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Histopathological Analysis and HER-2/neu Expression in Endoscopic Guided Upper Gastrointestinal Biopsies: An Observational Study

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ABSTRACT

This study presents a comprehensive analysis of a cohort of 90 patients who underwent upper gastrointestinal endoscopic biopsies. The aim was to investigate the demographic characteristics and histopathological findings within the upper gastrointestinal tract. Demographic data, encompassing age and gender profiles, were systematically gathered for the entirety of the study cohort comprising 90 cases. Histopathological findings in the oesophagus, duodenum and stomach were documented, with a focus on both non-neoplastic and neoplastic lesions. Additionally, the presence of HER-2/neu over expression was assessed using immunohistochemistry (IHC) scores. The study found the most common age for upper gastrointestinal endoscopy patients to be 40-60 years, with a nearly equal male-to-female ratio in esophageal biopsies and more males in duodenal and gastric biopsies. Esophageal biopsies often showed chronic esophagitis and Barrett's oesophagus, while chronic duodenitis and inflammatory polyps were common in duodenal biopsies. Gastric biopsies typically revealed chronic gastritis, with well-differentiated adenocarcinomas being the main neoplastic lesion. Gastric adenocarcinoma predominantly affected males in the 40-60 year group, usually in the pyloric antrum and most lacked HER-2/neu over expression. This study provides valuable insights into the prevalence and distribution of upper gastrointestinal lesions. The findings contribute to a better understanding of the demographic characteristics and histopathological features of these lesions, particularly in the context of gastric adenocarcinoma and HER-2/neu expression. Our study findings play an important role in improving clinical management and treatment strategies for patients with upper gastrointestinal disorders.

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Key Words
Upper gastrointestinal tract, histopathological findings, demographics, gastric adenocarcinoma, HER-2/neu over expression

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INTRODUCTION

Upper gastrointestinal tract (GIT) lesions and their histopathological characteristics play a crucial role in the diagnosis and management of various gastrointestinal disorders[1]. A comprehensive understanding of the demographics and histopathological findings associated with upper GIT lesions is essential for clinicians and researchers to guide clinical decision-making and further investigations[2]. In this study, we present a detailed analysis of a cohort of 90 patients who underwent upper GIT endoscopic biopsies, shedding light on the prevalence and distribution of lesions within this region.

The upper GIT, consisting of the esophagus, stomach, and duodenum, is susceptible to a range of non-neoplastic and neoplastic lesions[3,4]. These lesions may manifest with diverse clinical symptoms and can have a significant impact on the patient's health and well-being[5,6]. To provide optimal care to patients and advance our knowledge in the field, it is imperative to characterize the demographic profiles and histopathological features of these lesions.

Our investigation begins by examining the age and gender distribution of the study cohort. Understanding the age groups most commonly affected by upper GIT lesions can aid in clinical suspicion and early detection. Additionally, assessing gender distribution may reveal potential associations between gender and lesion types.

Histopathological findings in the upper GIT are diverse, encompassing non-neoplastic conditions such as chronic esophagitis, chronic gastritis, and chronic duodenitis, as well as neoplastic lesions including adenocarcinomas and squamous cell carcinomas[7]. Identifying the most common histopathological findings and their prevalence is crucial for accurate diagnosis and treatment planning.

Aims and objectives: To comprehensively investigate the histopathological features of upper gastrointestinal (GI) biopsies obtained through endoscopic procedures, considering factors such as biopsy site, patient age and gender. To assess the prevalence and extent of HER-2/neu over expression in gastric carcinoma using Immunohisto chemistry (IHC) as a diagnostic tool. To explore the potential associations and prognostic implications of HER-2/neu overexpression in patients diagnosed with gastric carcinoma by considering key clinicopathological parameters, including age, gender, histological grade, and tumor site.

MATERIALS AND METHODS

Study design: This research constitutes a hospital-based observational study with a cohort of 90 cases. The investigation primarily focuses on patients who under went upper gastrointestinal (GIT) endoscopic biopsies at King George Hospital in Visakhapatnam, covering the period from January 2021 to November 2022. The study meticulously adhered to predefined inclusion and exclusion criteria.

