Helicobacter pylori eradication in patients with chronic immune thrombocytopenic purpura

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AIM: To assess the effect of Helicobacter pylori (H. pylori) eradication on platelet counts in patients with chronic immune thrombocytopenic purpura (cITP).

METHODS: A total of 36 cITP patients were included in the study. The diagnosis of H. pylori was done by rapid urease test and Giemsa staining of the gastric biopsy specimen. All H. pylori positive patients received standard triple therapy for 14 d and were subjected for repeat endoscopy at 6 wk. Patients who continued to be positive for H. pylori on second endoscopy received second line salvage therapy. All the patients were assessed for platelet response at 6 wk, 3rd and 6th months.

RESULTS: Of the 36 patients, 17 were positive for H. pylori infection and eradication was achieved in 16 patients. The mean baseline platelet count in the eradicated patients was 88615.38 ± 30117.93/mm³ and platelet count after eradication was at 6 wk, 3 mo and 6 mo was 152562.50 ± 52892.3/mm³ (P = 0.003), 125578.95 ± 71472.1/mm³ (P = 0.0001), 150187.50 ± 41796.68/mm³ (P = 0.0001) respectively and in the negative patients, the mean baseline count was 71000.00 ± 33216.46/mm³ and at 6 wk, 3rd and 6th month follow up was 137631.58 ± 74364.13/mm³ (P = 0.001), 125578.95 ± 71472.1/mm³ (P = 0.005), 77210.53 ± 56892.28/mm³ (P = 0.684) respectively.

CONCLUSION: Eradication of H. pylori leads to increase in platelet counts in patients with cITP and can be recommended as a complementary treatment with conventional therapy.

Key words: Helicobacter pylori; Immune thrombocytopenic purpura; Platelet counts

Core tip: Immune thrombocytopenic purpura (ITP) is an autoimmune haematological disorder in which destruction of platelets is mediated by auto-antibodies in the reticuloendothelial system. Some studies have demonstrated improvement in the platelet count after Helicobacter pylori (H. pylori) eradication in ITP. The present study describes the effect of H. pylori eradication on the platelet count in patients with cITP. It was found that following H. pylori eradication there was a significant sustained rise in the platelet count at 6 wk, 3rd and 6th months following eradication. In patients where conventional therapy was administrated, although there was a significant rise in the platelet count at 6 wk and...
3rd month, it was found that at 6th month the platelet count was similar to the baseline pre therapy level.

Noonavath RN, Lakshmi CP, Dutta TK, Kate V. *Helicobacter pylori* eradication in patients with chronic immune thrombocytopenic purpura. *World J Gastroenterol* 2014; 20(22): 6918-6923 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i22/6918.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i22.6918

INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a spiral shaped microaerophilic gram-negative bacterium, first isolated from gastric biopsy by Robin Warren and Barry J. Marshall in 1984. *H. pylori* has been implicated in the aetiology of many upper gastrointestinal disorders like acid peptic disease, chronic gastritis and gastric lymphoma (MALToma). Recently, *H. pylori* has been found to be associated with various extra-intestinal and immune mediated diseases, including pernicious anemia, idiopathic thrombocytopenic purpura (ITP), rheumatoid arthritis, auto immune thyroiditis and Sjogren’s syndrome.

Some studies have shown an increased prevalence of *H. pylori* infection in patients with chronic ITP (cITP) compared to the general population. The prevalence of *H. pylori* infection in cITP patients varies according to the geographic region. Some studies have demonstrated significant improvement in the platelet count after *H. pylori* eradication in cITP patients. Several mechanisms have been proposed to explain the association of *H. pylori* infection and ITP. *H. pylori* surface antigen, such as cytotoxin associated gene A protein (CagA) evokes host systemic immune response that produces auto antibodies which cross-reacts with host platelets.

However, some studies have reported that there was no significant improvement of platelet counts after eradication of *H. pylori* infection in cITP patients. To the best of our knowledge, no studies have been reported from India regarding the association of *H. pylori* and cITP. Hence, this study has been done to evaluate the role of *H. pylori* infection in cITP and the response of *H. pylori* infected cITP patients to the eradication of *H. pylori*.

