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Pathology

HISTOPATHOLOGICAL STUDY OF ENDOSCOPIC BIOPSIES OF LESIONS OF UPPER GASTROINTESTINAL TRACT IN A TERTIARY CARE HOSPITAL.

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ABSTRACT **Background:** The gastrointestinal malignancies contribute enormously to the overall cancer burden and mortality compared to other malignancies. Early detection, however, greatly improves the survival rate of patients for which endoscopy with biopsy followed by histopathology are of enormous significance. **Methods:** This study was conducted in the department of Pathology at SKIMS Srinagar. The study material was the biopsy samples received in 10% formalin at department. The samples were processed in the tissue processor and paraffin embedded. Blocks were trimmed and stained with Hematoxylin and Eosin. Special stain was done wherever required. The tumors were staged as per 8th AJCC guidelines. Lesions of oral cavity were excluded. **Results:** The study had a total of 154 cases, out of which 75 were from stomach, 58 from esophagus, 13 from GE junction & 8 from duodenum. Majority of the patients were in the age group of 60-70 years (33.8%) with an M:F ratio of 1.7:1. The commonest symptom in our subjects was dyspepsia (61=39.6. The commonest site of lesion was stomach in our study (75 =48.7%). 58 cases (37.7%) endoscopically were ulceroproliferative lesions. The commonest histological diagnosis was adenocarcinoma (57.79%). **Conclusions:** Upper GIT endoscopy biopsy and histopathology is the gold standard for the diagnosis of endoscopically detected lesions. Hence, we can conclude that the combination of these two methods provide a powerful diagnostic tool for better patient care and management. Any person aged 60-70 years with symptoms should be evaluated by endoscopic biopsy to rule out the malignancy.

KEYWORDS : Gastrointestinal, Malignancies, Endoscopy, Biopsy, Histopathology, Stomach, Esophagus, Adenocarcinoma, Squamous cell carcinoma.

INTRODUCTION

The gastrointestinal system is essentially a muscular tube lined by a mucous membrane that exhibits regional variations, reflecting the changing functions of the system from mouth to anus. The GI tract has four distinct functional layers-mucosa, submucosa, muscularis propria & adventitia[1]. Malignancies here contribute enormously to the overall cancer burden and mortality compared to other malignancies[2]. Worldwide, these rally among the leading cancers, and constitute about 15-25% of the total cancer burden[3]. Gastrointestinal malignancies, although considered a disease of the elderly, have been on the rise in young due to swiftly changing lifestyles and food habits. Early detection, however, greatly improves the survival rate of patients[4].

Kashmir valley has traditionally been considered an endemic cancer zone having a peculiar cancer profile[5], with a flagrant prevalence of gastrointestinal malignancies, ranging from 45.4%[6] to 65.25%[7] of all cancers, which is very high compared to the rest of the country, with frequencies reported varying from 5.8% in Amritsar to 14.36% in Kerala.[7]. Esophageal, gastric s and colorectal malignancies are the leading cancers of this region, as has been consistently recounted by many studies[5, 8, 9] .Cancers of the esophagus and stomach are the prime malignancies[5, 8, 10], attributed to the cultural and lifestyle related factors prevalent here, including drinking hot beverages, consumption of traditional salted tea, preserved sundried and smoked foodstuffs, propensity for spicy food, and a high prevalence of tobacco usage in various forms[10, 11]. Esophageal malignancies are traditionally seen in the elderly age group with a mean age of diagnosis 68 years[12], however there are reports validating an increasing trend in a younger subset of people[13]. Currently, SCC is the most common type of esophageal cancer in the Indian subcontinent; the distal third of the esophagus being the most common site[14]; however adenocarcinomas of this region have been steadily rising, and the incidences are higher than squamous cell carcinomas in some high human development index (HDI) countries[15]. With increasing recognition of Barrett's mucosa it is apparent that most adenocarcinomas occur in the lower third of the esophagus or esophago-gastric junction[16] due to specialized intestinal metaplasia[17].

