Original article:

Study of High sensitivity C Reactive Protein Levels in Patients with Chronic Dyspepsia and Its Correlation with Helicobacter Pylori Infection

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Abstract

Background: Affection of gastric mucosa by helicobacter pylori infection can cause systemic inflammatory response. This study aimed to examine hs – CRP levels in patients with chronic dyspeptic symptoms and its correlation with Helicobacter pylori(HP) positivity.

Methods: All patients with age more than 18 years presenting with dyspeptic symptoms admitted in Department of Internal Medicine during the period September 2017 to August 2019 were included in this study. A total of 60 study subjects with dyspeptic symptoms for more than 4 weeks and completing short form leeds dyspeptic questionairre were classified as H. Pylori positive and negative patients and then hs – CRP levels were compared in them.

Results: Out of 60 patients studied, 22 patients were HP positive and 38 were HP negative. 17 HP positive and 12 HP negative patients had hs – CRP levels more than 0.01 and 5 HP positive and 26 HP negative had hs – CRP levels less than 0.01. It was found to be statistically significant with p value < 0.5.

Conclusion: hs – CRP levels were significantly higher in patients with HP positivity than HP negative, thus increasing the risk of cardiovascular risks in such patients.

Keywords: hs – CRP, Helicobacter pylori, Dyspepsia, Inflammation.

INTRODUCTION:

Dyspepsia is a term used to denote upper abdominal discomfort that is thought to arise from the upper-gastrointestinal tract. It encompasses a variety of more specific symptoms, including epigastric discomfort, bloating, anorexia, early satiety, belching or regurgitation and nausea.H pylori infection can be seen in 77.2% of the dyspeptic patients in India.[1] In many studies H. Pylori has been established organism causing gastritis, peptic ulcers and gastric mucosa associated lymphoma (MALToma). Recently there have been controversial studies suggesting systemic inflammatory response due to H. pylori infection leading to extra digestive pathologies including atherosclerotic vascular diseases and coronary artery disease.

C – reactive protein (CRP) an acute phase reactant originating from the liver is the marker of the systemic inflammation. Measurement of high sensitivity C reactive protein (hs – CRP) can reveal subclinical inflammatory states that might provide a clue to vascular inflammation and atherosclerosis. Little is known about effect of H. Pylori infection on inflammatory markers and its role in atherosclerosis. CRP has many clinical and biological effects and can be used for the diagnosis and follow-up of various inflammatory and traumatic processes.[2]. There is strong evidence that CRP is a powerful predictor of incident cardiovascular events independent of levels of LDL cholesterol, all levels of the Framingham risk score, and the metabolic syndrome.[3] The basal CRP level in individuals free from acute illness is reproducible [20].[4] Age and smoking

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are its major determinants [21][5], while substantial heritability (35–40%) was also reported in familial aggregation studies [22].[6]

Examining the association between *H. pylori* infection and serum CRP levels seemed important to elucidate the relevance of *H. pylori* infection with coronary heart disease, especially atherosclerosis. The previous studies on the association, however, provided inconsistent results.

The study was done to evaluate if any correlation exists between H. Pylori infection and hs-CRP levels in patients with chronic dyspepsia.

METHODS:

The study was carried out in a tertiary care hospital in Western India between September 2018 and August 2019. All patients with age more than 18 years and referred for upper gastrointestinal endoscopy (UGIE) for chronic dyspeptic symptoms of more than 4 weeks duration were included in the study. Institutional Ethics committee approval was taken prior to the commencement of the study and written informed consent were taken from all the participants. Patients with chronic kidney and liver diseases, k/c/o malignancy, acute infections, with history of major surgeries of gastrointestinal tract including gastrectomy (partial or total), History of regular use of Proton pump inhibitors, H2 Blockers, drugs used for eradication of HP in past 4 weeks were excluded from the study. A total of 60 study subjects with dyspeptic symptoms for more than 4 weeks were included. All patients were made to fill up the Short-form Leeds Dyspepsia questionnaire. UGIE was done for all the patients. Gross findings on endoscopy were noted. Two biopsies were taken from the antrum of the stomach. Rapid Urease Test (RUT) was done on one antral biopsy sample by a commercially available RUT-kit. (Yellow to Pink colour change of the slide within 24 hours was read as H. Pylori positive) The other antral biopsy was sent for histopathological examination for detection of H. Pylori. The study subjects were classified as H. Pylori positive if both RUT and HPE were positive for H. Pylori. Highly sensitive C- Reactive Protein was done by Nephelometry method for all the study subjects. All routine investigations were also done for these patients. The study subjects were divided into two groups – H. Pylori positive and H. Pylori negative and statistical tests were applied to study the association between H.Pylori and hs-CRP. Data analysis was done using Microsoft excel sheet. Pearson chi-square test was used for categorical variables. A “p” valueless than 0.05 was considered to be statistically significant.

