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RESEARCH ARTICLE
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EXPLORING THE ASSOCIATIONS OF AGE, GENDER, AND BLOOD GROUP WITH PEPTIC ULCER DISEASE: A COMPREHENSIVE STUDY OF FREQUENCY, CLINICAL MANIFESTATIONS, RISK FACTORS, AND ULCER TYPES

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Abstract

Background: Peptic ulcer disease (PUD) is an alimentary tract problem resulting from mucosal injury brought about by gastric acid and pepsin production. The most common etiologies of peptic ulcer disease are NSAIDS and H Pylori Infections.

Objective: To find the frequency, risk factors, clinical presentations, ulcer types of peptic ulcer patients presenting at gastroenterology OPD of a tertiary care hospital.

Methodology: This is a Cross-Sectional Observational study, conducted over a period of 6 months. The sample size of 464 participants was acquired through consecutive convenient (purposive) sampling. For each subject the data was recorded on a Performa after taking a detailed history, thorough physical examination, and investigations. Informed consent was obtained from the participants before enrolling them to the study. The data was then analyzed using Excel Spread Sheets and SPSS Version 26.

Results: Out of the 464 participants, 214 were male, and 250 were females. Among them, 78.23% participants had a positive family history. The frequency of peptic ulcer disease in this study was

recorded to be 59.91%, of which 24.4% participants had blood type O and 60.07% had duodenal ulcer. The common clinical presentations were of acidity (72.66%), indigestion (72.66%) and pain (44.96%). It was also noted that caffeine intake and dyspepsia were among the common risk factors.

Conclusion: Our study concluded that peptic ulcer disease has not just been an issue of the developed world, it is also prevalent in the developing nations, with duodenal ulcer being the commonest presentation. PUD was found to be present among every age group, hence its association is majorly with the unhealthy lifestyle of the patients (like use of analgesics, stress, intake of caffeine and spice).

Keywords: Peptic Ulcer Disease, Clinical Manifestations, Risk Factors, Duodenal Ulcer, Pakistan.

Introduction

Peptic ulcer disease (PUD) is an alimentary tract problem resulting from mucosal injury brought about by gastric acid and pepsin production. It most commonly occurs in the gastric region and proximal duodenum; less frequently, it occurs in the lower segment of esophagus, distal duodenum, or jejunum, or in ectopic gastric mucosa as occurs in Meckel's diverticulum, unopposed hyper secretory states such as Zollinger-Ellison syndrome or hiatal hernias. (1) This disease develops when the defensive mechanisms of the mucosa, prostaglandins, antioxidants are compromised by the damaging impacts such as excessive gastric acid, gallbladder fluid, H Pylori, elevated free radicals and pepsin. (2,3) Following Western research, 5-10% of people will acquire a peptic ulcer during their life. (4) A study conducted in Peshawar showed that 32% of the cases showed positive endoscopic findings while 65% of the cases tested positive for H Pylori infection. (5) Peptic ulcer disease can be caused by a variety of aetiologies, the most common of which are the use of NSAIDs and Helicobacter pylori infection. (6) Aside from NSAIDs and H. pylori, researchers have found different risk factors that can be generally controlled i.e., modifiable risk variables including coffee, corticosteroids, regular use of aspirin, anticoagulants, smoking, alcohol, spicy meals, stress, and use of dirty water. Other non-modifiable risk factors include genetics, age, gender, and a history of PUD and people with blood group O are found to have increased risk of duodenal ulcer. (7-9) The main complaint of patients with Peptic Ulcer is epigastric discomfort. Bloating, indigestion, nausea, premature satiety, bleeding, and heartburn are some of the other symptoms. (2) Proton pump inhibitors, anti-acid drugs, H-2 blockers, and gastro-protective agents are among the medications used to treat peptic ulcers. In cases of poor drug compliance, complications develop such as gastrointestinal bleeding (GIB), perforation, stomach obstruction, and the development of gastric cancer. (3) Keeping in mind the increased burden of peptic ulcer in developing countries, this study was directed to find the frequency, risk factors, clinical presentations, ulcer types of peptic ulcer patients presenting at gastroenterology OPD of a tertiary care hospital. The study also aims to emphasize the association of age, gender and blood groups with peptic ulcer disease.

Methodology

Over a period of six months, from April to September 2023, a cross-sectional observational study was carried out at Tertiary Care Hospitals in KPK, Pakistan. Ethical Approval was obtained from Institutional Review Board and Ethics Committee, Northwest School of Medicine. The required sample size was calculated as 457, having 99% confidence level and 22.1% anticipated frequency (n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1) +p*(1-p)]) (10). The sample was acquired through consecutive convenient (purposive) sampling. For each patient receiving a check-up, a thorough history and physical assessment were conducted.

