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Aetiology and Pattern of Presentation of Upper Gastrointestinal Tract Ulcers among Patients Attending the Gastroenterology Department of BSMMU-A Tertiary Level Hospital

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Abstract **Original Research Article**

Background: Upper gastrointestinal endoscopy is the most common procedure performed in Gastroenterology department for numerous indications and ulceration of the upper GI tract is one of the major pathological findings during endoscopy. Early diagnosis of upper GI ulcers with definite cause is the mainstay of therapy for patient's cure and prevention of complications. Different clinical features are observed in different types of ulcer. ***Objective:*** The objective of this study is to find out the causes of different types of ulceration in the upper gastrointestinal tract along with their clinical presentation. ***Methods:*** This cross-sectional study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of July 2016 to April 2017. Patients referred for upper GI endoscopy for different indications were primarily selected. Consecutive 220 patients having ulcers anywhere in the upper GIT were finally included in the study. Ulcer diseases were diagnosed through analysis of morphology of the ulcers, histopathology of biopsy materials, relevant clinical history and further investigations if required. All the findings were documented in predesigned data collection sheet. Any association between various types of ulcers with age, gender, BMI, lifestyle, location of ulcer, different signs and symptoms was assessed. ***Results:*** Out of 220 patients duodenal ulcer was found in 45.9%, gastric ulcer in 30.0%, oesophageal ulcer in 7.7%, ulceration at multiple sites in 13.6%, and stomal ulcer in 2.7% cases. Among the aetiologies H. pylori infection (62.8%), NSAIDs (14.6%) and malignant ulcers (9.1%) were found in majority of cases. Less common causes were tubercular ulcer, lymphoma, GIST, Crohn's disease and caustic injury. Aetiology could not be identified in 6.8% cases. Among various presenting complaints epigastric pain, early satiety, anorexia, vomiting and GI bleeding were the symptoms that differ significantly in patients with ulcers of different aetiologies. ***Conclusion:*** In majority of the cases the underlying cause of ulcer could be identified. However, in some cases the exact aetiology could not be detected. Clinical presentations were also different in patients with various types of ulcer.

Keywords: Ulcer, Upper Gastrointestinal Tract, Endoscopy, Peptic Ulcer Disease.

INTRODUCTION

An ulcer in the gastrointestinal (GI) tract may be defined as a 5 mm or larger break in the lining of the mucosa, with appreciable depth at endoscopy or with histologic evidence of submucosal extension [1]. There are numerous causes of ulceration in the upper gastrointestinal tract. Common examples are peptic ulcer disease, drug induced ulcers (e.g. NSAIDs, some antibiotics), malignant ulcers, infectious diseases (e.g. tuberculosis), Crohn's disease, corrosive injury and foreign bodies [2]. Some ulcers are acute, some are chronic; they may be single or multiple in numbers, benign or malignant, may be uncomplicated or associated with various complications. Complications of gastrointestinal ulcer include bleeding, perforation, obstruction and malignant ulcers may metastasize locally or in distant sites. Early diagnosis of GI ulcers is essential for prompt and definitive treatment including surgical intervention [3]. Esophageal ulcers most commonly occur as a result of gastroesophageal reflux disease (GERD) with a reported prevalence of 2% to

7%. Other causes of esophageal ulcers include peptic ulcer disease, NSAIDs, antibiotics, carcinoma, corrosive substances, foreign body, tuberculosis, candidiasis and radiation therapy [4]. Most common cause of ulceration in the stomach and proximal duodenum is peptic ulcer disease. Peptic ulcer disease is most frequently associated with Helicobacter pylori infection or the use of NSAIDs. Peptic ulcers are sites of loss of continuity of the mucosa of the gastrointestinal tract exposed to the gastric acid-peptic secretion. The organs affected are more frequently the stomach and the duodenum. Under some conditions it is also possible to observe peptic lesions in the esophagus and jejunum among other less common sites. Lesions are chronic and single in the majority of cases but can be multiple in about 5% to 20% of cases, simultaneously affecting the stomach and the duodenum or even other segments, as occurs in the Zollinger-Ellison Syndrome [5]. Most patients experience severe refractory heartburn and epigastric pain, often accompanied by profound diarrhea, which is a result of the combination of osmotic load of high gastric acid secretion as well as a malabsorptive component from inactivation of pancreatic digestive enzymes by the acid [6]. Tuberculosis in the upper GI tract may present with ulceration. The symptoms are usually retrosternal pain, dysphagia and odynophagia [7]. Tuberculosis of the stomach is rare (0.4%-2%) because of the bactericidal property of the gastric acid. Morphologically many types are seen, the commonest one is ulcerative lesion along the lesser curvature and pylorus [8]. Duodenal involvement is seen in 2%-2.5% of all gastrointestinal TB cases. Morphologic findings may be ulcerative, hypertrophic or ulcerohypertrophic [9]. Crohn's disease (CD) mainly affects the ileum and colon, but may involve any part of the GI tract. The reported rate of UGI lesions in CD varies from 1% to about 80% [10]. UGI lesions of CD include aphthae, erosions, ulcerations, strictures and notch like appearance [11]. Gastrointestinal tract is the most common extranodal site involved by lymphoma accounting for 5%-20% of all cases. Stomach is the most commonly involved site (60%-75%) in gastrointestinal tract. The presentations of gastric lymphoma are epigastric pain, weight loss, nausea and vomiting [12]. The clinical features of small intestinal lymphoma include colicky abdominal pain, nausea, vomiting, weight loss and diarrhoea [13]. In a cross- sectional study by Goenka and his colleagues from Kolkata, India with 128 patients of ulcer diseases showed that 57.8% had gastric and 42.2% had duodenal ulcers. In this study, H. pylori positivity rate was 61%. The proportion of H. pylori- negative with no history of NSAID use was 45.9% in gastric ulcer and 29.6% in duodenal ulcer patients. The etiology of H. pylori-negative ulcers was not further investigated [14]. Hassan *et al.,* [15] conducted a survey on peptic ulcer in a rural community in Bangladesh. The prevalence of duodenal ulcer disease was 11.98% and that of gastric ulcer was 3.58%. Both duodenal ulcer and gastric ulcer subjects were predominantly males. In another cross-sectional study by Carli and his co-workers from Brazil assessed the endoscopy records of a hospital in the period 2007-2010. They found peptic ulcer disease in 20.2% cases, of them 52.8% was associated with H. pylori infection, 28.4% were NSAID induced, and 18.8% were labeled as idiopathic ulcer [16].

