Topographic, Clinico-Pathological Profile And Status Of Risk Factors Of Patients Having Gastric Malignancy

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Abstract
Background: *Gastric cancers are the third common gastro-intestinal cancers with high mortality. Helicobacter pylori, the strongest risk factor for the development of gastric cancers, mainly affects the population of low socio-demographic profile countries. With the advancement of socio-economy, H. pylori infection is expected to be low in Bangladesh. This might have impact on pattern of topographic distribution of gastric malignancy also with their histological pattern. This area has not been well explored in Bangladesh and this study is undertaken to see the situation.*
Objective: *The objective of the study was to know the topographic, clinico-pathological profile and risk factors and their effect on gastric malignancies.*
Methods: *This cross-sectional study was done in the Department of Gastroenterology, Shaheed Suhrawardy Medical College Hospital involving confirmed cases of gastric malignancy. Statistical analyses were done by using appropriate statistical tool. Data was expressed in frequency, percentage and mean as applicable.*
Results: *A total of 74 patients were enrolled in the study with age range from 35 to 85 years. Maximum patients' (66.2%) age range was from 50 to 85 years. Male to female ratio was 2.5:1. Upper GI endoscopy showed that most of the patients (45.9%) had diffuse involvement in stomach. Adenocarcinoma (93.2%) was the common histological type. Maximum gastric malignancy was of grade-3/poorly differentiated (44.6%). Maximum patients (60.8%) were from rural area. Sixty six percent male were smoker. 66.67% female had used chewable tobacco products. Practice of taking added salt in foods was found in 55.4% patients. Family history of malignancy was present in 9.5% patients. The most common symptom was anorexia (87.8%) followed by weight loss (83.8%), generalized weakness (79.7%), dyspepsia (78.4%), abdominal pain (60.8%). Common signs were anaemia (73%) and ascites. Liver metastasis was present in 6.8% patients.*
Conclusion: *Gastric malignancy was found common in fifth to seventh decade of life with male predominance. Topographically most patients had diffuse involvement. Nearly two-thirds patients have H. pylori infection. Histologically most of the gastric malignancies were adenocarcinoma with poor differentiation.*

I. Introduction

An estimated 19.9 million new cases and 9.7 million deaths related to cancers occurred worldwide in 2022. Cancers of the gastrointestinal (GI) tract represent more than one-quarter (26%) of the global cancer incidence and more than one-third (35%) of all cancer-related death, according to Global Cancer Observatory [1].

On the basis of three databases, GLOBOCAN, Cancer Incidence in Five Continents and the World Health mortality database, incidence and mortality trends of GI cancers varied by geographic location. In 2018,

Asia predominated over Europe and North America in new cases (63% vs 26%) and deaths (65% vs 23%). Malignancy of the oesophgus, stomach and liver cancers were more prevalent in Asia, while colorectal and pancreatic cancers were more common in Europe and North America [2].

World is changing in both the age composition and growth of the population. According to these expected changes, the total number of new cases of, and deaths from GI cancers are predicted to increase by 58% and 73%, respectively, by 2040 [1].

Cancers of the oesophagus and stomach are among the most lethal of all malignancies [3]. Gastric cancer remains the third most common cause of malignancy related death in the world [4, 5]. Gastric cancer incidence ranked 7th of all malignancies. Its incidence varies widely and is predicted to cause a higher burden in developing countries than in industrialized nations [5]. GLOBOCAN stated that in 2018, estimated worldwide gastric cancer incidence was 5.7% and their death was 8.2% [6]. In 2018 GLOBOCAN, Bangladesh showed that 18.7% of total cases of new cancers were from oesophagus and stomach origin. Death from gastric malignancies was 6.3%. Death from gastric cancers predominated over other malignancies [7].

Globally, there is wide variation of ages among the gastric cancer bearing patients. But in general there is a tendency to have more frequently among elderly patients. More than 95% of all new cases are diagnosed at 40 years or more[5, 8]. From these observations, gastric malignancies are generally thought to be the disease of elderly, though some studies have shown 2-15% incidence of gastric carcinoma among individuals of age 45 years or less [9, 10, 11, 12, 13]. In Bangladesh, we don't have adequate data in this regard.

