Clinicopathological correlation of upper gastrointestinal biopsies: Experience from a tertiary hospital in Kerala

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Abstract

Background: The symptoms of upper gastrointestinal(GI) tract are often the subject of clinical consultation. Histopathology along with endoscopy remains the definitive method of diagnosing upper GI lesions. However there is a dearth of region specific data from Kerala.

Aim: To describe the histopathology of upper GI biopsies of a tertiary care hospital in Kerala and to correlate them with their endoscopic and clinical presentations.

Methods: This was a descriptive cross-sectional study in which 200 successive upper GI endoscopic biopsies were examined. The samples of tissues were treated and classified based on WHO guidelines. Other parameters observed were the *H. pylori* infection, intestinal metaplasia, atrophic changes, neutrophilic activity, parietal cell hyperplasia, and dysplastic changes. Data analysis was done using descriptive statistics and correlated with their patient records.

Results: The sample mainly included patients over 40 (80.5%), with a minor preponderance of males (1.2:1). The most common complaint was abdominal pain (48.5%), in those with antral gastritis (48.5%), and in the pyloric region (70.5%). About 70% of inflammatory lesions were attributable to chronic gastritis. Malignant neoplasms comprised 24%, which was most frequent. About 4.5% of samples had benign polyps, and 1.5% pre-malignant lesions. *Helicobacter pylori* was found in 30% cases of chronic gastritis, intestinal metaplasia was found in 7%, and dysplasia in 1.5%.

Conclusion: There was a higher incidence of inflammatory pathology, but malignancies represented a large share of cases in persons over 40 years. Early identification and management of pre-malignant changes and *H. pylori infection highlight the importance of biopsy,* emphasizing its urgency and regular follow up.

Abbreviations: EGD: Esophagogastroduodenoscopy; GERD: Gastroesophageal reflux disease; GI: Gastrointestinal; H&E: Hematoxylin & eosin; PAS: Periodic acid schiff; SCC: Squamous cell carcinoma; UGI: Upper gastrointestinal; WHO: World Health Orgnization

Introduction

One of the most common clinical manifestations that necessitates patients globally to visit healthcare facilities is upper gastrointestinal (UGI) symptoms, with the prevalence being estimated to be around 25 percent of patients who have to consult the medical institution each year [1]. Dyspepsia-related conditions, such as peptic ulcer disease, gastroesophageal reflux disease (GERD), and upper gastrointestinal neoplasms, continue to be a significant cause of gastrointestinal morbidity and mortality [2]. The most common clinical manifestations include upper abdominal pain or discomfort in 8%– 54%, heartburn and regurgitation in 10%–48% and 9%–45% of individuals respectively [3,4]. However, these clinical presentations are usually non-specific and overlap in a range of benign, premalignant and malignant entities. The correct interpretation of them requires access to the environmental exposures, dietary pattern, and other factors like immune status, hence the need for dependable diagnostic modalities.

One of the most important developments in the field of gastroenterology occurred in 1968 with the introduction of flexible fibre-optic endoscopy, which was the revolutionary form of examination in case of oesophageal, gastric and duodenal disease. [5]. The gold standard for investigating persistent or alarming upper GI symptoms is esophagogastroduodenoscopy (EGD). This is a minimally invasive procedure that allows a direct visualisation of the oesophagus, stomach and proximal duodenum, and its indications includes evaluation of dysphagia, gastrointestinal bleeding, refractory GERD, esophageal strictures, coeliac disease as well as unexplained diarrhea [6]. In addition to its diagnostic value, EGD biopsy under direct visualisation allows the use of histopathological evaluation which is more sensitive for identifying mucosal pathology compared to imaging modalities [7,8]. It is particularly helpful in the detection of inflammatory diseases like oesophagitis, gastritis, and duodenitis and vascular malformations, Mallory-Weiss tears, and early neoplasia.

