

Histopathological analysis of chronic gastritis and correlation of pathological features with helicobacter pylori

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Abstract

Introduction: Helicobacter pylori (HP) infection is a major cause of various gastroduodenal pathologies. The objective of our study is to evaluate various histopathological parameters of chronic gastritis using the updated Sydney system and to correlate it with presence of HP.

Materials and Method: Total 250 cases of chronic gastritis was evaluated retrospectively from January 2015 to December 2015 in a tertiary care centre. Histopathological examination of all antral gastric biopsies using Hematoxylin and Eosin, and Giemsa stain for grading of various parameters and for detection of HP was carried out.

Result: Chronic inflammation was identified in 100% of cases with varying intensity. Intensity of activity showed an incremental trend with density of HP. Forty percent of cases with intestinal metaplasia showed the presence of HP. Atrophy was documented in only one case. A strong association between chronic inflammation, activity, intestinal metaplasia and lymphoid follicle with HP was established.

Conclusion: The updated Sydney classification provides an objective mean of classifying chronic gastritis and increases the likelihood of detection of HP. Presence of intense grade of inflammation, activity and lymphoid follicle should hint the histopathologist to search for HP. And also the presence of one of these features is a strong indicator for the presence of the other.

Keywords: Chronic gastritis, Helicobacter pylori, Sydney classification

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Introduction

Helicobacter pylori (HP) are associated with several gastroduodenal lesions. Nearly half of the world's population is infected with HP.⁽¹⁾ Chronic gastritis being a more common disorder and usually manifest as a pathologic spectrum of lesions ranging from active chronic gastritis to erosions and malignancy. Helicobacter pylori colonises gastric mucosa leading to production of pro-inflammatory cytokines causing direct epithelial cell injury resulting in gastritis.⁽²⁾ As there is an effective specific treatment for HP associated gastroduodenal disorders, pathologists are usually requested to identify the organism on endoscopic biopsies. The perplexity in detection of HP on routine hematoxylin and eosin stain (H&E) has led to development of various special stains like Giemsa and Warthin Stary.⁽³⁾ The histopathological classification of gastritis was rather simplified from many conflicting nomenclatures to one, the Sydney System. Combination of topographical, morphological and etiological factors in the diagnosis of chronic gastritis was used in The Sydney System (1990).⁽⁴⁾ An up gradation of The Sydney System in 1994 at Houston, Texas gave a more appropriate classification system for gastritis including endoscopic findings.

It was seen that HP, chronic inflammatory infiltrate, neutrophilic infiltration, presence of lymphoid follicles and aggregates and surface epithelial damage are strongly associated with each other. The presence of one of these histological features is a strong indicator

for presence of other features. Thus in this study by correlating the various parameters we can suggest the most predictive parameter associated with HP infection.

Aims and Objectives

1. To evaluate histopathological parameters of chronic gastritis according to the updated Sydney system
2. To correlate various histopathological parameters with presence of HP.

Materials and Method

The present study is a retrospective descriptive study conducted from January 2015 to December 2015. All endoscopic antral biopsies received in the department of Pathology, Sri Venkateshwaraa Medical College Hospital & Research Centre, Puducherry were reviewed with reference to light microscopic findings. Two slides were examined for each case, one H & E and Giemsa stain for histopathological examination and detection of HP on gastric mucosa respectively. A total of 262 slides were analysed out of which 12 had features of malignancy and were excluded from the study. The remaining 250 cases with features of chronic gastritis were perceived.

The biopsies were evaluated for the presence and intensity of mononuclear inflammatory cell infiltrate, inflammatory activity, glandular atrophy, intestinal metaplasia, lymphoid aggregates and also for HP density. All parameters were graded according to Houston updated Sydney system modified by Aydinet

al⁽⁴⁾ to provide a more subjective score. Each morphological variable was scored as follows: absent (score 0), mild (score 1), moderate (score 2), severe (score 3). Lymphoid follicles were ranked by the index proposed by Wotherspoon et al.⁽⁵⁾