RESULTS:

Total sixty patients were included in the study. The mean age of the study subjects with dyspepsia was 50.08 ± 10.60 years. Maximum number of patients was in the age group of 41 to 60 years (68.33%). There were 34 (56.67%) females and 26 (43.33%) males in the study. The age and gender distribution of the study subjects is shown in Table 1.

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Table 1. - Age-wise and gender-wise distribution of study subjects

Age group (years)	**No of patients (%)**
18-30	2(3.33)
31-40	9(15)
41-50	23(38.33)
51-60	18(30)
>60	8(13.33)
Gender	**Number of patients (%)**
Males	26(43.33)
Females	34 (56.67)

Table 2. - Addictions in the study subjects

Addictions	Total (%)
Only Tobacco addiction	16 (26.67)
Only Alcohol addiction	14 (23.33)
Both tobacco and alcohol addiction	10 (16.67)
No Addictions	20(33.33)
Total	60

Table 2 shows other demographic parameters of the study subjects. Total 40 out of 60 patients had addictions. Total 14 patients were addicted to both alcohol and tobacco.

Average BMI was 28.90 ± 3.60 Kg/m^2. Total 8 patients had normal BMI (13.33%), 31 patients were overweight (51.67%) and 21 patients were obese (35%). The mean pulse rate was in normal range. Out of 60 subjects, 32 patients were normo-tensive and 28 patients were hypertensive. Biochemical parameters like haemoglobin, total leucocyte counts, Erythrocyte Sedimentation Rate, Liver function test and renal function tests were within normal limits. Mean hs – CRP levels were higher than normal (2.80 ± 5.14 mg/L).

Table 3. – Demographic and laboratory parameters in the study subjects

Parameter	Mean ± SD
BMI (Kg/m2)	28.9 ± 3.6
Pulse (per min)	87.23 ± 6.54
Haemoglobin(gm/dL)	11.70 ± 1.39
Total Leucocyte Count (per cubic mm)	7648 ± 1380
ESR (at the end of first hour in mm)	19 ± 8.50
hs – CRP mg/L	2.80 ± 5.14

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Average duration of dyspeptic symptoms in the study subjects was 36.3 ± 22.7 days. Epigastric burning pain was the most common symptom reported in 86.67% patients followed by indigestion in 83.33% and regurgitation in 23.33%. Nausea and vomiting were present in 12% patients.

All patients underwent UGIE to investigate dyspepsia. UGIE was abnormal in 55 patients. Gross findings matched with that of the histopathological findings. Five patients had gastric ulcers and 2 patients had duodenal ulcers. Seven patients had lower 1/3rd esophagitis. A total of 32 patients had acute changes and 23 patients had chronic changes of gastritis of the body and the antrum on endoscopic examination grossly.

On histopathological examination (HPE) 8 patients had esophagitis, 30 patients had acute gastritis of the body (12 had superficial erosive gastritis, 15 had haemorrhagic gastritis and 3 had superficial erythematous gastritis) and 21 patients had acute antral gastritis (12 had superficial erosive antral gastritis and 9 had haemorrhagic antral gastritis). 23 patients had chronic changes of gastritis of the body and the antrum on HPE.

H. Pylori infection was detected in 22 patients. (Proven with a positive Rapid Urease Test and detection of H. Pylori on HPE). HP infection prevalence rate was 36.67%.

Table 4. An association between H. Pylori infection and high Hs- CRP levels.

	hs-CRP < 0.01 mg/L	hs-CRP > 0.01 mg/L	P value
H. Pylori infection present	5	17	0.00064*
H. Pylori infection absent	26	12	

*Chi square test applied – P < 0.05

Table 4 shows that patients with HP infections had significantly higher hs – CRP level than HP negative patients. (P < 0.05)

Discussion:

This cross-sectional observational study was done for a period of 12 months with an aim to study high sensitivity C reactive protein levels in patients with chronic dyspepsia and its correlation with helicobacter pylori infection. Total 60 patients with dyspepsia were included in the study. UGIE was done for all the patients and antral biopsy sample was subjected to H. Pylori detection. HS-CRP was done for all the patients. A statistical correlation was sought between the HP infection and high hs-CRP levels.Mean age group of the study subjects in our study was 50.08 ± 10.60 years and maximum number of patients with dyspepsia were in the age group of 41 – 60 years (68.33%). In a similar study done by Al-Fawaeir et al., the mean age in HP positive patients was 50 ± 9.6 years and in HP negative study subjects was 49 ± 8.7 years and age groups varied between 35 – 70 years. This was comparable to our study.[7]