Although EGD would provide correct visualisation of the mucosal abnormalities, endoscopic impressions on their own might not be reliable in definitive diagnosis. Certain nonneoplastic and premalignant changes may resemble malignancies and some neoplastic lesions may resemble benign conditions. Therefore, histopathology of biopsy samples is essential in differentiating inflammatory, benign, premalignant, and

malignant ones [9]. Combined use of endoscopic and histopathological data is useful in the early detection, therapeutic decision making, and prognostic evaluation. It has been noted in numerous studies that there is a need to correlate endoscopic observations with histopathological verification in order to obtain diagnostic accuracy and the best management options for patients [10–15].

Jonnalagadda, et al. reports that endoscopic biopsy and histopathology is one of the most effective modalities that can be used to diagnose neoplastic and non-neoplastic lesions, especially malignancies, which enhances clinical outcomes[16]. Rauta and associates observed that non-neoplastic lesions are commonly diagnosed by increased use of histopathological diagnosis, despite the fact that malignant growths can be easily identified on endoscopy, which supports the diagnostic usefulness of endoscopy [17]. On the same note, Gunay and coauthors investigated the correlation between clinical and histopathological diagnosis and found that upper GI endoscopy is advisable with at least one of the red flag symptoms, but empirical treatment may be considered in younger patients who do not have the red flag symptoms [18]. These among other similar studies emphasise the significance of combining endoscopy and histopathological evaluation, particularly with the early detection of neoplastic change [19–21].

Though this is the case, there are still gaps that exist. A good part of what has been published in India and other neighbouring countries focuses on clinical or endoscopic appearances without correlating with histopathological diagnoses. Specifically, there are limited data from Kerala, despite the fact that the area has unique demographic and dietary patterns that can shape the manifestation of the disease. In addition, whereas the malignant lesions have been widely studied, there is a paucity of reports that describe the entire range of non-neoplastic and premalignant lesions that are essential in cancer prevention. Past research has also had limitations of small sample sizes or non-standardised histopathological parameters thus reducing comparability. By demonstrating such gaps, there is a need to incorporate region specific data that combine clinical presentation, endoscopic appearance, and histopathological observations to enhance the characterisation of upper GI pathology in the usual practice.

Considering these gaps, the current research was conducted to describe the histopathological range of upper GI biopsies in a tertiary care hospital in Kerala and to compare the results with the clinical presentation and endoscopic finding. The study will generate region-specific data to improve the diagnosis of diseases earlier, make clinical decisions, and guide surveillance measures for non-neoplastic and neoplastic diseases in the upper GI by integrating demographic, clinical, endoscopic, and histopathological data.

Materials and methods

Study design

The research is a descriptive cross-sectional study that is conducted following the STROBE reporting guidelines [22]. The main purpose was to define the range of histopathological lesions, which were detected in upper gastrointestinal (GI) biopsies and to determine their relations with clinical symptoms and endoscopic changes.

Study setting and duration

It was conducted in the Department of Pathology in a tertiary referral centre in Kerala over a period of 1 year from November 2022 to November 2023. The endoscopy unit of the hospital serves a heterogeneous group of patients across the central zone of Kerala, hence covering a wide range of upper GI disorders.

Ethical considerations

The study commenced after getting approved by the Institutional Ethics Committee. The additional tissue section examination did not charge any financial strain on the patients. The entire process was carried out in line with the institutional and national ethical guidelines of biomedical research. Anonymisation of patient information was done and data was only used in academic and clinical research. Informed consent was also taken according to institutional protocol during the time of biopsy.

Study population

The target population of the study consisted patients of all age group and gender with upper GI symptoms and endoscopic biopsy during the study period. All the specimens obtained were of the esophagus, esophagogastric junction, stomach and proximal duodenum. The cases not included in the study were those in which tissues were insufficient to carry out a histopathological examination.

Sample size and sampling

The sample size was calculated using the formula $n = 4pq/d^2$. Drawing on the prevalence of malignant lesions reported by Veerendrasagar, et al. [23] a prevalence (p) of 0.68 was adopted, with $q = 1 − p = 0.32$ and a margin of error (d) of 10 % (p = 0.068). Replacement of these values produced $n = 4* 0.68* 0.32/ 0.068^2 = 188$; 200 was therefore selected as a sample size. Two hundred upper GI biopsy samples in a sequence that met the inclusion and exclusion criteria were analyzed, utilizing consecutive sampling method to reduce selection bias.