Topographical distribution of gastric malignancy varies, with 40% being in the lower part, 40% in the middle part and 15% in the upper part [14]. In developing countries, this distribution is slightly different with relatively more occurrence in the lower part of the stomach probably due to H-pylori infection [15]. Cancers of the antrum and body of the stomach are decreasing in incidence and is increasing at the gastro-oesophageal junction[3]. In Bangladesh, due to improvement of socio-economic and environmental status, cancers of the antrum and body of the stomach also expected to reduce.

Histological types of gastric malignancies with their location in the stomach have been reported to be variable. Previously, majority of the gastric malignancies were of adenomatous type. Recently these have been changed to diffuse variety, most probably due to decreased prevalence of H. pylori infection.

Treatment modalities for gastric malignancy are dependent on their location and histological type. Several factors have a positive association with the incidence of gastric cancer e.g. diets rich in salt, smoked or poorly preserved foods, tobacco, alcohol, *H. pylori* infection and positive family history of gastric cancer [16]. Helicobacter pylori (H pylori) infection is considered to be the main risk factor for the development of gastric carcinoma and gastric mucosa associated lymphoid tissue lymphoma [17]. Fortunately *H. pylori* infection is decreasing in Bangladesh as evidence from a retrospective observational study among dyspeptic patients in Bangladesh and it was only 23% [18,19]. But its impact on location and histological type of gastric cancers are still unexplored.

In recent years trend of cumulative tobacco consumption is reducing in Bangladesh. According to Nigar Nargis et al. overall tobacco use went down from 42.4% to 36.3% from 2009 to 2012 [20]. In 2019 lancet Oncology also published a newsletter stating that 35% of adult Bangladeshis use tobacco [21].

Gastric malignancy is one of the common of all malignancies leading to high morbidity and mortality. Incidence of gastric malignancy rising in every year causing economic burden to family and thus to country through its diagnosis, treatment and workload. We, in Bangladesh, are lacking of information regarding true topographic distribution, histopathological pattern and associated risk factors for gastric malignancies

Therefore this study had been undertaken to unveil all these information which might help in making clinical guidance of patients' management and may also help to adopt the higher authority to adopt future national policy to address this problem appropriately.

General objective was to know the topographic, clinico-pathological profile and risk factors of patients having gastric malignancy**.**

Specific objectives were to determine demographic profile, topographic distribution of gastric malignancies, histologic type and grade of dysplasia, clinical features and risk factors status of gastric malignancy.

II. Materials And Methods

This was a cross sectional study. Adult patients ($\geq$ 18 years) with endoscopically and histologically proven newly diagnosed gastric malignancy were included. Sample size was 70 calculated on the basis of 4.8% expected events of gastric malignancy with 95% confidence interval and 5% allowable error. Exclusion criteria includes previous malignancy, current GI bleeding, any antibiotic consumption within 4 weeks and PPI/H2 blocker consumption within 2 weeks. Purposive sampling technique was adopted. Patients from OPD and inpatients of different departments, underwent upper GI endoscopy daily at the endoscopy suit of Department of Gastroenterology of Shaheed Suhrwardy Medical College Hospital. If suspicious malignant lesion is identified

at endoscopy, biopsy was taken from the lesion for histopathology to confirm the diagnosis. At the same time biopsy was taken from the healthy gastric mucosa for rapid urase test (RUT) to detect the H. pylori infection. Those patients with confirmed gastric malignancy by histopathology were enrolled in the study after getting written informed consent. Outcome variable included site of involvement of gastric malignancy, histologic types, age, gender, education level, area of residence, economic status, Helicobacter pylori infection status, smoking status, tobacco product consumption other than smoking, alcohol consumption and family history of malignancy, anorexia, generalized weakness, dyspepsia, dysphagia, early satiety, abdominal pain, weight loss, melaena, vomiting without blood, vomiting of blood, anaemia, Virchow's gland, ascites, abdominal lymphadenopathy and metastasis to liver. Written informed consent was obtained from the patients. Pre-tested questionnaire was used for data collection.

