

Gastric mucosal biopsies in non ulcer dyspepsia: A histopathologic study

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ABSTRACT

Background: Non-ulcer dyspepsia (NUD) is a major health problem and one of the most common causes of morbidity and economic loss. The aim of the study was to determine the pattern of gastric mucosal histopathologic alterations and frequency of *Helicobacter pylori* in patients with NUD. **Materials and Methods:** Patients presenting to Gastroenterology Out Patient Department over a period of one year with symptoms of dyspepsia but without any endoscopic lesion were taken up for the study and evaluated by obtaining two gastric mucosal biopsy specimens each from antrum and body mucosa. The specimens were processed and examined histologically using the updated Sydney system. **Results:** Gastric biopsies from 102 patients (63 females and 39 males) with NUD were studied. Histological examination of gastric mucosal biopsies showed that 82.3% of NUD patients had histopathological features of gastritis. Chronic inflammation was present in 84 (82.3%), activity was seen in 63 (61.7%), glandular atrophy was seen in 10 (9.8%) and intestinal metaplasia was seen in 4 (3.9%) patients with NUD on gastric biopsy. Maximum number of patients with NUD had Sydney score of less than 5 (68.6%). *H pylori* were identified on gastric mucosal biopsies in 49 (48.0%) patients with NUD based on H & E and Geimsa stained sections. **Conclusion:** NUD is a clinical problem which occurs in both sexes in all age groups; prevalence being low below 20 years of age. Patients with this condition have a high frequency of gastric mucosal inflammation and *H pylori* infection.

Key words: Non ulcer dyspepsia, Updated sydney system, *H pylori*

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INTRODUCTION

The term “dyspepsia” is derived from Greek words “dys” (bad) and “pepsis” (digestion) that refers to symptoms thought to originate in the upper gastrointestinal tract. Dyspepsia is often used to refer to pain or discomfort centered in the upper abdomen.¹ At least 50% of patients with dyspepsia who are seen in primary care settings have non-ulcer dyspepsia in which no definite structural or biochemical explanation for the symptoms can be identified.²

A number of hypotheses have been proposed to explain the pathogenesis of non-ulcer dyspepsia which includes gastric acid hypothesis, motor-disorder

hypothesis, the psychiatric hypothesis, the hypothesis of augmented visceral perception, and the food intolerance hypothesis.¹ *Helicobacter pylori* (*H pylori*) infection is also probably a causative agent for non-ulcer dyspepsia.³

H pylori is a small, curved and highly motile gram negative bacillus which survives on the surface of the mucosa in the layer of mucin and in the gastric pits.⁴ It is recognized to be associated with diverse upper gastrointestinal pathologies such as chronic gastritis, peptic ulceration, mucosal associated lymphoid tissue (MALT) lymphoma and gastric carcinoma.^{5,6} Therefore, investigation for this organism has become an integral part of upper gastrointestinal endoscopy.

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Non-ulcer dyspepsia is a major health problem and one of the most common causes of morbidity and economic loss. Patients with dyspepsia also have deterioration in the quality of their life. Hence the present study was carried out to determine the pattern of gastric mucosal histopathologic alterations in patients with non-ulcer dyspepsia and frequency of *H pylori* in these patients, which would help in better understanding and management of patients of non-ulcer dyspepsia.

MATERIALS AND METHODS

The study was conducted in the Postgraduate Department of Pathology and Gastroenterology division of the Postgraduate Department of Medicine, Government Medical College, Jammu. The study was prospective in nature, extending over a period of one year with effect from 1st November, 2009 to 31st October, 2010.

Patients presenting to Gastroenterology Out Patient Department over a period of one year with symptoms of dyspepsia were taken up for the study. Written consent was obtained from each patient after explaining him/her the nature and purpose of the study. Dyspepsia was defined as the presence of one or more of the postprandial fullness, early satiation, or epigastric pain or discomfort for the last three months with symptom onset at least six months before diagnosis according to the latest Rome III criteria.