Data collection

Patient records were used to extract clinical and demographic data, such as age, sex and presenting symptoms. Contemporary findings of endoscopy including biopsy site and appearance of the macroscopic lesions were recorded. All data were keyed in a tabulated proforma designed specifically to conduct this research.

Laboratory methods

Biopsy specimens were fixed in 10 % buffered formalin, underwent routine processing, and were embedded in paraffin wax. Sections were cut at 4-5 micrometer thickness, following which staining with haematoxylin and eosin (H&E) was done in accordance with the conventional histopathological procedures [24]. Appropriate special stains were used: *Helicobacter pylori* demonstrated with Giemsa or Warthin-Starry and intestinal metaplasia with periodic acid-schiff (PAS) or alcian blue [25-28]. Quality control was done using departmental policies such as verifying duplicate slides in instances of diagnostic doubt.

Variables and measures

The main outcome variable was the histopathological diagnosis of biopsy specimens and the explanatory variables were the patient demographics, presenting symptoms, endoscopic findings and the site of biopsy. The classification of lesions according to the WHO classification of tumours of the digestive system was inflammatory, benign neoplastic, premalignant, and malignant [29]. Inflammatory lesions were classified further as acute or chronic, or chronic active gastritis; intestinal metaplasia or dysplasia were defined as premalignant lesions, whereas malignant lesions were categorised using established histological criteria of upper GI tumours. Others noted were *Helicobacter pylori* infection, neutrophilicactivity, atrophy, and parietal cell hyperplasia.

Table 1. Additional histological features and clinico–pathological correlation (n = 200)

Endoscopic finding	n (%)	Site of biopsy	n (%)	Category	Diagnosis	n (%)
Antral/ periantral gastritis	97 (48.5)	Pylorus (including antrum/ canal)	141 (70.5)	Inflammatory (70.0)	Chronic gastritis	139 (69.5)
Ulceroproliferative growth	44 (22.0)	Body of stomach	19 (9.5)		Chronic inflammation	3 (1.5)
Normal study	18 (9.0)	Oesophagus	18 (9.0)	Benign neoplasms (4.5)	Hyperplastic polyp	6 (3.0)
Polyp/nodule	9 (4.5)	Gastroesophageal junction	11 (5.5)		Fundic gland polyp	2 (1.0)
Submucosal swelling	7 (3.5)	Cardia	1 (0.5)		Tubular adenoma	1 (0.5)
Pangastritis	6 (3.0)	Fundus	7 (3.5)	Premalignant (1.5)	Intestinal metaplasia/dysplasia	2 (1.0)
Atrophic gastritis	3 (1.5)	Duodenum (D1)	3 (1.5)		Barrett's oesophagus with dysplasia	1 (0.5)
Biliary gastritis	3 (1.5)			Malignant (24.0)	Gastric adenocarcinoma	31 (15.5)
Gastric outlet obstruction	2 (1.0)				Oesophageal squamous cell carcinoma (SCC)	15 (7.5)
Duodenitis	1 (0.5)				Carcinoma with neuroendocrine differentiation	1 (0.5)
					Gastrointestinal stromal tumour (GIST)	1 (0.5)
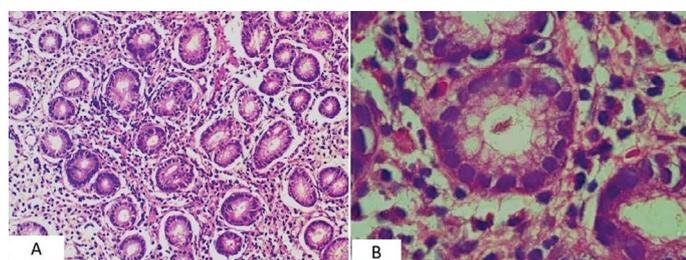
Figure 1. (A – B). Histological features of inflammatory lesions. (A) Chronic gastritis showing dense mononuclear infiltrates in the lamina propria (H&E, 200×). (B) Chronic gastritis with Helicobacter pylori organisms adherent to the gastric epithelium (H&E, oil immersion).

