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Original Article

Histopathological Evaluation of Gastric Biopsies and its Association with Endoscopic Findings

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ABSTRACT

Introduction: Gastrointestinal disorders include a range of conditions, both non-neoplastic and neoplastic, contributing to significant global morbidity and mortality. The prevalence of these gastric diseases exhibits geographical variability. Endoscopy has been proven to be a breakthrough in the diagnosis of gastric lesions, but histopathology is considered the gold standard. This study aims to shed light on the occurrence of diverse patterns of non-neoplastic and neoplastic gastric diseases in patients undergoing endoscopic biopsies at Patan Hospital.

Materials and methods: This cross-sectional study, conducted over 1 year in the Department of Pathology, Patan Academy of Health Sciences, included 117 patients undergoing endoscopic gastric biopsies.

Results: A diverse range of gastric diseases was observed across a broad age spectrum, spanning from 18 to 85 years, with a mean age of 57.2 years and a female preponderance of 0.7:1. Biopsy samples from the antrum constituted the majority at 55.6%. The prevalence of H. pylori was 20.5%. There was a statistically significant association between endoscopic findings and histopathological diagnosis (p-value <0.05) despite some discrepancies.

Conclusions: The association between endoscopic findings and histopathological diagnoses is robust, demonstrating high sensitivity and specificity. Based on the outcomes of this study, it can be inferred that the rationale behind targeted endoscopic biopsies is well-founded. Nevertheless, it is crucial to emphasize that endoscopy alone is insufficient, and the inclusion of biopsy and histopathology is imperative.

Keywords: Endoscopy; Gastric biopsy; Gastric diseases; Helicobacter pylori

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INTRODUCTION

Gastrointestinal disorders encompass a spectrum of conditions within the gastric region, ranging from non-neoplastic to neoplastic ailments contributing significantly to global morbidity and mortality rates. [1-3] Clinical encounters often involve a myriad of gastric epithelial lesions, such as gastritis, peptic ulcers, proliferative non-neoplastic polyps, and various non-invasive neoplastic entities, including dysplasia, adenomas, and invasive carcinoma exhibiting geographical variability.[1,4] *Helicobacter pylori* infection, affecting over half of the world's adult population, stands as a primary factor in the development of various gastric diseases.[1,5,7] The prevalence is variable among Asian countries with a reported prevalence of 30-70% in Nepal.[5,6]

Endoscopy provides an opportunity to visualize the mucosal surface of the gastrointestinal tract and has proved to be a major breakthrough in the diagnosis of gastric lesions.[2,3] Endoscopy is incomplete without biopsy and histopathology is the gold standard for the confirmation of diagnosis.[1,5,7] Histopathological study not only provides information regarding early pathological changes but also helps in monitoring the course, determining the extent of disease and response to therapy.[6,8,12] Few studies done in tertiary care centers of Nepal showed that endoscopic findings of benign gastric lesions poorly correlated with the histopathological diagnoses in comparison to malignant lesions.[6,9]

In PAHS only targeted endoscopic biopsies are taken from the suspicious lesion and sent for histopathological evaluation. This study aims to provide insight into the incidence of different patterns of non-neoplastic and neoplastic gastric diseases among patients undergoing endoscopic biopsies in Patan Hospital. It will provide baseline data for further in-depth study of various gastric pathologies. Based on the findings of the study we will be able to say whether or not a targeted endoscopic biopsy is justified.

MATERIALS AND METHODS

This is a cross-sectional study conducted over 1 year from 4th May 2022 to 4th May 2023 in the Department of Pathology, Patan Academy of Health Sciences, a tertiary care hospital in Lalitpur, Nepal including 117 patients undergoing endoscopic biopsies. Sample size was calculated using prevalence formula.[10] This study aimed to provide insight into the incidence of different patterns of non-neoplastic and neoplastic gastric diseases among patients undergoing endoscopic biopsies in Patan Hospital. Autolyzed samples, unlabeled samples, and patients refusing to give consent were excluded.

