CLINICOPATHOLOGICAL STUDY OF *HELICOBACTOR PYLORI* INFECTION AND GASTRIC CARCINOMA AT A TERTIARY CARE HOSPITAL IN KATHMANDU

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ABSTRACT

Gastric cancer is one of the most common malignancies worldwide and it is the fourth leading cause of cancer-related death. It is a multi-step process and multi-factorial disease, where both environmental and genetic factors can have an impact on its occurrence and development. A descriptive cross-sectional study was conducted in the Department of Pathology, Nepal Medical College Teaching Hospital (NMCTH), Nepal from January 2023 to September 2023. A total of 30 cases of gastric carcinoma confirmed by histopathological examination were included in the study. Ethical approval was taken from Institutional Review Committee of NMCTH. Detailed demographic information including age, gender, type and site of the lesions, and clinical features of the patients were noted. The observed findings were managed in MS Excel sheet and later analyzed using SPSS 17. The mean age of the patients enrolled was 60 ± 13.8 years ranging from 30 to 84 years with the male predominance (M: F=1.2:1). Physical weakness, signs of anemia, loss in appetite, weight loss and abdominal distension were the most common features of stomach cancer patients. Antrum was the most frequent site of tumor location whereas, adenocarcinoma is the common type of gastric carcinoma under histopathological examination. Regarding H. pylori infection, 14 (46.66%) cases were reported positive and the infection was not found to be significantly associated with the gastric cancer. Study with large sample size is necessary to establish the relation of H. pylori infection with gastric cancer in Nepal.

KEYWORDS

Adenocarcinoma, features, gastric cancer, *Helicobacter pylori*, Nepal

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INTRODUCTION

Gastric cancer (GC) is a highly aggressive, multi-factorial and the fourth leading cause of cancer-related deaths in which both environmental and genetic factors have an impact on its occurrence and development.[1] According to the Global cancer statistics 2018, stomach cancer is responsible for the over 1 million new cases and 783,000 deaths (1 in every 12 deaths across the globe) making it, the third leading cause of cancer deaths and the fifth commonly diagnosed cancer, and the rate of occurence in males is 2-times higher than in females.[2] *Helicobacter pylori* infection has an important role in gastric carcinogenesis because both diffuse type and intestinal type of gastric cancers originate from mucosa infected by *H. pylori* and then progress to gastric carcinoma.[3] The invasion and colonization of the gastric mucosa by *H. pylori* is strengthened by host factors, environmental factors and virulence factors like adhesion, translocation, and inflammation of the host gastric epithelium which changes the normal host immune response and cytokines to remain in the gastric epithelium for an extended period of time.[4] The human immune system identifies *H. pylori* as a foreign particle and provokes the inflammatory response to eradicate the bacterium from the body which induces the serious infection and may further progress to cancer.[5]

The chronic infection with *H. pylori* bacteria is the most important risk factor for the development of non-cardia gastric cancer and lower grade B-cell mucosa associated lymphoid tissue (MALT) lymphoma estimating 6,60,000 cancer cases in the year 2008 attributed to *H. pylori* and corresponding to 5.2% of the total burden from all cancers globally.[6] In Nepal, the prevalence of *H. pylori* was found to be lesser than that observed in other studies conducted in developing Asian countries, but the bacterium was remarkably seen in maximum number of duodenal ulcer, gastric ulcer and gastritis and the gastric cancer was significantly associated with *H. pylori* infection.[7] Our study was done to find out the prevalence of *H. pylori* infection in gastric carcinoma and to study its clinicopathological features at a tertiary care hospital in Kathmandu.

MATERIALS AND METHODS

This was a cross sectional hospital-based descriptive study conducted in the Department of Pathology, Nepal Medical College Teaching Hospital (NMCTH) over a period of 9 months (January 2023 to September 2023). The total number of cases included in the study were 30. Approval for the study was obtained from Institutional Review Committee (IRC) of NMCTH and informed consent was taken from the patients. Detailed history and demographic information including age, gender, type, site of the lesions and clinical features of all the enrolled patients were taken. History regarding triple therapy for *H. pylori* could not be confirmed, so all the cases were included irrespective of history of triple therapy. Patients undergoing upper GI endoscopy for suspicion of carcinoma of stomach were later confirmed by histopathological examination. Gastrointestinal biopsies from cardia, fundus, body and antrum of the stomach were kept in 10.0% formalin and received in the Department of Pathology for histopathology. After the specimens were fixed for at least six hours, gross examination of the specimen was carried out. Number of pieces and appearance of the specimen were noted and the tissue was processed in automated tissue processor (Yorco, 2L) for 16 hours. The next day the tissue block was prepared by embedding the tissue in paraffin wax and manual section of the tissue were obtained with the help of microtome (Slee Mainz) to obtain 4-5 um thick paraffin sections. The sections were then stained with Hematoxylin and Eosin (H and E) and Giemsa stain. The stained slides were mounted with Dibutylphthalate Polystyrene Xylene (DPX) and examined under the microscope for definitive diagnosis. All the findings were noted and *H. pylori* was specifically looked upon in the cases of histologically proven gastric carcinoma. All the received information of the patients was managed in MS Excel sheet and the data analysis was performed using SPSS 17 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics (mean ± standard deviation) was used to represent the quantitative outcomes. The qualitative data was presented with frequency and percentage.