Data was analyzed by computer with the help of SPSS (Statistical Package for Social Sciences) software version 22. Statistical analyses was done and data was expressed in frequency, percentage, and mean, median and mode as applicable.

Operational definitions:

Alcohol consumption: Current or ever drinker of any amount.

Anaemia: Pallor at palpebral conjunctiva

H. pylori infection status: Rapid Urase Test (RUT) was used to detect H. pylori infection. Name of the RUT kit is PYLO DRY, manufactured by Halifax research laboratory, 46/F/S-1 A, M, Dutta Road, Gorabazar, Kolkata-700028. Endoscopic gastric biopsy was taken from the apparently healthy mucosa preferably near the pyloric antrum. Biopsy was placed on yellow media of the kit with one drop of distilled water. Cover sticker was closed. It was observed for 10 minutes to 4 hours. Test was regarded positive if color change occurs from yellow to red or pink.

Melaena: Black tarry stool, on adding water it turns into red color.

Smoking status: Current or ever smoker of any amount.

Virchow's gland: The supraclavicular lymph nodes on the left side are called **Virchow's** nodes.

Weight loss: Any amount of weight loss within last six months.

III. Results

A total of 95 patients with suspected gastric malignancy on endoscopy was primarily enrolled. 18 patients had met exclusion criteria and were excluded. 3 patients' biopsy specimen failed to prove malignancy. Finally a total of 74 patients (male 71.6% & female 28.4%), having gastric malignancy, was enrolled. Demographic profile, clinical and pathological findings are described below.

Table I: Age of the patients:

Age of the patients (N=74)	Age range years	Mean years	Distribution of patients according to age range in % and (number)		
			35 yrs to 49 yrs	50 yrs to 69 yrs	70 yrs to 85 yrs
	35-85	56.59	23% (17)	66.2% (49)	10.8% (8)

Table I shows that patients' age was between 35 years to 85 years. Maximum patients (66.2%) age ranges was 50 years to 69 years.

Most of the patients (36.5%) were PSC pass, followed by JSC and SSC pass (27%). 4.1% patients were HSC pass. Twenty three percent patients were illiterate. Degree/Honors pass patients were 6.8%. 2.7 percent patients were Masters pass. Monthly income of the affected person/ family ranged from 1000 taka to 40000 taka. 26.5% patients' or their family monthly income was below 10000 taka. Only 21.9 % patients' or their family monthly income was above 20000 taka. Most of the patients (60.8 %) patients lived in rural area and 39.2% patients lived in urban area. Only 28.6% of total patients were smoker. Most of the male patients (66%) were smoker. Only 4.8% female patients were smoker. On the other hand, 36.5% of total patients use tobacco other than smoking. Among male it was 24.53% and among female it was 66.67%. More than half (55.4%) of total patients consumed added salt in their foods. Female were predominant over male in consuming salt (71.3% vs 49.05%). Only 7.55% of male patients consumed alcohol. None of the female ever consumed alcohol. Only 9.5% patients of gastric malignancy had family history of malignancy. Time elapsed between symptom onset and first consultation with registered physician ranges from 20 days to 180 days with a mean of 53±28 days.

Clinical features in patients of gastric malignancy

Clinical features	Number (Percentage)
Anorexia	65 (87.8%)
Generalized weakness	59 (79.7%)
Dyspepsia	58 (78.4%)
Dysphagia	10 (13.5%)
Early satiety	19 (25.7%)
Abdominal pain	45 (60.8%)
Weight loss	62 (83.8%)
Melaena	9 (12.2%)
Vomiting	24 (32.4%)
Vomiting of blood	8 (10.8%)
Anemia	54 (73%)
Virchow's lymph node	8 (10.8%)
Ascites	14 (18.9%)
Liver metastasis	5 (6.8%)