Study population: The study encompassed upper GI endoscopic biopsies collected from both inpatients and outpatients at the Gastroenterology department of King George Hospital. The research was conducted within the confines of a tertiary care hospital setting.

Study duration: The study had a two-year duration, commencing in January 2021 and concluding in November 2022.

Sample size: After rigorous application of inclusion and exclusion criteria, a total of 90 cases were included in the study.

Inclusion criteria:

- All endoscopy-guided biopsies of the upper GI tract were included

Exclusion criteria:

- Biopsies taken beyond the second part of the duodenum were excluded
- Biopsies with insufficient material were excluded
- Biopsies from patients who did not provide informed consent were excluded
- Biopsies lacking specific pathological findings were also excluded

Methodology: Informed consent was obtained from each patient. Clinical data were meticulously recorded according to the study protocol. Upper GI endoscopic biopsy samples were promptly placed in 10% neutral formalin for fixation and subjected to gross examination. Routine histopathological processing involved the following steps: Preparation of tissue sections. Dehydration using graded ethanol. Clearing with xylene. Wax impregnation. Embedding for block preparation. Section cutting and staining with hematoxylin and eosin. Immunohisto chemistry (IHC) procedure: Sections were labelled after poly-L-Lysine coating. Deparaffinization and rehydration of sections. Heat-induced antigen retrieval in TRIS/EDTA buffer. Washed in TRIS buffer. Endogenous peroxide quenching. Application and incubation of primary antibodies. Washed and addition of secondary antibodies. DAB solution for color development. Counter-staining with Harris's hematoxylin. Sections were dehydrated, cleared in xylene, and mounted with DPX.

Stringent precautions were taken throughout, including handling of carcinogenic substances,

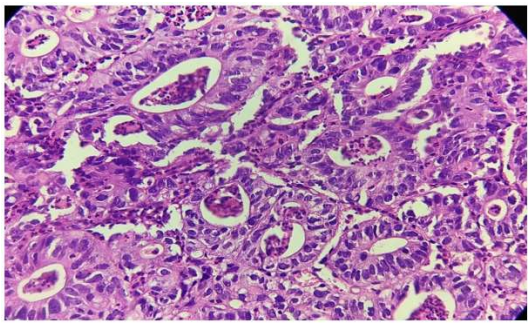

Fig. 1: Well differentiated Adenocarcinoma with Multiple Crowded Anaplastic Glands (H and E, 40X)

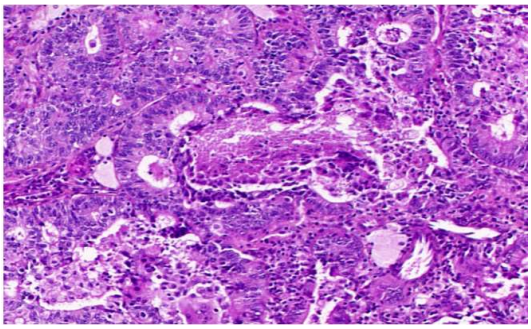

Fig. 2: Moderately differentiated Adenocarcinoma with few Anaplastic Glands and Solid sheets of Tumour Cells (H and E ,20X)

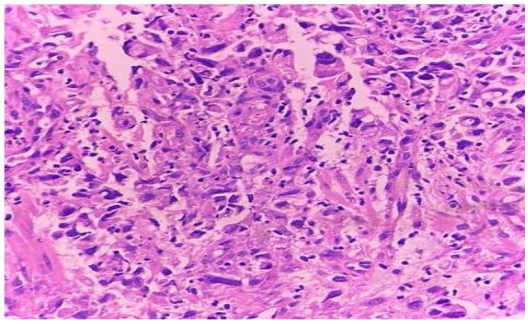

Fig. 3: Poorly differentiated Adenocarcinoma with discrete and solid sheets of Tumour cells with Anaplastic features (H and E,40x)

