solitary ulcers (in either the stomach or duodenum) are the same for both inpatients and outpatients

Table 3. Forrest Classification of Ulcers found in upper endoscopies done the Philippine General Hospital

	Inpatient	Outpatient	Overall
Gastric N, (% of Gastric ulcer)			
1A	0 (0)	0 (0)	0 (0)
1B	4 (2.86)	1 (0.81)	5 (1.89)
2A	6 (4.29)	0 (0)	6 (2.27)
2B	3 (2.14)	0 (0)	3 (1.13)
2B>1A	0 (0)	0 (0)	0 (0)
2B>1B	0 (0)	0 (0)	0 (0)
2B>2A	0 (0)	0 (0)	0 (0)
2B>2C	1 (0.71)	0 (0)	1 (0.37)
2B>3	2 (1.43)	0 (0)	2 (0.75)
2C	17 (12.14)	1 (0.81)	18 (6.81)
3	93 (66.43)	78 (63.90)	171 (64.77)
Healed/Healing	17 (12.14)	44 (35.48)	61 (23.10)
Total	**140**	**124**	**264**
Duodenal N, (% of Duodenal ulcer)			
1A	0 (0)	0 (0)	0 (0)
1B	2 (2.53)	0 (0)	2 (1.50)
2A	9 (11.39)	0 (0)	9 (6.76)
2B	2 (2.53)	0 (0)	2 (1.50)
2B>1A	0 (0)	0 (0)	0 (0)
2B>1B	0 (0)	0 (0)	0 (0)
2B>2A	2 (2.53)	0 (0)	2 (1.50)
2B>2C	0 (0)	0 (0)	0 (0)
2B>3	0 (0)	0 (0)	0 (0)
2C	9 (11.39)	5 (9.26)	14 (10.53)
3	49 (62.02)	37 (68.52)	86 (64.66)
Healed/Healing	8 (10.12)	12 (22.22)	20 (15.04)
	79	**54**	**133**

A test of independence was calculated comparing the severity of ulcers based on Forrest classification between inpatients and outpatients, A significant interaction was found using Pearson's Chi square statistics (χ^2 (3)= 45.2902, , p < 0.00001) and a strong dependence is seen using Cramer's V (Φ = 0.33775895). More severe ulcers seen in endoscopies done in admitted patients compared to outpatient endoscopies

Table 4. Helicobacter prevalence and associated endoscopic findings among patients tested using Rapid Urease test

	Positive	Negative
Inpatient		
Gastric and Duodenal ulcer	8	13
Gastric ulcer	24	31
Duodenal Ulcer	15	21
No ulcer	57	122
Total inpatient Helicobacter pylori (+)	104	187
Outpatient		
Gastric and Duodenal ulcer	1	4
Gastric ulcer	15	20
Duodenal Ulcer	7	7
No ulcer	41	117
Total outpatient Helicobacter pylori	64	148
Total Helicobacter pylori status	168 (33.40%)	335 (66.60%)

A chi square test of independence was calculated comparing the frequency of peptic ulcers between those infected with Helicobacter pylori and those who are not.

For inpatient endoscopies, a non significant interaction was found, χ^2 (1)= 3.0726, p = 0.07962. Helicobacter prevalence was similar for those with ulcers and those without ulcers.

However, for outpatient endoscopies, a significant interaction was found, χ^2 (1)= 9.4558, p = 0.002105. Helicobacter prevalence was higher among those with ulcers.

DISCUSSION

Peptic ulcer prevalence trends

In this study, the *overall* prevalence of peptic ulcer disease combining inpatient and outpatient endoscopies is 23.44%. This prevalence rate is similar to a previous study done by Daez et al in this same institution back in 1997[30]. This finding of a persistent peptic ulcer prevalence is different from a study done at a different tertiary hospital by Wong et al in 2002 [5] which showed a decreasing prevalence in peptic ulcers from 35.87% to 18.8% in a span of 6 years. The decrease in the peptic ulcer rate in the study by Wong et al was attributable to the decreasing infection rate by helicobacter pylori. The percentage of helicobacter pylori positive ulcers decreased from 71.90% to 34.6%

Comparing the trend of overall prevalence of Helicobacter infection in this institution, the previous prevalence rate of 42.1% by Daez is higher compared to the prevalence in this present study (33.4%). Even though there is a decrease in Helicobacter pylori infection, the peptic ulcer rate stayed the same. This could be caused by and increasing prevalence of other risk factors like NSAID use.