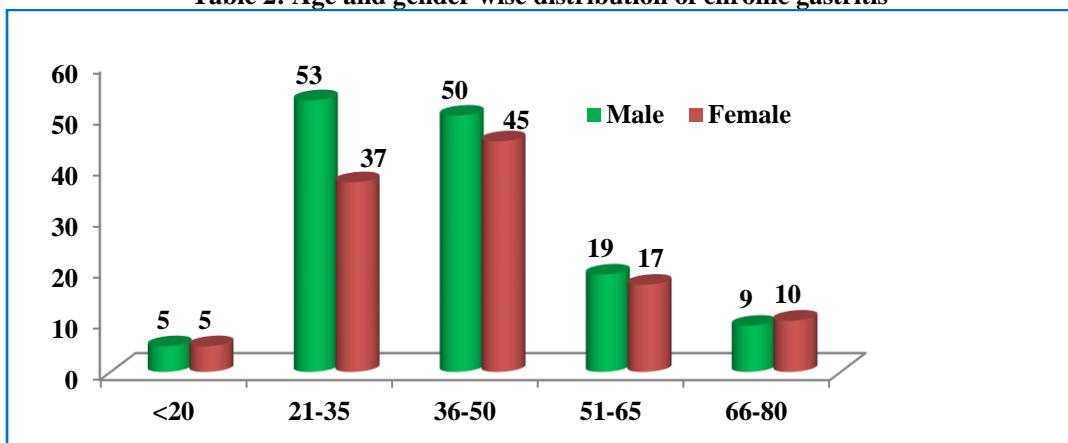
Statistical analysis: SPSS software (no 23) was used for statistical analysis. Chi square test was used to

assess the association between various morphological variables and HP infection. Correlation between histological findings and HP infection was done by using spearman's correlation. A probability value of less than 0.05 was taken as statistically significant.

Table 1: Grading criteria of gastric antral biopsies according to revised Sydney System as proposed by Aydinet al.⁽⁴⁾

Chronic inflammation	2-3 chronic inflammatory cells scattered randomly in the biopsy	nil
	10-15 chronic inflammatory cells/hpf	mild
	some areas with dense chronic inflammatory cells	moderate
	diffuse infiltration with dense chronic inflammatory cells	marked
Neutrophilic infiltrate	no neutrophils anywhere in the biopsy	nil
	scattered neutrophils in the biopsy	mild
	foci of dense neutrophilic infiltrate with scattered neutrophils in the rest of the biopsy	moderate
	several foci of dense inflammatory infiltrate in the biopsy with involvement of crypts	marked
Atrophy	no evidence of gastric gland loss	nil
	small areas where gastric glands have disappeared (< 25%)	mild
	25-50% of the biopsy shows loss of gastric glands	moderate
	> 50% of the biopsy shows loss of gastric glands	marked
Intestinal metaplasia	no intestinal metaplasia	nil
	focal areas of intestinal metaplasia (1-4 crypts)	mild
	multiple foci involving > 4 crypts but < 50% of the biopsy	moderate
	intestinal metaplasia involving > 50% of the biopsy specimen	marked
HP density	no HP identified	nil
	only a few HP seen in single or multiple foci	mild
	numerous HP seen in separate areas of foci	moderate
	> 50% of the surface area covered with HP	marked

Table 2: Age and gender wise distribution of chronic gastritis



Results

A total of 250 cases of chronic gastritis were reviewed. The mean patient's age was 41.6 (14 -80yrs). Most of the patients (38%) were in the age group of 36-50 yrs. There were 135 males and 115 female with a male: female ratio of 1.2:1 (Table 2).

Histopathological features of chronic gastritis were graded according to the Sydney system and are given in the Table 3.