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of July 2016 to April 2017. Patients referred for upper GI endoscopy for different indications were primarily selected. Consecutive 220 patients having ulcers anywhere in the upper GIT were finally included in the study. Ulcer diseases were diagnosed through analysis of morphology of the ulcers, histopathology of biopsy materials, relevant clinical history and further investigations if required. All the findings were documented in predesigned data collection sheet. Any association between various types of ulcers with age, gender, BMI, lifestyle, location of ulcer, different signs and symptoms was assessed. Peptic ulcer was diagnosed on the basis of relevant clinical features like dyspepsia, epigastric pain or burning sensation, periodicity, history of recent NSAIDs intake etc. Endoscopic features suggestive of peptic ulcer are typical location (lesser curvature, antrum or bulb of duodenum), clean based ulcer with clear cut margin and absence of irregularities. Ulcers that completely healed after appropriate treatment (e.g. anti H. pylori therapy) were also diagnosed as peptic ulcers. Meticulous clinical history was obtained from every patient and recorded in the data sheet. Further investigations were done in cases where endoscopy findings, histopathology and clinical history failed to reach a diagnosis. Tests included complete blood count, tumour markers, Chest X-ray P/A view, tuberculin test, Plain X- ray abdomen, USG of W/A, barium X-ray examination, colonoscopy in suspected cases of tuberculosis, lymphoma, Crohn's etc. Investigation findings were recorded in the data sheet. Patients with refractory ulcers on endoscopy having clinical suspicion of *Zollinger-Ellison syndrome* (ZES) were further evaluated by serum gastrin level and if doubtful, by secretin stimulation test. Specific history was obtained to ascertain ulcer due to caustic ingestion, previous radiotherapy or history of gastric surgery. Ulcer in the clinical setting of suspected immunodeficiency states (Diabetes, malignant disease, lymphoma, AIDS etc.) was further evaluated for possible fungal or viral aetiologies i.e. moniliasis, CMV, HSV etc. Temporal relationship was ascertained in cases of suspected pill induced ulcers by taking history of ingestion of drugs e.g. Doxycycline, Tetracycline, Clindamycin, calcium, Iron, Bisphosphonates, NSAIDs etc. Urea breath test (UBT) was done to find out H. pylori infection in all ulceration that was presumed to peptic ulcer disease on endoscopy.

Inclusion Criteria:

- Patients having ulceration in the upper gastrointestinal tract at endoscopy.

Exclusion Criteria:

- Age less than 18 years and more than 85 years.
- Patients who did not give informed consent.

Operational Definition

Upper Gastrointestinal Tract: On embryologic grounds, the upper gastrointestinal tract extends from mouth to major papilla in the duodenum (areas derived from the foregut). However, for the purposes of endoscopy oesophagus, stomach and duodenum up to the second part were regarded as upper GI tract for this study [17]. Upper GI tract is evaluated by esophagogastroduodenoscopy (EGD)--also called upper gastrointestinal (GI) endoscopy--which is performed with a flexible fiberoptic endoscope.

Ulcer: Ulcers was defined as a 5 mm or larger break in mucosa, with appreciable depth or with histologic evidence of submucosal extension. The size of the ulcer was approximated by the width of the tip of the biopsy forceps in open state, which is approximately 5 mm [1].

Peptic Ulcer Disease: The term peptic ulcer disease (PUD) is used to include ulcerations in the stomach and duodenum from a number of causes [1].

Upper GI Endoscopy: Upper endoscopy allows for examination of the lining of the upper part of the gastrointestinal (GI) tract, which includes the esophagus, stomach and duodenum (up to 2nd part). Endoscope is a thin, flexible tube containing a lens and light source, which projects images on a video monitor. Upper gastrointestinal endoscopy was done using a standard forward viewing endoscope (Olympus-GIF-H190).

Helicobacter Pylori Infection: Helicobacter pylori are gram negative, spiral, motile organisms and have multiple flagella at one end. These organisms produce large amounts of urease, an enzyme that hydrolyzes urea to alkaline ammonia and CO2, permitting the bacteria to modulate the local pH. Urease is the basis of clinical diagnostic tests (urea breath test and rapid urease tests) for H. pylori infection. It is the most common chronic bacterial infection in the world that is linked to peptic ulcer disease *[18]*.