Worldwide, gastric adenocarcinoma is the second most common cancer and carcinoma esophagus is the sixth leading cause of death[18, 19]. In India according to the National Cancer Registry, esophageal and gastric cancers are the most common cancers found in men while esophagus cancer ranks third among women after carcinoma of breast and cervix[20]. Gastric malignancy rates have also escalated amongst younger population with incidences ranging from 2-8% reported in different studies. Cancers of the stomach are not easy to diagnose in young people, as most of the patients are asymptomatic even in the advanced stages of the disease[21]. When histologically analyzed, gastric carcinomas occur in two principal patterns– the intestinal and the diffuse type. Intestinal variant is seen commonly, exhibiting a mean age of incidence 55 years and a male to female ratio of 2:1, major risk factors being environment especially H. pylori. The diffuse type occurs in slightly younger patients with a mean age 40 years, and nearly equal male to female ratio[7]. Most of the gastric cancers are sporadic with only 1-3% seen as part of inherited cancer syndromes like Hereditary Diffuse Gastric Cancer (HDGC) syndrome[22]. The different malignant conditions of the stomach can be gastric carcinoid tumors, adenocarcinoma, MALT lymphoma of the stomach, GI stromal tumors or a metastatic lesion to upper gastrointestinal tract. Endoscopy provides numerous small mucosal biopsies to diagnose and monitor the course of a variety of gastrointestinal tumors. To improve the prognosis of esophageal and gastric malignancies which are confined to the mucosa or submucosa, early diagnosis is essential which can be easily done with endoscopic biopsy and histopathology. In view of an increasing trend of gastrointestinal malignancies in the young population worldwide[16, 21, 23, 24, 25] early detection and diagnosis needs to be established. Population based registries are currently not available in Kashmir, and the data related to the cancer patterns is gauged after analysis from the hospitals[8]. So this study is an important one as it gives us an insight to the problem in this geographical area.

Aims and Objectives

1. To analyze the spectrum of various malignant lesions of upper GIT.
2. To analyze the prevalence of these lesions in different age groups.
3. To see the gender difference in prevalence of these lesions.
4. To analyze the site wise prevalence of these lesions.

MATERIALS AND METHODS

This study was conducted in the Department of Pathology at Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, which is the largest tertiary care hospital in Kashmir. It extended over a period of one and a half year of prospective analysis, from July 2017 to December 2018. It had a total of 154 cases, out of which 75 were from stomach, 58 from esophagus, 13 from GE junction & 8 from duodenum. The study material was the biopsy samples received at our department. Relevant clinical details were noted from the requisition forms as per the proforma. The samples were received in 10% formalin, and kept for overnight fixation. After fixation, the

samples were packed in cassettes for processing in the tissue processor, and paraffin embedded. After embedding, the paraffin blocks were trimmed and three to four micron-thick sections were obtained by microtome, and stained with Hematoxylin and Eosin. The slides were then mounted and the cases analyzed. Special stains like PAS, and immunohistochemistry was done wherever required. The tumors were staged as per 8th AJCC guidelines. Lesions of oral cavity were excluded.

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel). It was then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD, and categorical variables were summarized as frequencies and percentages. Frequency distribution tables, bar diagrams and pie charts were used for data presentation. The results are summarized in the tables 1 to 10 below which are self explanatory.

RESULTS AND OBSERVATIONS (with tables)

Table 1: Age distribution of study patients

Age (years)	Frequency	Percentage
< 50	30	19.5
50-60	28	18.2
60-70	52	33.8
70-80	35	22.7
≥ 80	9	5.8
Total	154	100
Mean±SD (Range)=59.8±12.85 (27-90).		

Table 2: Gender distribution of study patients

Gender	Frequency	Percentage
Male	96	62.3
Female	58	37.7
Total	154	100
Male:Female=1.7:1		

Table 4: Distribution of study patients as per tumor site

Tumor Site	Frequency	Percentage
Stomach	75	48.7
Esophagus	58	37.7
GE Junction	13	8.4
Duodenum	8	5.2
Total	154	100

Table 5: Showing endoscopic findings of study patients

Endoscopic Findings	Frequency	Percentage
Ulceroproliferative	58	37.7
Ulceroinfiltrative	37	24.0
Polypoid	15	9.7
Ulcerated	13	8.4
Infiltrative	12	7.8
Nodular	10	6.5
Proliferative	3	1.9
Edematous	2	1.3
Not available	4	2.6
Total	154	100

