



## IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION

### General Medicine

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### ABSTRACT

**Introduction:** The relationship between H.pylori infection and ITP was initially described in 1998 in an Italian study. According to the Maastricht III consensus conference ITP is one of the two extra-intestinal diseases for which H.pylori infection and eradication is indicated. We have determined the frequency of H.pylori infection in ITP patients to ascertain significant association with H.pylori. The prevalence of H.pylori infection and its association with ITP was studied in a series of 50 ITP patients on regular follow up in the Hematology department in RGGGH. They were subjected to endoscopy. Antral biopsy was taken and rapid urease test was performed to confirm the H.pylori status of the patients. **Aim :** To study the association between Immune Thrombocytopenic Purpura and Helicobacter pylori infection. To determine the prevalence of Helicobacter pylori infection in Indian patients with ITP. To evaluate if H. Pylori infected patients with ITP could be identified by symptoms referable to the GI tract. To study the clinical profile of ITP patients. **Results :** 18 of the 50 ITP patients (36%) were found to be H.pylori positive. The p value was calculated using the 't' test which was found to be 0.048 which shows significant association of H.pylori infection with ITP. Hence all ITP patients should be screened for H.pylori and steps to eradicate H.pylori must be undertaken. Bacterium eradication provides a new good option for a non-immunosuppressive treatment in some ITP patients. **Conclusion :** The present study confirms the existence of association between H.pylori and ITP ( $P < 0.05$ ). Our study also showed a significant association between the platelet counts at presentation in H.pylori positive ITP patients. 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.

### KEYWORDS

Immune Thrombocytopenic Purpura, Helicobacter pylori, Rapid urease test, Thrombocytopenia

### INTRODUCTION:

Immune thrombocytopenic purpura (ITP) also known 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.

Helicobacter pylori is an ubiquitous gram positive bacterium which was initially discovered in 1982. It colonizes the stomach of about half of the world's human population throughout their lifetimes. H.pylori has been clearly recognized as the main cause of gastritis and most cases of peptic ulcer. It also plays a role in the pathogenesis 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. Relevant to this Gasbarrini et al recently conducted a study and showed a high prevalence of H.pylori infection in patients with ITP and also reported a good response to bacterium eradication in most of the cases.

The relationship between H.pylori and ITP was initially described in 1998 in an Italian study. However discrepant reports have been produced by subsequent studies. In countries like Japan and Italy where the prevalence of H.pylori is high, the association between H.pylori and ITP was more frequent that is 70% and 50% respectively. Whereas in United States where the incidence of H.pylori is low the association was only 22%. Thus H.pylori prevalence in ITP patients mirrored the prevalence of H.pylori in the general population. However studies from France and Spain where the prevalence of H.pylori was high, did not show significant improvements in platelet count after eradication therapy. Hence the association of H.pylori and ITP is still controversial. 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. All these possibilities have been suggested by different studies. In this study we aim to find the prevalence of H.pylori in ITP patients in our set up.

### AIM AND OBJECTIVES

1. To study the association between Immune Thrombocytopenic Purpura and Helicobacter pylori infection.
2. To determine the prevalence of Helicobacter pylori infection in Indian patients with ITP.
3. To evaluate if H. Pylori infected patients with ITP could be identified by symptoms referable to the GI tract.
4. To study the clinical profile of ITP patients.

### MATERIALS AND METHODS

This study was conducted in the Medicine department of Madras Medical college in collaboration with Department of Hematology and Department of Gastroenterology. It was a cross sectional study conducted over a period of 6 months. The study population included the patients admitted with acute onset ITP in the medical wards and ITP patients who were on regular follow up in the Hematology department of Rajiv Gandhi Government General Hospital.

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

### INCLUSION CRITERIA

Patients with ITP in whom the secondary causes of ITP have been ruled out

### EXCLUSION CRITERIA

APLA, HIV patients, Hepatitis C virus positive patients, SLE, Lymphoproliferative disorders, Drug induced thrombocytopenia, Children < 10 years, Pregnant women, Chronic renal disease, Chronic liver disease patients, Pseudothrombocytopenia, SLE

### RESULTS:

#### TABLE 1- GENDER

| Gender      | H.Pylori Positive cases |
|-------------|-------------------------|
| Male (11)   | 4                       |
| Female (39) | 14                      |
| Total (50)  | 18                      |
| p value     | >0.05 Not sig           |

Out of the 50 patients 39 were female and 11 were male. The female: male ratio was 3.5:1. The frequency of H.pylori infection was equal among females (35.89%) and males (36%) all though ITP was more common among females. No significant difference between male and

female regarding H pylori positive cases. p value >0.05.