The study was conducted with the necessary ethical considerations and received approval from the Institutional Review Committee (IRC) of PAHS with reference number PML2205031612. Informed consents were obtained from all participants who willingly agreed to take part in the research.

The received endoscopic biopsy samples in 10% neutral buffered formalin were assigned a unique histopathology number. Overnight fixation in the 10% formalin was done followed by grossing as per the small biopsy grossing protocol. The tissues were subjected to tissue processing in automated Histokinet (Medite) for 12 hours. The paraffin embedding was done the following day and the blocks were prepared. Trimming was done followed by cutting sections of 4 microns by semi-automated rotatory microtome (HMM5E) and all the prepared slides were stained by Hematoxylin and Eosin stain as well as Giemsa stain. A special stains were done whenever required. The prepared slides were evaluated under a light microscope and *H. pylori* was screened in oil immersion.

The collected data were entered in EPI-INFO and analyzed in EPI-INFO and Easy R software. The categorical variables were presented in frequency and percentage (%). The chi-square test was used to find the association between categorical variables. P values of < 0.05 were considered statistically significant. Sensitivity, specificity, and predictive values between endoscopic findings and histopathological diagnosis of non-neoplastic and neoplastic gastric diseases were calculated using respective formulas.

RESULTS

In this study, a total of 117 patients who underwent endoscopic biopsies were included. The age of the patients ranged from 18 to 85 years, with a mean age of 57.2 years. A significant majority, accounting for 100 (85.5%) of the patients with gastric diseases, were above the age of 40 years. Out of the 117 patients, 51(43.59%) individuals were male, and 66(56.41%) individuals were female. This distribution resulted in a male-to-female ratio of 0.7:1.

During the endoscopic procedure within the study population, the predominant portion of patients—specifically, 100(85.47%) individuals showed non-neoplastic findings. Conversely, 17(14.53%) patients were diagnosed with neoplastic findings, as detailed in Table 1.

Table 1. Endoscopic findings of non-neoplastic and neoplastic gastric diseases

Endoscopic findings		Frequency (%)
Non-neoplastic	Normal	2 (1.7%)
	Erosion	19(16.2%)
	Erosion with gastropathy	1(0.9%)
	Erythema	28(23.9%)
	Atrophy	1(0.9%)
	Ulceration	20(17%)
	Nodular gastritis	2(1.7%)
	Polyp	25(21.4%)
	Hemorrhagic gastropathy	1(0.9%)
	Pangastritis	1(0.9%)
Neoplastic	Suspicious growth	1(0.9%)
	Ulcero-proliferative growth	2(1.7%)
	Ulcerative growth	6(5.1%)
	Linitis plastica	1(0.9%)
	Malignant growth	7(5.9%)
Total		**117(100%)**

The histopathological evaluation of the study population indicated a predominant diagnosis of non-neoplastic diseases in 101(86.32%) patients and neoplastic diseases in 16(13.68%) patients, as outlined in Table 2. The most common non-neoplastic disease was chronic gastritis, identified in 73 (62.38%) patients, followed by polyps, noted in 19(16.23%) patients. Among patients undergoing endoscopic biopsies, the prevalence of *H. pylori* was determined to be 20.5%. Figure 1 depicts chronic active gastritis associated with *H. pylori*, and the presence of micro-organisms is highlighted in the Giemsa stain. To investigate the association between *H. pylori* infection and the degree of acute and chronic inflammation, the Chi-square test was employed. The obtained p-values were < 0.05, indicating statistical significance.

