HISTOPATHOLOGICAL ANALYSIS OF GASTRIC MUCOSAL BIOPSIES IN NON ULCER DYSPEPSIA

Tariq Sarfraz, Muhammad Hafeez*, Nighat Shafiq*, Humaira Tariq*, Muhammad Azhar*, Kamran Nazir Ahmed*, Nighat Jamal*

Army Medical College/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Combined Military Hospital Kharian/ National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To find out the pattern of gastric mucosal histopathological findings in gastric biopsies of patients with non ulcer dyspepsia.

Study Design: Prospective descriptive study.

Place and Duration of Study: Histopathology department Combined Military Hospital (CMH) Kharian Pakistan from Jan to Dec 2015.

Material and Methods: One hundred patients presenting at outpatient gastroenterology department with dyspepsia having no endoscopic lesion were included in the study. Two gastric mucosal biopsies from antrum and two from corpus were taken. The specimens were processed and examined histologically to see the changes. *Results:* Gastric biopsies of 100 patients including 65 males and 35 females presenting with non ulcer dyspepsia were studied. Most of the patients were between the age group of 31–50 years. Histological examination of gastric biopsies revealed 70% of patients having histological features of gastritis, while 30% having no significant histological finding. Chronic inflammation was seen in 70 cases (70%), activity in 15 cases (15%), glandular atrophy in 2 cases (2%) and intestinal metaplasia in 2 cases (2%). *H.Pylori* were identified in 25 cases (25%) based on haematoxylin and eosin (H & E) staining and modified giemsa staining.

Conclusion: Most the cases of non ulcer dyspepsia show histological evidence of gastritis, however a significant number of patients showed no gastric mucosal histological abnormality. A significantly low frequency of *H. Pylori* in gastric biopsies noted in non ulcer dyspepsia cases may be due to more frequent use of antibiotics and acid suppressant drugs used by general practitioners at some stage of disease.

Keywords: Gastric biopsy, Gastritis, H. Pylori, Non ulcer dyspepsia.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Dyspepsia described as recurrent epigastric discomfort and fullness usually after meals and narrated by patient as indigestion¹. The term 'Dyspepsia' is derived from Greek words 'dys' (bad) and 'pepsis' (digestion) and is referred to discomfort or pain centred in upper abdomen². It is one of the commonest symptom presented by patients in general medical and gastroenterology outpatient departments. About 50% of dyspepsia cases have non ulcer dyspepsia with no structural biochemical finding and are considered functional3. There are different hypothesis regarding etiopathogenesis of non

Correspondence: Dr Tariq Sarfraz, Associate Professor of Pathology Dept, Army Medical College Rawalpindi, Pakistan *Email: tskhan_65@yahoo.com*

Received: 04 Jul 2016; revised received: 19 Jul 2016; accepted: 20 Jul 2016

ulcer dyspepsia. The factors including gastric acid, motor disorder, psychiatric factors, food intolerance and *H.Pylori* infection are considered to be probable causative agents⁴. Non ulcer dyspepsia is one of the commonest health problem causing significant morbidity and economic loss with deterioration in quality of life. Endoscopy is incomplete without gastric biopsy, which is the gold standard to determine the underlying pathology⁵. This study was carried out to analyze the histological findings in gastric mucosal biopsies done in non ulcer dyspepsia cases. Outcome of this study can help in better understating and management of non ulcer dyspepsia cases.

MATERIAL AND METHODS

This prospective descriptive study was carried out at histopathology department and

gastroenterology division of Combined Military Hospital Kharian Pakistan. The study extended over a period of one year with effect from January to December 2015. Patients presenting to gastroenterology outpatient department with dyspepsia were taken for study during a period of one year. Total 100 patients were selected by non-probabilty purposive sampling. Dyspepsia was defined according to latest Rome III criteria including one or more of symptoms including postprandial fullness, early satiation, epigastric discomfort or pain for last three months with symptoms starting at least 6 months before diagnosis. After explaining the purpose and nature of study, written consent was taken from the patients. A detailed clinical history and thorough physical examination was done fallowed by carrying out relevant investigations.

