# Clinicopathological Study of Upper GI Malignancy in Tertiary Care Centre of Nepal

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## ABSTRACT

## Introduction

Upper gastrointestinal malignancies are among the most common causes for cancer related morbidity and mortality. These cancers rapidly progress to advanced stages even in the absence of significant symptoms, thus leading to delayed diagnosis and dismal prognosis. The aim of this study was to determine the prevalence, type and clinicopathological characteristics of upper gastrointestinal tumors.

#### Methods

This was a three year cross-sectional study involving 66 patients of upper gastrointestinal cancer. The study was conducted from March 2018 to February 2021 at the college of medical sciences-Teaching Hospital, Nepal. Relevant clinical information, Endoscopic pattern and histological characterization were recorded. SPSS version 25.0 was applied for statistical analysis.

## Results

Total 66 patients were enrolled into this study. The mean age of the population was 59.13± 13.38 years with male predominance (M:F-1.36:1). Common presenting symptoms were abdominal pain (76%), significant weight loss (61%), vomiting (40%). About 77% of the tumors were located in the stomach, 17% in the esophagus and 6% in the first and second part of the duodenum. Most common endoscopic pattern of upper gastrointestinal lesion was ulceroproliferative type (53%). Tissue histology showed adenocarcinoma as the commonest histological pattern with 82% followed by squamous cell carcinoma 10%.

## Conclusions

These malignancies can rapidly progress to advanced stages even in the absence of serious symptoms and endoscopy is needed in suspected patients to avoid delayed diagnosis and improve the disease outcome.

Keywords: upper gastrointestinal malignancies; histopathological types; endoscopy.

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## INTRODUCTION

GI malignancies constitute one of the major tumor burdens to world and are among the most lethal of all malignancies.<sup>1</sup> Malignant tumors of the oesophagus are one of the commonest types of cancer (sixth and ninth among cancers in men and women).<sup>2</sup> Gastric cancers are the commonest upper gastrointestinal (UGI) malignancy and are the second most common cause of cancer related death worldwide.<sup>3</sup>

Despite advances in diagnosis and treatment, gastrointestinal (GI) malignancies are known for frequently progressing to advanced stages even in the absence of serious symptoms, thus leading to delayed diagnoses and dismal prognoses.<sup>4</sup> Since there are very few studies in Nepal regarding upper gastrointestinal malignancies, this study is being conducted on such patients presenting to the College of Medical Sciences and Teaching Hospital, Nepal to study prevalence, clinical features as well as endoscopic and histological patterns.

## **METHODS**

This was a three year cross-sectional study involving 66 patients with upper gastrointestinal tumor. The study was conducted from March 2018 to February 2021 at the college of medical sciences-Teaching Hospital, Bharatpur, Nepal. Relevant clinical information such as age, gender, clinical presentations (like unexplained recent weight loss, abdominal pain or swelling, dysphagia, haematemesis or melaena and anaemia), smoking history, alcohol use, spices were obtained from the patients. Upper GI Endoscopy was performed in all the patients with Pentax EPK 700 model / Sonoscape HD 500 endoscope under 10% xylocaine anaesthetic spray of the oropharynx. The locations of the tumor were determined and recorded. Endoscopically lesions were classified as ulcerative, ulceroproliferative, polypoid and other types. Tissue biopsies were taken from the suspected lesions for histological confirmation and characterization. The tumors were classified by the predominant histological appearance into oesophageal squamous cell carcinoma/ adenocarcinoma or gastric squamous cell carcinoma/adenocarcinoma, Lymphoma or GIST. Further categorizations into differentiated, moderately differentiated, undifferentiated or poorly differentiated carcinomas were made.

An ethical clearance for this study was obtained from the Ethical and Research committee of College of Medical Sciences and Teaching Hospital, Bharatpur and all the patient's written consent were obtained for the study.

**Statistical analysis**: Collected data were stored in an electronic database (MS- Excel Sheet). Statistical analysis was performed with statistical software (SPSS 25.0 for windows). Results were statistically analyzed using descriptive and chi square test.

## **RESULTS**

During the study period 66 patients of upper gastrointestinal malignancy were evaluated. The mean age of the study population was **59.13** years ± 13.38 years (age ranged from 25 years to 88 years). Majority of patients (54.5%) were in the age group 60 years and above followed by age group 40-59 years (41%) and 18-39 years (4.5%). 50% male and 60% female were 60 years old and above.