Table 2. Histopathological findings of non-neoplastic and neoplastic gastric diseases with subgroupings

Histopathological diagnosis			N (%)
Non-neoplastic	**Gastric mucosa within normal limit**		2(1.71%)
	Chronic Gastritis	Chronic inactive gastritis	32(27.35%)
		Chronic active gastritis	8(6.84%)
		Chronic atrophic gastritis	3(2.56%)
		H. Pylori associated gastritis	24(20.51%)
		Chronic gastritis with intestinal metaplasia	5(4.27%)
		Chronic eosinophilic gastritis	1(0.85%)
	Gastropathy		1(0.85%)
	Polyp	Hyperplastic polyp	9(7.69%)
		Fundic gland polyp	9(7.69%)
		Inflammatory polyp	1(0.85%)
	Ulcerative lesion		5(4.27%)
	Parietal cell hyperplasia		1(0.85%)
Neoplastic	**Dysplasia**		2(1.71%)
	Adenoma		1(0.85%)
	Malignancy	Suspicious of adenocarcinoma	1(0.85%)
		Well-differentiated adenocarcinoma	1(0.85%)
		Moderately differentiated adenocarcinoma	3(2.56%)
		Poorly differentiated with signet ring	7(6%)
		Undifferentiated neoplasm	1(0.85%)
Total			**117**

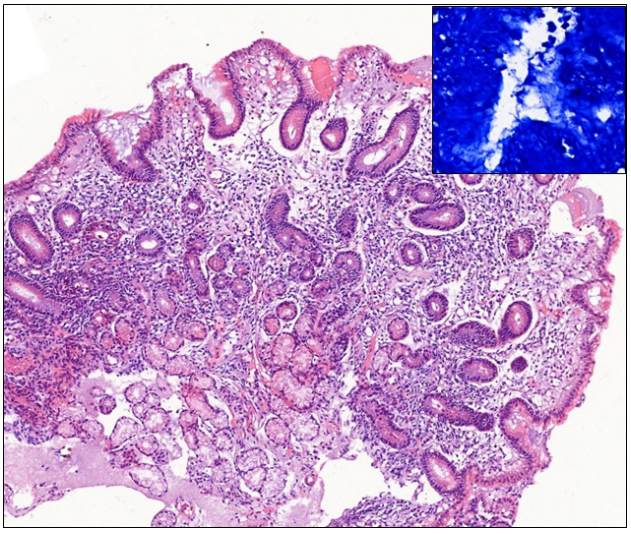

Figure 1: H. pylori associated chronic active gastritis (H&E, X10), inset showing H. pylori organism (Giemsa stain, X100)

The histopathological characteristics of neoplastic gastric disease were classified into dysplasia, adenoma, and malignancy, with their respective frequencies detailed in Table 2. Among these, adenocarcinoma emerged as the most frequently encountered gastric malignancy, particularly in the antrum. The prevailing form of adenocarcinoma observed was poorly differentiated, featuring a signet ring component, as illustrated in Figure 2. The distribution of both non-neoplastic and neoplastic gastric diseases based on anatomical site is presented in Figure 3.

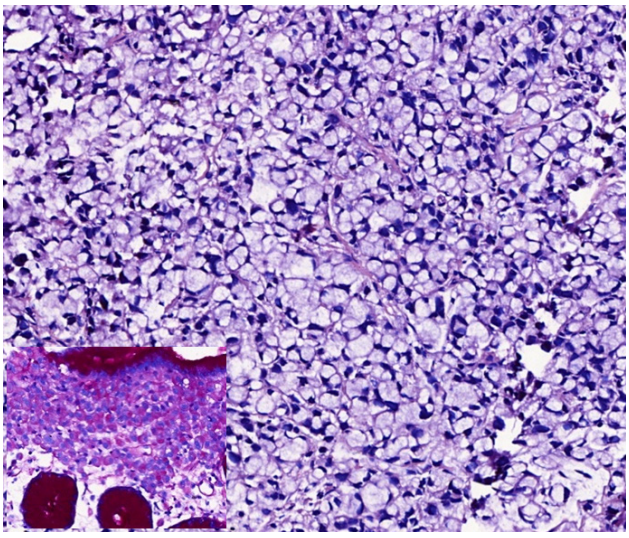

Figure 2: Poorly differentiated adenocarcinoma with signet ring component (H&E, x40), Inset showing PAS stain positive signet ring cells, (x40)