Table 6: Showing spectrum of various histopathological lesions in study patients

Diagnosis	Frequency	Percentage
PD Adenocarcinoma	45	29.2
MD Adenocarcinoma	32	20.8
WD Adenocarcinoma	11	7.1
PD Squamous cell carcinoma	5	3.2
MD Squamous cell carcinoma	37	24.0
WD Squamous cell carcinoma	10	6.5
Mucinous Adenocarcinoma	4	2.6
Squamous cell carcinoma basaloid	2	1.3
Neuroendocrine tumor	3	1.9
Adenocarcinoma in SITU	1	0.6
GIST	1	0.6
NHL	1	0.6
Mets Merkel cell carcinoma	1	0.6
Dysplasia	1	0.6
Total	154	100

Table 7: Showing correlation of endoscopic findings with histological diagnosis in study patients

Endoscopic Findings	Histological Diagnosis							Total
	Adeno-carci-noma	SCC	Neuro-endo-crine-tumor	GIST	NHL	Mets Merkel cell carci-noma	Dysp-lasia	
Ulceropro-liferative	29	26	2	1	0	0	0	58
Ulceroin-filtrative	21	15	0	0	0	1	0	37
Polypoid	8	6	1	0	0	0	0	15
Ulcerated	12	1	0	0	0	0	0	13
Infiltrative	10	1	0	0	0	0	0	11
Nodular	6	3	0	0	1	0	0	10
Proliferative	2	1	0	0	0	0	0	3
Edematous	1	0	0	0	0	0	1	2
Infiltrative	1	0	0	0	0	0	0	1
Not available	3	1	0	0	0	0	0	4
Total	93	54	3	1	1	1	1	154

Table 8: Showing prevalence of various lesions according to age (years) in study patients

Lesion	< 50 Yrs	50-60 Yrs	60-70 Yrs	70-80 Yrs	≥ 80 Yrs
Adeno-carcinoma	19 (20.4)	13 (14.0)	35 (37.6)	21 (22.6)	5 (5.4)
SCC	10 (18.5)	11 (20.4)	16 (29.6)	13 (24.1)	4 (7.4)
Neuroendocrine tumor	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	0 (0)
GIST	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
NHL	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Mets Merkel cell carcinoma	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
Dysplasia	0 (0)	1	0	0 (0)	0 (0)

Table 9: Showing gender wise prevalence of various lesions in study patients

Lesion	Male		Female	
	No.	% age	No.	%age
Adenocarcinoma	68	73.1	25	26.9
SCC	24	44.4	30	55.6
Neuroendocrine tumor	2	66.7	1	33.3
GIST	1	100	0	0.0
NHL	0	0.0	1	100
Mets Merkel cell carcinoma	1	100	0	0.0
Dysplasia	0	0.0	1	100

Table 10: Showing site-wise prevalence of various lesions in study patients

Lesion	Stomach	Esophagus	GE Junction	Dudenum
Adenocarcinoma	73 (78.5)	4 (6.8)	11 (11.8)	5 (5.4)
SCC	0 (0)	54(100%)	0	0
Neuroendocrine tumor	1 (33.3)	0 (0)	1 (33.3)	1 (33.3)
GIST	1 (100)	0 (0)	0 (0)	0 (0)
NHL	0 (0)	0 (0)	0 (0)	1 (100)
Mets Merkel cell carcinoma	0 (0)	0 (0)	1 (100)	0 (0)
Dysplasia	0 (0)	0 (0)	0	1 (100)

DISCUSSION & CONCLUSION

Upper gastrointestinal tract is a common site for various lesions, especially malignant tumors. Worldwide carcinoma stomach is the second most common cancer and carcinoma esophagus is the sixth leading cause of death. Early detection of malignancy greatly improves the survival rate of patients. Upper GI endoscopy with biopsy & histopathology is regarded as the most sensitive & specific diagnostic method for the early detection of esophageal, gastric & duodenal cancers, and in the management & surveillance and in the follow up of the patients.