Detection of Helicobacter Pylori Infection: Presence of H. pylori infection in the patients having ulceration in the upper gastrointestinal tract was diagnosed by urea breath test. Urea breath test is recommended for detection of H. pylori infection both during diagnosis and to confirm eradication [19].

Statistical Analysis

All data were checked and edited after collection. Statistical analysis was performed using SPSS (Statistical Package for Social Science). All continuous data were expressed as mean and standard deviation, whereas categorical data were expressed as frequency and percentage. Association between various types of ulcers with age groups, gender, BMI, lifestyle, location of disease, disease behavior were analyzed by Chi-square test. The student t-test or ANOVA test were used to compare mean age of patients, duration of illness, mean haemoglobin and ESR level between different groups of ulcers. A p-value of <0.05 was considered statistically significant.

RESULTS

Total 220 patients who met the inclusion criteria were enrolled for the study. Among the study patients, 101(45.9%) patients had duodenal ulcer (DU), 66(30.0%) had gastric ulcer (GU), 17(7.7%) had oesophageal ulcer (OU), 18(8.2%) had both gastric and duodenal ulcer, 8(3.6%) had both gastric and oesophageal ulcer, 4(1.8%) had both oesophageal and duodenal ulcer and 6(2.7%) patients had stomal ulcer [Table-1].

Table-1: Distribution of the patients by site of ulcer (N=220)

Site of Ulcer	Number	Percentage
Duodenal Ulcer	101	-45.90%
Gastric Ulcer	66	-30.00%
Oesophageal Ulcer	17	-7.70%
G.U. + D. U.	18	-8.20%
G.U. + O.U	8	-3.60%
O.U + D. U	4	-1.80%
Stomal ulcer	6	-2.70%

Table-2: Age, Sex and Smoking status distribution of patients with upper GI tract ulceration (n=220)

Age (Years)	Total patients (n=220) f (%)	Duodenal Ulcer (n=101) f (%)	Gastric Ulcer (n=66) f (%)	Oesophageal Ulcer (n=17) f (%)	p value
Unto 30	61(27.7%)	32(31.7%)	17(25.8%)	3(17.6%)	
31-40	47(21.4%)	28(27.7%)	12(18.2%)	1(5.9%)	
41-50	32(14.5%)	14(13.8%)	10(15.1%)	4(23.5%)	0.099*NS
51-60	26(11.8%)	11(10.9%)	6(9.1%)	4(23.5%)	
≥61	54(24.6%)	16(15.8%)	21(31.8%)	5(29.4%)	

Age (Years)	Total patients (n=220) f (%)	Duodenal Ulcer (n=101) f (%)	Gastric Ulcer (n=66) f (%)	Oesophageal Ulcer (n=17) f (%)	p value
Mean± SD	41.72±12.29	38.81±11.35	42.78±17.42	45.53±18.13	0.086**NS
Male	131(59.5%)	62(61.4%)	38(57.6%)	10(58.8%)	0.883 NS
Female	89(40.5%)	39(38.6%)	28(42.4%)	7(41.2%)	
Non-smoker	157(71.4%)	69(68.3%)	51(77.3%)	11(64.7%)	0.377NS
Smoker	63(28.6%)	32(31.7%)	15(22.7%)	6(35.5%)	

f=frequency, *p value derived from chi-square test, **p value derived from the one-way ANOVA test, NS=not significant p value derived from chi-square test.

NS=not significant

The mean (±SD) age of all patients was 41.72(±12.29) years in this study. Mean (±SD) age of patients having duodenal ulcer, gastric ulcer and oesophageal ulcer were 38.81±11.35, 42.78±17.42 and 45.53±18.13 years respectively. Mean age of patients with oesophageal ulcer in this study was higher than other groups, whereas mean age of duodenal ulcer group was lower than others, but these difference were not statistically significant (p=0.086). Patients aged ≥61years were more in GU group than DU group (31.8% vs. 15.8%) and patients aged ≤40 years were more in DU group than GU group (59.4% vs. 44.0%). Among the duodenal ulcer patients, the maximum no. of patients were found in the age group of below 30 years and the minimum no. were found in the group of 41-50 years. In the gastric ulcer group, the maximum numbers of patients were found in above 60 years group and minimum patients were found in 51-60 years group. Among the oesophageal ulcer patients, maximum were found in the age group of above 60 years and minimum were found in the group of 31-40 years. Among the total patients, 131(59.5%) were male and 89(40.5%) patients were female. There was no significant difference in distribution of male and female patients among three (gastric, duodenal and oesophageal) ulcer groups (p=0.883). Out of 220 patients 63(28.6%) patients had history of smoking, among them 32(31.7%) patients of duodenal ulcer group, 15(22.7%) patients of gastric ulcer group and 6(35.5%) of oesophageal ulcer group had history of smoking. No significant difference was observed between these groups regarding history of smoking (p=0.377) [Table-2].