Clinical history was elicited from each patient and complete general physical and systemic examination was done. This was followed by evaluation of relevant investigations.

Inclusion criteria

1. No evidence of organic disease from the history, physical examination or laboratory tests that is likely to explain the symptoms.
2. No evidence of any mucosal lesion in the esophagus, stomach or duodenum at upper gastrointestinal (G.I.) endoscopy.

Exclusion criteria

1. Patients whose symptoms were predominantly heart burn and/or regurgitation.
2. Peptic ulcer disease.
3. Patients whose dyspepsia had been investigated previously by radiology, endoscopy or other tests and specific diagnosis established.
4. Patients who had used non steroidal anti-inflammatory drugs (NSAIDs) in the last 2 weeks prior to endoscopy.

5. Attempt at *Helicobacter pylori* eradication or acid suppressive therapy in the last 2 weeks prior to endoscopy.
6. Absolute/relative contra-indication to upper G.I. endoscopy.

After overnight fasting, upper gastrointestinal endoscopy was performed on selected patients using Fujinon EG-265WR Endoscope under throat anaesthesia with 10% xylocaine spray. The esophagus, stomach and duodenum were visualized and mucosal findings noticed. Patients in whom no endoscopic lesion was found in the esophagus, stomach, duodenal cap and 2nd portion of the duodenum were further evaluated by obtaining two gastric mucosal biopsy specimens each from antrum and body mucosa. After each endoscopy, endoscopes and biopsy forceps were sterilized with 2% glutaraldehyde to prevent cross infection among patients.

The specimens were properly labeled, fixed in 10% formalin, processed using paraffin embedding technique, sectioned at 3 micrometer perpendicular to the mucosal surface and stained with haematoxylin and eosin (H & E). The histopathological parameters were graded using the updated Sydney system.⁷ Presence of *H pylori* was looked for on H&E stained sections and one section each from antral and body mucosa was also stained by modified Geimsa stain.⁸

RESULTS

A total of 102 patients who presented with dyspeptic symptoms and normal upper gastrointestinal endoscopy were included in the study. They consisted of 63 females (61.7%) and 39 males (38.2%). Their ages ranged between 18 to 70 yrs. 31-40 year age group comprised of the maximum number of the cases which were 34.3% followed by 22.5% cases in 41-50 year age group. Maximum number of cases both males and females were in the age group of 31-40 years which forms 28.2% in males and 38% in females.

Out of 102 patients with non ulcer dyspepsia, 17.6% had normal gastric mucosa on histopathology and 82.3% had histopathological features of gastritis. Out of 39 male patients, gastritis was present in 32 (82.0%) patients. Among 63 female patients, gastritis was seen in 52 (82.5%) patients.

Chronic inflammation (Figure 1a) was present in 84 (82.3%) patients of non- ulcer dyspepsia on gastric biopsy; out of which, 62 (73.8%) had mild, 22 (26.1%) had moderate

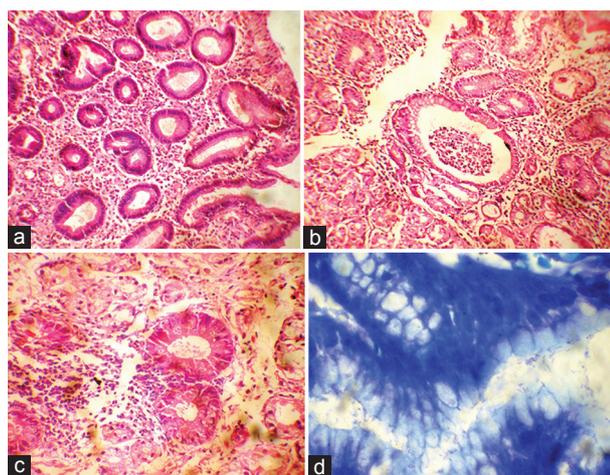


Figure 1: (a) Shows moderate chronic antral gastritis with lymphoplasmacytic infiltrate in lamina propria [H&E, 200X], (b) Shows severely active body gastritis, note the presence of crypt abscess [H&E, 200X], (c) Shows chronic gastritis; focal glands show intestinal metaplasia with presence of goblet cells and paneth cells [H&E, 200X], (d) Shows numerous H pylori on the surface of gastric mucosa [Modified Geimsa, 100X]