Table 3: Histological grading of chronic gastritis according to updated Sydney system

Histological variables	Total	%	Grade	No.	%
Chronic Inflammation	250	100	Mild	91	36.4
			Moderate	126	50.4
			Severe	33	13.2
Activity	81	32.4	Mild	41	16.4
			Moderate	30	12
			Severe	10	4
Intestinal Metaplasia	57	22.8	Mild	35	14
			Moderate	18	7.2
			Severe	4	1.6
Atrophy	1	0.4	Mild	1	0.4
			Moderate	Nil	Nil
			Severe	Nil	Nil
HP	89	35.6	Mild	19	7.6
			Moderate	57	22.8
			Severe	13	5.2

Chronic inflammation was observed in all (100%) cases of chronic gastritis. Majority around 126 (50.4%) of them had moderate inflammation. Activity as defined by the presence of polymorphonuclear infiltrate in the glands was seen with varying severity in 81 biopsies. Chronic gastritis cases with mild activity (16.4%) outnumbered the rest with moderate and severe in our study (Fig. 1). Fifty seven (22.8%) cases showed intestinal metaplasia of varying severity – 35 had mild, 18 had moderate and 4 had severe intestinal metaplasia (Fig. 2). Atrophy was observed in only one case (0.4%) and it was of mild degree only (Fig. 3). However no HP was detected in gastritis case with atrophy. Lymphoid follicle was present in 36.4% of cases. (Fig. 4)

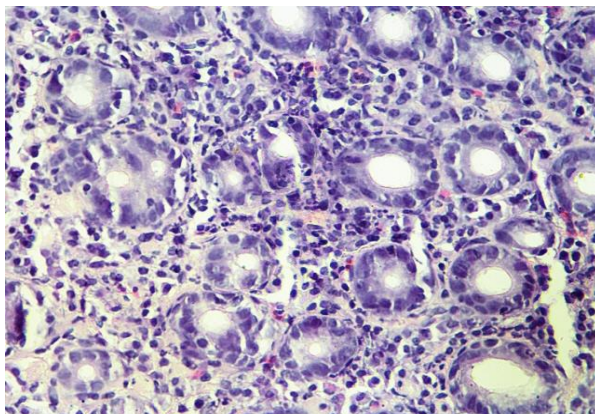


Fig. 1: Photomicrograph of gastric biopsy showing intraepithelial neutrophils. Magnification 400X (H&E)

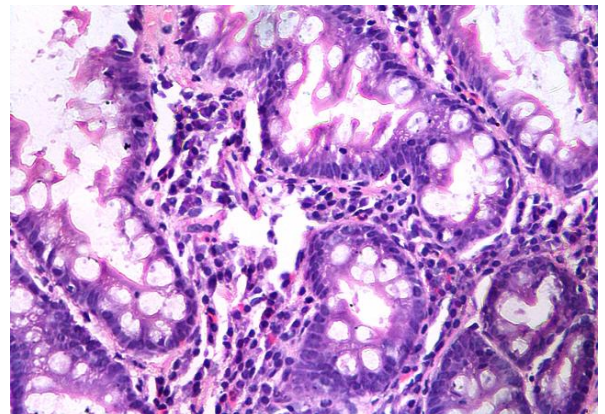


Fig. 2: Photomicrograph of gastric biopsy showing intestinal metaplasia. Magnification 400X (H&E)

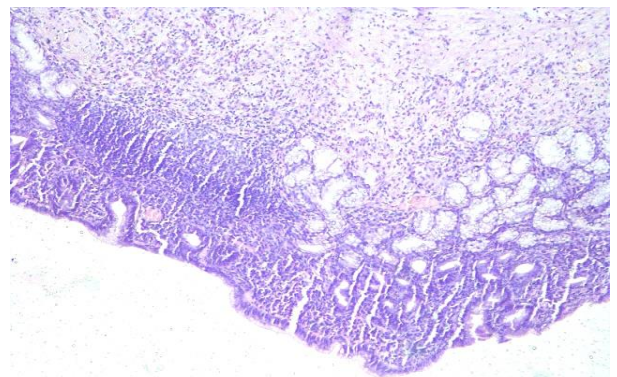


Fig. 3: Photomicrograph of gastric biopsy showing focal atrophy. Magnification 400X (H&E)

In our study we also established the association and correlation of HP with the individual histological parameters. We found the density of chronic inflammation had an influence on the presence of HP

(Table 4). Positivity for HP was high (93.93%) in severe grade of inflammation. A statistically significant association was accomplished between chronic inflammation and presence of HP, activity and lymphoid follicle ($p < 0.01$). (Table 6)