Table-3: Aetiological distribution of upper GI ulcer patients (N=96)

Category Name	Number	Percentage
NSAID	18	8.20%
Other Drug	7	3.20%
H.pylori + NSAID	14	6.40%
Malignant (Adenocarcinoma)	20	9.10%
Lymphoma	5	2.30%
Tubercular	3	1.30%
Crohn's	2	0.90%
GIST	4	1.80%
Corrosive	2	0.90%
GERD	6	2.70%
Idiopathic	15	6.80%

Various aetiologies of upper GI tract ulcer were found among the study patients which were diagnosed on the basis of endoscopic findings, relevant clinical history, histopathology of ulcer tissue, urea breath test and other laboratory findings. Majority of upper gastrointestinal ulcer cases (56.4%) were induced by Helicobacter pylori infection. Other causes of ulcer were also found in the study patients. Out of 220 patients 18(8.2%) patients had NSAID-induced ulcer, 7(3.2%) patients had drug induced ulcer other than NSAID, 14(6.4%) ulcer cases had history of NSAID intake and also found H. pylori positive, 20(9.1%) patients of ulcer were diagnosed as adenocarcinoma in histopathology report, 5(2.3%) patients were diagnosed as lymphoma (non-Hodgkin's), 3(1.3%) patients had tubercular ulcer, 2(0.9%) were patients of Crohn's disease manifested with upper gastrointestinal ulceration, 4(1.8%) patients of GIST found to have upper gastrointestinal ulceration, 2(0.9%) ulcer cases were due to corrosive injury and 6(2.7%) patients had ulceration as a complication of reflux oesophagitis. Out of the 220 ulcer cases, no specific causes were found in 15(6.8%) patients and were labelled as idiopathic ulcer [Table-3].

Table-4: Aetiology of Duodenal Ulcers (n=101)

Aetiology	Number of patients	Percentage
Helicobacter pylori infection	73	72.27
NSAID-induced	7	6.93
H. pylori + NSAID induced	8	7.92

Aetiology	Number of patients	Percentage
Malignant ulcer (Adenocarcinoma)	2	1.98
Lymphoma	1	0.99
Tubercular	1	0.99
Crohn's disease	2	1.98
GIST	1	0.99
Idiopathic	6	5.94

Among the patients of duodenal ulcer 73(72.27%) were induced by H. pylori infection, 7(6.93%) patients had history of NSAID ingestion, 8(7.92%) cases were H. pylori positive and had history of NSAID intake, 2(1.98%) cases of ulcer were malignant (adenocarcinoma), 1(0.99%) patient was diagnosed as lymphoma (non-Hodgkin's), 1(0.99%) patient had tubercular ulcer, 2(1.98%) patients had Crohn's disease, 1(0.99%) patient was diagnosed as GIST and in 6(5.94%) ulcer cases no specific causes were found [Table-4].

Table-5: Aetiology of Gastric Ulcers (n=66)

Aetiology	Number of patients	Percentage
H. pylori infection	29	43.9
NSAID-induced	5	7.6
Other Drug-induced	1	1.5
H. pylori + NSAID induced	3	4.5
Malignant ulcer (Adenocarcinoma)	16	24.2
Lymphoma	3	4.5
Tubercular	1	1.5
GIST	3	4.5
Idiopathic	5	7.6

Out of 66 patients of gastric ulcer 29(43.9%) were induced by H. pylori infection, 5(7.6%) patients had NSAID-induced ulcer, 1(1.5%) had drug induced ulcer other than NSAID, 3(4.5%) cases had history of NSAID intake and also found H. pylori positive, 16(24.2%) patients of gastric ulcer were diagnosed as adenocarcinoma, 3(4.5%) patients were diagnosed as lymphoma (non-Hodgkin's), 1(1.5%) patients had tubercular ulcer, 3(4.5%) patients of GIST found to have gastric ulcer, and in 5(7.6%) patients no causes were found [Table-5].

Table-6: Aetiology of Oesophageal Ulcers (n=17)

Aetiology	Number of patients	Percentage
H. pylori infection	1	5.9
NSAID-induced	2	11.8
Other Drug-induced	4	23.5
Malignant ulcer (Adenocarcinoma)	1	5.9
Tubercular	1	5.9
Caustic injury	2	11.8
GERD	6	35.3

Among the patients with oesophageal ulcer 1(5.9%) ulcer was induced by H. pylori infection, 2(11.8%) patients had NSAID-induced ulcer, 4(23.5%) patients had drug induced ulcer other than NSAID, 1 (5.9%) case was diagnosed as malignant ulcer, 1(5.9%) patient had tubercular ulcer, 2(11.8%) were patients of corrosive substance injury and 6(35.3%) patients had ulceration as a complication of reflux oesophagitis [Table-6].

Table-7: Distribution of malignant ulcers by site (N=24)

Malignant ulcer type	Total (n=24)	Duodenal Ulcer (n=3)	Gastric Ulcer (n=19)	Oesophageal Ulcer (n=1)	Stomal ulcer (n=1)
Adenocarcinoma	20	2(10.0%)	16(80.0%)	1(5.0%)	1(5.0%)
Lymphoma	4	1(25.0%)	3(75.0%)	0(0.0%)	0(0.0%)

In our study, malignant causes ulceration were found in 24 patients. Out of them 20 cases were adenocarcinoma and 4 cases were lymphoma. Among 20 cases of adenocarcinoma 2(10%) were found in the duodenum, 16(80%) were present in the stomach, 1(5%) in the oesophagus and 1(5%) case was found in gastrojejunostomy stoma. Of the 4 cases of lymphoma,

1(25%) was present in duodenum and 3(75%) were present as gastric ulcer [Table-7].