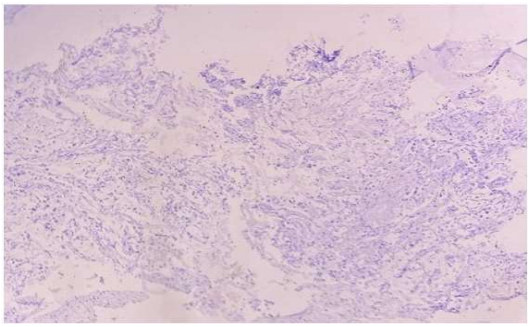

Fig. 4: Well differentiated Adenocarcinoma with her-2 /neu IHC marker score “0”(negative) 40x

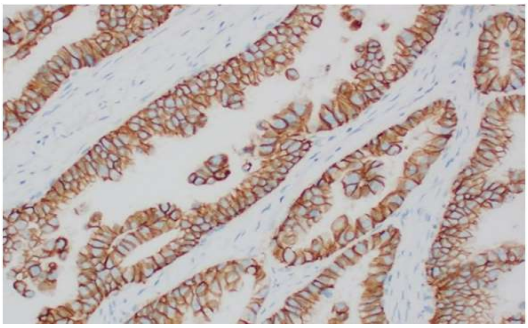

Fig. 5: Well differentiated Adenocarcinoma with positive her-2/neu IHC marker (score 3+) 40x

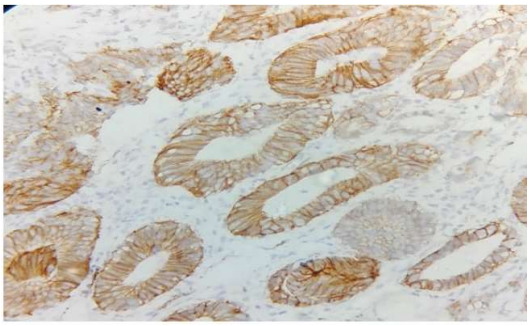

Fig. 6: Well differentiated Adenocarcinoma with positive her-2/neu IHC marker (score 3+) ,40x

antibody storage, buffer preparation and inclusion of positive/negative controls. HER-2/neu stain expression was scored following the Hoffman. Sxcoring system (Table 1).

Ethical considerations: This study was approval by the Institutional Ethics Committee of King George Hospital, Visakhapatnam, Andhra Pradesh. All patients provided informed consent for the collection and future utilization of their biopsy specimens for research purposes.

Statistical analysis: Descriptive statistics played a crucial role in our analysis, allowing us to express data as percentages. This method highlighted patterns, prevalence and trends within our data-set, aiding in clear data presentation and paving the way for deeper inferential analysis, ultimately enhancing our study’s significance and understanding.

RESULTS

In this study, we investigated a cohort of 90 patients who underwent upper gastrointestinal endoscopic biopsies. The demographic characteristics and histopathological findings were comprehensively analyzed, providing valuable insights into the prevalence and distribution of lesions within the upper gastrointestinal tract.

Table: 1 Hoffman. scoring for HER2/neu staining

Grade	Staining attern	HER-2/neu overexpression assessment
0	No reactivity in any tumor cell	Negative
1+	Tumor cell cluster with faint or barely perceptible membranous reactivity, irrespective of the percentage of tumor cells staine	Negative
2+	Tumor cell cluster with weak to moderate complete basolateral membranous reactivity, irrespective of the percentage of tumor cells staine	Equivocal
3+	Tumor cell cluster with strong complete lateral or basolateral membranous reactivity, irrespective of the percentage of tumor cells stained positive	Positive

Table 2: Demographics and Histopathological Findings in Upper GIT Endoscopic Lesions

Category	Esophagus (n = 12)	Duodenum (n = 14)	Stomach (n = 64)	Total (n = 90)
Age group	30-50 years (Most common)	40-60 years (Most common)	40-60 years (Most common)	40-60 years (Most common)
Gender distribution	1:1 (Male: female ratio)	More male cases	More male cases	65.1% male cases
Most common	Chronic esophagitis (n = 4)	Chronic duodenitis (n = 8)	Chronic gastritis (n = 30)	Chronic gastritis (most common)
Histopathological findings		Mild dysplasia (n = 3)	Eosinophilic duodenitis (n = 1)	Non-specific gastritis (n = 6)
			Well-differentiated Adenocarcinoma (n = 14)	Inflammatory polyps (n = 3)
		Inflammatory polyps (n = 3)	Chronic esophagitis (n = 4)	Barrett's esophagus (n = 3)
Neoplastic Lesions	Moderately differentiated Squamous cell carcinoma (n = 1) Adenocarcinoma (n = 1) Adenocarcinoma (n=1)	Moderately differentiated Adenocarcinoma (n = 1) Poorly differentiated Adenocarcinoma (n = 1)	Well differentiated Adenocarcinoma (n = 14)	Adenocarcinoma (n = 1) Moderately differentiated