MATERIALS AND METHODS

All the patients attending the haematology clinic of JIPMER hospital, Puducherry in-between September 2011 to July 2013 with the diagnosis of cITP were included in the study. The diagnosis of cITP was confirmed by a haematologist according to the standard criteria proposed by the American Society of Haematology guidelines. cITP was defined as ITP that persists for more than 6 mo. The study was conducted after obtaining clearance from the Institute Research Council and Ethics Committee. Informed written consent was obtained from all the patients included in the study.

After enrolment in the study, all the patients had baseline platelet counts, complete blood count and serology for hepatitis B, hepatitis C and human immunodeficiency virus analysis done. A baseline platelet count of less than 120000/mm$^3$ and stable treatment for 3 wk prior to study entry were included in the study.

Patients with other causes of thrombocytopenia such as Hepatitis C virus, Human Immunodeficiency virus or Hepatitis B virus infections were excluded. The patients also were excluded if they had received eradication therapy for *H. pylori* infection within the previous 2 years of enrolment or an antibiotic or proton pump inhibitor within the previous 4 wk. Those patients who had active life threatening bleeding at the time of enrolment were also excluded.

All cITP patients underwent diagnostic upper gastrointestinal endoscopy (UGIE). Four gastric mucosal biopsies were taken (two from the antrum and two from the body) and subjected to rapid urease test and histology by Giemsa staining for the diagnosis of *H. pylori* infection. A biopsy of mucosa is taken from the stomach and placed into the solution containing urea with phenol red as indicator and observed for 24 h. The urease produced by *H. pylori* catalyzes the urea to ammonia, which raises the pH of the solution, and changes the colour from yellow (negative) to red (positive). This urease test was earlier standardized in our institution, which contained 250 mg urea, 400 µL of gentamycin (40 mg/mL), and 400 µL of phenol red in 15 mL of distilled water.

Any one or both above mentioned tests, if positive, were considered to be positive for *H. pylori* infection. Eradication of *H. pylori* was defined when a patient was negative for urease test and *H. pylori*. After endoscopy and biopsy, the patients were divided into two groups.

Study group - *H. pylori* positive patients (Cases) were given standard first line eradication therapy for *H. pylori* (capsule- amoxicillin 1 gm twice daily, tablet- clarithromycin 500 mg twice daily, and capsule- omeprazole 20 mg twice daily for 14 d).

Control group - This group included cITP patients negative for *H. pylori*. The conventional therapy for ITP was continued (Prednisolone/Dapsone/azathioprine) for them.

Regular follow up was done at the end of 6 wk, 3 mo, and 6 mo following completion of eradication therapy. Study group were subjected for repeat UGIE with rapid urease test and histology by Giemsa stain to confirm the eradication of *H. pylori* at the end of 6 wk. The patients who continued to be positive for *H. pylori* on second endoscopy received second line salvage regime with amoxicillin 1 mg twice daily, levoflaxacin 500 mg twice daily, and omeprazole 20 mg twice daily for 14 d, to eradicate *H. pylori*. In both the groups the platelet counts were estimated at 6 wk, 3 mo and 6 mo follow up.
Table 1 Prevalence of Helicobacter pylori in patients with immune thrombocytopenic purpura (n = 36)

| ITP Patients          | n (%) |
|-----------------------|-------|
| H. pylori positive    | 17 (47.2) |
| H. pylori negative    | 19 (52.8) |
| Total                 | 36 (100) |

ITP: Immune thrombocytopenic purpura; H. pylori: Helicobacter pylori.

Statistical analysis
Statistical analysis was done by using SPSS 19.0 software version for windows. The following variables were analyzed to identify factors associated with the improvement in the platelet count after eradication therapy: age, sex, disease duration, duration of H. pylori eradication therapy, platelet count before and after H. pylori eradication, endoscopic and histopathological findings.