Helicobacter pylori status among the study patients was detected by urea breath test. Out of total 220 patients, urea breath test was positive in 164(74.5%) patients. Among 101 cases of duodenal ulcer, 84(83.2%) patients were found H. pylori positive. Out of 66 gastric ulcer patients, 46(69.7%) patients were H. pylori positive. 5(29.5%) patients of oesophageal ulcer, 24(80.0%) patients who had ulceration in two or more different sites and 5(83.3%) patients who had ulceration in gatrojejunostomy stoma were found H. pylori positive [Figure-1].

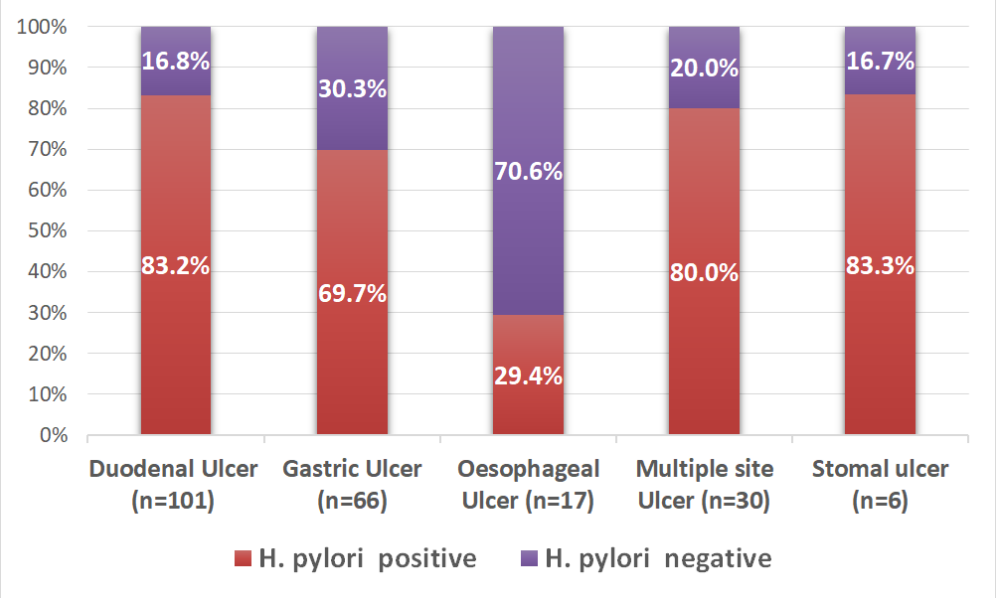

Figure-1: Bar diagram showing distribution of the patients by H. pylori status.

Table-8: Distribution of various drug-induced gastrointestinal ulcers (n=35)

Drug implicated	Oesophageal Ulcer (n=7) f(%)	Gastric Ulcer (n=12) f(%)	Duodenal Ulcer (n=16) f(%)
NSAIDs	3(42.8%)	6(50.0%)	7(43.8%)
NSAIDs + H. pylori	-	4(33.3%)	9(56.2%)
Aspirin	1(14.3%)	-	-
Steroids	1(14.3%)	1(8.3%)	-
Doxycycline	2(28.6%)	-	-
Bisphosphonates	-	1(8.3%)	-

Drug-induced upper gastrointestinal ulcers were found in 35 patients. Majority of these are NSAID-induced, either alone (n=16) or in association with H. pylori infection (n=13). Out of 7 cases of drug-induced oesophsgeal ulcers 3(42.8%) are due to NSAID, 1(14.3%) is due to Aspirin, 1(14.3%) from corticosteroids and 2(28.6%) from Doxycycline intake. Among 12 patients of drug-induced gastric ulcer, 6(50.0%) were NSAID-induced, 4(33.3%) had history of NSAID ingestion and also H. pylori infection, 1(8.3%) from Steroid and 1(8.3%) from Bisphosphonate ingestion. 16 patients had drug-induced duodenal ulcers, of them 7(43.8%) were NSAID-induced and 9(56.2%) patients who had history of chronic NSAID ingestion, were also found H. pylori positive [Table-8].

Table-9: Comparison of presenting complaints among different group of patients (N=220)

Presenting complaints	Total patients (n=220) f(%)	Duodenal Ulcer (n=101) f(%)	Gastric Ulcer (n=66) f(%)	Oesophageal Ulcer (n=17) f(%)	p value
Epigastric pain	174(79.1%)	83(82.2%)	57(86.4%)	7(41.2%)	0.001
Postprandial fullness	136(61.8%)	62(61.4%)	44(66.7%)	9(52.9%)	0.547NS
Early satiety	90(40.9%)	37(36.6%)	35(53.0%)	5(29.4%)	0.061NS
Abdominal bloating	102(46.4%)	45(44.6%)	37(56.1%)	3(17.6%)	0.016
Nausea	78(35.4%)	32(31.7%)	26(39.4%)	8(47.1%)	0.358NS
Anorexia	59(26.8%)	21(20.8%)	24(36.4%)	5(29.4%)	0.084NS
Vomiting	29(13.2%)	13(12.9%)	11(16.7%)	2(11.7%)	0.755NS
Heartburn	57(25.9%)	16(15.8%)	21(31.8%)	11(64.7%)	0.0001