Statistical analysis

The information was recorded and stored in Microsoft Excel sheets. Descriptive statistics were used, and the categorical variables, including demographic characteristics, clinical symptoms, endoscopic results, and histopathological diagnoses were summarised with the help of frequencies and percentages. The continuous variables such as the age was represented in terms of means with standard deviations. Such variables as age group, sex, presenting symptoms (dysphagia, reflux, dyspepsia, abdominal pain, nausea/vomiting, anorexia/weight loss, haematemesis/melena), biopsy site, type of lesion, presence of *Helicobacter pylori*, and histological variables (intestinal metaplasia, neutrophilic activity, atrophy, parietal cell hyperplasia, dysplasia) were also analysed. Besides, categorisation and quantification of endoscopy findings were also done. All findings were tabulated and the graphical forms of the same showed the distribution of these variables. Statistical tests were carried out in JAMOVI 2.5.3 at p 0.05.

Results

The study cohort comprised of 200 patients. Majority (80.5%) were aged above 40 years, with a mean age of 54.1 ± 12.2 years. The cohort was slightly male dominant with 111 males (55.5%) and 89 females (44.5%) producing a male to female ratio of 1.2:1.

The most frequent presenting symptom, reported by 97 patients (48.5%), was abdominal pain. This was followed by dyspepsia observed in 51 patients (25.5%), and dysphagia in 29 patients (14.5%). In 22 patients (11%) reflux was reported, in 34 patients (17%) nausea or vomiting, in 20 patients (10%) anorexia or weight loss, and in 18 patients (9%) haematemesis or melena. A hundred and thirty-five patients (67.5%) reported a single symptom, and 65 (32.5%), experienced multiple symptoms.

The most common endoscopic finding was antral/perinatal gastritis, followed by ulceroproliferative growths. Only a few patients showed duodenitis or gastric outlet obstruction and a minority of patients had normal studies. Pylorus was the major location of biopsy, and oesophageal and duodenal samples were underrepresented (see Table 1).

The histological findings found were mainly due to inflammatory lesions, which comprised 70 percent of all the biopsies, mostly representing chronic gastritis. Malignant lesions constituted 24% of cases, the most common type of which was gastric adenocarcinoma, and then squamous cell carcinoma of the oesophagus. Benign neoplasms were gastric polyps (4.5%), and the premalignant changes were rare (1.5%), which comprised of intestinal metaplasia, dysplasia, and Barrett's oesophagus with dysplasia (see Table 2, Figures 1 and 2).

Helicobacter pylori was identified in 60 cases (30%) among patients with chronic gastritis. Intestinal metaplasia was seen in 14 cases (7%) and neutrophilic activity was seen in 23 cases (11.5%). Less common were features of atrophy (1%), parietal-cell hyperplasia (2.5%), and dysplasia (1.5%). These histological changes were all related to chronic gastritis only (see Table 3).

The most common cases of chronic gastritis were found in patients who presented with abdominal pain and dyspepsia, and related in many cases to biopsies that were taken in the pylorus. A strong relationship was shown between malignant lesions and older age; (the lesions were observed in patients over 40 years old and with a strong male predominance with a male-to-female ratio of 3:1. Ulceroproliferative growths had nearly a perfect correlation with malignant histology by endoscopy, whereas antral/periantral gastritis was associated with inflammatory lesions (see Table 3, Figures 3-5).

Discussion

This study aimed to characterise the spectrum of histopathological lesions most frequently identified in upper gastrointestinal biopsies at a tertiary care centre in Kerala, and to evaluate how these diagnoses correlate with the patients' clinical presentations and endoscopic findings.. The statistics indicate that chronic gastritis was the dominant element of the inflammatory spectrum after which malignant neoplasms (mainly gastric adenocarcinomas and oesophageal squamous cell carcinomas) constituted about a quarter of all the cases. Premalignant changes like areas of intestinal metaplasia and Barrett's oesophagus with dysplasia were not common, but clinically important. Most of the patients were above 40 years in age, there was a slight dominance of males and the most common presenting symptom was abdominal pain.