RESULTS

A total of 950 histopathological samples were received in our Pathology Laboratory in 9 months' (January 2023 to September 2023) period of time. Thirty cases of histologically

Table 1: Age-wise frequency of the patients

Age group (Years)	n	%
31-40	3	10
41-50	6	20
51-60	3	10
>60	18	60
Total	**30**	**100**

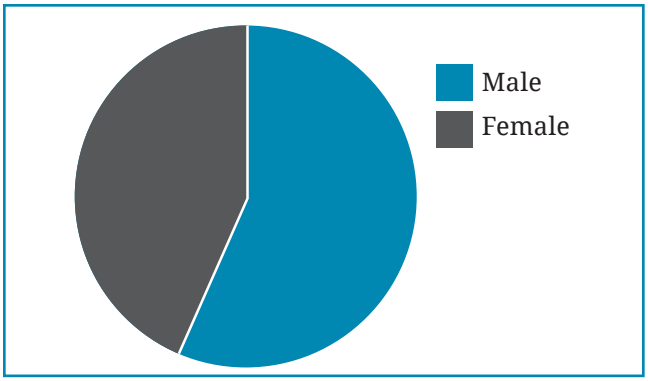

Fig. 1: Gender wise distribution of gastric cancer patients

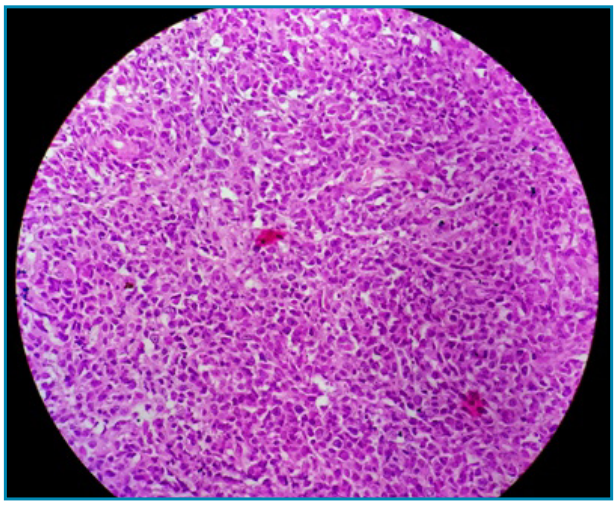

Fig. 3: Gastric biopsy showing non-Hodgkin's lymphoma (Hematoxylin and Eosin stain 400x)

Table 2: Sites of tumor location		
Site of lesion	**n**	**%**
Antrum	13	43.3
Body	6	20.0
Diffuse	5	16.7
Pylorus	4	13.3
Cardia	1	3.3
Fundus	1	3.3
Total	**30**	**100.0**

proven gastric carcinoma were included in the study. Among 30 cases, there were 17 males (56.0%) and 13 females (44.0%) with male: female ratio of 1.2:1 (Fig. 1). The mean age of the patients was 60 ± 13.8 years ranging from 30 to 84 years with the highest frequency of age group above 60 years (Table 1).

Regarding the distribution of predominant site of gastric carcinoma lesions, 13 (43.3%) cases were from antrum, 6 (20.0%) cases from body, 5 (16.7%) cases were with diffuse presentation, 4 (13.3%) cases from pylorus, 1 (3.3%) case each from fundus and cardia region (Table 2).

