

Original Article

Prevalence of High-Risk Groups for Gastric Carcinoma – A Biopsy Finding

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ABSTRACT

Introduction: Gastric carcinoma is leading cause of death world wide including Nepal. The 5 years survival rate of gastric carcinoma (25%) is drastically decreased compared to early gastric cancers (90-90%) hence implying the need for early detection. Atrophic gastritis and intestinal metaplasia are considered as major high-risk factors and has a precancerous lesion along with Helicobacter pylori. This study tries to look at the distribution of atrophy and intestinal metaplasia across age and gender and their occurrence in Helicobacter pylori positive cases.

Materials and Methods: It is Cross-sectional study of a retrospectively collected data at KIST medical college and GRP poly clinic private limited from April 2008 till March 2018. Total of 10,683 cases were included. The slides were stained with Hematoxylin and Eosin stain and Giemsa stain and evaluated by two pathologists. Statistical analysis was done using SPSS vs 21.

Results: Total numbers of cases studied were 10,683 with male to female ratio of 1.04:1. The most common age group of the study was 18-40 years (n=6206; 58.8%). Atrophy was seen in 81 (0.8 %) cases, Intestinal metaplasia in 298 (2.8 %) cases and Helicobacter Pylori was positive in 4459 (42.2%) cases. The incidence of atrophic gastritis was more in H. pylori positive group 54 (0.5%) group where as intestinal metaplasia was more in H. pylori negative 190(1.8%) group.

Conclusions: Atrophic gastritis and intestinal metaplasia, high-risk factors for gastric carcinoma, were not the common findings. Atrophic gastritis was seen in 0.8% and intestinal metaplasia was seen in 2.8% of the total study population.

Keywords: Atrophic; Carcinoma; Gastritis; Intestinal; Metaplasia; Precancer

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Submitted: 19th September 2018

Accepted: 15th October 2018

Published: 1st December 2018

Conflict of Interest: None

Sources of Support: None



Citation: KC Geetika, KC Shiva R, Gyawali P. Prevalence of high-risk groups for gastric carcinoma – a biopsy finding. Nep Med J 2018;1:82-5. DOI: 10.3126/nmj.v%vi%i.21600

INTRODUCTION

Gastric carcinoma is the fourth leading cause of cancer deaths and has high incidence in Eastern Asia.¹ It is the sixth leading cause of morbidity, worldwide, while it is the second most common cause of death preceded by lung cancer.² In Nepal, Gastric cancer is the 5th most common cancer with 1546 recorded new cases in 2018. According to 2018 data, it is the 5th most common cancer and 3rd most common cause of cancer related death in Nepal.³ It is seen that, the 5 years survival among gastric carcinoma patients is only 25 percent. In stark contrast to that, the early gastric cancers (EGC) have a 5 years survival rate of 90-95% 4-6 implying detection at the later stage of the disease.⁷

Risk factors for gastric carcinoma include Helicobacter pylori infection, smoking, alcohol, salt intake, family history of gastric

cancer, atrophic gastritis (AG) and intestinal metaplasia (IM).⁸ The later two, intestinal metaplasia and atrophic gastritis, are the consequence of prolonged exposure to Helicobacter Pylori and other irritants. Both, atrophy and intestinal metaplasia are considered two premalignant conditions.^{9,10} Transformation from atrophy and intestinal metaplasia into carcinoma requires prolonged exposure to the carcinogens. Hence, detection of gastric atrophy and intestinal metaplasia and timely management of the condition decreases the incidence of gastric cancer.

AG and IM are reported in a regular basis in the gastric biopsy specimen particularly because the updated Sydney system of classification is followed world wide. Both AG and IM have

Table 1: Distribution of atrophy and intestinal metaplasia according to the gender

Gender	Atrophy		P value	Intestinal Metaplasia		P value
	Positive	Negative		Positive	Negative	
Male	39 (0.36%)	5326	>0.05	124 (1.17%)	5241	<0.01
Female	42 (0.39%)	5148		174 (1.64%)	5016	
Total	81 (0.8%)	10474 (99.2%)		298 (2.8%)	10257 (97.2%)	

Table 2: Distribution of Atrophy and intestinal metaplasia in relation to H.pylori infection.