<b>Table 1.</b> Distribution of the age $(n = 66)$ .				
Age Group	Total	Percent		
18-39 years	3	4.5%		
40-59 years	27	41%		
60 and above	36	54.5%		
Total	66	100%		
Mean age = 59.13 years $\pm$ 13.38; Minimum age = 25 years, Maximum age = 88 years				

In this Study 38 (58%) males and 28 (42%) females. The male to female ratio was 1.36:1.

The risk factors identified in this study included; smoking in 35 (53%) cases which is followed by alcohol in 33 (50%) cases, with smoked meat consumer 16 (24%) and spicy meal taker 19 (29%). Whereas more than 1 risk factors were present in 35 (53%) of cases. This study showed abdominal pain as a presenting symptom in 76 % of patients followed by significant weight loss in 61% of patients, vomiting (40%), loss of appetite in 46% of patients, along with melena (20%), dysphagia (15%), hematemesis (6%) and other symptoms (8%) including ascites, diarrhea etc. In this study, 43 (64%) patients presented with anemia, 8 (12%) patients presented with abdominal lump and there were enlarged left supraclavicular lymph nodes in only 6 (9%) patients. Duration of illness was less than 3 months in 34(52%) cases and more than 3 months in 32 (48%) cases.

 $1/3^{rd}$  of esophagus. In duodenal, 3 (75%) cases were seen in D1 and 1 (25%) case was in D2.

<b>Table 3.</b> showing frequency of upper GI cancer according to location (n=66).				
Location	Frequency Percent			
Esophagus Upper 1/3 <sup>rd</sup> Middle 1/3 <sup>rd</sup> Lower 1/3 <sup>rd</sup> Total	0 7 4 11 (16.6%)	64% 36%		
Stomach Fundus Body Antrum Total	7 26 18 51 (77.3%)	13.7% 51% 35.3%		
Duodenum D1 D2 Total	3 1 4 (6.1%)	75% 25%		

Table 2. Presentation of upper GI cancer according to location of lesion (n=66).						
Signs/symptoms	Oesophageal Cancer	Stomach cancer	Duodenal cancer	Total	p-value	
Pain abdomen	2	45	3	50	0.020*	
Weight loss	9	29	2	40	0.264	
Vomiting	2	22	2	26	0.592	
Loss of appetite	6	22	2	30	0.775	
Melena	0	12	01	13	0.139	
Dysphagia	9	1	0	10	<0.001	
Hematemesis	1	3	0	4	0.463	
Other symptoms	1	3	1	5	0.507	
*p-value significant at level <0.05						

Majority of these tumors were located in the stomach (77%), followed by 17% in the esophagus and 6% in the duodenal. Of those located in the stomach, most common location was body of stomach with 26 (51%) cases, followed by 18 (35%) cases in antrum and 7 (14%) of cases in fundus. Within esophagus, middle 1/3<sup>rd</sup> was most common location with 7 (64%), followed by 4 (36%) in lower

In this study most common macroscopic/gross appearance of cancer was ulceroproliferative type, which was seen in 35 (53%) cases, followed by 11 (16.6%) cases of ulcerative type, 4 (6%) cases of gastric outlet obstruction, 6 (9%) cases of protruding lesion, 7 (10.6%) cases of polypoid type, whereas other lesion types including fungating were seen in 3 (4.5%) cases. Among esophageal cancer 5 (45%) cases were ulcerative type and 6 (55%) cases was protruding lesion. Among Gastric cancer cases, 31 (60%) cases were ulceroproliferative type, 6 (11%) cases were ulcerative type, 4 (8%) cases were gastric outlet obstruction, 7 (13%) cases were polypoid type and other types lesion were seen in 4 (8%) 37 (79%) cases out of 43 cases of stomach cancer were positive for H. pylori, while all 4 cases of duodenal cancer were positive.

In our study, histologically most cases revealed adenocarcinoma 54 (82%), followed by 7 (10%) cases of squamous cell carcinoma, all of which belongs to esophageal carcinoma, 3 cases of



![](_page_3_Figure_5.jpeg)

cases, that includes fungating and infiltrative type. All 4 cases of duodenum (100%) were ulceroproliferative type.