Another explanation for the seemingly lower helicobacter pylori infection rate is the possibility of false negative tests. In this institution, helicobacter pylori infection was determined using Prontodry. In this, patients were not excluded even if they have received proton pump inhibitors. Intake of proton pump inhibitors can cause false negative results when testing for helicobacter pylori either though urea breath test [31] urease test, histopathology [32] and even on stool antigen [33]. Taking two samples (one from antrum and another from the body) for Helicobacer pylori testing, does not eliminate the possibility of false negative test.

The persistent prevalence of peptic ulcer disease can either be (1) from the persistence of helicobacer pylori infection which was not detected due to false negatives or (2) increasing prevalence of other risk factors.

Distribution of Peptic ulcers

The prevalence of *gastric ulcers* in this study (16.59%) and duodenal ulcers (10.46%)is similar from the previous study by Daez (gastric ulcer 14.7%, duodenal ulcer 8.5%) [30]. Gastric ulcers are more prevalent compared to duodenal ulcers in both studies. This finding is consistent with other studies as well done in different institutions.[34-35]

In a previous study by Abrigo et al the number of peptic ulcers were investigated. In this 1985 study, multiple gastric ulcers were seen in 32.7% , while multiple duodenal ulcers were seen in 37.5% of patients. Comparing this with this present study, multiple Gastric ulcers and multiple duodenal ulcers were previously more prevalent. [36]

Forrest classification of ulcers

In the previous landmark study of Laine et al published 1994 in the new England journal of medicine, the prelavelence of ulcers based on Forrest classification is as follows: Active bleeding (18%), non bleeding visible vessel (17%), adherent clot (17%), flat spot (20%), and clean based ulcer (42%). In this study, rebleeding rate is as high as 55% and mortality rate as high as 11% for those ulcers with active bleeding [28].

This present study demonstrated that the prevalence of actively bleeding ulcers is much less than previous studies. Furthermore, ulcers were less severe in terms of Forrest classification. This is likely because during the time when Laine et al did their study, proton pump inhibitors (which are more potent that H2 receptor antagonists) are not yet available [37] Proton pump inhibitors particularly omeprazole were only introduced in the 1990s.

In this present review, 22 patients needed endoscopic therapy at the time of endoscopy (11 gastric ulcers and 11 duodenal ulcers). Most of them were controlled with epinephrine injection and use of hemoclips, with no recurrence of bleeding on repeat endoscopy. However in 3 patients, standard endoscopic therapy with epinephrine and hemoclip was unsuccessful and the enedoscopist had to use bovine clotting factors. Bovine activated clotting factors (Factors IIa/VIIa/IXa/Xa (brand name Seraseal/FastAct; by Wortham Laboratories, Chattanooga, Tennessee, USA). Have been approved by US FSA for use as a hemostatic agent usually in patients with impaired coagulation who bleed during operation. [38] This modality has been demosnstrated to be effective in endoscopic hemostasis for gastrointestinal bleeding in a proof of concenpt study by Ferlitsch, et al [39]. The use of Bovine clotting factors has been successful in controlling the bleeding.

During the review of records, no mortality from gastrointestinal bleeding was seen.

CONCLUSION

The prevalence of peptic ulcer disease remained persistent in this institution despite the overall decrease in Helicobacter pylori infection rate. The persistent of peptic ulcer disease may be due to increase in other risk factors, probably NSAID intake. However, despite the persistent prevalence of the disease, severity, morbidity and mortality from peptic ulcers have all decreased.

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