H. pylori	Atrophy		Intestinal Metaplasia		Total
	Positive	Negative	Positive	Negative	
Positive	54 (0.5%)	4405 (0.98%)	108(1%)	4351 (0.42%)	4459
Negative	27 (0.25%)	6069(0.57%)	190 (1.8%)	5906 (0.56%)	6096
Total	81 (0.8%)	10474(99%)	298 (2.8%)	10257 (97%)	10555

Table 3: Distribution of Atrophy and Intestinal metaplasia according to age group.

Age group (years)	Intestinal metaplasia	Atrophy
0-18	7 (0.66%)	0
18-40	142 (1.34%)	44(0.41%)
40-60	113 (1.07%)	28(0.26%)
>60	36 (0.34%)	9 (0.08%)
Total	298 (2.8%)	81(0.8%)

been graded into none, mild, moderate and severe according to this system. However, further systems have come up in this line, namely the Operative Link on Gastritis Assessment (OLGA) system and the Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) system that classified the grade and stage of atrophy and intestinal metaplasia respectively.^{11,12} These systems provide better prognostic and management evaluation, as higher stages of intestinal metaplasia and atrophy in the gastric biopsy specimens have higher risk of developing gastric carcinoma later in life.^{11,12} Proposals have been made regarding the frequency of follow up in patients with stage III/IV OLGA/OLGIM groups for early detection and treatment of gastric carcinoma.¹³⁻¹⁵

Hence, AG and IM are specific findings that need to be evaluated in detail. Helicobacter pylori (H. Pylori) which is seen to be commonly found in gastric biopsy is also associated with AG and IM.^{16,17} H. pylori has specific genetic makeup that produces CagA and VacA genes. These genetic groups are seen to have links to AG, IM and gastric carcinoma.¹⁷⁻¹⁹

In this study we are going to evaluate the incidence of AG, IM and H.pylori and their interrelationship with each other. We are also studying their distribution across age and gender of the study population.

MATERIALS AND METHODS

It is Cross-sectional study of a retrospectively collected data at KIST medical college and GRP poly clinic private limited of a total of 10,683 cases. Prior to the study, permission was obtained from the Institutional Review Board of KIST Medical College. All the cases from April 2008 till March 2018, of whose slides

could be retrieved, were included in the study. Demographic data were retrieved from the medical record. The slides stained with Hematoxylin and Eosin stain and Giemsa stain were evaluated by two pathologist and the findings were entered in Microsoft Excel. Statistical analysis of incidence, frequency was calculated using SPSS vs 21. P value was calculated wherever necessary.

RESULTS

Total number of cases studied was 10,683. Out of which 5451 (51.0%) were male and 5232 (49.0%) were female with male to female ratio of 1.04:1. Mean age of all the cases were 53.2 years. Out of these 10,683 cases, atrophy was seen in 81 (0.8 %) cases, Intestinal metaplasia was seen in 298 (2.8 %) cases and Helicobacter Pylori was positive in 4459 (42.2%) cases. Among 10,683 cases, 10,555 were non-neoplastic lesions and were included in the study.

Among male patients who underwent endoscopic biopsy, 39 patients (0.36%) had atrophic gastritis whereas 40 female patients (0.39%) had atrophic gastritis (Table 1). Incidence of atrophy was insignificant with gender ($p>0.05$). P value was significant for intestinal metaplasia in male and female ($p<0.01$).

The incidence of AG is more in H. pylori positive group 54 (0.5%) compared to H. pylori negative group (0.25%). In cases of IM, it is more in H. pylori negative group 190(1.8%) compared to H. pylori positive cases 108 (1%) (Table 2). Atrophic gastritis as well as intestinal metaplasia was slightly more frequent among females than in males.

The most common age group in our study population was in 18-40 years ($n=6206$; 58.8%) followed by 40-60 years ($n=3202$; 30.3%). Mean age of the study population with atrophic gastritis was 40.65 years with minimum of 20 years and maximum age being 84 years. Intestinal metaplasia was most prevalent in the age group of 18-40 years. Atrophic gastritis and Helicobacter were also the most common findings among the same age group (Table 3). Atrophy was encountered slightly more among patients below 40 years of age (44 vs. 37 cases). (Table 3)

Intestinal metaplasia was observed across all age groups. The mean age of patients with intestinal metaplasia was 42.21 years

with youngest being 15 years and oldest 85 years. Seven cases with intestinal metaplasia were observed among patients younger than 19 years, whereas atrophy was not seen in this population. Similarly, intestinal metaplasia was almost equally distributed in the patients below and above 40 years of age (149 cases).