In our study, majority of the patients were in the age group of 60-70 years (33.8%), followed by 70-80 years (22.7%). Only 9(5.8%) cases were above 80 years. The mean age was 59.8 years. In a study

conducted by Islam et al (2014)[26], the mean age was 54.46 years. Our results were also coherent with a study conducted by Kothari et al (2016)[27] where most of the malignant lesions were seen in the age group of 51-70 years.

We had 96 (62.3%) males in this study, with an M:F ratio of 1.7:1. The results were in coherence with studies conducted by Abilash et al(2016)[28] and Sheikh et al (2015)[29] where males constituted 66% & 65.8% of the total cases respectively. Hussain et al (2015)[30] had a study with 73.5% males.

The commonest presenting symptom in our subjects was dyspepsia (61=39.6%). Dysphagia was present in 29.2% cases followed by epigastric pain which was present in 16.9% of the patients. Hematemesis, postprandial distension & recurrent vomiting was seen in 7.1%, 4.5% & 2.6% , respectively. The results were similar with a study conducted by Syed Imtiyaz Hussain et al (2015)[30] with dyspepsia being the most common complaint in 37.9%, followed by dysphagia in 30.3% and epigastric pain in 18.2% in a study with 132 cases.

The commonest site of lesion was stomach in our study (75 =48.7%), followed by esophagus (58=37.7%), GE junction (13=8.4%). The least number of cases were from duodenum (8=5.2%). In a study conducted by Sheikh et al (2015)[29], of the 196 upper GI biopsy samples, 127(64.8%) cases were from stomach , 50(25.5%) cases from esophagus, 15(7.65%) cases from GE junction & 4 (2.04%) cases from duodenum. However, in a study by Sharma et al (2019)[31] of 109 cases, majority of the cases were from esophagus constituting 54(49.54%) cases followed by 35 (32.11%) cases from stomach, 17 (15.59%) cases from duodenum & 3(2.75%) cases from GE junction. The differences in the results can be explained by variation in sample size & exclusion of benign & non-neoplastic conditions (inflammatory, infectious, etc) in our study.

Majority of the cases (58=37.7%) endoscopically presented as ulceroproliferative lesion, followed by ulceroinfiltrative (24%) in our study. Our findings were in synchrony with a study conducted by Makhdoomi et al (2005)[32]. In a study by Rashmi et al (2013)[33], most of the lesions presented as ulcerated & ulceroproliferative lesions on endoscopy and one by Qizilbash & Stevenson(1979)[34], majority of the lesions were ulcerative on endoscopy.

In our study, the most common histological diagnosis was adenocarcinoma (89=57.79%), followed by squamous cell carcinoma (54=35.06%). In a study conducted by Sheikh et al (2015)[29], of 103 cases, majority was diagnosed as adenocarcinoma (56%), followed by squamous cell carcinoma (40.77%). Our results were also coherent with a study conducted by Krishnapa Rashmi et al (2013)[33]. We even found one case of mets merckel cell carcinoma in our study, with adenocarcinoma in situ, dysplasia, neuroendocrine tumor, NHL, GIST, mets merckel cell carcinoma, each constituting 1 case.

In our study, out of 58 ulceroproliferative lesions, 29 were diagnosed as adenocarcinoma. SCC constituted 26 of the total ulceroproliferative lesions. Of the 37 ulceroinfiltrative lesions, 21 were diagnosed as adenocarcinoma & 15 as SCC. Of the 15 polypoid lesions, 8 were diagnosed as adenocarcinoma on histopathology, 6 as SCC & 1 as neuroendocrine tumor. Of the 13 ulcerated lesions, 12 were diagnosed adenocarcinoma on histopathology & 1 as SCC. In a study conducted by Makhdoomi et al (2005)[32], SCC of esophagus presented as proliferative & ulceroproliferative lesions and in a study by Krishnappa Rashmi et al (2013)[33], adenocarcinomas endoscopically presented as ulcerative & ulceroproliferative lesions.