During this study, total 48 cases of gastric and duodenal cancers were tested for Helicobacter pylori RUT (rapid urease test), 87% (42 cases) of the study population were positive for H.pylori. GIST,1 case of carcinoid tumor, and 1 case of lymphoma. All 4 (100%) cases of duodenal carcinoma were adenocarcinoma, and 46 (90%) cases of gastric cancers were adenocarcinoma and among remaining 5 (10%) cases, 3 (5.8%) were gastrointestinal stromal tumor along with each carcinoid tumor and lymphoma.

Table 4. Association between biopsy findings and endoscopic location of different carcinomas.					
Pienes Andings	Endoscopic location				
biopsy findings	Esophagus	Stomach	Duodenum	p-value	
Adenocarcinoma	4 (6.1%)	46 (69.6%)	4 (6.1%)		
Squamous cell carcinoma	7 (10.6%)	0 (0%)	0 (0%)	0.010*	
Other types	0 (0%)	5 (7.6%)	0 (0%)		
*p-value significant at <0.05					

Only 26 Gastric adenocarcinoma cases were sub classified, 10 (38%) were poorly differentiated, 7 (27%) were moderately differentiated, 6 (23%) cases were signet ring cell carcinoma, 2 (7.7%) well differentiated and 1 (3.8%) undifferentiated.

Among all cases distant metastasis were observed in 7 (12%) cases. Intraabdominal lymph nodes were involved in 28 (48%) cases, among gastric cancers 26 (53%) were involved with nodal metastasis, 2(18%) in case of esophageal cancer and 1(25%) in case of duodenal cancer.

# DISCUSSION

Cancer incidence in general and GI cancer in particular varies widely in different parts of the world in different age groups. Studies from Nepal showed higher incidence compared to other parts of the world.<sup>5,6</sup>

In this study of 66 patients of upper GI malignancy, upper GI malignancy were seen more commonly in the male gender compared to the female counter part (1.36:1), the average age of patient was 59 years and peaked between 60 year and above age group (54.5%). Gastric carcinoma is extremely rare before the age of 30 years and most patients are above 50 years of age.<sup>7,8</sup>

There was a spectrum of median age incidence reported in different parts of the world. In the western world, it was 71 years in the USA, which is higher than this study. In Asian countries, median ages in different countries were low. Similar to this study was seen in Japan (61 years).<sup>9</sup> in TUTH Nepal (59.6±12.4 years),<sup>17</sup> in western region Nepal (age group 51-70 years)<sup>10</sup> Contrast to this study, in Pakistan (48 ± 4.47 years) and Saudi Arabia (47 years) incidence of cancer in early age population were seen.<sup>11,12</sup>

Compared to this study, male: female ratio was higher in Mizoram  $(2.7: 1)^{13}$  In Nigeria (2.5:1),<sup>14</sup> in Kashmir  $(3.3: 1)^{15}$  and in Saudi Arabia (2.2:

1)<sup>12</sup>. Similar to this study was seen in Pakistan  $(1.5: 1)^{16}$ , in western region Nepal  $(1.8:1)^{10}$  and TUTH Nepal  $(2:1)^{17}$  Presumably, this male preponderance could be attributed to the high incidence of risk factors in male (like; smoking >60%, alcohol >50%), with male to female smoking ratio of 1.7:1 in this study).

Majority of patients (53%) in this study had a history of smoking, and 50% with history of alcohol intake, consumption of smoked meat were seen in 24% cases, along with spicy meal consumption in 29% cases. Similarly, in a study from Nigeria Ajayi et al.14 identified Alcohol, smoking and spices are the three main risk factors for upper GI malignancy. Study from north eastern India showed overwhelming majority of patients (77.8%) had a history of consumption of smoked meat, and 67.7% of patients had history of consumption of dried, fermented fish, and smoking history in 67.6% of males and 44% of females.<sup>18</sup> Another study from Nepal also reported smoked meat, alcohol and smoking were associated with gastric cancer in more than 50% of cases (western region Nepal).<sup>10</sup>

Current study showed, dysphagia (82%) and weight loss (82%) were most common presentation of esophageal caarcinoma, in keeping up with the many studies as Dysphagia (86%) was reported as the most common presenting complaint of esophageal carcinoma by Durrani et al.<sup>16</sup> and study by Ajayi et al.<sup>14</sup> also reported similar stats. In Nepal, Thakur et al reported dysphagia was presenting complain in 98.5 % of cases of esophageal carcinoma.<sup>19</sup>

Most of our patients with gastric cancer presented with abdominal pain (88%), weight loss (57%), vomiting (43%), loss of appetite (%) and melena (57%), which is similar to many studies, Barad et al.<sup>18</sup>, Durrani et al.<sup>16</sup>, Ajayi et al.<sup>14</sup> In Nepali context Shah et al.<sup>17</sup>, revealed pain abdomen (87%), anorexia (81%), and weight loss (77%) which is very similar to our results. 51.9% of the patients in this study presented at the hospital within 3 months of the onset of symptoms while the only less than 15% presented after 6 months.