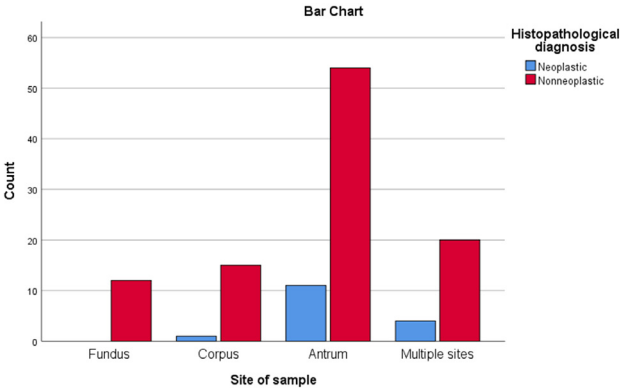

Figure 3: Bar diagram representing distribution of non-neoplastic and neoplastic gastric diseases as per anatomical site

The endoscopic evaluation identified 100 cases of non-neoplastic gastric diseases. Upon histopathological evaluation, 97(82.9%) cases were confirmed as non-neoplastic gastric diseases, while 3(2.6%) cases were diagnosed as neoplastic diseases. Similarly, among the 17 cases diagnosed as neoplastic by endoscopic evaluation, 13 cases were confirmed as neoplastic, while 4 were diagnosed as non-neoplastic gastric diseases as shown in Table 3. The sensitivity was 81.3%, specificity was 96%, positive predictive value was 76.4% and negative predictive value was 97%.

Table 3. Association of endoscopic findings with the histopathological diagnosis of non-neoplastic and neoplastic gastric diseases.

Endoscopic findings	Histopathological diagnosis			Chi-square (p-value)
	Neoplastic n (%)	Non-neoplastic n (%)	Total n (%)	
Neoplastic	13(11.1%)	4(3.4%)	17(14.5%)	0.001
Non-neoplastic	3(2.6%)	97(82.9%)	100(85.5%)	
Total	**16(13.7%)**	**101(86.3%)**	**117(100%)**	

DISCUSSION

A range of gastric conditions was observed across a broad age spectrum, spanning from 18 to 85 years, with an average age of 57.2 years. This aligns with findings from related studies, indicating mean age groups of 53.2 (Nazrin et al)[1], 52.52 (Poudel et al)[11], and 52 years (Hirachand et al)[12]. The variations in age might be attributed to diverse exposures to risk factors among distinct age groups. A significant proportion 100(85.5%) of patients with gastric ailments belonged to the age group above 40 years, consistent with findings from prior research studies.[2–4]

This study has revealed a slight predominance of gastric diseases in females, with a male-to-female ratio of 0.7:1. This aligns coincidently with the findings of Hussein et al, where the male-to-female ratio was 1:1.3 and it may be due to the role of various factors like diet, hormones and sensitivity of gut to stress.[13] In contrast, several prior studies, including those by Sharma et al[6]upper GI bleeding were included from August 2004 to August 2008. Results: A total of 2761 patient were evaluated, with mean age group of 40.57 years (range 8- 95 years with a male-to-female ratio of 1.4:1, Nazrin et al[1] with a ratio of 1.5:1, and Hirachand et al[12] with a ratio of 1.76:1, reported a higher prevalence among males.

In this study, targeted endoscopic biopsies were predominantly taken from the antrum (55.6%). The antrum was identified as the most common site of gastric diseases, consistent with findings from studies by Hussein et al[13], Bhattarai et al[14], Barad et al[15] and H Ganga et al[16]. The updated Sydney system, which offers guidelines for generating systematic, uniform diagnostic reports, recommends biopsies from five different sites, including two from the antrum, two from the body, and one from the incisura angularis. Biopsies from the incisura angularis are emphasized in the updated system due to its susceptibility to chronic inflammation and premalignant changes like intestinal metaplasia and atrophy.[17]

