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# PREVALENCE OF HELICOBACTER PYLORI INFECTION IN PATIENTS OF RHEUMATOID ARTHRITIS WITH UPPER GASTROINTESTINAL SYMPTOMS

Medicine

**Dr. Avinash Kulhar** Department of Medicine, Hindu Rao Hospital, Delhi

**Dr. Hemant Sharma*** Senior Physician, HOD Department of Medicine, Hindu Rao Hospital, Delhi
*Corresponding Author

## ABSTRACT

**Introduction**: Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown aetiology affecting approximately 0.5–1% of the adult population worldwide.[1] Helicobacter Pylori HP infection, one of the most common chronic bacterial infections in the world, is linked to peptic ulcer disease (PUD) and is a key constituent of the human micro biome.[5]

**Aims and objectives:** 1. To study the prevalence of Helicobacter pylori infection in confirmed cases of Rheumatoid Arthritis. 2. To study the relation between Helicobacter pylori infection and upper gastrointestinal symptoms (like nausea, vomiting, GERD and dyspepsia) in patients of RA receiving NSAID's and DMARD's therapy.

**Material and method: Inclusion Criteria** Patient on DMARDs or NSAIDS having upper GI symptoms like nausea, vomiting, GERD and dyspepsia. 2. Willing to give informed consent. 3. Willing to undergo the requisite investigation.

**ExclusionCriteria:1.**Uncooperative patients. 2. Not willing for endoscopy. 3. Contraindication of endoscopy.

**Results** There was no statistically significant association between HP infection and the duration of GI symptoms ($p = 0.850$). There was a statistically significant association between HP positivity and endoscopic examination ($p = 0.001$). There was a statistically significant association between HP infection and nausea ($p = 0.035$), and GERD ($p = 0.007$).

**Statistical Analysis**: The data was analysed using SPSS version 23 statistical software package. The statistical significance of continuous variables was determined by unpaired student test. Statistical significance of categorical variables was determined by Chi square test. The level of statistical significance was taken as $p \leq 0.05$.

**Conclusion:** RA patients with refractory upper GI symptoms and taking DMARD's and NSAID's; should undergo endoscopy and HP testing. If positive, they should be treated with triple therapy.

## KEYWORDS

## INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown aetiology affecting approximately 0.5–1% of the adult population worldwide.[1] A.N. Malviya et al in a study from rural Delhi reported the prevalence of RA as 0.75%, the maximum age specific prevalence of 2.5% was reported in age group of 25-29 years and 90.30% of those identified with RA were females.[2]The disease results from a complex interplay of genetic, environmental, and immunologic factors that lead to a deregulation of the immune system and thus a breakdown in self-tolerance.[3]. RA has a systemic nature, thus affecting a variety of organ systems.[4] HP infection, one of the most common chronic bacterial infections in the world, is linked to peptic ulcer disease (PUD) and is a key constituent of the human micro biome.[5] The clinical manifestations of HP infection include chronic gastritis, gastric ulcer (GU) and duodenal ulcer (DU), adenocarcinoma, and gastric mucosa–associated lymphoid tissue (MALT) lymphoma.[5] Nonetheless, most infected individuals remain asymptomatic for life despite developing chronic histological gastritis.[5] The prevalence of HP infection varies greatly; ranging from more than 80% in developing countries to less than 40% in developed countries. HP is very common in the Indian subcontinent. Exposure occurs in childhood and approximately 80% of adults have been infected at some time.[6]

## AIMS AND OBJECTIVES:

1. To study the prevalence of Helicobacter pylori infection in confirmed cases of Rheumatoid Arthritis. 2. To study the relation between Helicobacter pylori infection and upper gastrointestinal symptoms (like nausea, vomiting, GERD and dyspepsia) in patients of RA receiving NSAID's and DMARD's therapy.

## MATERIALS AND METHODS:

Patients of rheumatoid arthritis (based on 2010 revised American College of Rheumatology/European League Against Rheumatism criteria) with upper gastrointestinal symptoms, coming to the rheumatic clinic (from 01 – 08 – 2016 to 01 – 03 – 2018) were taken up for endoscopy and the prevalence of HP infection was studied by biopsy and kit method.Detailed clinical history has been taken by focusing on gastrointestinal symptoms. Detailed clinical examination was done. Investigations - all the patient were subjected to investigate for Hemogram, Liver Function Test; Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Alkaline Phosphatase, Kidney Function Test, Rheumatoid Factor, C Reactive Protein and Erythrocyte Sedimentation Rate.

