

Prevalence of *H. pylori* in Immune Thrombocytopenic Purpura (ITP) in a tertiary care center, South India

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Introduction: Immune thrombocytopenic purpura (ITP) has been linked with *Helicobacter Pylori* infection. **Objectives:** The objective of the present study was to determine the prevalence of *H. pylori* infection in adult ITP patients in a tertiary care center in South India. **Methods:** 50 adult patients with ITP in the Department Hematology, Madras Medical College were recruited for a cross-sectional study over a period of 6 months. Biopsy from the antrum was subjected to Rapid urease test to detect *H. pylori*. A total of 50 patients participated in the study. **Result:** The prevalence of *H. pylori* infection in ITP patients was 36%. The majority of patients were male (78%). **Conclusion:** The diagnosis of *H. pylori* in ITP patients may be considered in high prevalent areas.

Keywords: Immune thrombocytopenic purpura, *Helicobacter Pylori*, Urease test

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Introduction

Immune thrombocytopenic purpura (ITP) commonly called as idiopathic thrombocytopenic purpura, is an acquired disease of adults and children which is immune mediated and is characterized by transient or persistent decrease of the platelet count. The risk of bleeding increases depending upon the degree of thrombocytopenia.

When ITP occurs in the absence of an evident predisposing etiology it is known as primary ITP and when it occurs secondary to an identifiable cause it is known as secondary ITP. Pseudo thrombocytopenia should also be ruled out.

Helicobacter pylori have been clearly recognized as the main cause of gastritis and most of gastric adenocarcinoma and mucosa associated lymphoid tissue (MALT) lymphoma. It has also been implicated in the pathogenesis of some autoimmune diseases such as rheumatoid arthritis, autoimmune thyroid disease and ITP. Many studies have well documented that there is an association between ITP and *H. pylori* infection and showed a high prevalence of *H. pylori* infection in patients with ITP [1-4].

Recently, Khan Sheema et al conducted an interventional and prospective study and reported a good response to bacterium eradication in most of the cases. However discrepant reports have been produced by earlier studies from France and Spain where the prevalence of *H. pylori* was high, but there was no significant improvement in platelet count after eradication therapy [5, 6,7].

Studies from India pointed out that almost 80% to 90% of the population is infected with *H. pylori* in all age groups [8-11]. There is a relationship of *H. pylori* infection with hygiene lifestyle and socioeconomic conditions with a 45% yearly increase in incidence rate of *H. pylori* infection in developing nations compared to approximately 0.5% in developed and industrialized countries [12].

Thus *H. pylori* prevalence in ITP patients mirrored the prevalence of *H. pylori* in the general population. However, It is still not clear if *H. pylori* should be implicated as a secondary cause of ITP or it is just an alternative, additional or incidental finding in patients with ITP in our country particularly South India. In this study, authors aimed to find the prevalence of *H. pylori* in ITP patients and its association with clinical and demographic profiles.

Materials and Methods

Type of study: This was a prospective, cross sectional study where all adult patients with ITP in the Department of Hematology, Madras Medical College were reviewed and recruited over a period of 6 months.

Inclusion and exclusion criteria: The inclusion criteria included patients with ITP in whom the secondary causes of ITP had been ruled out. Patients who were previously included were not recruited again. Patients were not eligible if they had anti-phospholipid antibody syndrome, systemic lupus erythematosus, lymphoproliferative disorders, chronic renal disease or drug induced thrombocytopenia. Patients who are HIV positive, Hepatitis C virus positive or pregnant were also excluded.

Ethical consideration and permission: Informed consent was obtained from all patients and the study was approved by the Institute Ethics Committee.

Patients were asked questions as per a questionnaire and subjected to clinical examination. All the secondary causes of ITP were ruled out using appropriate tests. Patients were grouped as per age, sex and platelet counts. Patients who have dyspeptic symptoms were identified. Routine lab investigations were done. Platelets counts were done before endoscopy. Patients with stable platelet counts and no active bleeding were subjected to upper GI endoscopy in the Medical Gastroenterology Department and the findings were recorded. A biopsy was taken from the antrum and it was subjected to Rapid urease test to detect *H. pylori*. Patients who turn out to be positive were put on *H. pylori* regimen.

Statistical analysis: Shapiro-Wilk Test was used for normality of data for parametric variable analysis. Continuous variables were analyzed by Mann-Whitney U and categorical variables were analyzed by Chi-square test. *P* level of significance was considered at 5% level. Data analysis was performed on SPSS version 17.0.

Results

A total of 50 patients participated in the study. The patients' characteristics were analyzed. The median age was 30 years, 16 were in the third decade and 13 in the fourth decade.

