Journal of Population Therapeutics & Clinical Pharmacology

**RESEARCH ARTICLE**
**DOI: 10.53555/jptcp.v30i19.3652**

# HELICOBACTER PYLORI AND IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP); IS THERE ANY ASSOCIATION

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## ABSTRACT

**Background:** Idiopathic thrombocytopenic purpura (ITP) is a hematological condition characterized by platelet hypersensitivity, which is often accompanied by autoantibodies and results in platelet destruction. While the actual etiology of ITP is unknown, it has been associated to a number of medical disorders, including infectious infections. Helicobacter pylori (H. pylori) infection has recently appeared as a possible factor to ITP, with research showing that its eradication improves platelet counts.

**Objective:** To investigate the association between H. pylori infection and ITP.

**Study Design:** This case-control study.

**Duration and Place of the Study:** This study conducted at the Department of Gastroenterology, Lady Reading Hospital, Peshawar, from February 2021 to February 2023.

**Material and Methods:** The study included 37 patients with immune thrombocytopenia throughout a two-year period and compared with healthy controls in the ration 1:2. Male and female patients between the ages of 18 and 60 years with ITP were enrolled. Platelet counts of 150,000 cells per $mm^3$ was used to diagnose ITP after other causes of thrombocytopenia had been excluded. Data collection included demographic information, a medical history, and a focus on gastric symptoms.

**Results:** Among cases, male patients constituted (51.4%) over (48.6%) females. The control group included 74 non-ITP patients, the majority of them were between the ages of 18-45 (79.77%). The gender distribution was almost equivalent to cases, with 48.64% males and 51.35% females. Only 5 (6.75%) of the 74 healthy controls tested positive for H. pylori, compared to 18 (48.6%) of the 37 ITP patients. 59.46% (n=22) of the 37 ITP patients reported having gastric symptoms, whereas the remaining 40.54% (n=15) did not. The odds ratio was 13.0 with 95% CI 4.2-39.8 indicating significant association between ITP and H.pylori.

**Conclusion:** This study suggests a significant relationship between H. pylori and ITP. The study also stresses the need of healthcare practitioners addressing gastrointestinal diseases and genetic factors in ITP development. Recognizing these linkages may help healthcare practitioners monitor and manage ITP.

**Keywords:** Idiopathic thrombocytopenic purpura (ITP), Helicobacter pylori (H.pylori), Platelet Count.

## INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is a hematological condition that is distinguished by an increased susceptibility of platelets to autoantibodies, leading to their destruction and consequent reduction in platelet count. [1]. The exact cause of ITP is not fully recognized, but it is often associated with various underlying medical conditions, with infectious diseases being a significant factor. One such infection that has obtained attention in relation to ITP is Helicobacter pylori (H. pylori)[2,3]. Helicobacter pylori is a well recognized bacterium that establishes colonization in the gastric region of the human body. It is acknowledged as the most widespread chronic bacterial infection globally[4,5]. This condition is mostly linked to gastritis and peptic ulcers. Recent research has shown a possible correlation between the existence of Helicobacter pylori (H. pylori) and immunological thrombocytopenia (ITP), so inspiring more inquiry into the underlying processes that contribute to this relationship[6].

The invasive characteristics of H. pylori and its capacity to cause inflammatory reactions in the gastric mucosa have prompted researchers to investigate its possible involvement in ITP[7,8]. This relationship received significant attention due to a number of important results. It is noteworthy to add that prior studies have shown that infection with H. pylori has the potential to promote the aggregation of platelets and granulocytes below the epithelial layer of the stomach. This phenomenon has been suggested as a potential factor contributing to the observed reduction in platelet counts in persons with ITP[9]. This observation implies that H. pylori has both a localised and systemic effect on platelet function and formation.

Furthermore, the various strains of H. pylori have significant antigenic diversity, which has the potential to impact the immunological response of the host and their vulnerability to thrombocytopenia [10,11]. Certain individuals who are infected with H. pylori may encounter a decrease in their platelet counts, whilst others may not experience any changes. This observation underscores the need for a more comprehensive comprehension of the variables that contribute to this variability [12,13].