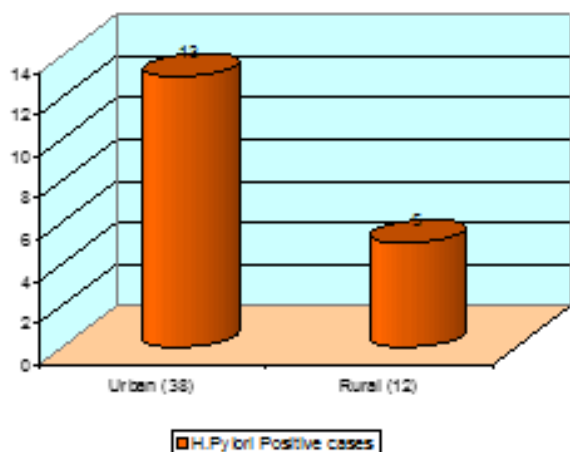
**TABLE 2-AGE**

| H. Pylori | Mean Age | SD              |
|-----------|----------|-----------------|
| Positive  | 32.4     | 12.1            |
| Negative  | 31.5     | 19              |
| p value   | 0.812    | Not significant |

Mean age of ITP was 31.9 years ( $\pm 12.42$ ). Mean age in males was 33.27 years and mean age in females was 31.5 years. Mean age of H.pylori positive ITP patients was 32.4( $\pm 12.1$ ) years and mean age of H.pylori negative ITP patients was 31.53( $\pm 19.0$ ) years. P value is 0.812 not significant.

**TABLE 3-RESIDENCE**

RESIDENCE VS H.PYLORI POSITIVE



In our study 38(76%) were from urban area and 12(24%) from rural area.

H.pylori positivity was more in rural population 41% (5 positive among 12) and it was 34% in urban area (13 positive among 38). P value is >0.05 not significant.

**TABLE -4 SOCIOECONOMIC STATUS:**

| Socio economic status | No.of cases   |
|-----------------------|---------------|
| Lower class (42)      | 15            |
| Upper class (8)       | 3             |
| p value               | >0.05 Not sig |

Applying the Kuppasamy's criteria it was found that 84% (42 of 50) were from the lower class and 16% (8 of 50) from upper class. The frequency of H.pylori positivity was equal in both the upper class (37.5%) and lower class(35.7%). P value is >0.05 not significant.

**TABLE -5 CLINICAL PROFILE:**

CLINICAL PROFILE



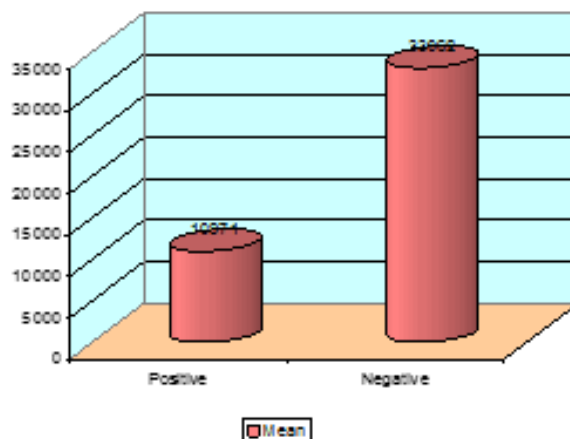
**Bleeding:** 88% (44 of 50) presented with bleeding and 12% (6 of 50) were asymptomatic. Among the patients with bleeding 50% had major bleed(GI bleed, genitor-urinary and intra cranial) and 50% presented with minor bleed (skin and mucous bleed).

**Skin rash:** 64%(32 of 50) of ITP patients had skin rash.

**Dyspepsia:** Out of 50 patients only 13(26%) had dyspepsia and 74% had no dyspepsia. Out of the 18 H.pylori positive patients only one had symptoms of dyspepsia.

**TABLE -6 PLATELET COUNT**

PLATELET MEAN VS H.PYLORI POSITIVE



In our study 60% (30 of 50) had platelet counts less than 30000 and 34% (17 of 50) had platelet counts between 31000 and 60000 and 6%(3 of 50) had platelet counts between 60000 and 100000. The mean platelet count of ITP patients was 27860( $\pm 17007.81$ ) cells/cu mm. All the 18 H.pylori positive patients had platelet counts less than 60,000, out of these 77%(14 of 18) had platelet <30000 and 23% (4 of 18) had platelet counts between 31000 and 60000. The mean platelet of H.pylori positive ITP patients was 10971( $\pm 12275$ )cells/cu mm and mean platelet of H.pylori negative ITP patients was 33062.5( $\pm 17709$ ) cells/cu mm. p value is 0.003 significant.

#### ENDOSCOPY (GASTRITIS):

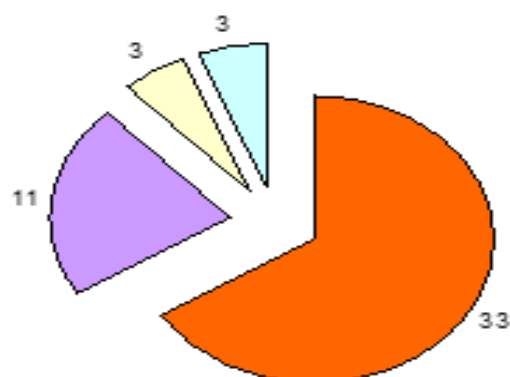
Out of 50 patients 21 (42%) had gastritis on endoscopy and of these 47% (10 of 21) were positive for H.pylori. The remaining 29 (58%) did not have gastritis on endoscopy and of these only 27% (8 of 29 ) were H.pylori positive. Out of 18 ITP patients positive for H.pylori 55% (10 patients) had gastritis on endoscopy.