The $\chi^2$ t tests was used for comparison of age and gender distribution, disease duration, and mean baseline platelet counts between H. pylori negative and H. pylori positive cITP patients. $\chi^2$ test was used for comparison of UGIE findings and platelet response between H. pylori eradicated and H. pylori negative cITP patients. Unpaired student $t$ test was used for comparing platelet count response between H. pylori eradicated and H. pylori negative patients during follow up period. A P value of less than 0.05 was considered as statistically significant.

RESULTS
A total of thirty seven patients were enrolled in the study. Out of these, 36 patients underwent UGIE and biopsies were taken and subjected to rapid urease test and histology by Giemsa stain for the diagnosis of H. pylori. After endoscopy and biopsy, patients were divided into two groups.

Total of seventeen patients were diagnosed to have H. pylori infection with cITP. Table 1 shows the prevalence of H. pylori infection in the study population (47.2%). The mean age in both the groups was similar. In H. pylori positive cITP patients the mean age was ± SD of 29.1 ± 10.9 years and in H. pylori negative patients the mean age was ± SD of 29.8 ± 9.2 years, ($p < 0.083$). Most of the patients 15/36 (41.5%) were in the age group of 21-30 years with a mean age of 29.5 ± 9.92 years (range: 14-52 years).

The gender distribution between the groups was similar. Among H. pylori positive patients, 2 were males and 15 were females and in H. pylori negative group, 5 were males and 14 were females ($p \leq 0.271$). In the present study, the most common symptom was gum bleeding 18 (52.9%) followed by menorrhagia 11 (32.4%), petechiae 4 (11.8%) and epistaxis 1 (2.9%).

The mean cITP duration between H. pylori positive and H. pylori negative patients was 2.09 ± 1.9 years vs 5.3 ± 6.4 years ($p \leq 0.057$). The mean baseline platelet count between H. pylori positive and H. pylori negative patients was 81588.2 ± 7100/mm$^3$ vs 34294.8 ± 33216.5/mm$^3$ ($p = 0.354$).

As regards UGIE findings, 18 (50.0%) had gastritis, 15 (41.7%) had normal study and 3 (8.3%) had ulcer. The UGIE findings were similar in both H. pylori positive and H. pylori negative patients and the difference was not significant ($p = 0.66$).

Comparison of the platelet count at 6 wk, 3 mo and 6 mo between H. pylori eradicated and H. pylori negative patients from the baseline count is shown in the Table 2, Table 3 and Table 4 respectively. Eradication of H. pylori in the patients with cITP achieved a significant increase in the platelet count at 6 wk, 3 mo and 6 mo follow up, whereas with conventional therapy in H. pylori negative patients although there was short term benefit in the platelet response at 6 wk and 3 mo follow up, the platelet count reduced a 6 mo follow up closer to the baseline counts ($p = 0.0001$).

Table 5 shows the comparison of platelet response in the patients with successful eradicated and H. pylori negative patients. Among sixteen H. pylori eradicated patients, 13 had a complete response (CR), 3 had partial response (PR) and in 19 H. pylori negative patients, 5 had complete response, 5 had partial response and 9 patients did not have any response (NR) ($p = 0.002$).

In the present study, platelet response (CR, PR and NR) was assessed between the successful H. pylori eradicated (13/5/0) and H. pylori negative patients (5/5/9), and it was statistically significant ($p = 0.002$). Assessment of platelet response was done as per the following criteria - CR - platelet count of at least 120000 for more than 2 mo, PR - platelet count of at least 20000 and at least doubling the base line count over a period of more than 2 mo. NR - platelet counts below 20000 or when the counts do not increase to more than 50% of the pretreatment level.

DISCUSSION
ITP is an autoimmune hematological disorder in which destruction of the platelets is mediated by anti-platelet auto-antibodies in reticuloendothelial system[13]. The mechanisms of anti-platelet auto-antibodies development are still not yet known. In recent years, several studies have proposed that H. pylori infection may be associated with extra gastrointestinal diseases, especially haematological disorders like iron deficiency anaemia and immune thrombocytopenic purpura[13].

