ENDOSCOPIC STUDY OF GASTRIC ULCER WITH REFERENCE TO MALIGNANCY

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ABSTRACT

BACKGROUND

It is fundamental that any gastric ulcer should be regarded as being malignant, no matter how classic the features of a benign gastric ulcer. Multiple well-targeted biopsies, as many as 10, should always be taken before an ulcer can be definitely accepted as benign, which can be detected by a simple outpatient procedure of upper gastrointestinal endoscopy.

MATERIALS AND METHODS

Cases undergoing upper GI endoscopy in the Department of General Surgery, M.K.C.G. Medical College Hospital, from June 2015 - July 2017 were included in the study to determine the malignancy developing in cases of gastric ulcer keeping in mind the above-mentioned facts.

RESULTS

Out of 1782 cases of total upper GI endoscopy performed, 197 cases were detected as gastric ulcer. The incidence of malignancy in a gastric ulcer in this study was 3.04%. Peptic ulcer disease was more common in male sex compared to females. Incidence of malignancy in gastric ulcer was higher in smokers and alcoholics. The patients with H. pylori were more prone to gastric ulceration and its subsequent malignant transformation are well established.

CONCLUSION

Gastric ulcer maybe a precursor lesion of gastric malignancy. Multiple well-targeted biopsy from ulcer at endoscopy may lead to detection of early gastric cancer.

KEYWORDS

Gastric Ulcer, Gastric Malignancy, Upper GI Endoscopy.

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BACKGROUND

Gastric ulcer are defects in gastric mucosa that may extend into submucosa or deeper, which maybe acute or chronic.[1] Peak incidence occurs between age 55 and 65 years. Conditions predisposing to gastric ulcerations are ingestion of mucosal barrier breaking drugs such as aspirin and other NSAIDS, abnormalities in acid and pepsin secretion, gastric stasis from delayed gastric emptying, coexisting duodenal ulcer, duodenal gastric reflux of bile, gastritis and infection with H. pylori. Some clinical conditions that predispose to gastric ulcerations include chronic alcohol intake, smoking, long-term corticosteroid therapy and infection with H. pylori. Acid and pepsin appears to play essential role in production of gastric ulcer.[2]

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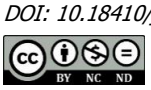

The population with gastric ulcers tend to be older. It is more prevalent in low socioeconomic groups and is considerably more common in the developing world than in the West.[3] Epigastric pain, vomiting, loss of weight, upper GI bleed, which maybe overt or occultare some of the clinical features. One of the classical features is periodicity. Symptoms may disappear for weeks or months to return again. This periodicity maybe related to the spontaneous healing of the ulcer. Chronic gastric ulcers are much more common on the lesser curve (especially over the incisura angularis) than on the greater curve and even when high on the lesser curve, they tend to be at the boundary between the acid-secreting and the non-acid-secreting epithelia. With atrophy of parietal cell mass, non-acid-secreting epithelium migrates up the lesser curvature.[3]

Gastric carcinoma is a common cancer worldwide. There is substantial geographic variation with very high rates in Japan and some parts of South America. Worldwide gastric cancer is the 4th most common cancer and second leading cause of cancer death.[3] It may be noted that gastric ulcer maybe a precursor lesion of carcinoma stomach, which in the early stages is curable by simple resection. Two clinical extremes can exist. First, there can be benign chronic gastric ulcer that undergoes malignant transformation and secondly

the patient maybe identified as having an ulcer in the stomach, either endoscopically or on contrast radiology, which is assessed as benign, but biopsies reveal malignancy. This situation is common.

It is fundamental that any gastric ulcer should be regarded as being malignant, no matter how classic the features of a benign gastric ulcer. Multiple well-targeted biopsies, as many as 10, should always be taken before an ulcer can be definitely accepted as benign, which can be detected by a simple outpatient procedure of upper gastrointestinal endoscopy.[4]

Keeping in mind, the above-mentioned facts, it was proposed to undertake an endoscopic study of gastric ulcers with special reference to gastric malignancy.

MATERIALS AND METHODS

The patient attending M.K.C.G. Medical College Hospital with a provisional diagnosis of gastric ulcer disease in surgical department from June 2015 - July 2017, consecutively of both sexes and all age groups were included in the study. Out of 1782 cases of total upper GI endoscopy done, 197 cases were detected as gastric ulcer and included in the study to determine the malignancy developing in cases of gastric ulcer.