Patients with no evidence of any organic clinical history, physical from examination, relevant investigations and those with no evidence of any mucosal lesion on upper gastro-intestinal endoscopy of oesophagus, stomach and duodenum were included in the study. Patients with peptic ulcer disease, those whose dyspepsia was investigated previously and using non steroidal anti inflammatory drugs (NSAIDs), antibiotics or gastric acid suppressants for last 02 weeks were excluded from the study. **Patients** having absolute or relative contraindication for upper gastrointestinal endoscopy were also excluded from the study.

After overnight fasting, upper gastro-intestinal endoscopy was done on selected patients with 10% Xylocaine spray as throat anaesthesia. Oesophagus, stomach and duodenum were visualized and mucosal findings noted. Patients with no obvious mucosal lesions in oesophagus, stomach, duodenal cap and 2nd part of duodenum were further evaluated by taking two mucosal biopsies from gastric antrum and two from corpus.

The specimens were labeled and fixed in 10% formalin. Paraffin blocks were made and sectioned at 3-5 micrometer thickness.

The sections were stained with haematoxylin and eosin (H&E). For highlighting the presence of *H.Pylori*, modified Giemsa stain was done on one section including antral and corporal mucosa⁶. The slides were examined by two histopathologists and the histopathological findings were noted.

Data were analyzed using SPSS version 17. Descriptive statistics were used to describe the results and in cases having gastritis, histopathological variables were graded according to updated Sydney system of gastritis⁷. Non graded variables like ulceration and granulomas were also looked for and mentioned descriptively without grading. Categorical variables were presented by frequency and percentage.

RESULTS

A total of 100 patients who presented with dyspepsia were analyzed. They included 65 (65%) males and 35 (35%) females. The age range was between 18–70 years. Maximum number of cases 45 (45%) were between 31–40 years, followed by 25 cases (25%) which were between 41–50 years.

Out of these 100 cases of non ulcer dyspepsia, gastric biopsies of 30 cases (30%) showed normal gastric mucosa with no significant pathology, while 70 cases (70%) had histopathological features of gastritis. Out of 65 male patients, 45 (69.23%) had gastritis and out of 35 female patients 25 (71.42%) had gastritis with almost equal male: female ratio.

Chronic inflammation was found in 70 cases (70%) of non ulcer dyspepsia, out of which 50 cases (71.42%) had mild, 15 (21.42%) had moderate and 5 (7.14%) had severe inflammation. Activity was seen in 15 cases (15%) of non ulcer dyspepsia, out of which 12 (80%) had mild activity and 3 (20%) had moderate activity. Severe activity was not seen in any patient. Glandular atrophy was seen in 2 cases (2.0%) which was mild in both cases. Intestinal metaplasia was seen in 2 cases (2.0%) which was mild in both patients.

H.Pylori were detected in gastric biopsies of 25 patients (25%) with non ulcer dyspepsia, out of which 15 cases (60%) had mild, 7 (28%) had moderate and 3 (12%) had severe colonization of H.Pylori. Out of 70 cases of gastritis, 60 (85.71%) had a Sydney Score of less than 5, while 10 cases (14.28%) had a score between 5-10. None had a score above 10. No non graded variables like ulceration and granuloma were noted. Regarding topography, out of 100 cases studied, 50 cases (50%) showed antral gastritis, 15 cases (15%) showed antral and corporal gastritis (pan gastritis) while 5 cases (5%) showed corporal gastritis. Rest of 30 cases (30%) had unremarkable gastric antral and corporal mucosa. Histological variables in gastric biopsies of patients in non ulcer dyspepsia are given in table.

DISCUSSION

Dyspepsia is one of the most common complaints encountered by general practitioner, medical specialists and gastroenterologists. The prevalence of non ulcer dyspepsia ranges from 42.5 years. This age incidence was in accordance with the result of a similar study carried out in India¹¹. Regarding the gender, in our study, most of the patients (65%) were males, which was likely due to main influx of patients from military set up, however the frequency of gastritis was almost equal in males and females presenting with non ulcer dyspepsia.

Biopsy sampling on endoscopic examination indicated the underlying pathology and provided valuable information regarding presence or absence of gastritis, its grade, activity, glandular atrophy, intestinal metaplasia, etiological factors like *H.Pylori* as well as topography. This information not only helps in management of these cases but also provides guidance to assess further risk for other gastric disorders¹².