In 1998 Gasbarrini, for the first time proposed that H. pylori infection be associated with ITP and showed that, there was a significant improvement of platelet counts in H. pylori positive ITP patients after eradication of H. pylori infection[3]. Emilia et al[18] have demonstrated that H. pylori eradicated cITP patients exhibited a significant increase in the platelet count. Sato et al[9] and Inaba et al[9], Demonstrated a favourable platelet response in the patients in whom H. pylori was successfully eradicated.

In the present study, the results are similar to that of
Table 2  Comparison of platelet count at 6 wk follow up between *Helicobacter pylori* eradicated patients and *Helicobacter pylori* negative patients (*n* = 32)

| Groups                  | n  | Platelet count (mean ± SD)/mm³ | P value 1 | CI        |
|-------------------------|----|--------------------------------|-----------|-----------|
| *H. pylori* eradicated  |    |                                |           |           |
| Baseline count          | 13 | 8615.38 ± 30117.93             | 0.003     | -89230.8 - 20000 |
| Count at 6 wk           |    | 143230.77 ± 52437.51           |           |           |
| *H. pylori* negative    | 19 | 71000.00 ± 33216.46            | 0.001     | -104526 - 2736.8 |
| Baseline count          |    | 137631.58 ± 74364.13           |           |           |
| Count at 6 wk           |    |                                |           |           |

1Unpaired t test. *H. pylori*: Helicobacter pylori.

Table 3  Comparison of platelet count at 3 mo follow up between *Helicobacter pylori* eradicated patients and *Helicobacter pylori* negative patients (*n* = 35)

| Groups                  | n  | Platelet count (mean ± SD)/mm³ | P value 1 | CI        |
|-------------------------|----|--------------------------------|-----------|-----------|
| *H. pylori* eradicated  |    |                                |           |           |
| Baseline count          | 16 | 84375.00 ± 33372.39            | 0.0001    | -100118.68 - 36256.32 |
| Count at 3 mo           |    | 152562.50 ± 52892.3            |           |           |
| *H. pylori* negative    | 19 | 71000.00 ± 33216.46            | 0.0050    | -91249.09 - 17908.79 |
| Baseline count          |    | 125578.95 ± 71472.1           |           |           |
| Count at 3 mo           |    |                                |           |           |

1Unpaired t test. Post salvage therapy 3 patients added to *H. pylori* eradication Group. *H. pylori*: Helicobacter pylori.

Table 4  Comparison of platelet count at 6 mo follow up between *Helicobacter pylori* eradicated patients and *Helicobacter pylori* negative patients (*n* = 35)

| Groups                  | n  | Platelet count (mean ± SD)/mm³ | P value 1 | CI        |
|-------------------------|----|--------------------------------|-----------|-----------|
| *H. pylori* eradicated  |    |                                |           |           |
| Baseline count          | 16 | 84375.00 ± 33372.39            | 0.0001    | -93120.40 - 38504.60 |
| Count at 6 mo           |    | 150187.50 ± 41796.68           |           |           |
| *H. pylori* negative    | 19 | 71000.00 ± 33216.46            | 0.6840    | -36862.56 - 24441.51 |
| Baseline count          |    | 77210.53 ± 56892.28           |           |           |
| Count at 6 mo           |    |                                |           |           |

1Unpaired t test. *H. pylori*: Helicobacter pylori.

Table 5  Comparison of platelet response in patients with successful eradication and *Helicobacter pylori* negative patients

| Groups                  | n  | Response | P value 1 | CI        |
|-------------------------|----|----------|-----------|-----------|
| Yes (CR/PR)             |    | 16 (13/3) | 0        | 0.002     | 0.2835-0.6308 |
| No (NR)                 |    | 10 (5/5)  | 9        |           |           |

1Unpaired t test. *H. pylori*: Helicobacter pylori.

the previous studies, and at 6 wk follow up in patients with *H. pylori* eradication there was a significant increase in the mean platelet count from the baseline value (8615 ± 30117/mm³ vs 143230 ± 52437/mm³, *P* ≤ 0.003), whereas, *H. pylori* negative patients also had a significant increase in the platelet count (137631 ± 74364/mm³) from the baseline value (71000 ± 33216/mm³, *P* ≤ 0.001).