Table 2. Distribution of histopathological diagnoses (n = 200)

Category	Diagnosis	n (%)
Inflammatory (70.0)	Chronic gastritis	139 (69.5)
	Chronic inflammation	3 (1.5)
Benign neoplasms (4.5)	Hyperplastic polyp	6 (3.0)
	Fundic gland polyp	2 (1.0)
	Tubular adenoma	1 (0.5)
Premalignant (1.5)	Intestinal metaplasia/dysplasia	2 (1.0)
	Barrett's oesophagus with dysplasia	1 (0.5)
Malignant (24.0)	Gastric adenocarcinoma	31 (15.5)
	Oesophageal squamous cell carcinoma (SCC)	15 (7.5)
	Carcinoma with neuroendocrine differentiation	1 (0.5)
	Gastrointestinal stromal tumour (GIST)	1 (0.5)

Table 3. Additional histological features (n = 200)

| Feature	Associated pathology	n (%)
Helicobacter pylori	Present in chronic gastritis	60 (30.0)
Intestinal metaplasia	Chronic gastritis	14 (7.0)
Neutrophilic activity	Chronic gastritis	23 (11.5)
Atrophy	Chronic gastritis	2 (1.0)
Parietal cell hyperplasia	Chronic gastritis	5 (2.5)
Dysplasia	Chronic gastritis	3 (1.5)
Abdominal pain	Chronic gastritis (pylorus)	Inflammatory > neoplastic
Dyspepsia	Chronic gastritis (pylorus)	Often non-specific
Dysphagia	Oesophageal SCC / GEJ adeno	Strong malignant association
Reflux symptoms	Chronic gastritis / Barrett's	Premalignant changes rare
Ulceroproliferative growth	Adenocarcinoma / SCC	High predictive value
Antral/periantral gastritis	Chronic gastritis	Strong correlation
Abdominal pain	Chronic gastritis (pylorus)	Inflammatory > neoplastic
Dyspepsia	Chronic gastritis (pylorus)	Often non-specific
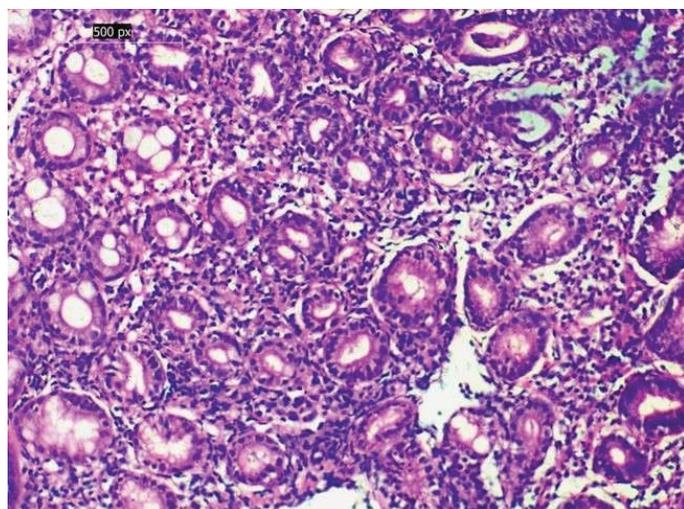
Figure 2. Premalignant change in chronic gastritis. Chronic gastritis with intestinal metaplasia, characterised by replacement of gastric epithelium by intestinal-type columnar cells with goblet cells (H&E, 400×)

Endoscopic analysis showed that antral gastritis was predominant and the pyloric region was the most frequent location of biopsy. *H. pylori* were also found to be a positive etiologic agent in gastric pathology, with approximately a third of chronic gastritis cases being positive.

The cohort was mainly composed of persons over 40 years (80.5%), with a high male preponderance. These finding agree with other recent Indian research findings that also demonstrated a greater occurrence of upper GI pathology in middle-aged and elderly adults, with a male predominance in both inflammatory and malignant lesions [2,16,30]. The commonest symptom was abdominal pain, which was followed by dyspepsia and dysphagia as in Rana et al. and Gunay et al. [1,18]. These observations reiterate the fact that nonspecific symptoms often cloud out major pathology and hence the importance of biopsy in symptomatic patients, especially above 40 years.