Each person underwent a comprehensive interview by consultant gastroenterologists' specialists about the existence of reflux or dyspeptic symptoms in the current period or having it in previous months. Complete Blood Count (CBC), Blood Serology (H. pylori IgG antibody) test, Urea Breath Test (C14 or C13), H. pylori Stool Antigen Test and endoscopies were performed. Skilled

endoscopists conducted the endoscopies using an Endoscope, following the subjects' overnight or at least 6-hour fast. It was unknown to the endoscopists whether the patients they were examining had symptoms or not. A set of biopsy forceps with a known span was opened in front of each gastroduodenal mucosal break to measure its length after the patients had a thorough examination for the presence of the breakage. A well-defined ulcer crater and a confined mucosal breach with a diameter of at least 5 mm were the hallmarks of acute peptic ulcer illness. A chronic ulcer was described as having scarring, deformity, and an ulcer with or without slough at the base. If an endoscopy showed a scar, with or without deformity, a healed ulcer was assumed. Every stomach ulcer seen during an endoscopy was biopsied and examined histologically.

This study's inclusion criteria involved individuals aged 10 to 90 years. Participants were required to either possess a previously confirmed history of peptic ulcer disease or have a current diagnosis, substantiated by both medical laboratory tests and Oesophago-gastroduodenoscopy (OGD). Obtaining informed written consent was also mandatory, ensuring that individuals were fully informed about the study's nature and willingly agreed to participate. Pregnant women, individuals unwilling to participate, critically ill individuals with altered mental status, and those with stomach or duodenal conditions like gastroenteritis, gastritis, gastroparesis, or malignancies were excluded from the study. Additionally, individuals who were using histamine-2 receptor antagonists, sucralfate, proton pump inhibitors, prostaglandin analogues, prokinetic or anticholinergic agents, or antacids within the previous month were also excluded. Other possible causes of the subject's symptoms were excluded through a thorough medical history, a physical assessment, and the relevant laboratory testing. This included conditions such as irritable bowel syndrome, pancreatitis, and oesophageal cancer etc.

Data was collected using specifically designed proforma. For every subject, the following information was filled in the Performa: age, gender, level of education, occupation, family history of PUD, blood group, alcohol use, consumption of tobacco, previous history of PUD, dyspepsia, stress, caffeine intake, spicy foods intake, and use of non-steroidal anti-inflammatory drugs (NSAIDs) within previous 4 weeks of endoscopy. Signs of clinical presentations (i.e., Acidity, Indigestion, Severe upper abdominal pain that has persisted for more than two weeks either lately or during the previous five years and is eased by food and/or antacids, Fever, Nausea and Vomiting, Loss of Appetite, Passage of Bloody Stools, Constipation, Abdominal Distension, Weight Loss, Shocked state at presentation (SBP < 90 mmHg), Common signs and symptoms of peritonitis were also recorded on the Performa. Verbal informed consent was taken from every participant, and every participant was informed regarding the purpose of the study. Data analysis was carried out using Excel® Spread Sheet and Statistical Package for the Social Sciences (Version 26). Frequencies, Mean, and Standard Deviation were among the descriptive statistics used in the variable analysis.

Results

During the 6-month period, data from a total of 464 participants was obtained. The majority (53.9%) of our sample were female. The mean age of our patient group was 34.7 years. Many of our patients had received no form of formal education (39.2%) and were unemployed (45.0%). Although most patients were not aware of their blood group, among those that were aware, Blood type O was the most common (22.8%). A great majority (78.2%) of the patients had a family history of Peptic Ulcer Disease (Table 1).

Table 1: Demographics of all participants.

Demographic		**Frequency (%)**
Sex	Male	214 (46.12)
	Female	250 (53.87)
Age (Mean + S.D)		34.7 + 13.1 years
Education	Illiterate	182 (39.2)
	Basic Education	115 (24.8)
	Secondary Education	87 (18.7)
	Higher Education	80 (17.2)
Occupation	Employed	181 (39.0)
	Unemployed	209 (45.1)
	Retired	74 (15.9)
Blood Group	A	35 (7.5)
	B	22 (4.7)
	AB	54 (11.6)
	O	106 (22.8)
	Don't know	247 (53.2)
Family History positive for Peptic Ulcer Disease		363 (78.2)

A total of 278/ 464 (59.9%) of our patients were diagnosed with peptic ulcer disease after further work up. A larger portion of these participants were male (153 participants). The most common location of the ulcer was the duodenum (60.1%), while the least common was Esophageal. This pattern was seen in both genders (Table 2).

Table 2: Location of Ulcer.