In the present study, at 3 mo follow up in the patients with *H. pylori* eradication there was a significant increase in the mean platelet count from the baseline value (84375 ± 33372/mm³ vs 152562 ± 52892/mm³, *P* ≤ 0.0001), whereas, *H. pylori* negative patients also had a significant increase in the platelet count (125578 ± 71472/mm³) from the baseline value (71000 ± 33216/mm³, *P* ≤ 0.005).

In the present study, at 6 mo follow up in the patients with *H. pylori* eradication there was a significant increase in the mean platelet count from the baseline value (84375 ± 33372/mm³ vs 150187 ± 41796/mm³, *P* < 0.0001), whereas, *H. pylori* negative patients also had a significant increase in the platelet count (77210 ± 56892/mm³) from the baseline value (71000 ± 33216/mm³, *P* < 0.0001).
whereas, in H. pylori negative patients who received conventional therapy had a drop in mean platelet count close to the baseline value (71000 ± 33216/mm³ vs 77210 ± 56892/mm³, \( P < 0.684 \)).

It appears from the present study, in the short term such as at 6 wk and 3 mo follow up, H. pylori eradication therapy or conventional therapy achieved a significant increase in the platelet count. However, at 6 mo follow up it was found that patients without H. pylori infection who received conventional therapy had a drop in platelet count close to the baseline level, whereas in patients with H. pylori eradication there was sustained increase in the platelet counts. Eradication of H. pylori was achieved in 94% of patients with standard triple therapy and salvage therapy. This could be due to long term effect of H. pylori eradication therapy in H. pylori positive chronic ITP patients.

In contrast to our study, Stasi et al\(^{[7]}\) reported that H. pylori eradication therapy had no effect on the platelet counts in the patients with cITP. Ahn et al\(^{[11]}\) too reported a poor response to H. pylori eradication therapy in patients with cITP in Western countries.

The prevalence of H. pylori infection in cITP patients varies according to the geographical location\(^{[5]}\). The prevalence of H. pylori in cITP patients in most of the Asian countries such as Japan, Iran and South Korea is high at 50% to 85%\(^{[10,18-21]}\). However, the prevalence of H. pylori in cITP patients in the Western countries is lower at 22% to 30%\(^{[10,18-21]}\). In the present study, the prevalence of H. pylori infection in cITP patients was 47.2%. This was lower than the prevalence of H. pylori in cITP patients in other Asian countries\(^{[10,18-21]}\). This may be due to differences in the socioeconomic status, hygiene factors, H. pylori strains and widespread use of antimicrobials for treatment of various infections in the childhood\(^{[22,31]}\).

Stasi et al\(^{[3]}\) and Fujimura et al\(^{[2]}\) reported better platelet response in patients with shorter duration of cITP and mild thrombocytopenia than in patients with long duration of cITP and severe thrombocytopenia. In the present study, there was no significant difference between the H. pylori positive and H. pylori negative patients with regard to duration of cITP (\( P < 0.057 \)) and the baseline platelet count (\( P < 0.354 \)).

In H. pylori positive and H. pylori negative patients with cITP did not show difference in the baseline characteristics such as age, gender, symptoms and UGIE findings.

The main limitations of the present study are: (1) the sample size of the study was not larger (\( n = 36 \)); and (2) follow up period of the study was limited.

The eradication of H. pylori in the patients with cITP was effective in restoring platelet counts at 6 mo follow up (\( P \leq 0.0001 \)), whereas in H. pylori negative patients with cITP there was a transient improvement in the platelet count with conventional therapy (\( P < 0.684 \)). The persistent increase in the platelet count in H. pylori eradicated patients could be due to long term efficacy of H. pylori eradication therapy in cITP patients.

Therefore we conclude that H. pylori eradication therapy was effective in H. pylori positive cITP patients in increasing the platelet count. Further studies are required to identify other possible causative factors involved in the platelet recovery, and to understand the mechanism underlying the response to eradication therapy.