The following scheme was followed in recording the cases.

Inclusion Criteria

1. Abdominal pain (nonradiating) burning quality, located in epigastrium.
2. Pain increases with intake of food.
3. Nausea, weight loss, bloating.
4. Stool positive for occult blood.

Exclusion Criteria

1. Haemodynamically unstable patients.
2. Pain radiating to back and pressure sensation.
3. Regurgitation of undigested food.
4. Dysphagia for solid and liquid foods at the same time.
5. Unstable cardiac disease and recent MI attack.
6. Uncorrected coagulopathy.
7. Unable to obtain informed consent.
8. Intubated or terminally-ill patients.

METHOD

After taking proper history and complete general and systemic examination, upper gastrointestinal endoscopic evaluation was done. Each patient was explained about the procedure beforehand and informed consent was obtained in all cases. The following routine was followed out in each case. The patient was not allowed to take anything orally 4-8 hours prior to endoscopic procedure. In all patients, lignocaine viscous spray was sprayed 10 minutes before the procedure. The patient was sedated if anxiety was expected. Prophylactically, antibiotics to prevent infective endocarditis were given. With patient in left lateral supine position, scope was introduced through a mouthguard, which protect the scope from being bitten after lubricating with lignocaine gels. Scope was introduced under direct vision of the monitor, into oesophagus, then to stomach and first part of duodenum finally visualising second part of duodenum. The mucosal interior surface of stomach was seen carefully and systematically.

Endoscopic Biopsy- Multiple targeted biopsies were taken from ulcer placing the biopsy forceps vertically to the mucosal surface of stomach to prevent slipping.

RESULTS

Out of 1782 cases of total upper GI endoscopy done, 197 cases were detected as gastric ulcer and included in the study.

Total No. of UGIE Done	Total No. of Gastric Ulcers	Total No. of Histopathological-Proved Malignancy	Incidence of Gastric Malignancy in Gastric Ulcer Cases
1782	197	6	3.04%

Table 1. Incidence Malignancy

The incidence of malignancy amongst the patients diagnosed with gastric ulcer was 6/197 x 100 = 3.04%.

Age Group (in yrs.)	Number of Patients	Percentage (%)	Malignancy Positive
18-20	2	1.0	0
21-30	14	7.1	0
31-40	15	7.6	0
41-50	35	17.8	3
51-60	47	23.9	2
61-70	63	32	1
71-80	21	10.6	0
Total	**197**	**100**	**6**

Table 2. Age Distribution

The cases were grouped into following age groups 18-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, respectively. Majority of the patients (66.5%) fell in the age group 50-70 years.

The age of the 6 patients diagnosed with a malignant gastric ulcer were 48, 52, 57 and 71 years (males) and 42 and 49 years (females).

Sex	Number of Cases	Percentage	Malignancy Positive
Male	146	74.1	4
Female	51	25.9	2
Total	**197**	**100.0**	**6**

Table 3. Sex Distribution

In this study, the sex ratio was 2.86:1. Four male patients and two female patients were diagnosed with an ulcer that proved to be malignant on biopsy.

Incidence of malignancy in a gastric ulcer in males = 4/146 x 100 = 2.73%.

Incidence of a gastric ulcer being malignant in females = 2/51 x 100 = 3.92%.

	Malignancy Positive	Malignancy Negative
Alcoholic	3	86
Nonalcoholic	1	107
Total	**4**	**193**

Table 4. Alcoholism and Malignant Gastric Ulcer

Out of 197 patients studied, 89 patients had history of alcohol consumption (past/present) and rest 108 patients were nonalcoholics.

Incidence of malignant gastric ulcer in alcoholics = 3/89 x 100 = 3.37%.

Incidence of malignancy in a gastric ulcer in non-alcoholics = 1/108 x 100 = 0.92%.

	Malignancy Positive	Malignancy Negative
Smokers	2	57
Nonsmokers	2	136
Total	**4**	**193**

Table 5. Smoking and Malignancy in a Gastric Ulcer

In this study, out of 197 patients, 59 patients had a positive smoking history, whereas 138 were nonsmokers.

Incidence of cancer in smokers with a gastric ulcer = 2/59 x 100 = 3.38%.