Demographics and histopathological findings in upper git endoscopic lesions (n = 90): Our analysis revealed that the age group between 40-60 years was the most common among patients undergoing endoscopic evaluation of the upper gastrointestinal tract, consistently observed across all biopsy sites, including the esophagus, duodenum and stomach.

Gender distribution demonstrated that while there was a nearly equal male-to-female ratio in esophageal biopsies, both duodenal and gastric biopsies showed a predominance of male cases.

Histopathological findings in esophageal biopsies were marked by chronic esophagitis, mild dysplasia and Barrett's esophagus. Chronic esophagitis emerged as the most frequent non-neoplastic lesion, while neoplastic lesions included moderately differentiated squamous cell carcinoma and adenocarcinoma.

Duodenal biopsies exhibited chronic duodenitis as the primary non-neoplastic lesion, with inflammatory polyps also observed. In gastric biopsies, chronic gastritis was the dominant non-neoplastic finding. Neoplastic lesions in the stomach were primarily well-differentiated adenocarcinomas (Table 2).

Demographics and histopathological findings in gastric adenocarcinoma (n = 20): Among the subset of patients diagnosed with gastric adenocarcinoma the most prevalent age group was again between 40 to 60 years. The male population was more frequently affected, and the pyloric antrum emerged as the most common site of carcinoma.

Histologically, most cases of gastric adenocarcinoma were well-differentiated, though moderately differentiated and poorly differentiated adenocarcinomas were also identified in a smaller

Table 3: Demographics and Histopathological Findings in Gastric Adenocarcinoma

Category	Gastric Adenocarcinoma (n = 20)
Age group	40-60 years (most common)
Gender distribution	More male cases
Most common site of carcinoma	Pyloric antrum (n = 13)
Histological grade of adenocarcinoma	Well differentiated (n = 14)
	Moderately differentiated (n = 3)
	Poorly differentiated (n = 3)
HER-2/neu IHC score distribution	Positive score +3 (n = 2)
	Negative score (n = 18)

Table 4: Association and prognostic significance of HER-2/neu overexpression in gastric carcinoma

Parameter	Gastric Adenocarcinomas (n = 20)
Age group (years)	
40-60	12 (60%)
Most common age group	40-60
Sex distribution	
Male	15 (75%)
Female	5 (25%)
Male-female ratio	3:1
Most common site	Pyloric antrum (n = 13)
Histopathological differentiation	
Well-differentiated	14 (70%)
Moderately differentiated	3 (15%)
Poorly differentiated	3 (15%)
HER-2/neu IHC score distribution	
IHC Score+3	2 (10%)
IHC Score+2	0
IHC Score+1	0
IHC Score 0	18 (90%)

Table 5: Age Distribution in upper gastrointestinal biopsies (n = 90)

Age group	No. of case	Percentage
10-20 years	2	2.3
21-30 years	3	3.3
31-40 years	11	12.8
41-50 years	28	32.6
51-60 years	27	29.7
61-70 years	12	13.2
71-80 years	6	6.6
81-90 years	1	1.2
Total	90	100.0

Table 6: Sex distribution of patients

Sex	No of patients
Male	59
Female	31

subset of patients. HER-2/neu immunohistochemistry (IHC) score distribution demonstrated a majority of cases with a negative score, indicating the absence of HER-2/neu over expression (Table 3).

Association and prognostic significance of her-2/neu overexpression in gastric carcinoma: In our evaluation of gastric adenocarcinomas, we found that the age group between 40-60 years was most commonly affected, with a higher incidence in male patients, resulting in a male-to-female ratio of 3:1. The majority of cases were localized in the pyloric antrum.