**REFERENCES**

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984; i: 1311-1315 [PMID: 6145023 DOI: 10.1016/S0140-6736(05)60004-9]
2. Gasbarrini A, Franceschi F, Tartaglione R, Landolfi R, Pola P, Gasbarrini G. Regression of autoimmune thrombocytopenia after eradication of Helicobacter pylori. Lancet 1998; 352: 878 [PMID: 9742983 DOI: 10.1016/S0140-6736(05)60004-9]
3. Emilia G, Lungo G, Luppi M, Gandini M, Morselli M, Ferrara L, Amarrin S, Cagossi K, Torelli G. Helicobacter pylori eradication can induce platelet recovery in idiopathic thrombocytopenic purpura. Blood 2001; 97: 812-814 [PMID: 11157503 DOI: 10.1182/blood.V97.3.812]
4. Suzuki H, Marshall BJ, Hibi T. Overview: Helicobacter pylori and extragastric disease. Int J Hematol 2006; 84: 291-300 [PMID: 17118754 DOI: 10.1532/IJH.97.06180]
5. Menaker RJ, Sharaf AA, Jones NL. Helicobacter pylori
infection and gastric cancer: host, bug, environment, or all three? Curr Gastroenterol Rep 2004; 6: 429-435 [PMID: 15522671 DOI: 10.1007/s11894-004-0063-9]

6 Fujimura K, Kuwana M, Kurata Y, Imamura M, Harada H, Sakamaki H, Teramura M, Koda K, Nomura S, Sugihara S, Shimomura T, Fujimoto TT, Oyashiki K, Ikeda Y. Is eradication therapy useful as the first line of treatment in Helicobacter pylori-positive idiopathic thrombocytopenic purpura? Analysis of 207 eradicated chronic ITP cases in Japan. Int J Hematol 2005; 81: 162-168 [PMID: 15765787 DOI: 10.1532/IJH97.04146]

7 Inaba T, Mizuno M, Take S, Suwaki K, Honda T, Kawai K, Fujita M, Tamura T, Yokota K, Oguma K, Okada H, Shiratori Y. Eradication of Helicobacter pylori increases platelet count in patients with idiopathic thrombocytopenic purpura in Japan. Eur J Clin Invest 2005; 35: 214-219 [PMID: 15733077 DOI: 10.1111/j.1365-2362.2005.01471.x]

8 Sato R, Murakami K, Watanabe K, Okimoto T, Miyajima H, Ogata M, Ohitsuka E, Kodama M, Saburi Y, Fujikota J, Nasu M. Effect of Helicobacter pylori eradication on platelet recovery in patients with chronic idiopathic thrombocytopenic purpura. Arch Intern Med 2004; 164: 1904-1907 [PMID: 15451766 DOI: 10.1001/archinte.164.17.1904]

9 Takahashi T, Yujiri T, Shinohara K, Inoue Y, Sato Y, Fujii Y, Okubo M, Zaitsu Y, Ariyoshi K, Nakamura Y, Nawata R, Oka Y, Shirai M, Tanizawa Y. Molecular mimicry by Helicobacter pylori CagA protein may be involved in the pathogenesis of H. pylori-associated chronic idiopathic thrombocytopenic purpura. Br J Haematol 2004; 124: 91-96 [PMID: 14675413 DOI: 10.1111/j.1365-2457.2003.04735.x]

10 Michel M, Cooper N, Jean C, Frissora C, Bussel JB. Does Helicobacter pylori initiate or perpetuate autoimmune thrombocytopenic purpura? Blood 2004; 103: 890-896 [PMID: 12920031 DOI: 10.1182/blood-2003-05-0900]

11 Ahn ER, Tiede MP, Jy W, Bidot CJ, Fontana V, Ahn YS. Platelet activation in Helicobacter pylori-patient-associated idiopathic thrombocytopenic purpura: eradication reduces platelet activation but seldom improves platelet counts. Acta Haematol 2006; 116: 19-24 [PMID: 16809885 DOI: 10.1159/000092433]