Among the 117-study population undergoing endoscopic procedure, non-neoplastic findings 100(85.5%) were more common than the neoplastic findings 17(14.5%) which is in concordance with the studies of Hirachand et al[12], H Ganga et al[16]. The most common non-neoplastic endoscopic findings were erythema (23.9%) followed by polyps (21.4%) and erosion (16.2%) whereas the most common neoplastic endoscopic findings were malignant growth (6%) followed by ulcerative growth (5.1%) and ulceroproliferative growth (1.7%).The endoscopic findings are variable in comparison to the other studies.[2–4] It may be because of multiple personnel involved in the endoscopic procedures, may be due to variation in the reporting pattern as per the institute and may be due to lack of submission of tissues for histopathological evaluation.

As per the histopathological evaluation, the most prevalent non-neoplastic diagnosis was chronic gastritis noted in 73(62.3%) patients and polyps noted in 19(16.2%). Among the varieties of chronic gastritis, chronic inactive gastritis was the most frequent diagnosis noted in 32(27.4%) patients followed by *H. pylori* associated gastritis noted in 24(20.51%) patients. The finding is variable in comparison to the study of Hirachand et al[12] where chronic active gastritis was the most common gastritis accounting to 35.16%. The variation in the result could be due to the limited sample size of the study population.

The prevalence of *H. pylori* organisms was 20.51% which is lower in comparison to various previous studies conducted by Shrestha et al(68%)[5], Poudel et al(41.8%)[11], M et al(43%)[18]. This is at the lowest end of the range earlier reported in our country with two possibilities. The previous studies showed wide variation in the prevalence of *H pylori* ranging from 30-80%.[5,6] A retrospective study done in Nepal in 2005 showed that the prevalence of *H. pylori* was 33.9% with a sample size of 224 in dyspeptic patients attending the hospital.[19] The finding was almost similar with slightly decreasing prevalence by 4.5% in another study done in tertiary hospital of Nepal in 2013 with *H. pylori* prevalence of 29.4% with a sample size of 2820.[20] One of the possibilities could be an indication that the prevalence of *H. pylori* in local setup might not be very high as was projected from a decade old data. This could be due to the development of the 'westernization' of the life style or use of proton pump inhibitors or antibiotics.

H. pylori organisms can be identified through both non-invasive and invasive diagnostic techniques. Non-invasive methods encompass serology, urea breath test, and stool antigen test. Invasive techniques involve endoscopic biopsies, rapid urease test, and culture.[8,9] The lower prevalence of *H. pylori* among patients undergoing endoscopic biopsies at Patan Hospital might be attributed to several factors. One possibility is that many patients with dyspeptic symptoms are initially assessed for *H. pylori* using non-invasive techniques, such as the urea breath test. Additionally, even when endoscopy is performed, biopsies may not be taken from areas with normal mucosa, contributing to the lower observed prevalence during endoscopic evaluations.

H. pylori-negative chronic active gastritis was observed in 8% of cases, a finding consistent with the study conducted by Hirachand et al.[12] This occurrence might be attributed to the prolonged use of proton pump inhibitors by the study population before undergoing endoscopic biopsy or the potential challenges in detecting *H. pylori* in tissue specimens, given its patchy colonization of the gastric mucosa. In routine practice, it is recommended to employ at least two staining methods for *H. pylori* diagnosis, typically using H&E stain and Giemsa stain. Giemsa stain, commonly used in routine practice, is favored for its simplicity, consistency, higher sensitivity, and cost-effectiveness. However, it is important to note that it is associated with interobserver variability. On the other hand, immunohistochemistry, a more specific technique with less interobserver variability, is not commonly used in day-to-day practice due to various limitations. These limitations include higher costs, which pose a financial burden to patients,

longer turnaround times, and dependence on the skills of the operator.[8,9]

In this study, second most common histopathological non-neoplastic finding was gastric polyp. Out of 15 non-neoplastic gastric polyps, 7 were hyperplastic polyps, 7 were fundic gland polyps and 1 was inflammatory polyps which is variable in comparison to other published studies. In Camarack et al study[21], hyperplastic polyps (77%) were more common than fundic gland polyps (17%) which is in contrast to the study of Sherpa et al[22] and Cao et al[23] where the number of fundic gland polyp seem to be in increasing trend. The variation in the results could be due to the variation in the geography, exposed risk factors and the number of the study population.