Recent studies have also shown the fascinating potential for cross-reactivity between antibodies that specifically target proteins of H. pylori, including the Cag A protein, and antigens found on platelets [14]. This observation indicates a pathogenic mechanism by which H. pylori may contribute to the development of ITP, underscoring the need of exploring this correlation. The recognition of the likely participation of Helicobacter pylori (H. pylori) in immunological thrombocytopenia (ITP) has significant significance in the treatment of patients[15]. Corticosteroids are often used as the principal therapeutic intervention for immune thrombocytopenia (ITP); nevertheless, it is worth noting that their administration may potentially worsen Helicobacter pylori infection and its associated symptoms [16]. The main aim of this study is to investigate the prevalence of Helicobacter pylori (H. pylori) infection in individuals who have been diagnosed with immune thrombocytopenic purpura (ITP). Additionally, this research seeks to explore potential associations between these two medical disorders, therefore elucidating a possible pathophysiological relationship and facilitating the development of enhanced treatment approaches.

## METHODOLOGY

Case-control design was chosen to carry out this study. 37 Cases (with ITP) were compared with 74 controls (healthy individuals without ITP) at Lady Reading Hospital, Gastroenterology Department, Peshawar recruited during the period February 2021 to February 2023. ITP was diagnosed when

platelet counts were <150,000 cells per $mm^3$, eliminating other causes thrombocytopenia. The research included participants in the age range 18 to 60 years. Participation in the study provided informed consent. Except for ITP, patients with thrombocytopenia from malaria, dengue, chronic liver diseases, HIV, co-existing autoimmune disorders, leukemia's, lymphomas, and aplastic anemia were excluded. To ensure that the study's participants correctly reflected the target population and minimized confounding factors, precise inclusion and exclusion criteria were used. Age, gender, and other variables were gathered to characterize the research population. A detailed medical history was collected, focusing on gastrointestinal symptoms and family history of gastric complaints or cancer. Diagnoses of H.pylori included serological, breath, stool antigen, and gastric biopsies. The findings divided people into H. pylori-positive and negative groups and compared between cases and controls.

## DATA ANALYSIS

Descriptive statistics were utilized to summarize the research population's demographics and Comparative analyses were conducted to investigate the correlation between H pylori and ITP by assessing the relative frequencies of positive and negative cases within the two groups. A chi-squared test was used to examine whether H. pylori infection was associated with ITP. To measure the strength of H. pylori-ITP relationship, odds ratios was determined.

## RESULTS

Among cases, 32.4% of the patients were aged between 18 and 30, while 40.5% fell within the age bracket of 31 to 45. The remaining 27.0% of the sample had an age distribution spanning from 46 to 60 years. In relation to gender, the proportion of male patients (51.4%) exceeds that of female patients (48.6%). Table 1 presents the demographic characteristics of the cases.

**Table 1:** Demographic Characteristics of ITP Patients (Cases), n = 37

| Characteristic | Frequency | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| 18-30 | 12 | (32.4%) |
| 31-45 | 15 | (40.5%) |
| 46-60 | 10 | (27.0%) |
| **Gender** | | |
| Male | 19 | (51.4%) |
| Female | 18 | (48.6%) |

The control group included 74 non-ITP patients, the majority of them were between the ages of 18-45 (79.77%). The remaining 20.27% were between the ages of 46-60 years. The gender distribution was almost equivalent to cases, with 48.64% males and 51.35% females. Because these demographic parameters were similar to those of the ITP patient group, a more precise comparison between the two groups was possible (Table 2).