The majority of patients were male (78%) (Table 1).

Table-1: Baseline demographic and clinical characteristics of study patients.

Variables	H. Pylori Negative	H.Pylori Positive	P value
Age	30.0 (21- 40)	30.0 (24.75 - 40.75)	0.671
Economic status			0.609
Upper	5 (62.5%)	3 (37.5%)	
Lower	27 (64.3%)	15 (35.7%)	
Gender			0.621
Male	25 (64.1%)	14 (35.9%)	
Female	7 (63.6%)	4 (36.4%)	
Platelet count	31000 (16250 - 46500)	20000 (9750 - 24250)	0.009
Bleeding			0.285
Yes	27 (61.4%)	17 (38.6%)	
No	5 (83.3%)	1 (16.7%)	
Skin rash			0.049
Yes	18 (54.5%)	15 (45.5%)	
No	14 (82.4%)	3 (17.6%)	
Dyspepsia Yes	10 (76.9%)	3 (23.1%)	0.216
No	22 (59.5%)	15 (40.5%)	
Endoscopy (gastritis)			0.124
Yes	11 (52.4%)	10 (47.6%)	
No	21 (72.4%)	8 (27.6%)	
Blood group			0.053
A Positive	6 (85.7%)	1 (14.3%)	
AB Positive	2 (100%)	0 (0%)	
B Negative	1 (50%)	1 (50%)	
B Positive	10 (90.9%)	1 (9.1%)	
O Negative	0 (0%)	1 (100%)	
O Positive	13 (48.1%)	14 (51.9%)	
Duration	20.0 (12.25 - 39.0)	17.0 (7.5 - 46.5)	0.793

Prevalence of *H. pylori* in ITP patients: Analysis of patient's clinical profile was done and an antral biopsy and was subjected the specimen to rapid urease test, to detect the *H. pylori* status of the ITP patients. Out of the 50 ITP patients 18 were *H. pylori* positive that is the prevalence was 36%. The frequency of *H. pylori* infection was equal among females (35.89%) and males (36%) although ITP was more common among females.

Demographic profile of ITP patients: Applying the Kuppusamy's criteria it was found that higher percentage of people (84%) were from the lower economic class and 16% from upper economic class. The frequency of *H. pylori* positivity was almost equal in both the upper class (37.5%) and lower class (35.7%).

In the present study, most of the patients were from urban area (76%). However, *H. pylori* positivity was more common in rural population, 41% (5 positives among 12) in ITP patients from rural areas and 34% (13 positives among 38) in urban area. Median platelet count was 21000 cells/cu mm in *H. pylori* positive individuals from both urban and rural population.

Among demographic profile of ITP patients, there was no significant difference between *H. pylori* positive and negative patients in terms of age, gender, economic status.

Clinical profile of ITP patients

Bleeding: 88% (44 of 50) presented with bleeding and 12% (6 of 50) were asymptomatic. Among the patients with bleeding 50% had major bleed (GI bleed, genitor-urinary and intra cranial) and 50% presented with minor bleed (skin and mucous bleed).

H.pylori positivity was more frequent in patients with bleeding 38% (17 of 44 positive) than patients without bleeding 16% (1 of 6). Median platelet in ITP patients with bleeding and *H. pylori* infection was 20000 cells/cmm.

Skin rash: Among 64% (32 of 50) of ITP patients with skin rash *H. pylori* positivity was seen in 47% (15 positives of 32) of these patients. *H. pylori* positivity among patients without skin rash was only 16.6%.

Dyspepsia: Out of 50 patients, only 13(26%) had dyspepsia and 74% had no dyspepsia. *H. pylori* positivity was only 7% among patients with dyspepsia as compared to 46% positivity in patients without dyspepsia.

Platelet count: All the 18 *H. pylori* positive patients had platelet counts less than 60000, out of these 77% (14 of 18) had platelet < 30000 and 23% (4 of 18) had platelet counts between 31000 and 60000. Significant low median platelet count (20000 cells/cmm) in ITP patients with *H.pylori* positivity was observed compared to ITP patients who were *H.pylori* negative (31000 cells/cmm) (P < 0.009).

Endoscopy (Gastritis): Out of 50 patients, 21 (42%) had gastritis on endoscopy and of these 47% (10 of 21) were positive for *H.pylori*. the remaining 29 (58%) patients did not have gastritis on endoscopy and only 27% (8 of 29) were *H.pylori* positive.

Out of 18 ITP patients positive for *H. pylori*, 55% (10 patients) had gastritis on endoscopy.