In our study, majority of the adenocarcinomas (35) were in the age group of 60-70 years followed by 21 cases in the age group of 70-80 years. Majority (16) of the squamous cell carcinomas in our study were in the age group of 60-70 years followed by 13 cases in the age group of 70-80 years. Neuroendocrine tumors affected almost all age groups. In a study conducted by Monal Trisal et al (2018)[35], patients with esophageal cancer presented with ages ranging from 3rd to 8th decade. Patients with gastric cancer presented with ages ranging from 2nd to 9th decade. Patients with pyloro-duodenal neoplasms presented with a mean age of 73 years. In another study conducted by Anoja Aparjita et al(2016)[36], highest incidence of esophageal and gastric malignancy was seen between 51-60 years of age.

Adenocarcinoma was predominantly found in males constituting 73.1% but SCC was found predominantly in females constituting 55.6%. Out of 3 NE tumors, 2 were males. In a study conducted by Hussain et al (2015)[30], males constituted about 84.6% of the total adenocarcinoma cases. However, SCC was also found predominantly in males.

In our study, out of a total of 58 cases from esophagus, 54(94.7%) were diagnosed as SCC. 4(6.8%) cases were diagnosed as adenocarcinoma. None of the cases was diagnosed as adenosquamous or neuro-endocrine etc. Of the 75 cases from stomach, 97.3% of the cases were diagnosed as Adenocarcinoma, one was diagnosed as GIST and one as neuroendocrine tumor. Of the 13 GE junction biopsies, 11 were diagnosed as adenocarcinoma, 1 as dysplasia & 1 as neuroendocrine tumor. One was diagnosed as metastatic deposits of Merckel cell carcinoma. Of 8 duodenal biopsies, 5 were diagnosed as adenocarcinoma, 1 as neuroendocrine tumor, 1 as NHL and 1 as dysplasia

In a study, conducted by Gull et al (2019)[37], squamous cell carcinoma constituted about 84.7% of the total cases followed by adeno-carcinoma of about 12.2% from esophagus. In a study conducted by Kothari et al (2016)[27], 86.6% of the cases were SCC. Adenocarcinoma constituted 13.4%. In a study conducted by Sk Md Jaynul Islam et al(2014)[26], all the malignant lesions from stomach were diagnosed as adenocarcinoma. Aparjita A et al (2016)[106], Sadhana L Kothari (2016)[27], Qureshi et al (2007) & Gulia SP et al (2012)[113] in their studies also reported adenocarcinoma as the most common histological type in gastric malignant lesions.

In a study of Bilal A Sheikh et al (2015)[29], with 15 biopsies from GE junction, 11 were adenocarcinoma, 3 Barretts esophagus & 1 reflux esophagitis. In study conducted by Sunita Sharma et al (2019)[31], all the 3 GE junction biopsies were diagnosed as adenocarcinoma.

In a study conducted by Sadhana L Kothari (2016)[27] of duodenal biopsies, most common histological diagnosis was adenocarcinoma. In another study by Sheikh (2015)[29], out of 4 duodenal biopsies, 2 were diagnosed as celiac disease, 1 as adenocarcinoma & 1 as tubular adenoma.

Upper gastrointestinal tract endoscopy helps in visualisation of specific site of mucosal lesions. Endoscopy is incomplete without biopsy and histopathology is the gold standard for the diagnosis of endoscopically detected lesions. Hence, we can conclude that the combination of these two methods provide a powerful diagnostic tool for better patient management. Endoscopic examination and histopathological examination should go parallel and neither should be a substitute of each other. Limitations in diagnostic interpretation are encountered at times due to tiny biopsy material, handling and processing artifacts. However multiple bits of endoscopic biopsies from abnormal looking mucosa are recommended to establish a definitive diagnosis.

Endoscopic biopsies can detect changing patterns in the spectrum of lesions besides detecting upper GI mucosal lesions at an early stage especially atrophy, intestinal metaplasia and dysplasia so as to prevent progress of these lesions to invasive cancer.

Hence, we can draw a conclusion that any person aged 60-70 years especially a male, with dyspepsia, dysphagia or epigastric pain should be evalvated by endoscopy to rule out any possible lesion. And if any lesion, biopsy must be taken to rule out the malignancy.

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