Presenting complaints	Total patients (n=220) f(%)	Duodenal Ulcer (n=101) f(%)	Gastric Ulcer (n=66) f(%)	Oesophageal Ulcer (n=17) f(%)	p value
Dysphagia	33(15.0%)	5(4.9%)	14(21.2%)	10(58.8%)	0.0001
Constipation	56(25.4%)	30(29.7%)	18(27.3%)	3(17.6%)	0.586NS
Melaena	21(9.5%)	11(10.9%)	8(12.1%)	1(5.9%)	0.762NS
Haematemesis	17(7.7%)	4(3.9%)	10(15.1%)	1(5.9%)	0.033

p value derived from chi-square test.
NS=not significant

Various types of complaints were presented by different groups of ulcer patients. Out of 220 ulcer patients 174(79.1%) patients had epigastric pain, among them 83(82.2%) patients of duodenal ulcer, 57(86.4%) patients of gastric ulcer and 7(41.2%) patients of oesophageal ulcer experienced this symptom. Difference between these groups for epigastric pain was significant (p=0.001). 62(61.4%) of duodenal ulcer group, 44(66.7%) of gastric ulcer group and 9(52.9%) of oesophageal ulcer group had postprandial fullness. There was no significant difference among these groups (p=0.547). 37(36.6%) patients of duodenal ulcer, 35(53.0%) patients of gastric ulcer and 5(29.4%) patients of oesophageal ulcer experienced early satiety. 102(46.4%) patients experienced abdominal bloating, 45(44.6%) patients of duodenal ulcer group, 37(56.1%) of gastric ulcer group and 3(17.6%) of oesophageal ulcer group had this symptom with significant difference among these groups (p=0.016). 78(35.4%) of ulcer patients had nausea, out of them 32(31.7%) patients of duodenal ulcer, 26(39.4%) patients of gastric ulcer and 8(47.1%) patients of oesophageal ulcer had this symptom without significant difference (p=0. 358). 21(20.8%) patients of duodenal ulcer group, 24(36.4%) of gastric ulcer group and 5(29.4%) of oesophageal ulcer had anorexia. 29(13.2%) patients of upper gastrointestinal ulcer had vomiting. Among them 13(12.9%) patients of duodenal ulcer, 11(16.7%) of gastric ulcer and 2(11.7%) of oesophageal ulcer group had this symptom with no significant difference (p=0.755). 16(15.8%) patients of duodenal ulcer, 21(31.8%) patients of gastric ulcer and 11(64.7%) patients of oesophageal ulcer experienced heartburn. There was significant difference for this symptom among these groups (p=0.0001). 5(4.9%) patients of duodenal ulcer, 14(21.2%) patients of gastric ulcer and 10(58.8%) patients of oesophageal ulcer had dysphagia. Difference between these groups was significant (p=0.0001). 56(25.4%) patients had constipation, out of them 30(29.7%) patients of duodenal ulcer, 18(27.3%) patients of gastric ulcer and 3(17.6%) patients of oesophageal ulcer experienced constipation. No significant difference was found (p=0.586). 11(10.9%) patients of duodenal ulcer, 8(12.1%) of gastric ulcer and 1(5.9%) of oesophageal ulcer had history of melaena. Haematemesis was present in 17(7.7%) patients, among them 4(3.9%) patients of duodenal ulcer, 10(15.1%) of gastric ulcer and 1(5.9%) of oesophageal ulcer group had this symptom. There was significant difference in these groups (p=0.033) [Table-9].

Table-10: Presence of comorbidities with upper GI ulceration (N=77)

Comorbid conditions	Number of patients	Percentage
Chronic liver disease /Cirrhosis	24	10.9
Chronic kidney disease	10	4.5
Cardiovascular disease (IHD, heart failure)	17	7.7
Chronic obstructive airway disease	3	1.4
Diabetes mellitus	19	8.6
Rheumatic disease (RA, SLE, PSS)	4	1.8

In many cases various comorbid illnesses were present along with gastrointestinal ulceration. Comorbidities found in this study were chronic liver disease in 24(10.9%) ulcer patients, chronic kidney disease in 10(4.5%) patients, cardiovascular disease in 17(7.7%) patients, COPD in 3(1.4%) cases, diabetes mellitus in 19(8.6%) patients and rheumatic disease in 4(1.8%) ulcer cases [Table-10].

DISCUSSION

Patients referred for upper GI endoscopy for different indications from inpatient and outpatient department of Gastroenterology, who met the inclusion criteria were primarily selected for the study. Consecutive 220 patients found to have ulcers anywhere in the upper GIT were finally included in this study. The differences in clinical, morphological, histopathological and laboratory parameters between the ulcer subgroups were also compared. In this study it was found that, duodenal ulcer was present in 101(45.9%) patients, gastric ulcer in 66(30.0%) and oesophageal ulcer in 17(7.7%) patients. Combined gastric and duodenal ulcer were present in 18(8.2%) cases, gastric and oesophageal ulcer in 8(3.6%), oesophageal and duodenal ulcer in 4(1.8%) and stomal (gastrojejunostomy stoma) ulcer in 6(2.7%) patients. This finding was consistent with the findings of Uyanikoglu *et al.*, [20]. They found that out of 140 cases, ulcer was located in duodenum in 96(68.5%), in stomach in 40(28.6%), and both duodenum and