Location of Ulcer	**Frequency (%)**	**Males (%)**	**Female (%)**
Esophageal Ulcer	24 (8.6)	9 (5.9)	15 (12.0)
Gastric Ulcer	87 (31.3)	50 (32.7)	37 (29.6)
Duodenal Ulcer	167 (60.1)	94 (61.4)	73 (58.4)

When looking at the age distribution of patients diagnosed with Peptic Ulcer Disease, the prevalence of PUD was highest in the 21-30 years group, closely followed by 31-40 years and 31-50 years old. 10.1% of the patients diagnosed were aged 81-90 years old (Table 3)

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Table 3: Age distribution of patients diagnosed with peptic ulcer disease.

Age group	**Frequency (%)**
10-20 years	14 (5.0)
21-30 years	54 (19.4)
31-40 years	52 (18.7)
41-50 years	50 (18.0)
51-60 years	30 (10.8)
61-70 years	34 (12.2)
71-80 years	16 (5.8)
81-90 years	28 (10.1)

Many of our diagnosed patients were unaware of their blood group, however among those who did know theirs (123 patients), Peptic Ulcer Disease was clearly the most common in Blood Group O (68 patients) (Table 4).

Table 4: Blood Group of patients diagnosed with Peptic Ulcer Disease.

Blood Groups	Peptic Ulcer (%)
A Type	16 (5.8)
B Type	14 (5.0)
AB Type	25 (9.0)
O Type	68 (24.4)
Don't Know	155 (55.8)

The most common presenting signs and symptoms for those diagnosed with Peptic Ulcer Disease were Acidity and Indigestion (72.7%) of patients. Symptoms suggesting complications of Peptic Ulcer Disease were also seen (such as passage of bloody stools, weight loss and severe abdominal pain). A small portion of the patients presented with signs of shock (4.3%) and peritonitis (1.4%) (Table 5).

Table 5: Signs and symptoms of patients with peptic ulcer disease at the time of presentation.

Clinical Presentation	Frequency (%)
Acidity	202 (72.7)
Indigestion	202 (72.7)
Severe Abdominal Pain	125 (45.0)
Abdominal Distension	89 (32.0)
Nausea and Vomiting	64 (23.0)
Fever	39 (14.0)
Passage of Bloody Stools	32 (11.5)
Loss of Appetite	25 (9.0)
Constipation	21 (7.6)
Weight Loss	16 (5.8)
Shocked state at presentation (SBP < 90 mmHg)	12 (4.3)
Classical signs of generalized peritonitis	4 (1.4)

An assessment of the risk factors for peptic ulcer disease was done among these patients. The most common risk factor was Caffeine Intake which was present among 247 (88.8%) of those diagnosed with Peptic Ulcer Disease. Chronic dyspepsia and NSAID use were also present in many patients. Subjectively high stress levels were another extremely common factor observed in 70.9% of patients. Alcohol use was reported in 0 patients (Table 6).

Table 6: Associated Risk Factors

Associated Risk Factors	Frequency (%)
Alcohol use	0 (0)
Cigarette smoking	86 (30.93)
Use of NSAIDS	191 (68.70)
Previous History of Peptic Ulcer	41 (14.74)
Dyspepsia	202 (72.66)
Stress	197 (70.86)
Caffeine Intake	247 (88.84)
Spicy Food Consumption	127 (45.68)

Discussion

The frequency of Peptic Ulcer Disease in our study population was 59.9%. It is stated that globally there has been a significant decrease in Peptic Ulcer Disease, likely due to the development of Proton