Histological evidence of gastritis was noted in majority of gastric biopsies (70%), while a significant number of gastric biopsies (30%) revealed unremarkable gastric mucosa with no significant pathology. This indicates that gastritis

Table: Histological variable in gastric biopsies showing gastritis in non ulcer dyspepsia.

Histological Variables	Grade				
	None (0)	Mild (1)	Moderate(2)	Severe (3)	Total (Positive) (%)
Chronic inflammation	30	50	15	05	70 (70%)
Activity	55	12	03	00	15 (15%)
Glandular atrophy	68	02	00	00	02 (2.0%)
Intestinal metaplasia	68	02	00	00	02 (2.0%)
H.Pylori	55	15	07	03	25 (25%)

20–30% among the general population⁸. In North America, about 60% of the patients with dyspepsia are those who have non ulcer dyspepsia⁹. This pathology is not only common, but at the same time is a costly affair, accounting for use of costly drugs like inhibitors of gastric acid secretion, expensive tests and utilization of time thus causing a real clinical challenge for the patient as well as health care providers¹⁰.

In this study, most cases of non ulcer dyspepsia were between the age group of 31–50 years and this disease was most common in 4th decade (31-40 years) with a mean age of about

is not the sole cause in all cases of non ulcer dyspepsia and other etiopathogenetic factors may also be considered and searched for by doing further studies.

Chronic inflammation was present in 70 cases of non ulcer dyspepsia, which was comparable to chronic inflammation noted in 66.70% cases of non ulcer dyspepsia in a study conducted at Nigeria¹³. In another similar study carried out at India, chronic inflammation in non ulcer dyspepsia cases was 82.30¹⁰, which is higher as compared to our study. Neutrophilic infiltration (activity) was present in 15.0% of non

ulcer dyspepsia having gastritis in our study, which is quite low as compared to similar study done in India showing 61.7% activity in gastritis with non ulcer dyspepsia. Another study done by Touken et al also showed higher activity (65%) in gastritis with non ulcer dyspepsia¹⁴. Glandular atrophy was noted in only 2 cases (2.0%) and was mild in both. The prevalence of glandular atrophy was much less in our study as compared to a similar Indian study showing 9.8%11. Another study revealed 2.5% glandular atrophy noted in non ulcer dyspepsia cases¹⁵, which is comparable with the percentage noted in our study. Intestinal metaplasia was noted in 2.0% cases in our study, which is comparable to intestinal metaplasia noted in gastric biopsies of non ulcer dyspepsia cases in other studies^{11,15}. H.Pylori were identified in 25% cases in our study. This number is significantly less as compared to one study showing presence of H.Pylori in 48% of gastric biopsies done in cases of non ulcer dyspepsia¹¹, 67% in another study¹⁶ and 66.1% in yet another study¹⁷. As the patients with symptoms of dyspepsia are now a days getting antibiotics and acid suppressing drugs more frequently from general practitioners at some stage of disease, which may be a cause of lesser frequency of H.Pylori found in gastric biopsies done in non ulcer dyspepsia cases. According to another study, the prevalence of H.Pylori infection is declining¹⁸. A wide range of H.Pylori prevalence (37.5-75%) is shown in non ulcer dyspepsia cases in different studies^{19,20}. Regarding topography, antral gastritis was most common followed by antral and corporal gastritis (Pangastritis) and these finding were in comparison with other studies¹⁹.

CONCLUSION

Most the cases of non ulcer dyspepsia show histological evidence of gastritis, however a significant number of patients showed no gastric mucosal histological abnormality. A significantly low frequency of *H.Pylori* in gastric biopsies noted in non ulcer dyspepsia cases may be due to more frequent use of antibiotics and acid

suppressant drugs used by general practitioners at some stage of disease.