Incidence of malignant ulcer in nonsmokers = 2/138 x 100 = 1.44%.

	Positive for Malignancy	Negative for Malignancy
H. pylori positive	6	161
H. pylori negative	0	30
Total	**6**	**191**

Table 6. H. Pylori and Malignant Gastric Ulcers

In this study, out of 197 patients with gastric ulcer, 84% of patients (167) were positive for H. pylori.

All of the 6 gastric ulcers, which were proved to be malignant on biopsy were positive for H. pylori.

	Positive for Malignancy	Negative for Malignancy
NSAIDs consumption - Positive	3	107
NSAIDs consumption - Negative	3	84
Total	**6**	**191**

Table 7. NSAIDs and their Role in Development of Malignancy in a Gastric Ulcer

Out of 197 patients, 110 (55.8%) patients were found to have a previous or present history of NSAID consumption.

Out of 110 patients on NSAIDs, 3 patients were found to have a gastric ulcer that turned out to be malignant on HP study, while out of 87 patients who did not consume NSAIDs, 3 were tested positive for a malignant gastric ulcer.

Incidence of malignancy in a gastric ulcer in NSAID users = 3/110 x 100 = 2.72%.

Incidence of a malignant gastric ulcer in patients who did not use NSAIDs = 3/87 x 100 = 3.44%.

Blood Group	Rh Typing Positive	Rh Typing Negative	Total	Positive for Malignancy
AB	11	3	14	0
A	26	0	26	2
B	75	1	76	1
O	75	6	81	3
			197	**6**

Table 8. Blood Group and Malignant Gastric Ulcers

Out of 197 ulcer patients, 41.1% patients were of blood group "O", 38.5% of the patients were of "B" blood group, while "A" and "AB" blood group accounted for 13.1% and 7.1%, respectively.

Out of the 6 patients with a malignant ulcer, 3 were of blood group "O", 2 were of "A" and 1 patient was "B" positive.

Incidence among blood group "O" = 3/81 x 100 = 3.7%.
Incidence among blood group "A"= 2/26 x 100 = 7.69%.
Incidence among blood group "B" = 1/76 x 100 = 1.31%.

Socioeconomic Class	Positive for Malignancy	Negative for Malignancy	Total
Low	5	171	176
High	1	20	21
Total	**6**	**191**	**197**

Table 9. Socioeconomic Class and Incidence of Malignancy in a Gastric Ulcer

In this study, 176 patients belong to low socioeconomic status, whereas 21 patients were of high Socioeconomic Status (SES). Out of 6 patients diagnosed with a malignant gastric ulcer, 5 belong to low SES, whereas only one (female) patient was of high SES.

Incidence of malignant degeneration of a gastric ulcer in low SES = 5/176 x 100 = 2.84%.

Incidence among high SES = 1/21 x 100 = 4.76%.

BMI (in kg/m^2)	Number of Patients	Positive for Malignancy
<18	31	0
18.5-24.99	88	2
25.0-29.99	63	2
30.0-34.99	12	2
>35	3	0
Total	**197**	**6**

Table 10. Obesity and Malignancy in a Gastric Ulcer

The majority of patients (60.4%) in this study had a BMI <25 kg/m^2, while 31.9% had a BMI in the range of 25-30 and 12 patients had a BMI 30-35 kg/m^2.

Of the 6 patients (19, 20.5, 25, 25.5, 30.5 and 31) diagnosed with a malignant ulcer, their BMI ranged from 18 to 35 kg/m^2. Thus, the chances of gastric cancer in an ulcer case increased with increase in BMI.

Type of Ulcer	Number of Patients	Positive for Malignancy
Type I	123	4
Type II	25	1
Type III	29	0

Type IV	14	1
Type V	6	0
Total	**197**	**6**

Table 11. Location of Gastric Ulcer and its Relevance in Development of Malignancy

Out of 197 gastric ulcers, 123 were type I (along the lesser curvature near incisura angularis), 25 were type II (body), 29 were of type III (prepyloric), 14 were type IV (high on the lesser curvature) and 6 ulcers were of type V (at any location). Among the six malignant ulcers, 4 were type I, 1 was of type II and 1 was of type IV.

DISCUSSION

The incidence of malignancy in a gastric ulcer in this study was 3.04%. Similar results were found in study done by LV Sx et al[5] with an incidence of 2.41%.