and none had severe chronic inflammation. Activity (Figure 1b) was seen in 63 (61.7%) patients of non-ulcer dyspepsia on gastric biopsy; out of which, 48 (76.1%) had mild, 11 (17.4%) had moderate and 4 (6.3%) had severe neutrophilic activity. Glandular atrophy was seen in 10 (9.8%) patients of non-ulcer dyspepsia on gastric biopsy and was of mild grade. Intestinal metaplasia (Figure 1c) was seen in 4 (3.9%) patients of non-ulcer dyspepsia on gastric biopsy and was also of mild grade.

H pylori (Figure 1d) were identified on gastric mucosal biopsies in 49 (48.0%) patients with non-ulcer dyspepsia; out of which, 33 (67.3%) had mild, 10 (20.4%) had moderate and 6 (12.2%) had severe H pylori colonization. Lymphoid follicles and lymphoid collections were seen in 16 (15.6%) patients of non-ulcer dyspepsia.

Maximum number of patients with non-ulcer dyspepsia had Sydney score of less than 5 (68.6%). 17.6% patients had score zero; 13.7% had score between 5 and 10 and none had score above 10.

DISCUSSION

Dyspepsia is among the most common complaints evaluated by both the general practitioner and gastroenterologist. The magnitude of non-ulcer dyspepsia is impressive and the annual incidence is over 1%.⁹ The prevalence of functional dyspepsia ranges from 20%-30% in the general population.¹⁰ Non-ulcer dyspepsia (NUD) is not only common, but costly, because it often results in empiric treatment intended to heal peptic ulcers, including

potent inhibitors of gastric acid secretion,¹¹ and accounts for expensive tests and utilization of time.¹² Altogether, dyspepsia is an important health issue and constitutes a significant clinical problem in primary care.

In our study, 31-50 years age group comprised the maximum number of the cases of non-ulcer dyspepsia (56.8%) with peak in 4th decade and the mean age being 42.9 yrs. Non-ulcer dyspepsia occur with a similar frequency in both sexes up to 60 years, but less common in older people of both sexes.¹³ In the present study, the maximum number both of male and female patients was in the age group of 31-40 years which forms 28.2% in males and 38.0% in females. 42.9 yrs was the mean age of male and 42.3 yrs. was the mean age of female patients. Least number of cases in both male (5.1%) and female (1.5%) patients in our study was seen up to 20 years of age.

Biopsy sampling of the gastric mucosa at diagnostic endoscopy provides information that cannot be obtained otherwise. The most common indication for gastric biopsy is the need to know whether the patient is infected with *Helicobacter pylori* or not and whether the stomach shows gastritis or not.¹⁴ Some studies could not find any correlation between endoscopic or histologic gastritis and dyspeptic symptoms¹⁵ while others have reported a correlation between histological inflammation of the gastroduodenal mucosa and dyspeptic symptoms.¹⁶ Microscopic examination of gastric biopsy specimens gives, in addition to H pylori status, information about the grade, extent, and topography of gastritis- and atrophy-related alterations in the gastric mucosa. This information helps in management and provides further possibilities for the assessment of risk and likelihood of various gastric disorders.¹⁴ Results from the Cochrane Collaboration systemic review shows that a one to two week course of H. pylori eradication therapy has a small but statistically significant effect in H pylori positive non ulcer dyspepsia.¹⁷

In our study, histological examination of gastric mucosal biopsies showed that 82.3% had histopathological features of gastritis. This is consistent with other studies where histopathological features of gastritis was observed in the range of 70- 92% in patients with NUD.¹⁸⁻²⁰ Chronic gastritis alone was seen in 21(20.5%) patients, both acute and chronic gastritis in 63 (61.7%) and 18 (17.6%) patients had normal mucosal biopsies in the present study.