Table XII shows that 87.8% patients of gastric malignancy had anorexia.
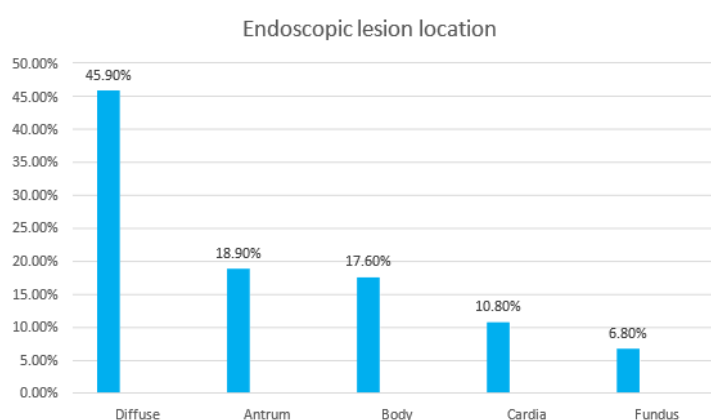

Figure I: Endoscopic lesion location among patients with gastric malignancy.

Figure I: Bar chart showing endoscopic lesion location among patients with gastric malignancy. Most of the patients (45.9%) with gastric malignancy presents with diffuse involvement in the stomach and this was followed by involvement of antrum (18.9%), body (17.6%), cardia (10.8%) and fundus (6.8%).

Table XXVI: CLO/ RU test among patients with gastric malignancy.

CLO test	Number	Percentage
Positive	46	62.2%
Negative	28	37.8%
Total	74	100%

Table XXVI shows that 62.2% patients with gastric malignancy had positive CLO test.

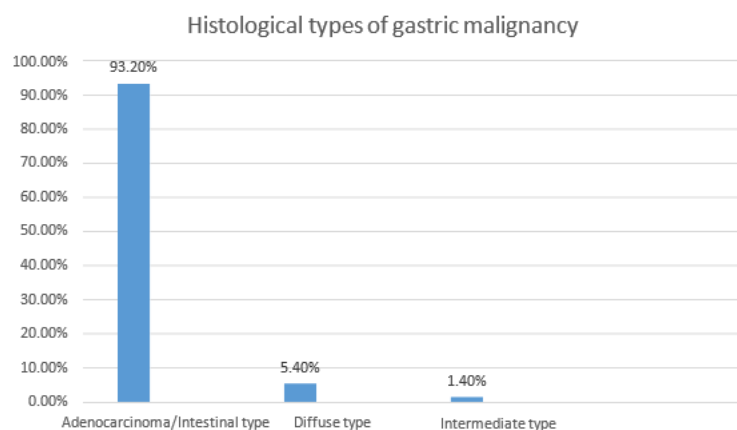**Figure II: Histological types of gastric malignancy in the study.**

Figure II shows that most of the gastric malignancy was adenocarcinoma/ intestinal type (93.2%). It was followed by diffuse type (5.4%) and intermediate type (1.4%).

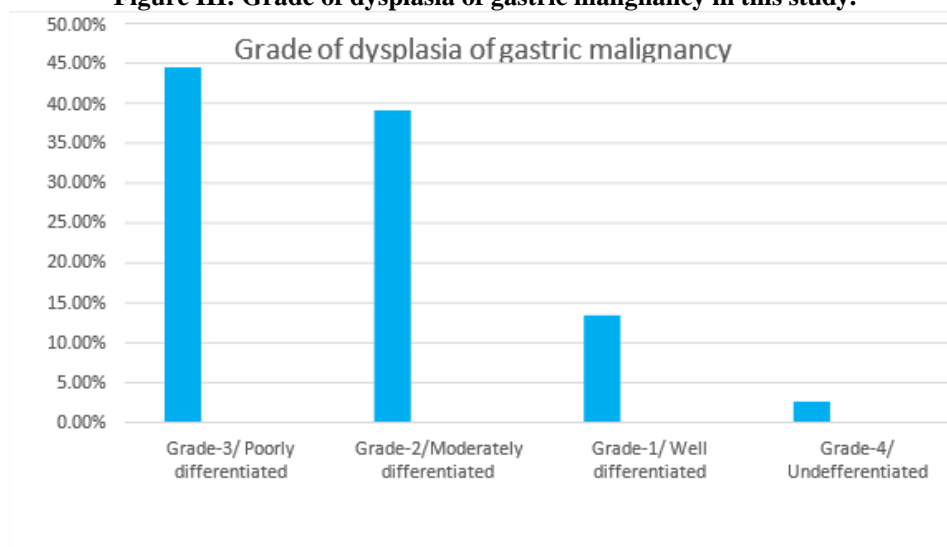**Figure III: Grade of dysplasia of gastric malignancy in this study.**

Figure III shows Bar chart showing maximum gastric malignancy was of grade-3/poorly differentiated (44.6%) followed by grade-2/ moderately differentiated (39.2%), grade-1well differentiate (13.5%) and gade-4/ undifferentiated (2.7%) in nature.