Nearly, 70% of the patients were in the age group 51-80 years. This is in accordance to the study done by Brock J et al,[6] which stated gastric ulcer disease affected mainly older individuals peaking around age 70 years.

Out of 146 males in the study, 4 were diagnosed with a malignant ulcer, whereas out of 51 female patients, malignancy was detected in 2 of them, male-to-female ratio in the studied patients was 2.86:1, which complies with the fact that peptic ulcer disease is more common in male sex compared to females also described by Rodrigo et al.[7]

The incidence of malignant ulcer in alcoholics was 3.37% compared to 0.92% in nonalcoholics.

Smokers are about twice as likely to develop PUD as nonsmokers, which can be explained by the fact that smoking increases gastric acid secretion and duodenogastric reflux and decreases both gastroduodenal prostaglandin production and pancreatic-duodenal bicarbonate production.

In this study, 84% of the total patients were positive for H. pylori and 100% of the patients who were diagnosed with a malignant ulcer were positive for H. pylori on histological analysis or on rapid urease test. These results are favoured by the study done by Uemura et al[8] who observed that gastric cancer develops in persons previously infected with H. pylori, but not in uninfected persons.

Incidence of malignant degeneration of gastric ulcer in NSAID users was lower (2.72%) compared to patients that did not give any history of NSAID use (3.44%). Thus, this study shows NSAID use may have some protective effect on gastric cancer development. The study done by Wu CY et al[9] also showed that patients with peptic ulcer who never used NSAIDs had a higher risk of gastric cancer compared with general population and regular NSAID use was an independent protective factor for gastric cancer development, especially in H. pylori infected patients.

Majority of the ulcer patients in this study were of blood group "O" (41%) and "B", whereas blood group "A" accounted for only 13% of the total cases; the incidence of malignant ulcer in blood group "A" was the highest (7.69%) compared to blood group "O" (3.7%) and "B" (1.31%). These results are in accordance to the study conducted by Zhiwei et al,[10] which stated blood group "A" patients had more chances of developing gastric malignancies than non-A blood groups and Edgren et al,[11] which reported gastric ulcer to be more common in patients of the blood group "O".

In general, gastric carcinoma is more prevalent in low socioeconomic class, but the higher incidence of cancer in a gastric ulcer observed in this study may be explained by the fact that the carcinoma diagnosed was of diffuse variety and the patient affected was a female of high SES, which is in accordance with the Laurens classification of gastric carcinoma, which states that the diffuse variety of adenocarcinoma affects more commonly the female sex, high SES and has a worse prognosis as compared to the intestinal variety of adenocarcinoma.

Apart from two patients (BMI of 19.0 and 20.5), rest four patients were overweight with a BMI >25 kg/m^2. Thus, obesity is a risk factor for an ulcerated gastric malignancy. The study done by Hoyo et al[12] also showed obesity as an independent risk factor for oesophagogastric cancers, including the cardia. Abdominal fat may directly cause GERD, a risk factor for oesophageal and cardia-gastric cancer. Moreover, fat is metabolically active and produces numerous compounds like insulin-like growth factor and leptins have been associated with various malignancies through the induction of pro-growth changes in the cell cycle, decreased cell death and pro-neoplastic cellular changes.[13]

Most of the malignant ulcers being of type I can be explained by the fact that type I gastric ulcers are more common.

CONCLUSION

- Thus, increasing age is a risk factor for both gastric ulcer and gastric malignancy.
- Malignant degeneration of a gastric ulcer is more in males.
- Incidence of malignancy in gastric ulcer is higher in smokers and alcoholics.
- The patients infected with H. pylori are more prone to gastric ulceration and its subsequent malignant transformation is well established.
- Blood group "A" patients have reduced-immune response to tumour cells than other blood group types, so more prone for malignancy.
- Incidence of cancer in a gastric ulcer is more in high Socioeconomic Status (SES).
- Obesity (BMI >25 kg/m2) is a risk factor for an ulcerated malignancy.
- Most of the malignant ulcers are type I (along the lesser curvature near incisura angularis). Gastric ulcer maybe a precursor lesion of gastric malignancy. Multiple well-targeted biopsy from ulcer at the endoscopy may lead to detection of gastric cancer earlier.

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