Non ulcer dyspepsia is a very common and challenging medical problem encountered by general practitioners and gastroenterologists. Patient with this condition have a high frequency of gastric mucosal inflammation, however, there is a significant number of cases showing no histological alterations. This brings a need to look for other etiopathogenetic factors responsible for non ulcer dyspepsia with further studies. Gastric antral mucosa is the most common site of inflammation. *H.Pylori* prevalence is decreasing with increase in use of antibiotics against *H.Pylori* and acid suppressant drugs.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

- Tack J, Talley NJ, Camilleri M, Holtmann G, Hu P, Malagelada J, et al. Functional gastroduodenal disorders. Gastro-enterology. 2006; 130: 1466.
- Fisher RS Parkman HP. Management of non ulcer dyspepsia. N Eng J Med. 1998; 339: 1376-1381.
- Richter JE. Dyspepsia: organic causes and differential characteristics from functional dyspepsia. Scand J Gastro-enterol 1991; 26: 11-16.
- Marshall BJ. The 1995 Albert Lasker medical research award. Helicobacter pylori. The etiologic agent for peptic ulcer. JAMA 1995; 274: 1064-1066.
- Pailoor K, Sarpangala KM, Naik CN. Histopathological diagnosis of Gastric Biopsies in Correlation with Endoscopy - A Study at Tertiary Care Centre. Adv Lab Med Int. 2013; 3(2): 21-31.
- Gray SF, Wyatt JI, Rathbone BJ. Simplifi ed techniques for identifying Campylobacter pyloridis. J Clin Pathol. 1986; 39: 1279-1280.
- 7. Dixon MF, Genta RM, Yardley JH, Correa P. Classifi cation and grading of gastritis. The updated Sydney system. International Workshop on the Histopathology of Gastritis, Houston 1994. Am J Surg Pathol. 1996; 20: 1161–81.
- 8. Hammer J, Talley NJ. Non ulcer dyspepsia. Curr Opin Gastroenterol. 1999; 15: 492-96.
- 9. Bazaldua OV, Schneider FD. Evaluation and management of dyspepsia. Am Fam Physician. 1999; 60: 1773-84, 1787-8.
- Talley NJ, Piper DW. A prospective study of social factors and major life event stress in patients with dyspepsia of unknown cause. Scand J Gastroenterol 1987; 22: 268-272.
- 11. Singh P, Goswami KC, Gupta BB. Gastric mucosal biopsies in non ulcer dyspepsia: A Histopathological Study. Ascian J of Medical Sciences, 2016; 7(2): 80-84.
- Elta GH, Appelman HD, Behler EM. A study of the correlation between endoscopic & histological diagnosis in gastroduodenitis Am J Gastroenterol 1987; 82: 749-753.

- Nwokediuko SC, Okafor OC. Gastric mucosa in non ulcer dyspepsia: A Histopathological study of Nigerian patients. The Internet Journal of Gastroenterology. 2006; 5 (2): 1-6.
- 14. Toukan AU, Kamal MF, Amr SS, Arnaout MA, Abu-Romiyeh AS. Gastroduodenal infl ammation in patients with nonulcer dyspepsia. A controlled endoscopic and morphometric study. Dig Dis Sci. 1995; 30: 313-320.
- Arruda SMB, Forones NM, Juca NT, Barros KSC. Could gastric histology be a useful marker for making decision on Helicobacter pylori eradication therapy in patients with dyspepsia? Arq Gastroenterol. 2009; 46: 209-213.
- 16. Sultana A, Badrudoza SM, Rahman F. Correlation Between Endoscopic and Histological Findings in Different Gastroduodenal Lesions and its Association with Helicobacter

- Pylori. AKMMC J. 2011; 2 (2): 6-10.
- 17. Tani NF, Ndip LM, Clark AMM, Nandoo N, Mkwetshana N, Green E, et al. Helicobacter Pylori Prevalance in Dyspeptic Patients in Eastern Cape Province Race and Disease Status. SAMJ. 2010; 100(11): 734-37.
- Walker MM, Harris AK, Edward GC, Talley NJ. A GP primer for understanding upper gastrointestinal tract biopsy reports. AFP. 2015; 44 (10): 706-11.
- Loffeld RJLF, Potters HVPJ, Arends JW, Stobberingh E, Flendrig JA, Van Spreeuwel JP. Campylobacter associated gastritis in patients with non-ulcer dyspepsia. J Clin Pathol. 1988; 4: 85-88.
- Amin K, Alam Z, Nagra MH, Hussain I, Javed M. Association of Helicobacter pylori with non- ulcer dyspepsia. The Professional 2003; 10: 1-4.

.....