stomach in 4(2.9%) patients. However, Goenka *et al.,* [14] showed different finding in their study. They assessed the proportion of non-NSAID, non-H. pylori peptic ulcer disease in India. Their study observed that among the enrolled 128 patients 74(57.8%) had gastric ulcer (GU) and 54 (42.2%) had duodenal ulcer (DU). In a study on oesophageal ulcer by Higuchi *et al.,* [4] conducted in an urban hospital of Detroit, Michigan from 1991 to 2001, oesophageal ulcers were seen in 88(1.2%) patients. A study was conducted by Chung *et al.,* [21] in South Korea regarding ulcers following gastrectomy. They found that the incidence of marginal ulcers after gastrectomy was 8.6%. The mean age of the total patients, patients of DU group, GU group and OU group were 41.72±12.29, 38.81±11.35, 42.78± 17.42 and 45.53± 18.13 years respectively. There was no significant difference in mean age between these groups (p = 0.086). In contrast to our observation, the mean age was much higher in the research findings of Kim *et al.,* [22]. The lower mean age of the patients may be due to involving the lower age group that was enrolled in this study. Another factor is that people of developing countries acquire H. pylori infection earlier. Yang *et al.,* [23] stated that more than 50% of the world's population has been infected by H. pylori and the prevalence of infection in developing countries is greater than 80% in adults over 50 years of age. Among the total patients, 131(59.5%) were male and 89(40.5%) patients were female. There was no significant difference in distribution of male and female between gastric, duodenal and oesophageal ulcer group (p = 0.883). In a Prospective multicentre study of patients with peptic ulcer disease in 32 French general hospitals over 1 year conducted by Charpignon *et al.,* [24] found that out of 713 enrolled patients 57.9% were male and 42.1% were female. These results were comparable to our study result. This observation is closer to another study by Uyanikoglu *et al.,* [20]. They enrolled 140 patients diagnosed with peptic ulcer in a prospective study and found that 78 (55.7%) patients were male and 62 (44.3%) were female. In the present study 63 (28.6%) patients had history of smoking. No significant difference was observed between different groups of ulcer in history of smoking (p=0.377). This finding was supported by Konturek *et al.,* [25]. To examine the association between gastroduodenal ulcers and H. pylori infection, NSAID use, smoking and age, Konturek *et al.,* [25] designed a study with 5967 dyspeptic patients and found that the H. pylori prevalence was significantly higher in smokers (76%) than in non-smokers (67%) and the ulcer risk was also significantly higher in smokers than in non-smokers. Various aetiologies of upper gastrointestinal tract ulcer were diagnosed in the study patients. Majority of ulcer cases (56.4%) were induced by Helicobacter pylori infection. Among other causes 18(8.2%) patients had NSAID-induced ulcer, 7(3.2%) patients had drug induced ulcer other than NSAID, 14(6.4%) had history of NSAID intake and also found H. pylori positive, 20(9.1%) patients of ulcer were diagnosed as adenocarcinoma, 5(2.3%) patients had lymphoma, 3(1.3%) patients had tubercular ulcer, 2(0.9%) were patients of Crohn's disease manifested with upper gastrointestinal ulceration, 4(1.8%) patients had GIST found to have upper gastrointestinal ulceration, 2(0.9%) were due to corrosive injury and 6(2.7%) patients had ulceration as a complication of reflux oesophagitis. No specific causes were found in 15(6.8%) patients and were labelled as idiopathic ulcer. Charpignon *et al.,* [24] analyzed the epidemiological and clinical characteristics of 713 patients with ulcer disease in 32 French general hospitals. They classified patients into four groups: 40.0% had only H. pylori infection; 18.7% only gastro toxic drugs; 19.8% had both and 21.6% neither H. pylori infection nor gastro toxic drug intake ('idiopathic ulcers'). In one study on oesophageal ulcers conducted by Higuchi *et al.,* [4] in Detroit, Michigan, oesophageal ulcers were seen in 88 (1.2%) patients. The aetiology of oesophageal ulcers included the following: gastroesophageal reflux disease (65.9%), drug induced (22.7%), candidal (3.4%), caustic injury (2.3%), herpes simplex virus, HIV, marginal ulcer, and unknown etiology (1.1% of each). Kim *et al.,* [22] found that the rate of idiopathic peptic ulcer without evidence of H. pylori and NSAIDs was 40.6%. Kim *et al.,* [22] evaluated the risk factors and general characteristics of patients diagnosed as PUD. Among them adenocarcinoma were found in 2(10%) patients in the duodenum, 16(80%) in the stomach, 1(5%) in the oesophagus and 1(5%) case was found in gastrojejunostomy stoma. Of the 4 cases of lymphoma, 1(25%) was present in duodenum and 3(75%) were present as gastric ulcer. Sruthi *et al.,* [26] conducted a descriptive study on gastric neoplasm in Karnataka, India. This study included gastric biopsies of 163 patients with suspected gastric malignancy of which 157 were neoplastic. There was a male predominance with a peak in the 5th to 7th decade. The commonest site of origin was antrum & prepylorus (59.87%) and commonest endoscopic finding was ulcerative growth (62.42%). Of the 157 neoplasms, 153 (97.45%) were adenocarcinomas. The other cases comprised of 2 cases of gastric carcinoid, one case each of gastric lymphoma and GIST. The associated findings noted were H. pylori infection (22.87%), chronic atrophic gastritis (23.52%) and intestinal metaplasia (9.15%). Chung *et al.,* [21] conducted a study to determine the incidence of endoscopic ulcers following gastrectomy. A total of 78 patients with endoscopic ulcers were found. Out of them 72 patients had Marginal ulcer and 6 patients were diagnosed with gastric stump cancer. The incidence of endoscopic ulcers after gastrectomy was 9.3% and that of marginal ulcers was 8.6%. Helicobacter pylori status among the study patients was detected by urea breath test. Out of total 220 patients, urea breath test was positive in 164(74.5%) patients. 84(83.2%) patients of duodenal ulcer, 46(69.7%) patients of gastric ulcer and 5(29.5%) patients of oesophageal ulcer were found H. pylori positive. 24(80.0%) patients who had ulceration in two different sites and 5(83.3%) patients who had