Chronic inflammation was present in 84 (82.3%) patients of non ulcer dyspepsia on gastric biopsy in the present study. However, a study in Nigeria observed that chronic inflammation was present in 66.7% of patients with non ulcer dyspepsia.²¹ Some studies have shown chronic gastritis, as characterized by an increase in round cell infiltration, in

dyspeptic patients.^{22,23} The implication of gastric mucosal inflammation in patients with non ulcer dyspepsia is not clear because of lack of comparison with an appropriate control group made up of healthy subjects.²¹ Toukan *et al.*¹⁶ in their study of gastroduodenal inflammation in patients with non ulcer dyspepsia found no significant difference in the gastric mucosal round cell numbers between dyspeptic patients and normal controls.

Neutrophilic infiltration was seen in 63 (61.7%) patients of non ulcer dyspepsia on gastric biopsy in our study which is in concordance to that stated by Toukan *et al.*¹⁶ who observed a significant increase in gastroduodenal mucosal neutrophilic count in patients with non ulcer dyspepsia. In biopsy studies of normal people, few or no neutrophils are usually seen by subjective means.^{24,25} Some authors see the presence of increased neutrophil infiltration as implying that the inflammatory process is active, particularly if seen in the epithelial cell layer.²⁶ This mucosal inflammation may account for the symptoms in patients with non ulcer dyspepsia.¹⁶

Glandular atrophy was seen in 10 (9.8%) patients of non ulcer dyspepsia on gastric biopsy and was of mild grade in the present study. Other studies stated atrophic gastritis in 2.5%¹⁹ and 14.5%²⁷ NUD patients. However, Nwokediuko & Okafor²¹ reported glandular atrophy in 42.7% patients of non ulcer dyspepsia and it was of mild grade in 28.1%, moderate grade in 53.1% and severe grade in 18.7% patients. Shafii *et al.*²⁸ reported that patients with mild chronic gastritis are less probable to reflect atrophy which is similar to the observation made in our study. Even when extensive biopsy protocols are used, inevitable sampling errors may affect the documentation of the atrophic foci, which are frequently patchy.²⁹

In the present study, intestinal metaplasia was seen in 4 (3.9%) patients of non ulcer dyspepsia on gastric biopsy and was also of mild grade. This is in concordance with other studies which reported intestinal metaplasia in 2.5%¹⁹ and 8%²¹ NUD patients.

In our study, maximum number of patients with non ulcer dyspepsia had Sydney score of less than 5 (68.6%). 17.6% patients had score zero; 13.7% had score between 5 and 10 and none had score above 10. Nwokediuko & Okafor²¹ reported Sydney score zero in 29%, less than 5 in 34.7%, between 5 and 10 in 33.3% and more than 10 in 2.7% patients of non ulcer dyspepsia.

In our study, *H pylori* were identified on gastric mucosal biopsies in 49 (48.0%) out of 102 patients with non ulcer dyspepsia based on H & E and Geimsa stained sections. Various studies show the prevalence of *H pylori* in NUD patients between 37.3% to 75%.³⁰⁻³²

The so called post-infection functional dyspepsia occurring after acute gastrointestinal infection postulates that inflammation may cause alterations in the enteric nervous system and visceral sensation by modifying signaling in the brain-gut axis. *H pylori* induced inflammation of the gastric mucosa in functional dyspepsia falls into the same logic, suggesting that acute and chronic inflammation seem to play some role in the functional dyspepsia pathogenesis.^{33,34}

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Authors Contribution:

PS- Concept and design of the study, collected data, reviewed the literature, manuscript preparation and critical revision of the manuscript; **KCG-** Concept of study, review of literature and critical revision of the manuscript; **BBG-** Conceptualized study, selection of cases and review of study

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