According to the histopathological assessment of 117 cases, 16 were identified as neoplastic gastric diseases. Among these, two cases showed low-grade dysplasia, one was diagnosed as adenoma, and the remaining cases were histopathologically confirmed as malignant. The low incidence of dysplasia could be due to targeted biopsies and the infrequent submission of biopsy samples for histopathological analysis, as dysplastic lesions and flat adenomas are often challenging to detect through endoscopic examination. Gastric adenocarcinoma emerged as the most prevalent malignant diagnosis, aligning with findings from other studies conducted by Hirachand et al[12], Bhattarai et al[14], Barad et al.[15]

Biopsies were conducted in areas exhibiting specific endoscopic features such as erythema, erosions, ulcers, polyps, or growths to determine potential histological counterparts to these endoscopic findings. Out of the 117 cases examined, endoscopy identified 85.5% (100 cases) as non-neoplastic lesions, with 82.9% (97 cases) histologically confirmed as non-neoplastic, and 2.6% (3 cases) as neoplastic lesions. Interestingly, two cases with endoscopically normal mucosa were histologically diagnosed as chronic inactive gastritis and chronic active gastritis, respectively. Similarly, two cases initially identified as ulcer and erythema through endoscopy were histologically diagnosed as low-grade dysplasia. Additionally, a benign polypoidal lesion was found to be an adenoma upon histological examination. This underscores the significance of histopathology in evaluating inflammation levels and early precursor changes in symptomatic patients, even when the endoscopic examination indicates normal gastric mucosa.

In a study involving 117 cases, endoscopic examinations identified neoplastic lesions in 14.5% of the cases. Histological analysis confirmed 11.1% of these as neoplastic and 3.4% as non-neoplastic. Notably, discrepancies were observed between endoscopic findings and histological diagnoses. Instances included a suspicious lesion being identified as chronic gastritis with intestinal metaplasia, an ulcero-proliferative growth as atrophic gastritis, an ulcerative growth as *H. pylori* associated gastritis, and a malignant growth as gastric mucosa within normal histological limits. These findings highlight the importance of relying on histopathological examinations for accurate diagnoses of ulcers or gastritis, as opposed to relying solely on endoscopic observations. The observed discrepancies are attributed to potential sampling errors between the biopsied site and the identified endoscopic abnormality.

Despite some discrepancies, our study demonstrated a strong correlation between endoscopic findings and histopathological diagnoses. This alignment could be attributed to the proficiency involved in both the endoscopic procedure and the interpretation of histopathological results. The association between non-neoplastic and neoplastic endoscopic findings and histopathological diagnoses was statistically calculated using the Chi-square test, yielding a significant p-value of 0.001.

The sensitivity of the endoscopic procedure was 81.3%, with a specificity of 96%, a positive predictive value of 76.4%, and a negative predictive value of 97%. Notably, these figures exhibit variability compared to other studies.[6,11] Such differences could be attributed to the distinct populations studied, as well as variations in the results of endoscopic and histological findings. Additionally, sampling errors may have occurred between the actual site biopsied and the observed endoscopic abnormality.

CONCLUSIONS

Endoscopy offers a valuable chance to observe the mucosal surface of the gastrointestinal tract, representing a significant advancement in diagnosing gastric lesions. The endoscopic observations exhibit a robust correlation with histopathological diagnoses, demonstrating high sensitivity and specificity. Drawing from the study's results, it can be inferred that targeted endoscopic biopsies are justified. However, it is important to highlight that endoscopy is insufficient without biopsy, and histopathology, recognized as the gold standard, should always accompany endoscopy. Neither should serve as a substitute for the other in confirming a diagnosis.

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