Blood group: In the present study majority of the patients had O positive (54%) and B positive blood groups (22%). 14% were A positive, 4% AB positive, 4% B negative and 2% O negative respectively. 14 out of the 18 *H. pylori* positive patients were O positive (77%).

Duration of ITP: In the present study, 66% (33 of 50) had chronic ITP, 22% (11 of 50) had persistent ITP, 6% (3 of 50) had ITP of less than 3 months duration and 6% (3 of 50) had splenectomy done for refractory ITP. The median duration of ITP patients included in the present study was 18 months.

61% (11 of 18) *H. pylori* positive ITP patients had chronic ITP, 22% (4 of 18) had persistent ITP 11% (2 of 18) had acute ITP and 6% (1 of 18) had steroid refractory ITP.

H. pylori frequency was more among patients with acute ITP (66.66%) when compared to patients with persistent ITP (36.66%), chronic ITP (33.33%) and refractory ITP (33.33%).

In analyzing the clinical profile there was no significant difference between *H. pylori* positive and negative patients in terms of bleeding risk, dyspepsia, endoscopic findings and duration of ITP. However, a statistically significant difference between *H. pylori* positive and negative patients in terms of platelet counts were observed.

Discussion

Several studies have shown that ITP patients infected with *H. pylori* were found to be significantly older than ITP patients not infected with *H. pylori* [13-15]. Prevalence of *H. pylori* increases with increasing age and is mostly seen in patients more than 30 years of age. In the present study median age of *H. pylori* positive and *H. pylori* negative patients was 30 years.

Similar to other studies, no significant difference was demonstrated in the prevalence of *H. pylori* infected males and females. Duration of ITP is important in monitoring response to treatment of *H. pylori*. Shorter the duration better is the response. The median duration of *H. pylori* positive patients was 20 months and *H. pylori* negative patients was 17 months.

Significant association between *H. pylori* positivity and dyspepsia was reported by Patel P et al [17], but not by Stasi et al [18]. In the present study there was no significant association between *H. pylori* and dyspepsia ($P < 0.38$). No studies showed any significant association between the initial platelet count and *H. pylori* positivity [19] but most of the *H. pylori* infected ITP patients presented with severe form of ITP at the time of diagnosis. In the present study 14 of 18 (77.77%) *H. pylori* ITP patients presented with severe ITP at the time of diagnosis and their platelet counts were < 30000 cells/cmm and it is statistically significant, P value < 0.003 .

H. pylori has been implicated in a number of autoimmune diseases like ITP [20]. The first association was proved in 1998 by Gasberrini et al [21]. Small study by Emilia et al (13 positive of 30) also proved significant association [22]. In the present study 18 (36%) were positive out 50 ITP patients. Similar to other studies, the present study also proves significant association between *H. pylori* and ITP.

Most of the studies had found a high frequency of *H. pylori* infection in patients with ITP and it was observed that in most of them after the eradication of *H. pylori* there was a significant increase in platelet count [23-25]. Worldwide analysis had found that 65.7% of ITP patients are infected with *H. pylori*. In contrast some studies from USA [26] and France [27] have reported only a low frequency of *H. pylori* infection. The possible explanation for this could be the low prevalence of *H. pylori* infection in this population. The reason for such discordant reports is uncertain but it might reflect the results of studying diverse patient groups, failure to stop concomitant treatment and the genetic diversity of *H. pylori*.

The frequency of *H. pylori* association with ITP reflected the prevalence of *H. pylori* in that geographical area. *H. pylori* positivity was proportionate to the general population. This explains why most of the reports are from Japan and Italy. Successful *H. pylori* eradication led to good platelet response in areas where *H. pylori* infection rate in ITP patients was higher than in those where no association was found.

Conclusion

The present study confirms the existence of association between *H. pylori* and ITP.

A significant association between the platelet counts at presentation in *H. pylori* positive ITP patients was observed.

What the study adds to the existing knowledge?

There was no significant association with other parameters like sex, age, residence, socioeconomic status, bleeding, dyspepsia and endoscopy findings. Considering the low costs and non-invasiveness of the diagnostic test and the favorable toxicity profile of eradication compared to the standard treatment for ITP the detection and eradication of *H. pylori* should be considered in high prevalent areas. The British society of Hematology also recommends *H. pylori* eradication and screening as a treatment in ITP.

Author's contribution

Dr. K Chenthil: Study design. **Dr. Anny Antony:** Sample collection. **Dr. Margaret C.:** Data collection. **Dr. R. Karthikeyan:** Data analysis. **Dr. Anny Antony:** Manuscript writing. **Dr. Muhammed Ali:** Revision of manuscript.

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