IV. Discussion

A total of 74 patients with gastric malignancy was finally included in the study. Patients' age range was between 35 years to 85 years. Maximum patients (66.2%) age ranges was between 50 years to 69 years. This age status of the patients reflects advanced age is still be a risk factors for gastric malignancy. Study conducted in Bangladesh by ZiaulHaque, et al showed that age range of the patients with gastric malignancy ranged from 18 years to 65 years with maximum involvement in age group of 41years to 60 years and it was 84.27%.[22] Age range was almost similar to a study conducted by Mir SA et al. in Srinagar, India and it was ranged from 33 to 83 years.[23] But age range was also different in other studies. Study conducted in Algeria by Safia Fehim et al showed that the age distribution varied from 21 years to 90 years with a mean age of 58.96±14.75 years.[24] Chand et al conducted a study in the hilly state of Himachal Pradesh, India and showed that age range of the affected patients was from 29 years to 83years with maximum involvement seen in the age group of 45 to 65 yrs.[25] Study conducted in Yemen by A. Kassim et al showed 34.9% patients' age between 50 years to 69 years, but 49.6% patients' age was ≥ 70 years.[26]

Male was found affected predominantly and it was 71.6% with male to female ratio was 2.5:1. This male predominance patients with gastric malignancy may reflect the underprivileged women in our society to get healthcare facilities. Study conducted in Bangladesh by ZiaulHaque, et al showed that male to female ratio was 4:1. [22] Mir SA et al. in Srinagar, India also showed male predominance (58.4%) with a male female ratio was1.4:1.[23] Study conducted in Algeria also showed male predominance (57.76% vs 42.4%) with a male female ratio of 1.37:1.[24] Chand A et al in India also showed male was commonly affected with male to female ratio was nearly 2:1.[25] Study in Yemen by A. Kassim*et al.*alsoshowed male predominant (71.5% vs 28.5%) with male to female ratio was 2.5:1.[26] In this study most of the patients (36.5%) were PSC pass, followed by JSC and SSC pass (27%).

4.1% patients were HSC pass. 23 percent patients were illiterate. Degree/Honors pass patients were 6.8%. 2.7 percent patients were Masters pass. This also reflects that patients with low level educational background are main healthcare seeking consumer in our tertiary care hospital.

Most of the affected patients were from rural areas (60.8 %) and 39.2% patients were from urban area. This reflects most of the population of our country reside in rural area. Mir SA et al. in Srinagar, India also showed that 53.98% patients lived in rural area and 46.01% patients lived in urban area.[23] Study from Yemen showed that 86.9% patients were from rural area and only 13.1% patients were from urban area.[26]

Monthly income of the affected person/ family ranges from 1000 taka to 40000 taka with mean income 14851±7810 taka. 26.5% patients' or their family monthly income was below 10000 taka. 51.6% patients' or their family monthly income was between 10000 taka to 20000 taka. Only 21.9% % patients' or their family

monthly income was above 20000 taka. This low level economic status of patients also reflects that poor patients are the main healthcare consumer in our tertiary care hospital.Study from the hilly state of Himachal Pradesh, India showed that majority of the patients (75.80%) belonged to the low socioeconomic groups followed by middle income groups (24.2%).[25]

In this study only 28.6% of total patients were smoker. Among male patients, 66% were smoker and among female only 4.8% patients were smoker. 36.5% of total patients use tobacco other than smoking. Among male it was 24.53% and among female it was 66.67%.This reflects male and female patients almost equal tobacco consumer but in different forms. Mir SA et al showed that 71.68% patients had present or past history of smoking. Study by A. Kassim*et al from* Yemen showed that 43.1% patients were smoker. Among male 55.9% and among female 10.8% were smoker. [26]

Out of total patients, 55.4% consumed added salt in their foods. 49.05% of male and 71.43% female patients consumed added salt.