In this study, most common presenting Symptom of upper GI malignancy noted was abdominal pain (75%), followed by weight loss (60%), vomiting (39%), loss of appetite (45%) and melena in 19% of cases. Similar to our study, abdominal pain was most common presentation in Nigeria (Ajayi et al.)<sup>14</sup> 64% of cases with anemia on presenting symptom was higher in our study than only 2.6% of anemia in same study, whereas abdominal lump was present in only 12% of cases in our study, which is lower than 30.8% reported by Ajayi et al.<sup>14</sup>

The prevalence of oesophageal malignancies in this study was low (16%) in keeping with a similar study from Nigeria where oesophageal carcinoma were present in 16.6% of upper gastrointestinal tumors. Contrast to our study, Durrani et al.<sup>16</sup> reported higher incidence (43.3%) of esophageal cancer, which also included cases of upper GI cancers. Other studies from Nepal also reported lower incidence, where incidence ranges from 1.6% to 10.7%.<sup>6,20</sup>

Gastric malignancies are important cause of mortality from cancer and one of the most deadly malignant neoplasm worldwide and in Nepal. The prevalence of gastric malignancies in this study was quite high (77%). Which is comparable to similar studies, in Nigeria by A. Ajayi et al.(67.9%),<sup>14</sup> in Punjab by Durrani et al.(57.6%)<sup>16</sup> The incidence of stomach cancer is said to be highest in Japan, China, South America and the Eastern Europe. The high prevalence obtained here was in sharp contrast to 13.3% recorded in Nigeria by Atoba et al.<sup>21</sup>, 12% recorded in Lagos by Abdulkareem et al.,<sup>2</sup> and 4.6% in maharastra by Khatib et al.<sup>22</sup> In Nepal the incidence of gastric carcinoma recorded ranges from 4% to 15.1%.<sup>6,20</sup> The prevalence of duodenal carcinoma in this study was extremely low (6%), which is comparable to low incidence reported in Nigeria in similar study population by Ajayi et al.<sup>14</sup>

In this study, most common site for esophageal cancer was middle one third (64%) followed by lower third (36%). Our findings are similar to many other studies where middle third was commonest site followed by lower third. Mchembe et al.<sup>23</sup>, Kuwano et al.<sup>24</sup>, Ajayi et al.<sup>14</sup> and Durrani et al.<sup>16</sup> Contrast to our study, in Kashmir by Mustafa et al.<sup>25</sup> reported distal third (45%) as the most common site followed by middle (34.8%). Similar finding of distal esophagus as a commonest site of esophageal cancer was reported in Nepal by Pun et al.<sup>5</sup>

Among esophageal cancers, in our study most common endoscopic/macroscopic appearance of cancer were protruding lesion (55%) and 50% cases of ulcerative lesions. As only few studies mentioned esophageal gross lesion, in Tanzania by Mchembe et al.(2013),<sup>23</sup> unlike this study, most common macroscopic appearance of esophageal cancer was ulcerative type 132 (40.3%) ,similar finding were seen by Mustafa et al.(2016),<sup>25</sup> who reported localized ulcerative lesion as the most common appearance (50%) followed by protruding lesion (19%)

Similary in Nepal, Pun et al. (2012)<sup>5</sup> reported gross findings in squamous cell carcinoma were either exophytic or ulcerative lesion with deep irregular ulcers.