## ENDOSCOPIC GUIDED BIOPSY OF UPPER GASTROINTESTINAL TRACT:

Informed consent was taken for performing an upper gastrointestinal endoscopy to rule out the presence of gastrointestinal lesions. After an overnight fast, endoscopy was performed with the help of a forward-viewing instrument (Olympus). During endoscopic examination, a total of four biopsy specimens were obtained from the gastroduodenal mucosa of normal appearance; two specimens from the greater curvature of the upper body and two from the antrum of the stomach, using biopsy forceps (Olympus).Then these specimen's sensitivity to H. pylori was checked via kit method. The name of the kit used was "PYLO DRY (Rapid Agglutination Test)"; which detects the urease enzyme of HP.[7]

## INCLUSION CRITERIA

Patients satisfying 2010 revised ACR (American college of Rheumatology) and EULAR (European League against Rheumatism) criteria for diagnosis of rheumatoid arthritis.1.Patient on DMARDs or NSAIDS having upper GI symptoms like nausea, vomiting, GERD and dyspepsia. 2. Willing to give informed consent. 3. Willing to undergo the requisite investigation.

## EXCLUSION CRITERIA:

**1.** Uncooperative patients. 2. Not willing for endoscopy 3. Have done endoscopy already for HP infection. 4. Contraindication of endoscopy. 5. History of recent use of drugs for management for HP infection. 6. Patients of CKD, CLD, Heart failure or other diseases causing upper GI Symptoms.

## STATISTICAL ANALYSIS:

The data was analysed using SPSS version 23 statistical software package. Descriptive data analyses of the selected characteristics (means and SDs for continuous variables and proportions for categorical variables) were done among the total sample comparing the groups of "HP positive" and "HP negative". The statistical significance of continuous variables while comparing the means between two groups (HP positive and HP negative) was determined by

unpaired student t test. Similarly, the statistical significance of categorical variables between both groups (HP positive and HP negative) was determined by Chi square test. The level of statistical significance was taken as $p \leq 0.05$.

**RESULTS:**

A total number of 100 patients satisfying the 2010 revised ACR (American college of Rheumatology) and EULAR (European League against Rheumatism) criteria for diagnosis of rheumatoid arthritis were included in the study.There were 76% of females and 24% of males in the study sample; showing a greater prevalence of females in the sample. Age of the study sample varied from 17 years to 65 years with a mean age of 40.91 years and a standard deviation of 11.56.The highest prevalence of males (41.7%) was in the age group of 41-50 years, whereas for females (30.3%) the highest prevalence was in the age group of 31-40 years. Disease duration since diagnosis of cases ranged from 0.06 year (3 weeks) to 25 years with a mean duration of 6.35 years and a standard deviation of 5.19. Median disease duration was 5 years and a mode of 2 years. Majority of the study sample (43%) had a disease duration of 0 – 5 years.

32% of the study sample was RF negative whereas 68% was RF positive.86% of the study sample was CRP negative whereas 14% was CRP positive. The prevalence of Helicobacter Pylori infection in the study sample was 30%. Prevalence of NSAID usage**.** The number of RA patients using NSAID's was 71%.. The duration of DMARD's usage varied from 0.06 to 25 years, with a mean of 4.65 years and a standard deviation of 4.60 years. The prevalence of anemia in the study sample was 60%.In the study sample, there is a higher prevalence of females (46%) who are anemic as compared to males (14%).

Majority of the study sample (83%) had an acute occurrence (less than a year) of GI symptoms rather than chronic symptoms. The frequency of occurrence of GERD in the study sample is 73%.The frequency of occurrence of nausea in the study sample was 75%.and of vomiting was 25%.The frequency of occurrence of dyspepsia in the study sample was 45%.Majority of the sample had no LFT and KFT derangements. A vast majority of the study sample (89%) had normal endoscopic findings. The various other findings include duodenitis (7%), duodenal ulcer (2%), antral gastritis (1%) and small hiatal hernia (1%).There was no statistically significant association between HP infection and the duration of RA ($p = 0.694$).There was no statistically significant association between HP infection and the duration of DMARD's usage ($p = 0.851$).There was no statistically significant association between HP infection and the duration of NSAID's usage ($p = 0.075$).