Table 4: Association of HP and degree of chronic inflammation in chronic gastritis

Chronic inflammation	No. of cases	HP positive	%
Mild	91	3	3.2
Moderate	126	55	43.65
Severe	33	31	93.93

p value <0.01

Table 5: Association of HP and degree of activity in chronic gastritis

Activity	No. of cases	HP positive	%
Mild	41	28	68.29
Moderate	30	24	80
Severe	10	9	90

p value <0.01

Table 4: Summary of association among various histological parameters with each other

Parameters	Chronic inflammation	Lymphoid follicle	Activity	Intestinal metaplasia	HP
Chronic inflammation	---	P=0.000	P=0.000	P=0.023	P=0.000
Lymphoid follicle	P=0.000	---	P=0.000	P=0.025	P=0.000
Activity	P=0.000	P=0.000	---	P=0.015	P=0.000
Intestinal metaplasia	P=0.231	P=0.252	P=0.153	---	P=0.000
HP	P=0.000	P=0.000	P=0.000	P=0.000	---

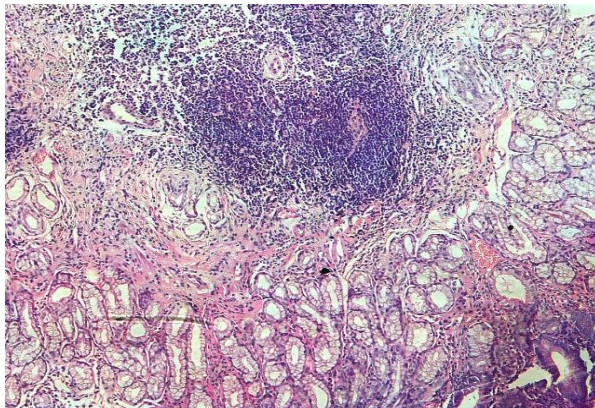


Fig. 4: Photomicrograph of gastric biopsy showing lymphoid aggregates. Magnification 100X (H&E)

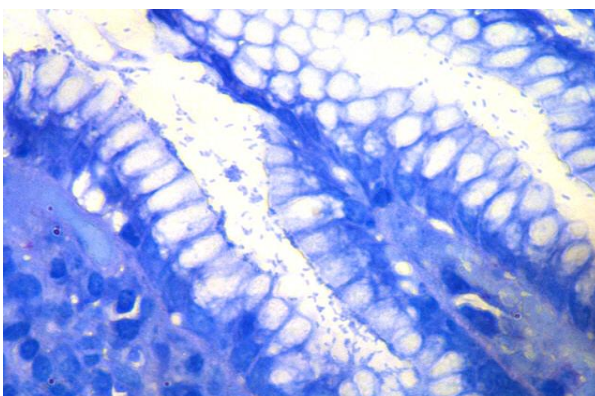


Fig. 6: Photomicrograph of gastric biopsy showing Helicobacter pylori (Giemsa stain). Magnification 1000X

On studying the association of HP with activity, > 50% of cases with activity were positive for HP. An incremental trend towards the presence of HP and severity of polymorphonuclear infiltrate was observed (68.29% - 90%) (Table 5). A strong positive correlation was evidenced between activity and presence of HP. The association of activity with HP, lymphoid follicle and intestinal metaplasia was found to be statistically significant ($p=0.000$). (Table 6)

Intestinal metaplasia was observed in 22.8% of cases. Twenty two cases (40%) showed the presence of HP and their association was found to be statistically significant ($p=0.000$) (Table 6). However intestinal metaplasia did not show any association with rest of the histological parameters.

Because of the small number of atrophy cases (1/250) encountered in our study no statistical significance could be obtained in its association with presence of HP.