Table 3: Histological typing and *H. pylori* infection			
Histological typing	**n cases**	**Presence of *H. pylori***	**Absence of *H. pylori***
Adenocarcinoma	27 (90.0%)	14 (46.7%)	13 (43.3%)
Non Hodgkin lymphoma	3 (10.0%)	0 (0.0%)	3 (10.0%)
Total	**30 (100.0%)**	**14 (46.7%)**	**16 (53.3%)**

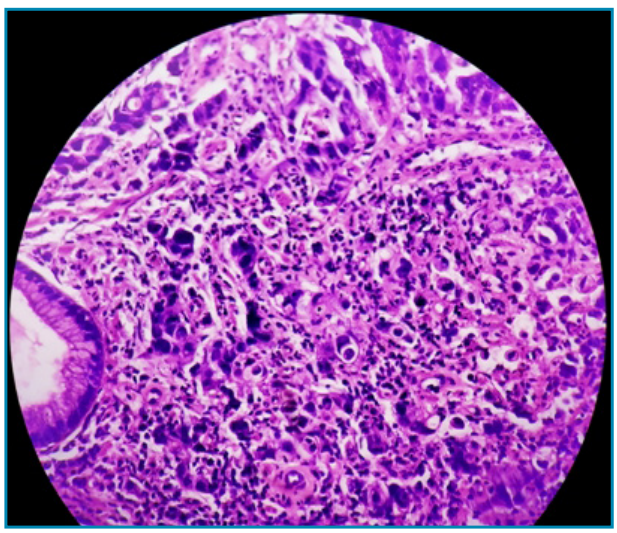

Fig. 2: Gastric biopsy showing poorly differentiated adenocarcinoma (Hematoxylin and Eosin stain 400x)

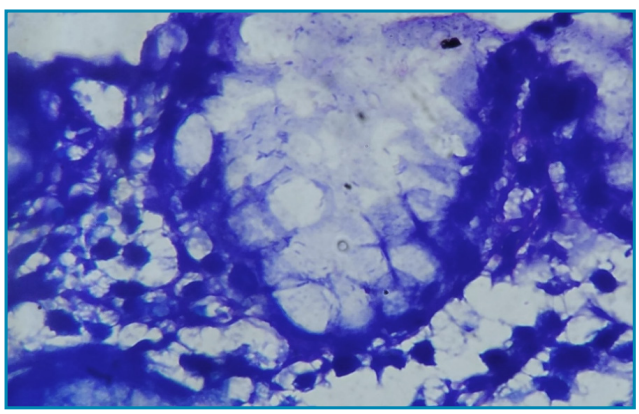

Fig. 4: Gastric biopsy showing *Helicobacter pylori* (Giemsa, 1000X).

Table 4: Clinical findings of Gastric carcinoma patients

Clinical features	n	%
Abdominal pain	29/30	96.7
Decreased appetite	25/30	83.3
Weight loss	22/30	73.3
Abdominal distension	5/30	16.7
Fatigue, weakness, lethargy and features of anemia	30/30	100.0

Out of 30 histopathologically diagnosed cases of gastric cancer, 27 (90.0%) cases were adenocarcinoma type (Fig. 2) whereas, remaining 3 (10.0%) cases were non-Hodgkin lymphomas (Fig. 3). Among 27 adenocarcinoma of stomach, *H. pylori* infection (Fig. 4) was observed in 14 (46.7%) cases but not seen in 13 (53.3%) cases. In case of non-Hodgkin lymphomas type of gastric cancer, *H. pylori* infection was absent in all the specimens. Overall, 53.3% cases of gastric carcinoma did not show any association with *H. pylori* infection (Table 3).

Talking about the clinical features of stomach cancer, all the patients complained to be physically weak, fatigue, lethargic and presented with features of anemia. Similarly, abdominal pain was observed in 29 cases, decreased appetite in 25 cases, weight loss in 22 and abdominal distension in 5 cases (Table 4).

DISCUSSION

In the present study, the mean age of the patients was 60 ± 13.8 years with male predominance (M:F = 1.2:1). The maximum cancer cases were seen in patients above 60 years (60.0%). Bhattarai *et al*[8] reported 1.9 times more gastric cancer in males than females (M:F = 1.9:1) and the majority of cancer patients were of age group 51 to 70 years in their study. Similarly, Kafle *et al*[9] observed 46.0% of patients with gastric carcinoma were above 60 years of age. Likewise, in a Nepalese study by Ghosh *et al,*[10] the highest frequency of gastric tumors was seen in the age group 61 to 70 years (47.0%) with male predominance (M:F = 1.8:1).

Regarding the site of the gastric carcinoma in our study, the antrum (43.3%) was the commonest site of gastric lesion, followed by the body (20.0%), diffuse (16.7%) and pylorus (13.3%). Our findings were found to be similar with studies done by Thapa *et al,*[5] Bhattarai *et al*[8] and Ghosh *et al*[10] where antrum was the most common site of gastric cancer accounting for 48.0%, 70.0% and 72.5% cases respectively.