Histopathological differentiation revealed that the majority of cases exhibited well-differentiated adenocarcinoma, though moderately and poorly differentiated adenocarcinomas were also identified. HER-2/neu IHC score distribution showed that the majority of cases were negative for HER-2/neu over expression, with only a minority displaying a positive IHC score(Table 4).

Age distribution in upper gastrointestinal biopsies (n = 90): The age distribution across all upper gastrointestinal biopsies revealed that patients between 41-60 years were the most commonly affected group, with a substantial proportion of cases falling within this age range(Table 5).

Sex distribution of patients: The gender distribution analysis demonstrated a higher prevalence of male patients (59) compared to female patients (31) among the study cohort (Table 6).

Gender vs. Age distribution in upper gastrointestinal biopsies (n = 90): When examining the distribution of patients across different age groups, it was apparent that males were more prominently represented in nearly all age groups, with the highest male-to-female ratio observed in the age group of 51-60 years (Table 7).

Comparison of the number of cases vs. Site of biopsy (n = 90): The distribution of biopsies across different anatomical sites revealed that the stomach was the most commonly biopsied organ, accounting for 71.1% of cases, followed by the duodenum (15.6%) and the esophagus (13.4%) (Table 8).

Comparison of age distribution vs. Site of biopsy (n = 90): In the comparative analysis of age distribution with the site of biopsy, it was observed that patients within the age group of 41 to 60 years predominantly under went biopsies across all anatomical sites (Table 9).

Frequency of various histopathological findings (n = 90): Among the various histopathological findings, chronic gastritis emerged as the most common, affecting 33.33% of cases. Other prevalent findings included well-differentiated adenocarcinoma of the stomach (15.5%) and chronic duodenitis (8.8%) (Table 10).

Her-2/neu ihc score distribution in gastric adenocarcinomas: The distribution of HER-2/neu IHC scores in gastric adenocarcinomas indicated that the majority of cases had a negative score, with only a minority displaying a positive score of +3(Table 11).

DISCUSSIONS

we present a comprehensive analysis of various aspects related to upper gastrointestinal endoscopic lesions and HER-2/neu overexpression in gastric carcinoma.

Contextual introduction to gastrointestinal malignancies: Gastrointestinal malignancies represent a significant global health burden, with stomach cancer ranking as the fifth most common cancer worldwide. These malignancies are often characterized by late-stage diagnosis and high mortality rates. The complexity and diversity of these cancers necessitate the development and implementation of advanced diagnostic techniques and personalized treatment approaches. Understanding the histopathological characteristics and molecular profiles of these cancers is crucial for developing effective management strategies.

Detailed analysis of histopathological findings: In our study, chronic gastritis and well-differentiated adenocarcinoma were the predominant histopathological findings. This prevalence aligns with the trends observed in other regional studies, like those by Rajagopal *et al*.[8] and Yano *et al*.[9] but also highlights possible geographic variations in the histopathological spectrum of gastrointestinal malignancies. The comparison with other regional data suggests potential differences in genetic, environmental or dietary factors that could influence these variations.

Demographic insights and their clinical implications: The majority of lesions in our study were observed in the 40-60 year age group, with a higher prevalence in males. This demographic trend could be influenced by a combination of biological factors, lifestyle choices, and socio-economic conditions. Understanding these demographic patterns can be instrumental in developing targeted screening programs and early diagnosis strategies, potentially improving patient outcomes.

Comprehensive review of lesion sites: The stomach, particularly the pyloric antrum, emerged as the most common biopsy site in our study. This finding has

Table 7: Gender vs. age distribution in upper gastrointestinal biopsies (n = 90)

10-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years	Total
F	1	1	4	7	10	6	1	31
M	1	2	7	21	17	6	5	59
Total	2	3	11	28	27	12	6	90

Table 8: Comparison of the number of cases vs. Site of biopsy (n = 90)

Site of Biopsy	No of Cases	Percentage
Esophagus	12	13.4
Stomach	64	71.1
Duodenum	14	15.6
Total	90	100.0

Table 9: Comparison of age distribution vs. site of biopsy (n=90)

Age distribution	Site of biopsy	Duodenum	Esophagus	Stomach	Total
10-20 years	Duodenum	1	1	0	2
21-30 years	Esophagus	0	0	3	3
31-40 years	Duodenum	2	3	6	11
41-50 years	Duodenum	5	3	20	28
51-60 years	Duodenum	4	2	21	27
61-70 years	Duodenum	1	1	10	12
71-80 years	Esophagus	0	2	4	6
81-90 years	Duodenum	1	0	0	1
Total		14	12	64	90

Table 10: Frequency of various histopathological findings (n = 90).