DISCUSSION

Gastric carcinomas, like most of the other malignancies, have their own risk factors. Particularly well known ones are excessive salt intake, deficient ascorbic acid, insufficient carotene and most importantly *H. pylori* infections.¹⁶ In our study the *H. pylori* incidence was seen in 4475 (42.2%) of cases. In the study done comparing the Japanese and Nepalese population,²⁰ 167/309 (54.0%) cases were positive for *H. pylori* and the prevalence did not vary among Aryans and Mongolians. The bacterial virulence genes, cytotoxin-associated gene A [CagA] and vacuolating cytotoxin A [VacA], are found to have an important role in the pathogenesis of AG, IM and gastric carcinoma. CagA causes cytoskeletal changes and abnormal gastric epithelial cell proliferation by disrupting the phosphorylation-dependent and independent signaling pathway mechanisms.¹⁷ VacA has several subtypes (s1-2 and m1-2) unlike CagA. s1m1 is associated with increased epithelial damage, AG and IM.^{18,19} In our study we did not perform any genetic studies due to lack of resources.

There are several types of chronic gastritis and Updated Sydney system classification is the one we widely follow. Histopathologically it takes into consideration activity (neutrophil infiltration), chronic inflammation (mononuclear cell infiltration), glandular atrophy, Intestinal metaplasia and *Helicobacter pylori* density. The findings are graded into none, mild, moderate and severe using the visual analogue scale.^{21,22} Though widely used, this system does not give the prognosis of gastric cancer risk specially when atrophic gastritis as well as intestinal metaplasia are considered to be precancerous conditions.

Hence new systems were developed namely OLGA (Operative link on Gastritis Assessment) and OLGIM (the Operative Link on Gastric Intestinal Metaplasia Assessment) systems. According to these systems the patients are grouped into I to IV stages. They provided better management possibility such as OLGA/OLGIM stage III and IV are grouped for secondary preventive surveillance where as stage I and II are exempted from it.^{11,12,14}

The incidence of atrophic gastritis, in a meta-analysis including 14 studies, have been shown to be ranging from 0-10.9%.²³ The incidence varied according to the clinical set up. Lowest range was seen in patients treated for *H. pylori* and highest was

seen in peptic ulcer disease cases.²³ In our study the incidence of atrophic gastritis was 81(0.8%) of case, which is within the above mentioned range. The mean age group for AG in our study population included 18-44 years. Incidence of AG was more in *H. pylori* positive 54 (0.5%) than negative 27(0.25%) cases. This finding was similar to the study done by Adamu et al.²³

The intestinal metaplasia (IM) incidence was more in a *H. pylori* negative (n=190; 1.8%) cases compared to positive cases (n=108; 1%) in our study. Which was opposite to a study done in Netherlands, in which it was found more in *H. pylori* positive cases (33.9%) than in *H. pylori* negative cases (15.2%).²⁴ The reason for not finding correlation between *H. pylori* and IM may be due to the fact that environmental or host factors were more important risk factors for IM as some of the studies have reported.²⁵ The mean age positive for IM in our study was 42.21 years with a range of 15-85 years, which was lower than the study of Craanen et al, in which it was seen as 64 years of age.²⁴ Seven cases of IM were also seen in age lower than 19 years which was seen in atrophic gastritis.

In a study done in Korean population, prevalence of AG ranged from 20.1 to 42.5% and IM was 21.2 to 28.6%.²⁶ This finding was much higher than the one seen in our study. The mean age group for AG was 40.65 years with a range of 20-84 years. AG was almost equally distributed in our study in both male (0.36%) and female (0.39%) however, in the study done on Korean population it was slightly higher in male (42.7%) than female (38.1%).²⁶

Other studies have shown that the incidence of AG and IM increased with age, 27 however in our study we found that both the AG and IM were higher in the age group between 18-40 years and it did not show progressive increase in incidence with increasing age. This might be due to the bias created by the maximum number of (58.8%) cases in our study coming to the hospital in this age group.

CONCLUSIONS

Atrophic gastritis and intestinal metaplasia, high-risk factors for gastric carcinoma, were not the common findings. Atrophic gastritis was seen in 0.8% and intestinal metaplasia was seen in 2.8% of the total study population. Despite being low in incidence, early detection of these lesions via endoscopy and gastric biopsy can lead to a better management outcome. However, further large scale study and community based study on grading and staging of these precancerous lesions are also required.

ACKNOWLEDGMENT

Dr Gyanendra Lal Amatya, Consultant Gastroenterologist, GRP poly clinic private limited, Kathmandu.

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