Female preponderance was seen in study subjects 34 (56.67%) females and 23 (43.33%) males. Contrary to this, in a study by Al-Fawaeir et al. there was a male preponderance (65.6%).[7]Total 40 out of 60 patients had addictions. Total 16 patients were using tobacco (26.67%). In a study by Al-Fawaeir et al., 36.8% patients were smokers.[7] In a study by Ishida total 43.33% were smoker.[8]Total 23.33% patients were addicted to alcohol. In an African study by Wafula et al., 2.8% patients were cigarette smokers and 15.5% took alcohol.[9]

In our study 86.67% patients had BMI ≥25, on contrary to ishida study which had only 27.49% with BMI ≥25, [8] or in kebapcilar study which had mean BMI of 22.9 ± 4.5 in HP positive individuals and 23.7 ± 3.1,[10] or in al fawaeir et all which had 32.93% of patients with BMI ≥25. [7] This difference can be due to

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selection bias or different ethnicity which need to be further evaluated.In our study epigastric burning pain (Heartburn) was the most common symptom reported in 86.67% patients followed by indigestion in 83.33%. Which is comparable to a study by Bhumika et al Indigestion was present in 90%, heartburn in 96%.[11]

In a study by Babu Krishnan et al., diabetic patients had high prevalence of dyspepsia (63%). Only a minority presented with the classical symptoms of dysphagia and heartburn.[12]Study by Dawod HM et al., had heartburn, indigestion (42%) and burning (25.7%) as the main symptoms. Nausea (2.9%) and dysphagia (5.7%) were least commonly seen.[13]Average duration of dyspeptic symptoms was 36.3 ± 22.7 days which was not comparable to average duration in study by Bhumika et al which showed patient having average duration of dyspeptic symptoms of 7.68 ± 7.73 months

In our study 91.67% of patients had changes of gastritis (Acute and chronic) 11.67% had esophagitis, 8.33% had gastric ulcers and 3.33% patients had duodenal ulcers.

Study by Wafula et al., showed that 67.6% had gastritis, 25.7% had duodenitis, 11.3% had oesophageal candidiasis, 8.5% had reflux oesophagitis, 8.5% had ulcers and 1.4% had gastric malignancy.[9] Thus, gastritis was most common gross UGIE finding which was similar to the current study findings. In a study by Ogutu et al., a normal looking mucosa was the commonest single endoscopic finding, accounting for 34.2%, followed by gastritis 31.7% and duodenal ulcer 29.2%.[1430] HP positive study subjects in current study had statistically significantly different and higher hs-CRP levels compared to HP negative patients. (4.74 ± 5.47 vs 0.48 ± 2.51) ($P < 0.05$)

Study by Raut et al demonstrated significantly higher levels of hs-CRP in gastritis with *H. pylori* as compared to that without, but also noted that, 55% of patients with *H. pylori* positive gastritis had serum levels of hs-CRP in intermediate to high cardiovascular risk range as compared to only 35% in *H. pylori* negative gastritis.[15] Study by Jafarzadeh A et al indicated that mean serum levels of hs-CRP in H pylori positive peptic ulcer and asymptomatic groups were significantly higher than that observed in an H. pylori negative control group.[16]

A study on the effects of *H. pylori* eradication among 78 patients in Turkey reported that serum CRP was significantly reduced among 57 participants with successful eradication, but not among 21 participants in whom the eradication failed.[17]It is also found that HP positive patients had high risk for cardiovascular disease than those with HP negative patients ($P<0.05$) . Few other studies also showed that hs-CRP levels were higher in HP infected patients.[8,10] CRP is a marker of inflammation and HP infection of the gastric antrum induces a potent inflammatory reaction. Thus, hs-CRP levels tend to rise in chronic HP infection. Higher hs-CRP levels are risk factors for coronary heart disease and stroke. Therefore, it can be concluded that HP infection causing high levels of hs-CRP may also be a potential risk factor for metabolic derangements which eventually lead to CHD. Limitations of study were selection bias as there were no control group and overall patients had high BMI compared to other studies but that can be attributed to ethnicity of the study subjects. Also, alcohol was not excluded in this study which can alter the endoscopic findings in study subjects.

Conclusion:

hs – CRP levels were significantly higher in patients with HP positivity than HP negative, thus increasing the risk of cardiovascular risks in such patients.

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