The most typical biopsy site was the pylorus (70.5%), as the percentage of patients who reported abdominal pain and dyspeptic symptoms was high. Antral gastritis was the most frequent endoscopic finding with almost half the patients having this condition. Other Indian series show better proportions of oesophageal biopsies [17,20]. These regional variations would probably be variations in patterns of referrals, diet, and exposure to risk factors.
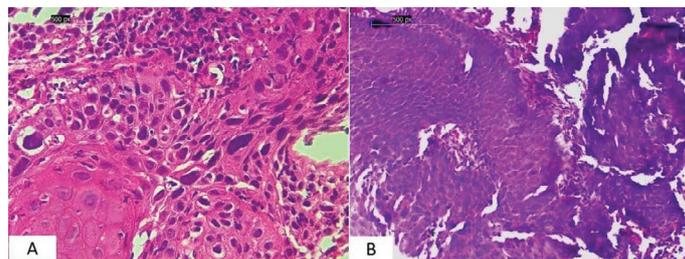
Figure 3. (A – B). Oesophageal squamous cell carcinoma. (A) Well-differentiated squamous cell carcinoma with keratin pearl formation (H&E, 400×). (B) Poorly differentiated squamous cell carcinoma showing marked pleomorphism and high mitotic activity (H&E, 200×)
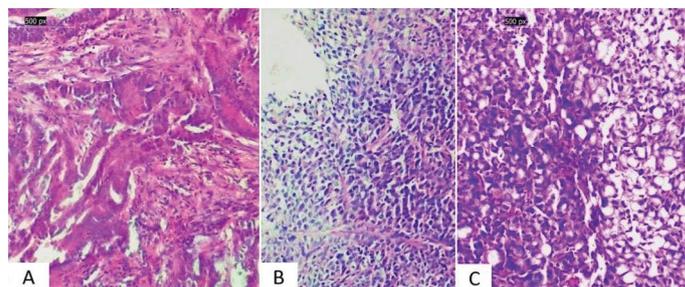
Figure 4. Gastric adenocarcinoma spectrum. (A) Gastric adenocarcinoma showing glandular architecture (H&E, 200×) (B) Poorly cohesive adenocarcinoma with loss of gland formation (H&E, 200×) (C) Signet ring cell carcinoma characterised by intracytoplasmic mucin displacing the nucleus (H&E, 200×)
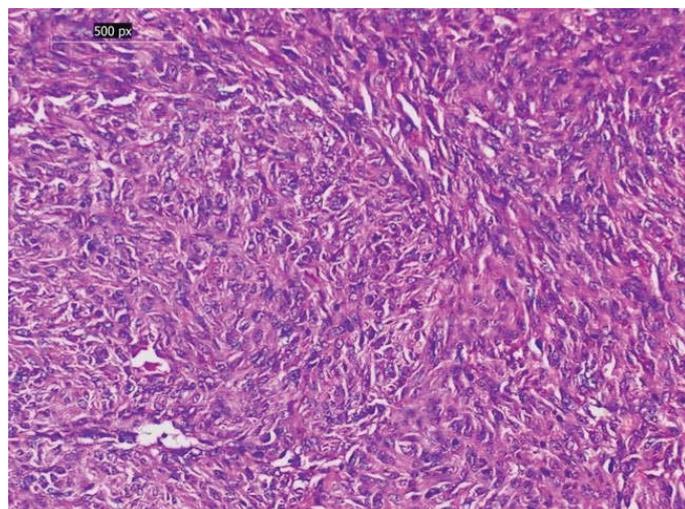
Figure 5. Gastrointestinal stromal tumor (GIST). Proliferation of spindle-shaped cells arranged in fascicles, consistent with GIST (H&E, 200×)

Histopathological diagnosis revealed inflammatory lesions (70%), and chronic gastritis was the most common subtype (97.8%). This trend is consistent with the findings of other Indian cohorts and studies in the region where gastritis is the most common biopsy result [2,19]. *H. pylori* has been detected in about a third of chronic gastritis which is similar to South Asian studies, but lower than global prevalence estimates which frequently exceeds 50% [21,26]. The regional differences in prevalence might reflect the advances in sanitation, nutrition, exposure to antibiotics, and the diagnostic techniques. Notably, other features such as intestinal metaplasia, neutrophilic activity, and atrophy were also detected, thus highlighting their contribution to the cascade of Correa towards gastric carcinogenesis [27,28].