**Table -1: Association Of Helicobacter Pylori Infection With Nsaid's (using "chi Square Test")**

| | HP infection positive (N = 30) | | HP infection negative (N = 70) | | P value |
|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | |
| NSAIDS (not taken) | 2 | 6.7 | 27 | 38.6 | 0.001 |
| NSAIDS (taken) | 28 | 93.3 | 43 | 61.4 | |

There was a statistically significant association between HP infection and NSAIDS ($p = 0.001$). There was no statistically significant association between HP infection and the duration of GI symptoms ($p = 0.850$).

**Table-2: Association Of Helicobacter Pylori Positivity With Endoscopic Examination (using "chi Square Test")**

| | HP infection positive (N = 30) | | HP infection negative (N = 70) | | P value |
|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | |
| Endoscopic examination (normal) | 20 | 66.7 | 69 | 98.6 | 0.001 |
| Endoscopic examination (abnormal) | 10 | 33.3 | 1 | 1.4 | |

There was a statistically significant association between HP positivity and endoscopic examination ($p = 0.001$). There was a statistically significant association between HP infection and nausea ($p = 0.035$).and also between HP infection and GERD ($p = 0.007$).There was no statistically significant association between HP infection and vomiting ($p = 0.493$).There was no statistically significant association between HP infection and dyspepsia ($p = 0.332$).

**Discussion:** NSAIDS and DMARDS are the corner stone of drug therapy in RA and also contribute to the variety of gastrointestinal side effects like nausea, vomiting, dyspepsia and GERD. Recent studies have grappled with possible implication of H pylori infection on the clinical course of RA.

A total of 100 patients were included in the study out of which 76% were females and 24% were males. The mean age of the study population was 40.9111.56 years. A.N. Malviya et al[2] in a study from rural Delhi reported the prevalence of RA as 0.75%, the maximum age specific prevalence of 2.5% was reported in age group of 25-29 years and 90.30% of those identified with RA were females.[2] In our study prevalence of RA was highest in the females between age group of 31 and 40 years. In our study the duration of disease had a range between 3 weeks and 25 years with a mean of 6.35 +/- 5.19 years. The prevalence of Rheumatoid factor in the study population was 68%.

In the present study the prevalence of HP in RA patients was 30%. In a meta-analysis published by James K Y Hoi et al on global prevalence of H Pylori infection, which included 407 patients from India, estimated the prevalence of H pylori infection in India at 63.5%.[8]Hongyan wen et al found that the patients of rheumatic diseases were significantly more likely to suffer from HP infection than health control (89 vs 42%, $P < 0.01$).[9] .

A detailed history of occurrence of GI symptom was obtained. The most frequently reported complaints were GERD, dyspepsia, nausea and vomiting. Study by Abraham et al also concluded that the most commonly recognized manifestation of *H. pylori* infection in India is peptic ulcer disease, particularly duodenal ulcer disease, which outnumbers gastric ulcers between 8:1 and 30:1.[10]

The Endoscopic examination revealed presence of duodenitis in 7 patients, duodenal ulcers in 2 patients, antral gastritis was found in 1 patient and hiatal hernia was present in 1 patient. 89% patients had normal endoscopy. Out of 11 patients with abnormal endoscopic findings, 10 patients were HP positive. H. pylori infection was, however found in 20 patients with normal endoscopy findings. The study found a statistically significant association between HP positivity and endoscopic findings ($p=0.001$). An endoscopic study conducted to find the HP infection found that; 79.3% diagnosed with endoscopic gastritis had HP infection whereas 12.7% with normal endoscopic findings had HP infection.[11]The prevalence of H. pylori infection in patients with gastritis was significantly higher than in those with a normal stomach ($p<0.05$).[11]

The study found a statistically significant association between the NSAID's usage among symptomatic patients and HP infection ($p=0.001$), showing that HP infection is more prevalent with increased usage of NSAID's. A study has found that HP infection and NSAID's has a synergistic action which leads to ulcer formation and complications.[12] . We also found that there was an association between GERD and presence of H pylori infection. 27 patients with H pylori infection had GERD and 48 patients with no H pylori infection had GERD. The association was significant and p value was 0.007. A study conducted to find out if there was any relationship between GERD and HP infection; found that there was not only a statistically significant association but an association between the grade of GERD with HP positivity.[13]

**CONCLUSION**:

The disease course of RA and the gastrointestinal symptoms were not influenced by presence of H Pylori infection except GERD and Nausea. RA patients with refractory upper GI symptoms and taking DMARD's and NSAID's; should undergo endoscopy and HP testing. If positive, they should be treated with triple therapy.

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