12 Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, Bussel JB, Cines DB, Chong BH, Cooper N, Godeau B, Lechner K, Mazzucconi MG, McMillan R, Sanz MA, Imbach P, Blanchette V, Kühne T, Ruggeri M, George JN. Standardization of terminology, definitions and outcome criteria in idiopathic thrombocytopenic purpura of adults and children: report from an international working group. Blood 2009; 113: 2386-2393 [PMID: 19005182 DOI: 10.1182/blood-2008-07-162503]

13 Suzuki T, Matsushima M, Masui A, Watanabe K, Takagi A, Ogawa Y, Shirai T, Mine T. Effect of Helicobacter pylori eradication in patients with chronic idiopathic thrombocytopenic purpura-a randomized controlled trial. Am J Gastroenterol 2005; 100: 1265-1270 [PMID: 15929755 DOI: 10.1111/j.1572-0241.2004.41641.x]

14 Jones VS, Kate V, Ananthakrishnan N, Badrinath S, Amanath SK, Ratnakar C. Standardization of urease test for detection of Helicobacter pylori. Indian J Med Microbiol 1997; 15: 181-183

15 Herschk I, Ianculovich M, Souroujon M. A hematologist's view of unexplained iron deficiency anemia in males: impact of Helicobacter pylori eradication. Blood Cells Mol Dis 2007; 38: 45-53 [PMID: 17067833 DOI: 10.1016/j.bcmd.2006.09.006]

16 Emilia G, Luppi M, Zucchini P, Morselli L, Potenza L, Forghieri F, Volzone F, Jovic G, Leonardi G, Donelli A, Torelli G. Helicobacter pylori infection and chronic immune thrombocytopenic purpura: long-term results of bacterium eradication and association with bacterium virulence profiles. Blood 2007; 110: 3833-3841 [PMID: 17652264 DOI: 10.1182/blood-2006-12-063222]

17 Stasi R, Rossi Z, Stipa E, Amidori S, Newland AC, Provan D. Helicobacter pylori eradication in the management of patients with idiopathic thrombocytopenic purpura. Am J Med 2005; 118: 414-419 [PMID: 15808140 DOI: 10.1016/j.amjmed.2004.09.014]

18 Yim JY, Kim N, Choi SH, Kim YS, Cho KR, Kim SS, Seo GS, Kim HU, Baik GH, Sin CS, Cho SH, Oh BH. Seroprevalence of Helicobacter pylori in South Korea. Helicobacter 2007; 12: 333-340 [PMID: 17669107 DOI: 10.1111/j.1532-5078.2007.00504.x]

19 Russo A, Eboli M, Pizzetti P, Di Felice G, Ravagnani F, Spinielli P, Hotz AM, Notti P, Maconi G, Franceschi S, Ferrari D, Bertario L. Determinants of Helicobacter pylori seroprevalence among Italian blood donors. Eur J Gastroenterol Hepatol 1999; 11: 867-873 [PMID: 10514119 DOI: 10.1097/00042737-199908000-00010]

20 Michel M, Khellaf M, Desforges L, Lee K, Schaeffer A, Godeau B, Bierling P. Autoimmune thrombocytopenic Purpura and Helicobacter pylori infection. Arch Intern Med 2002; 162: 1033-1036 [PMID: 11996614 DOI: 10.1001/archinte.162.9.1033]

21 Graham DY, Malaty HM, Evans DG, Evans DJ, Klein PD, Adam E. Epidemiology of Helicobacter pylori in an asymptomatic population in the United States. Effect of age, race, and socioeconomic status. Gastroenterology 1991; 100: 1495-1501 [PMID: 2019355]

22 Fraser AG, Scragg R, Metcalf P, McCullough S, Yeates NJ. Prevalence of Helicobacter pylori infection in different ethnic groups in New Zealand children and adults. Aust N Z J Med 1996; 26: 646-651 [PMID: 8958339 DOI: 10.1011/j.1445-5994.1996.tb02934.x]

23 Malaty HM, Graham DY, Wattigney WA, Srinivasan SR, Osato M, Berenson GS. Natural history of Helicobacter pylori infection in childhood: 12-year follow-up cohort study in a biracial community. Clin Infect Dis 1999; 28: 279-282 [PMID: 10064244 DOI: 10.1086/515105]

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