The proportion of benign lesions were 4.5% of biopsies, and all were presented in the form of polyps or nodules on endoscopy. Hyperplastic polyps had the highest rate than fundic gland polyps and tubular adenomas as per the distribution by Jonnalagadda, et al. and Rani, et al. [16, 15]. Premalignancies were infrequent (1.5%), but seemed to have clinical importance, such as Barrett oesophagus with dysplasia, and chronic gastritis with underlying foci of dysplasia. This proportion is lower than some studies conducted in India and the West, but lack of systematic sampling as per the Sydney protocol might have led to under-detection [11,12]. Given the established progression of intestinal metaplasia and Barrett's oesophagus to carcinoma, these lesions warrant close post-diagnostic surveillance.

At least 24% of the cases were diagnosed with malignancies, mostly in patients who were of age over 40 years, and in males. The most common neoplasm was gastric adenocarcinoma, which is followed by oesophageal squamous cell carcinoma and gastroesophageal junction adenocarcinoma. This distribution reflects regional epidemiological patterns, with gastric adenocarcinoma remaining highly prevalent, while squamous cell carcinoma continues to predominate among oesophageal cancers [31,32]. The histological subtyping showed that the majority of gastric cancers were adenocarcinomas, including poorly cohesive carcinomas with signet ring morphology, which was not the first time that consonant results were obtained in India [2,19]. The fact that all the oesophageal SCCs were presented as ulceroproliferative lesions, with the majority being moderately differentiated, is consistent with those by Jonnalagadda, et al. [16], and Rauta, et al. [17]. These correlations between endoscopic appearance and histologic subtype can be used to give useful hints at early suspicion and directed biopsy.

The finding that *H. pylori* has remained relevant in gastric pathology and that eradication therapy has a role to play in reducing long-term risks of ulceration and malignancy is supported by the fact that it has been identified in a significant proportion of cases. In addition to this, the premalignant changes though rare in occurrence have been detected which underscores the need to have systematic biopsy procedures and follow-up measures which will enable timely intervention. To clinicians in Kerala and similar environments, the findings recommend caution in the assessment of dyspeptic patients especially those who are above 40 years and those who exhibit persistent or numerous symptoms.

This study has some strengths such as its real-life design, consecutive sampling and systematic correlation of histopathology, clinical presentation and endoscopic information. Weaknesses include small sample size compared to the overall number of biopsies done within the institution, non-systematic sampling in terms of the Updated Sydney System, and no follow-up of premalignant lesions. The study is a single-centre study, and the results might not be applicable to the wider population.

Future studies would include multicentric cohorts, increase sample sizes and standardised biopsy procedures in order to improve the detection of premalignant conditions. It is recommended that longitudinal follow-up of patients with intestinal metaplasia patients or those with Barrett's oesophagus be done in an attempt to gain a better understanding of the progression to malignancy. Moreover, the risk of the disease in various regions could be further explained by molecular investigations of *H. pylori* strains and host susceptibility factors.

Conclusion

Finally, the histopathology of upper GI biopsies in this Kerala cohort is almost entirely dominated by inflammatory lesions, especially chronic gastritis, but malignant lesions represent a significant burden. Although they are less prevalent, benign and premalignant lesions are still clinically significant with regard to cancer prevention. These results highlight the importance of histopathology as being an indispensable component of clinical and endoscopic assessment, early detection of neoplastic change, and a method of determining the correct approach to patient management when the patient presents with upper GI symptoms.

Acknowledgement

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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