ulceration in gatrojejunostomy stoma were found H. pylori positive. In a cross-sectional study by Goenka *et al.,* [14] from Kolkata, India with 128 patients of ulcer diseases found that 78 (60.9%) cases were H. pylori positive. The proportion of ulcer with H. pylori positivity was 54.1% in gastric ulcer patients and 70.4% in duodenal ulcer patients. Chung *et al.,* [21] describes characters of endoscopic ulcers following gastrectomy. A total of 78 patients with stomal ulcers that were found, H. pylori infection (%) were present in 34.5% cases. The most frequent presenting complaints of the total patients were epigastric pain (79.1%) and postprandial fullness (61.8%). Epigastric pain was present similarly in gastric and duodenal ulcers groups (86.4% and 82.2% respectively) but differ significantly in oesophageal ulcer groups (41.2%). There was also significant difference in presenting complaints between three ulcer groups regarding abdominal bloating (p=0.016), heartburn (p=0.0001) and dysphagia (p=0.0001) and haematemesis (p=0.033). There was no significant difference between the groups in the presence of postprandial fullness (p=0.547), early satiety (p=0.061), nausea (p=0.358), anorexia (p=0.084), vomiting (p=0.755), constipation (p=0.586) and melaena (p=0.762). A clinical study of peptic ulcer disease and its complications by Mukherjee *et al.,* [27] in Karnataka, India, 80 patients with peptic ulcer disease were analyzed with respect to presenting complaints and clinical signs. Among the duodenal ulcer patients, vomiting was a complaint in 47.7% at one time. In patients with duodenal ulcers, the duration of symptoms was between 1-5 years in maximum no. of patients (56.2%). Nausea, anorexia and weight loss were common in patients with tubercular ulcer. In Crohn's ulcer patients the main presenting features were abdominal pain, vomiting and weight loss. These findings were consistent with study of Mukherjee *et al.,* [27] where patients with peptic ulcer most commonly presented with abdominal pain and loss of appetite, whereas vomiting and weight loss were less common presenting features. In a study by Sah *et al.,* [28] in Nepal, the presentation of gastric malignant ulcers were analyzed. In this study various drug-induced upper gastrointestinal ulcers were found in 35 patients. Majority of these are NSAID-induced, either alone (n=16) or in association with H. pylori infection (n=13). Among drug-induced oesophsgeal ulcers 3(42.8%) are due to NSAID, 1(14.3%) is due to Aspirin, 1(14.3%) from corticosteroids and 2(28.6%) from Doxycycline intake. In gastric ulcer group, 6(50.0%) were NSAID-induced, 4(33.3%) had history of NSAID ingestion and also H. pylori infection, 1(8.3%) from Steroid and 1(8.3%) from Bisphosphonate. In duodenal ulcer group, 7(43.8%) were NSAID-induced and 9(56.2%) had both history of NSAID and also H. pylori positive. In a study on oesophageal ulcer by Higuchi *et al.,* [4] in Detroit, out of 88 ulcer patients, drug-induced oesophageal ulcers were found in 20 cases. In this study, various comorbid illnesses were present in association with gastrointestinal ulceration. Comorbidities found in this study were chronic liver disease in 24(10.9%) ulcer patients, chronic kidney disease in 10(4.5%) patients, cardiovascular disease in 17(7.7%) patients, COPD in 3(1.4%) cases, diabetes mellitus in 19(8.6%) patients and rheumatic disease in 4(1.8%) ulcer cases. Charpignon *et al.,* [24] analyzed different characteristics of 713 patients with ulcer disease in 32 French general hospitals. They found comorbidities in 148(21.6%) ulcer patients. Out of them 58(8.1%) patients had cirrhosis of liver, 40(5.6%) had chronic renal failure, 27(3.8%) patients had cardiac failure, 7(1%) had recent stroke, 21(3.0%) patients were in intensive care support, 35(4.9%) patients were malnourished and 10(1.4%) patients were receiving chemotherapy.

CONCLUSION

The current study showed that peptic ulcers are the predominant ulcers occurring in the upper gastrointestinal tract; H. pylori infection and chronic use of NSAIDs are the common causes for peptic ulcer in our country. Malignant lesions were also found but relatively less common than peptic ulcers. There were variations in pattern of clinical presentations among the patients with different types of ulcer regarding their site and aetiology. In some cases the exact aetiology of the ulcer could not be identified. So a further study on large sample with extensive investigations and follow-up is needed to identify the underlying cause of such idiopathic ulcers.

Limitation

- The study was carried out in a single center.
- The study period was short.
- The sample size of the study was small.
- Follow-up studies were not performed.

RECOMMENDATION

A multi-center study with large sample size may be undertaken to make representation of the whole population. Further evaluation and follow-up study period should be done to find out the causes of idiopathic ulcers and who are not adequately response to treatment.

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