#### BLOOD GROUP:

In our 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%).

**TABLE -7 DURATION OF ITP:**

DURATION OF ITP DISTRIBUTION

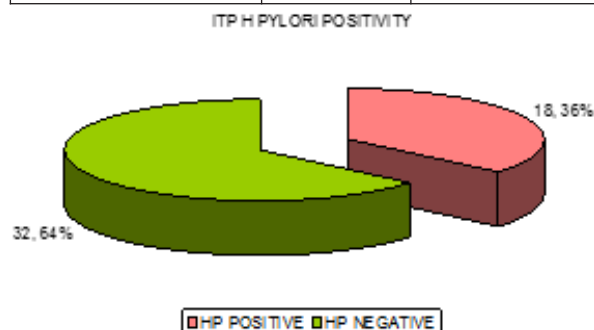


|             |                |
|-------------|----------------|
| Chronic ITP | Persistent ITP |
| < 3 months  | Refractory ITP |

In our 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 refractory ITP that is had splenectomy done. The mean duration of ITP patients included in our study was 29.44(±25.331) 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 refractory ITP.

**TABLE – 8 PREVALENCE OF H.PYLORI IN ITP:**

| ITP         | FREQUENCY | PERCENTAGE |
|-------------|-----------|------------|
| HP POSITIVE | 18        | 36         |
| HP NEGATIVE | 32        | 64         |



Out of the 50 ITP patients 18 were H.pylori positive that is the prevalence was 36%. 32(64%) were H.pylori negative.

## DISCUSSION

### CLINICAL CHARACTERISTICS:

**AGE:** 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.<sup>8, 14</sup> Prevalence of H.pylori increases with increasing age mostly seen in patients more than 30 years. In our study mean age in H.pylori positive was 32.14 years and in H.pylori negative patients was 31.59 years and P value was 0.8 and hence was not statistically significant.

**SEX:** None of the studies demonstrated any difference in the prevalence of H.pylori infected males and females. The P value in our study was 1 and was not statistically significant.

**DURATION:** Duration of ITP is important in monitoring response to treatment of H.pylori. Shorter the duration better is the response.<sup>8</sup> The mean duration of H.pylori positive patients was 31 months and H.pylori negative patients was 28.5 months. P value was 1 and was not significant.

**DYSPEPSIA:** Significant association between H.pylori positivity and dyspepsia was reported by Michel et al<sup>6</sup>, but not by Stasi et al<sup>8</sup>. In our study there was no significant association, P value was 0.38.

**PLATELET COUNT:** There were no studies which showed any significant association between the initial platelet count and H.pylori positivity.<sup>8, 14</sup> but most of the H.pylori infected ITP patients presented with severe form of ITP at the time of diagnosis. In our study 14 of 18(77.77%) H.pylori ITP patients presented with severe ITP at the time of diagnosis and their platelet counts were <30000cells/cu mm and it is statistically significant, P value is 0.003.

Other parameters like residence, socioeconomic status, bleeding and presence of skin rashes were assessed, but were not clinically significant. The endoscopic finding of gastritis was also assessed in H.pylori positive and negative cases but was not significant.

### P values

| Parameters          | P value | Interpretation |
|---------------------|---------|----------------|
| Mean age            | 0.8     | NS             |
| Mean duration       | 0.76    | NS             |
| Mean platelet count | 0.003   | S              |

NS- not significant S-significant

### ASSOCIATION BETWEEN H.PYLORI AND ITP:

Recently H.pylori has been implicated in a number of autoimmune diseases like ITP.<sup>11</sup> The first association was proved in 1998 by Gasberrini et al<sup>19</sup>. Small study by Emilia et al<sup>14</sup> (13 positive of 30) also proved significant association. In our study 18 (36%) were positive out

50 ITP patients. The P value was 0.048 and hence was statistically significant. So similar to other studies our study also proves significant association between H.pylori and ITP. Most of the studies in literature have 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.<sup>12-15</sup> In World this association has been found in 27 other studies. A consolidated analysis of these studies shows that 65.7% of ITP patients are infected with H.pylori. In contrast some studies from USA<sup>17</sup> and France 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.<sup>8</sup>

|          | OBSERVED N | EXPECTED N | RESIDUAL |
|----------|------------|------------|----------|
| POSITIVE | 18         | 25.0       | - 0.7    |
| NEGATIVE | 32         | 25.0       | 0.7      |

### Test Statistics:

|                           | RUT   |
|---------------------------|-------|
| CHI - SQUARE              | 3.920 |
| Df                        | 1     |
| ASYMPTOMATIC SIGNIFICANCE | 0.048 |

### CONCLUSION:

The present study confirms the existence of association between H.pylori and ITP (P < 0.05). Our study also showed a significant association between the platelet counts at presentation in H.pylori positive ITP patients. 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 recommends H.pylori eradication and screening as a treatment in ITP.

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