Unlike western countries,In Asia still Oesophageal squamous cell carcinoma (OSCA) is the predominant histologic type of oesophageal malignancy, in Iran by Pedram et al.<sup>26</sup> reported 81.3% cases of squamous cell carcinoma, 16.3% cases of adenocarcinoma, in japan Kuwano et al.<sup>24</sup> also reported esophageal squamous cell carcinoma as commonest histological type with 91.6 %, in India by Cherian et al. also reported similar findings as squamous cell carcinoma were seen in 92%. Among very few studies done in Nepal, Pun et al.5a total of 106 cases of esophageal cancer were received in the department of pathology, BP Koirala Memorial Cancer Hospital. Relevant clinical data were retrieved from computer database of the hospital.Results: A total of 106 cases of esophageal carcinomas were diagnosed during a three years period. There were 68 (64.15% also reported similar study as 64 % of squamous cell carcinoma. This study showed 64% cases of esophageal adenocarcinoma, which is contrast to the many Asian studies mentioned above, may reflect small study sample or changing trend of cancer pattern in our part of the world due to increase in risk factors that are associated with the occurrence of esophageal adenocarcinoma. As reports from Asian countries have also shown a decline in incidence of SCC. Similar to study by Pun et al.<sup>5</sup> where the maximum number of SCC were seen in middle esophagus and the maximum number of adenocarcinoma was seen in distal esophagus, our study also showed all squamous cell carcinoma in middle third and maximum number of adenocarcinoma in distal esophagus followed by middle esophagus.

Unlike in the USA where proximal stomach is the commonest site of cancer in stomach, in this study, distal part including body of stomach (51%) and antrum (35%) were common site followed by fundus (17%). Similarly, in Nigeria by Ajayi et al. (2016)<sup>14</sup> 62.3% were in the antrum while 37.7% were in the corpus. Likewise, Barad et al.<sup>18</sup> in India, the most common site of gastric cancer was antrum (50.6%). in Nepal antrum was the commonest site of involvement (70%) by Gosh A et al. (2010)<sup>10</sup>, lower third of stomach was common site for gastric cancer (61.5%) followed by middle third (20%) and upper third (15%) Sah et al.(2015).<sup>17</sup>

In this study, 60% of gastric lesions were

ulceroproliferative type, 11% ulcerative type, 8% gastric outlet obstruction. Similar to our study Qureshi et al. showed 35.5% ulceroproliferative, 26% proliferative, 31% ulcerative, and 7.4% infiltrative lesions in Kashmiri patients.<sup>15</sup> Shaha A et al.<sup>11</sup>, Ulcerative lesion was 57.8% followed by ulceroproliferative lesion 24.9% and polypoidal lesion 17.3%. Another study done by Kabir et al.<sup>27</sup> showed that ulcerative lesion was 56%, ulceroproliferative lesion 10%, and polypoidal lesion 34%.Unlike our report, Ghosh A et al.<sup>10</sup> reported type IV (40%) as most common gastric cancer in Nepal, followed by type III (33%) and type II (27%)

In this study, histologically majority (82%) were found to be adenocarcinoma consistent with other studies, Ajayi et al.<sup>14</sup> reported 83 % as adenocarcinoma, Barad et al.<sup>18</sup> 95.6% adenocarcinoma, in Nepal Ghosh A et al.<sup>10</sup> reported 100% adenocarcinoma, Sah et al.<sup>17</sup> also showed 100% adenocarcinoma. Majority of the tumours in our study were poorly differentiated and moderately differentiated, similar to other studies (Ghosh et al.<sup>10</sup>, Barad et al.<sup>18</sup>).

In this study, 12% had distant metastasis and majority (48%) had locally advanced gastric cancers at the time of presentation. This figure is higher to 9-17% seen in western countries and much higher to the prevalence of Japan where mass screening programmes for gastric cancer are in place. These studies suggest that patients with gastric adenocarcinomas usually present with advanced disease unfavorable histopathology.

H. pylori positivity in this study for those with gastric cancer was 79% and 100% for duodenal cancer. This was significant statistically. In Bangladesh, Talukdar et al. showed that the prevalence of H. pylori was 66% out of 50 cases of gastric cancer.<sup>27</sup> Kabir et al.<sup>27</sup> showed prevalence of H. pylori in 71.8% of gastric cancer patients.

Ajayi et al.<sup>14</sup> also showed 71.7% were positive for H.pylori in gastric cancer patients.

## CONCLUSIONS

Upper GI malignancy mainly gastric cancers are apparently predominant in our part of the world. In view of the fact that upper GI tumors

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can rapidly progress to advanced stages even in the absence of serious symptoms, early esophagogastroduodenoscopy is needed in high risk cases to avoid delayed diagnosis and improve the disease outcome.

## Conflict of Interest: None.

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