5.4% of total patients ever consumed alcohol. Among male it was 7.55%. None of the female ever consumed alcohol.

In this study 9.5% patients of gastric malignancy had family history of malignancy.This reflects most of the gastric malignancies are sporadic. Study conducted in Bangladesh by ZiaulHaque, et al showed that 11.42% patients had positive family history of carcinoma stomach.[22] Study from Srinagar, India also showed that 8.85% patients had family history of gastric malignancy. [23] A. Kassim*et al.* from Yemen also showed 3.1% patients with gastric malignancy had family history of gastric cancer.[26]

Time elapsed between symptom onset and first consultation with registered physician ranges from 20 days to 180 days with a mean of 53±28 days. Consultation seeking behavior was variable depending on awareness of health status, economic status and educational background of the patients.

Among patients with gastric malignancy the most common symptom was anorexia (87.8%) followed by weight loss (83.8%), generalized weakness (79.7%), dyspepsia (78.4%), abdominal pain (60.8%), vomiting (32.4%), early satiety (25.7%), dysphagia (13.5%), melaena (12.2%) and vomiting of blood (10.8%). Study conducted by Ziaul Haque, et al showed that most common symptom was vomiting (98.57%) followed by epigastric discomfort (97.14%), anorexia (92.85%), generalized weakness (70%), epigastric pain (60%), haematemesis and melaena (10%) and dysphagia (7.14%).[22] Study conducted in Srinagar, India revealed the most common symptom was dyspepsia (40.70%) followed by anemia (25.6%), melaena (10.6%), haematemesis (7.96%), recurrent vomiting (5.3%), dysphagia (3.5%).[23] SafiaFehim et al from Algeria showed that the most common symptom of patients with gastric malignancy was epigastric pain (57.8%) followed by vomiting, gastrointestinal bleeding and dysphagia which had occurred in 17.2%, 12.1% and 6% respectively.[24] Study conducted in the hilly state of Himachal Pradesh, India showed that anorexia was the most common symptom (70.96%) followed by vague abdominal pain (69.35%) and weight loss (66.12%). Nausea/vomiting were seen in (64.51%) cases. In this study early satiety was reported in 46.77% of the patients which is characteristic of tumors involving the stomach wall diffusely.[25] Symptoms among patients with gastric malignancy were epigastric pain 81.5%, weight loss 74.6%, dyspepsia 65.4%, vomiting 49.2%, dysphagia 46.9% and vomiting of blood 20% revealed by A. Kassim*et al.* from Yemen. [26]

The most common sign of the patients with gastric malignancy in this study was anaemia (73%) followed by ascites (18.9%), and Virchow's lymph node (10.8%). Liver metastasis was present in 6.8% patients. Study conducted in Bangladesh by ZiaulHaque, et al also showed that anaemia (97.4%) and weight loss (97.4%) were the most common sign among patients with gastric malignancy followed by ascites (8.57%) and Virchow's gland (7.14%).[22] Mir SA et alalso showed that liver metastasis was seen in 1.76% patients with gastric malignancy.[38] Study from Algeria showed that 6.9% patients with gastric malignancy had ascites.[24] Chand A et al also showed that anemia was (69.35%) and supraclavicular lymph node was 4.84% in patients with gastric malignancy.[25]Ascites, Virchow's gland and liver metastasis indicate advanced disease.

In this study, some clinical features are predominated in female including generalized weakness (90.47% vs 75.47%), dyspepsia (90.47% vs 73.58%), vomiting of blood (14.28% vs 9.43%), anaemia (90.47% vs 66.03%), ascites (33.33% vs 13.2%) and Virchow's lymph node (14.28% vs 9.43%) reflecting advanced disease in female. This also suggest either poor awareness of self-health status or underprivileged healthcare facilities in female of our country.