Histopathological findings	No of Cases	Percentage
Non-specific gastritis	2	2.22
Barrett's esophagus	3	3.33
Chronic duodenitis	8	8.8
Chronic esophagitis	4	4.4
Chronic gastritis	30	33.33
Eosinophilic duodenitis	1	1.1
Hyperplastic antral polyp	2	2.2
Hyperplastic polyp of duodenum	1	1.1
Inflammatory polyp of stomach	6	6.6
Pyloric gland adenoma	2	2.22
Mild dysplasia of esophagus	3	3.33
Adenocarcinoma of esophagus	1	1.1
Moderately differentiated squamous cell carcinoma of esophagus	1	1.1
Well differentiated adenocarcinoma of stomach	14	15.5
Moderately differentiated adenocarcinoma of stomach	3	3.3
Poorly differentiated adenocarcinoma of stomach	3	3.3
Total	90	100.0

Table 11: HER-2/neu IHC score distribution in gastric adenocarcinomas

IHC Score	No of cases
+3	2
+2	0
+1	0
0	18

significant clinical implications, as it can guide endoscopic surveillance strategies and influence therapeutic approaches[10]. Additionally, understanding the specific types of lesions prevalent in different parts of the upper gastrointestinal tract can aid in the development of more precise treatment protocols.

Her-2/neu expression and its clinical relevance: The 10% positivity rate for HER-2/neu expression observed in our study is an important finding, particularly given the global range of 6-35% for this expression. The reasons behind this specific rate could be explored in terms of genetic predispositions or environmental influences. The HER-2/neu status has substantial implications for personalized treatment, especially the use of targeted therapies like trastuzumab, which can significantly improve outcomes in positive cases. Hsu *et al*.[11], Bang *et al*.[12].

Exploration of clinical parameters and their associations: The lack of a significant association between HER-2/neu status and gender or age warrants further investigation. This finding, compared with studies like those of Indu Rajagopal *et al*.[8] and Rüschoff *et al*.[13], suggests complex underlying biological mechanisms. The correlation between tumor differentiation and HER-2/neu overexpression also needs further exploration to understand its implications in tumor behaviour and treatment response[14].

Gender dynamics in gastric cancer: The higher incidence of gastric cancer in males observed in our study aligns with global trends. Investigating the role of hormonal factors, such as oestrogen, could provide insights into the protective effects against gastric cancer in females and lead to novel preventative strategies[15,16].

Critical appraisal of study limitations: Our study's limitations, including the small sample size and the exclusion of resected specimens are critical factors that might have influenced the outcomes. Future research could address these limitations by including larger

patient cohorts and a broader spectrum of specimen types to enhance the generalizability of the findings.

Future research directions and global implications: Future research should focus on larger, multicentric studies involving diverse populations to validate and expand upon your findings. The study's insights could significantly influence global clinical practices, contributing to the development of more effective diagnostic and treatment protocols for gastrointestinal malignancies.

CONCLUSION

In our study of 90 upper gastrointestinal endoscopic biopsies, chronic gastritis and well-differentiated adenocarcinoma were the most common diagnoses. Gastric carcinomas were prevalent in the 40-60 age group, predominantly among males (75%), with 65% located in the pyloric antrum. Most gastric carcinomas (70%) were well-differentiated adenocarcinomas and only 10% exhibited HER-2/neu positivity. Despite the low positivity rate, HER-2/neu assessment is crucial for therapeutic and prognostic purposes in gastric carcinoma, especially in well-differentiated adenocarcinomas of the pyloric antrum in the 40-60 age group.

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