Pump Inhibitors. (11) However, when looking at the global burden, there has been a 25.8% increase in frequency from 1990 to 2019. (12) Peptic Ulcer Disease remains a challenge in Low-Income and Low-Middle Income countries such as Pakistan. (13) We can see in our study that 70.9% of our patients reported a high stress level. In a study done by Levenstein et al. studying the factors other than H. Pylori that contribute to peptic ulcer disease in patients with a low socioeconomic status. Adjustment for life stress/psychological characteristics eliminated 56.5% of the risk of peptic ulcer disease. (14) It is interesting to note the relatively lower numbers of Cigarette smokers (compared to the other risk factors), where health risk behaviors are thought to also be a major contributor in lower socioeconomic status. This may indicate the effectiveness of no-smoking campaigns in our country. However, this may also be simply a result of underreporting due to social concerns, as a study done by Khan et al in 2016 reported the implementation and adherence to tobacco control laws to be poor. (15) Alcohol use being reported as 0% is understandable due to the religious and social implications, as well as the sale of it being illegal in this part of the world. It continues to be a challenge to assess the extent it may be affecting our patients. (16) The dietary habits in Pakistan are huge factors in Peptic Ulcer Disease being so common. The rampant use of caffeine in the form of tea, and the widespread use of spices in most foods is present in most households, which can be seen in our results in Table 6. A cross-sectional study done by Chen et al. in Islamabad. 87.5% of their patients with GERD consumed tea, and that increased intake of fried and spicy food was also prominent. NSAIDs use for pain has been a longstanding contributor to peptic ulcer disease. (17) The widespread availability of NSAIDs and sporadic use of stronger NSAIDs without proper guidance from medical professionals is adding to the issue. Zamir et al. emphasized this issue when they assessed the preference of NSAIDs, where 40.8% participants stated Mefenamic Acid was the first drug they would use for pain (mostly headaches). (18) A study done by Yakoob et al. investigated patients that presented to their Gastroenterology department from 1999 to 2001. Of the 2260 patients, 415 patients (18.4%) had a diagnosis of either gastric ulcer or duodenal ulcer. (19) The large difference in number of cases (18.4% vs 59.9% in our study) may be due to the large difference in NSAIDs use: 39 patients (18.0%) in the study in Karachi had significant NSAID use vs the 191 patients in our study (68.7%). Other possible explanations could be a regional difference, the difference in other risk factors or the different time frame for the studies. Aside from the established risk factors that we assessed for, Ahmad et al.'s work has indicated that recent changes in the quality of groundwater (which would be the source for most of our patients) may also be a contributor to increased incidence of certain diseases, including Peptic Ulcer Disease. (20) In Table 4, we can see that among the patients that were aware of their blood group, there were more cases of peptic ulcer disease in patients with the blood group O. The increased inflammatory response to H. Pylori and increased density of colonization of cells are both reported as reasons by this by Alkout et al. (21)

Table 2 shows the locations of the ulcers. It is very clear that duodenal ulcers are the most common type for us (60.1% of ulcers), like the global trend reported. (22) We can also note that the proportion of male patients with duodenal ulcers is slightly higher. Table 5 shows us the common presenting symptoms. As our study was conducted in patients presenting to the outpatient department, only a small majority of our patients had presented with a complication of peptic ulcer disease. The most common symptoms were Acidity and Indigestion, which are expected symptoms of Peptic Ulcer regardless of its location. However, a large portion of our patients did present with red flag symptoms. Weight loss, severe abdominal pain, loss of appetite and symptoms indicating gastrointestinal bleeds are considered warning signs for impending/developed complications. (23) Peptic Ulcer perforation can introduce infection in the sterile peritoneum, leading to peritonitis. A retrospective study in 2017 by Rohit et al. in India showed the mortality of patients operated on for peritonitis secondary to perforated peptic ulcer to be 11.1%. (24) This, and hypovolemic shock are the deadly complications of Peptic Ulcer Disease. 4 patients were presented with symptoms indicative of Peritonitis, and 12 were found to be in shock. These patients had to be urgently managed to prevent mortality. Educating patients with regards to the warning signs so that they may seek timely treatment is an important

aspect of the management of peptic ulcer in developing countries. As of data published in 2020, Peptic Ulcer Disease has caused 5450 deaths (0.37%) in Pakistan. (25)

Strengths of our Study: The strengths of our study are that it is one of the first in our region to investigate the frequency of peptic ulcer disease extensively. The wide variety of symptoms that Peptic Ulcer Disease may present with is also shown, to help keep healthcare professionals aware of the possible presentations. We have also been able to pinpoint the more prominent risk factors in our patients, to help focus efforts into mitigating them for all our patients.

Study Limitations: The limitations of this study are the sample size and specific study population. To get a better idea of the frequency, as well as reduce biases, there is a need to reach out extensively to the population as we may have missed many patients who do not have access to healthcare. Our study also did not include H. Pylori status, as the records were incomplete for this information. We plan on including this information in future information when following up the outcomes of our patients after treatment. A large number of patients were not aware of their blood group, although we were able to still able to display the link between Blood Group O and Peptic Ulcer Disease.

Conclusion

Our study concluded that peptic ulcer disease has not just been an issue of the developed world, it is also prevalent in the developing nations, with duodenal ulcer being the commonest presentation. PUD was found to be present among every age group, hence its association is majorly with the unhealthy lifestyle of the patients (like use of analgesics, stress, intake of caffeine and spice). It was also noted that patients with a positive family history, Blood Type O and males (specifically for duodenal ulcers) were slightly more prone to developing peptic ulcer disease. Given the significant frequency identified in our study, there is a compelling argument for the judicious use of proton pump inhibitors (PPIs) globally. However, it is crucial to acknowledge that indiscriminate use of PPIs may contribute to additional health concerns, such as nephropathies, as indicated by contemporary research. Therefore, a balanced and informed approach to the prescription and consumption of PPIs is warranted to mitigate potential risks while effectively managing peptic ulcer disease on a global scale.

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