Presence of lymphoid follicle is taken as a marker of active infection. Around 64.8% of cases with presence of lymphoid follicle were positive for HP. A significant association between the presence of HP and lymphoid follicle was attained statistically. (Table 6)

Discussion

Infection with HP invariably results in chronic gastritis. Social and economic status of the population determines the prevalence of HP infection in different countries.^(6,3) The present study was intended to evaluate the various parameters of chronic gastritis and to elucidate its association with HP. In our study,

chronic gastritis was commonly seen in 36-50 years with a mean age of 41 years, which was in accordance to the studies done by Garg et al⁽⁷⁾ and Aydin et al.⁽⁴⁾ The incidence of HP was more frequent in males with an M : F ratio of 1.2:1 which is consistent with studies done by Sharma et al⁽²⁾ and Chen XY et al⁽⁸⁾ who reported ratio of 1.7:1 and 1.8:1 respectively.

We have concentrated only on antral biopsies in our study because literature evidence reports antrum to be the most likely site of histopathological gastritis.^(1,9)

Direct epithelial damage by HP results in liberation of epithelium derived proinflammatory cytokines leading to recruitment of inflammatory cells. Presence of chronic inflammatory infiltrates was perceived in all cases with the majority (50%) having moderate inflammation while severe inflammation was noticed in 33% of the cases. A study done by Witteman et al⁽¹⁰⁾ observed chronic infiltrate in all biopsies with majority having moderate inflammation. Statistically significant association between chronic inflammation and acute inflammatory infiltrate, lymphoid follicle and density of HP was obtained akin to work done by Garg et al.⁽⁷⁾ An increase in the positivity of HP with increasing grade of inflammation was notable in our study. Also chronic inflammation showed a strong positive correlation next only to activity for the presence of HP.

Similar to studies by Garg et al⁽⁷⁾ activity was observed in 32.5% of chronic gastritis. The density of HP showed increasing trend with the severity of polymorphonuclear infiltrate. Mysorekar et al⁽¹¹⁾ and Sharma et al⁽²⁾ substantiated our findings of having a significant association between the presence of neutrophils with chronic inflammation, lymphoid follicles and density of HP. Neutrophils are a very sensitive indicator for presence of HP and its disappearance is taken as evidence of cure of infection.⁽¹²⁾

Intestinal metaplasia was seen in 22.8% of cases which was of slightly higher percentage when compared to reports by Atisook et al⁽¹³⁾ and Sharma et al⁽²⁾ who have observed in only 8.2% and 7.8% respectively. Intestinal metaplasia observed in patients with inappropriate and superfluous long term use of proton pump inhibitors is a reputable fact.⁽¹⁴⁾ This might be the probable explanation for higher incidence of intestinal metaplasia in our study population.

Our study ascertained 35.6% of HP positive chronic gastritis while the studies done by Kumar et al⁽⁹⁾ and Gill et al⁽¹⁵⁾ showed positivity in 78% and 65% of cases respectively. This low prevalence of HP could be ascribed to inadvertent use of antibiotics by the patients without any ratification.

Atrophy as defined by the loss of specialized glands in the subepithelium was established in only one case in the present study. Atrophy usually appears in long standing HP infection. Diverse views were expressed by Garg et al⁽⁷⁾ and Sharma et al⁽²⁾ in their studies who have observed atrophy in 12.3% of cases.

Discordance can be substantiated by the fact that large scale screening programs and early endoscopic examination of patients has been followed in our hospital setup which could facilitate detection of HP in a much earlier stage.

The formation of germinal centre is a morphologic indication of lymphocyte response to antigen. Evidences in literature shows that proliferation of T cells and macrophages is induced by *H. pylori*, which release several cytokines (interleukin 2 and 6) which leads to proliferation of B cells and development of lymphoid follicles.^(8,5) Scattered lymphoid aggregates were excluded and only germinal centre formation which is a morphological indicator of lymphocyte response to antigen was considered. Sixty four percent of the cases with the presence of lymphoid follicle were positive for HP. Similar to Mysorekaret al⁽¹¹⁾ we also noticed strong association between the presence of lymphoid follicle and mucosal inflammation, activity and HP infection.

Conclusion

To conclude, our study has determined a strong association of chronic inflammation, activity, intestinal metaplasia and lymphoid follicle with HP. So the presence of any of the above parameters should allude the histopathologist to search for HP. By establishing a strong inter association among the parameters except for intestinal metaplasia, the presence of one parameter should clue the observer to search for the presence of other parameter and also for the presence of HP.

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