Upper GI endoscopy showed that most of the patients (45.9%) present with more than one area of stomach (diffuse) involvement and was followed by involvement of antrum (18.9%), body (17.6%), cardia (10.8%) and fundus (6.8%). This findings also suggest late presentation of the patients of gastric malignancy. Ziaul Haque, et al showed that most common area of involvement was antrum (55%) followed by body and fundus 35% and cardiac 10%.[22] Study conducted in Srinagar, India revealed that most common location of tumor on endoscopy was antrum (57.52%) followed by body (19.46%), fundus (12.38%), cardia (6.19%) and diffuse (4.42%).[23] Safia Fehim et al from Algeria showed that tumor topography was presented mainly in the antral and fundic regions accounting for 40.9% and 22.7% respectively. 15.5% of tumors were present at the level of the

antropyloric region and 9.1% of them were of an antrofundic site.[24] Chand A et al showed that Proximal (cardiac and fundus) was 17.7%, body was 25.8% and distal/ antrum was 68.06%.[25] A. Kassim*et al.* from Yemen showed that involvement of body was 21.2%, antrum was 17.2%, cardia was 8.6%, diffuse 7% and cardia and fundus was 46.1%.[26]

This study revealed that 62.2% patients with gastric malignancy had positive CLO test indicating active H.pylori infection and represent high prevalence of H. pylori infection. A. Kassim*et al.* from Yemen showed that H.pylori positivity was found in 66.1% patients with gastric carcinoma.[26]

Histopathology showed that most of the gastric malignancy was adenocarcinoma/ intestinal type (93.2%). It was followed by diffuse type (5.4%) and intermediate type (1.4%). No gastric lymphoma was detected in this study. This may be due to referral bias. Study from Bangladesh showed that 95% gastric malignancy were adenocarcinoma, 5% were squamous cell carcinoma.[22] SafiaFehim et al showed that that 72% of cases were adenocarcinoma, 11.2% were MALT lymphoma, 9.3% were linitisplastica and 7.5% were gastrointestinal stromal tumors (GIST).[24] Study by Chand A et al in the hilly state of Himachal Pradesh, India showed that 58.07% cases were of intestinal type, 38.70% were diffuse type.[40]Study from Yemen revealed that gastric malignancy of intestinal type was 76.2%, diffuse was 16.2%, squamous was 1.5%, GIST was 1.5%, lymphoma was 4.6%.[26]

In this study maximum gastric malignancy was of grade-3/poorly differentiated (44.6%) followed by grade-2/ moderately differentiated (39.2%), grade-1well differentiate (13.5%) and gade-4/ undifferentiated (2.7%) in nature. No early gastric malignancy was detected. Presentation at advanced grade of differentiation and no early gastric cancer also reflect poor self-health awareness or poor access to healthcare facilities in Bangladesh. Chand et al showed that 16.12% gastric malignancy was well differentiated, 45.16% cases had moderately differentiated tumors and 38.70% cases had poorly differentiated tumors.[25]A. Kassim*et al.* from Yemen showed that well differentiated was 31.7%, moderately differentiated was 11.7%, poorly differentiate was 30%, undifferentiated was 6.7%, mucinous was 6.7%, and Papillary was 2.5%.[26]

V.   Conclusion

Gastric malignancy was common in third to fifth decade of life with male predominance. Female patients presented at advanced stage. Topographically most patients present with diffuse involvement. Nearly two-thirds patients have H. pylori infection. Smoking is common in male patients but tobacco consumption other than smoking is common in female patients. Histologically most of the gastric malignancies were intestinal type with poor differentiation.

Limitation Of The Present Study

This study was conducted on a limited number of patients in a tertiary care hospital where most of the medical care seeking patients were poor leading to scarcity of data from affluent patients. Observer variation may lead to gastric cancer topographic distribution variation. Histology of the biopsy specimen was also done in different centers that may lead to variation in type and grade of malignancy.

Recommendation

Patients with dyspepsia should be screened for Helicobacter pylori and should be treated accordingly. Elderly patients with anorexia, weight loss, dyspepsia and anemia should under gone surveillance for gastric malignancy with appropriate diagnostic tools. Screening for gastric malignancy at early age may be appropriate if the large nationwide data also reveals occurrence of gastric malignancy at early age.

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