After analyzing the histological subtypes of the gastric cancer specimens, gastric adenocarcinoma was found in 90.0% cases whereas, non-Hodgkin lymphomas was seen in 10.0% cases. Similar to our study, Kassim *et al*[11] and Shah *et al*[12] reported majority of the gastric cancers with adenocarcinoma type comprising of 75.3% and 92.4% of total cases.

Out of 30 cases of gastric cancer, *H. pylori* infection was observed in 46.7% cases. In the case of Non-Hodgkin lymphomas, *H. pylori* infection was not seen. Overall, 43.3% cases of gastric carcinoma did not show the presence of *H.pylori* infection. Zhang *et a1*[13] reported that *H. pylori* infects more than half of the world's population and the infection is usually acquired in childhood and remains for life long. Similarly, Tiwari *et al*[14] mentioned that younger patients (less than 45 years) from the Indian sub-continent infected with *H. pylori* have higher risk of developing gastric carcinoma while, Thapa *et al*[4] found the common age group for the *H. pylori* infection in both the sexes is between 61-70 years and the infection is highly prevalent in distal gastric carcinoma.

In the present study, 46.66% diagnosed cases of adenocarcinoma patients were found to be *H. pylori* infected suggesting gastric carcinoma do not have any association with *H. pylori* infection. A Gram-negative bacterium, *H. pylori* has numerous virulence factors that help in adherence and translocation of pathogen into gastric epithelial cells that causes gastritis to gastric carcinoma by invading and colonizing the gastric mucosa.[4] *H. pylori* infects the mucosal layer of stomach and causes pathological gastritis, and the infection usually persists lifelong causing chronic inflammation of gastric mucosa that leads to gastric adenocarcinoma and other varieties of gastrointestinal tract diseases.[3] In Asia, *H. pylori* infection is considered as an important etiological factor for the occurrence of non-cardia gastric adenocarcinoma but prevalence of infection is not always true because high sero-prevalence rate of *H. pylori* infection paradoxically had low incidence of gastric carcinoma considering the environmental factors, host susceptibility, bacterial virulence factors and immune response are also responsible of the disease occurrence.[15]

Although there is high prevalence of *H. pylori* infection, no any significant differences in infection between genders was observed and

the peptic ulcers are often seen in males which have higher rate of *H. pylori* colonization.[16] The molecular analysis of premalignant stages and gastric cancer by using DNA microarray based gene expression profiling in tumors and adjacent mucosa specimens suggested chronic gastritis shows distinct mitochondrial gene expression which may be linked to pathogenesis of *H. pylori.*[17]

Despite high *H. pylori* prevalence, there is low gastric cancer burden because host gastric factors would play a significant role in the gastric cancer pathogenesis providing relative protection to particular race against development of cancer.[18] The Indian enigma referred to the observations that the Asian countries like Thailand, India, Bangladesh, Pakistan reported a high frequency of *H. pylori* infection but low incidence of gastric cancer whereas, in areas such as China, Korea and Japan the prevalence of gastric cancer was common.[19] Furthermore, Shrestha *et al*[7] reported the prevalence of *H. pylori* infection in Nepal was lower than shown in other studies of developing Asian countries but found to be significantly associated with gastritis, peptic ulcers and gastric cancer in our country.

In this study, as clinical features of gastric cancer, all the patients had physical weakness, fatigue, lethargy and presented with features of anemia. In addition, abdominal pain was observed in 96.7% patients followed by decrease in appetite in 83.3%, weight loss in 73.3% and abdominal distension in 16.7% of total cases. Our findings were similar to the study by Jayant *et al*[12] which reported more than two-thirds of patients had anorexia, weight loss and/or vomiting and abdominal pain. Likewise, Kassim *et al*[11] found epigastric pain, weight loss, vomiting, dysphagia, palpable epigastric mass and hematemesis as the most frequent clinical features of gastric adenocarcinoma patients.

Carcinoma of stomach can be highly aggressive. It is considered as a leading cause of death worldwide and adenocarcinoma is the most common type. Although *H. pylori* infection was seen in nearly half of the cases, its association with gastric cancer was not found to be statistically significant in our study. *H. pylori* infection alone is not only a single factor responsible for gastric carcinogenesis. Dietary factor, genetic factor and other factors may act together with *H. pylori* for the development and progression of gastric carcinoma.

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