**Table 2:** Demographic Characteristics of Control Group (Non-ITP Individuals), n = 74

| Characteristic | Frequency | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| 18-30 | 28 | 37.88% |
| 31-45 | 31 | 41.89% |
| 46-60 | 15 | 20.27% |
| **Gender** | | |
| Male | 36 | 48.64% |
| Female | 38 | 51.35% |

The relationship between H. pylori infection and ITP is seen in Table 3. Only 5 (6.75%) of the 74 non-ITP patients tested positive for H. pylori, compared to 18 (48.6%) of the 37 ITP patients. This suggests that ITP patients have a much greater prevalence of H. pylori infection than non-ITP patients. The remaining 19 ITP patients (51.4%) and 69 non-ITP patients (93.24%) tested negative for H. pylori. Overall, the findings point to a substantial link between H. pylori infection and ITP. The odds ratio and 95% confidence interval (CI) for the connection between H. pylori infection and ITP are shown. The odds ratio of 13.07 indicates that there is strong statistically significant link between H. pylori infection and ITP. The 95% confidence interval (CI) extends from 4.29 to 39.80, meaning that the real odds ratio might fall within this range with 95% certainty. This shows that there exist strong link between H. pylori infection and ITP.

**Table 3:** Association between H. pylori Infection and ITP

| H. pylori Status | ITP Patients (n=37) | Non-ITP Patients (n=74) | Chi square p value | Odds ratio (95% CI, LB-UB) |
|---|---|---|---|---|
| Positive | 18 (48.6%) | 5 (6.75%) | <0.001 | 13.07 (4.29-39.80) |
| Negative | 19 (51.4%) | 69 (93.24%) | | |
| Total | 37 (100%) | 74 (100%) | | |

Table 4 shows the occurrence of gastric symptoms in the ITP patient group, as well as a family history of gastric complaints or malignancy. 59.46% (n=22) of the 37 ITP patients reported having gastric symptoms, whereas the remaining 40.54% (n=15) did not. Furthermore, 40.54% (n=15) of ITP patients had a family history of gastric symptoms or malignancy, but the remaining 59.46% (n=22) did not.

**Table 4:** Gastric Symptoms and Family History of ITP Patients

| Variables | Number of ITP Patients (n=37) | Percentage (%) |
|---|---|---|
| Gastric Symptoms | | |
| Present | 22 | (59.46%) |
| Absent | 15 | (40.54%) |
| Family History of Gastric Complaints or Malignancy in ITP Patients (Cases) | | |
| Present | 15 | (40.54%) |
| Absent | 22 | (59.46%) |

## DISCUSSIONS

The findings indicated that 48.6% of patients diagnosed with immune thrombocytopenic purpura (ITP) had a positive test result for Helicobacter pylori (H. pylori) infection. On the contrary 6.75% individuals in the control group showed positive infection. This finding indicates a possible association between infection with H. pylori and ITP.

The results of this study align with other research that has also shown a possible correlation between H. pylori infection and ITP. [17] According to a research conducted by Stasi et al.[18] it was shown that 22% of patients with ITP tested positive for H pylori, whereas only 20% of patients in the control group without ITP exhibited the same infection. In a study conducted by Emilia et al.[19], it was shown that the prevalence of H. pylori infection was greater in patients with ITP (60%) compared to a control group of healthy patients (30%). The aforementioned investigations, in conjunction with the current research, indicate a potential association between H. pylori infection and the onset of ITP.

Regarding demographic features, the current investigation revealed that a significant proportion of patients diagnosed with ITP fell within the age range of 18 to 45 years. Furthermore, a marginal disparity was seen between the genders, with a slightly greater representation of men than females. The results of this study align with other research that has similarly shown a greater occurrence of ITP in younger persons and a slightly elevated frequency in males by Cines et al.[20]

The current research also investigated the occurrence of gastric symptoms and the prevalence of gastrointestinal complaints or malignancies in patient with immune thrombocytopenia (ITP). The findings of the study indicated that a majority of patients diagnosed with immune thrombocytopenia (ITP), particularly 59.46%, reported the occurrence of gastric symptoms. Additionally, a significant proportion of patients, specifically 40.54%, had a family history of gastrointestinal complaints or malignancy. The results of this study indicate a possible association between gastrointestinal disorders and immune thrombocytopenia (ITP), along with a potential genetic influence on the onset of ITP. This assertion is substantiated by prior research, which has also shown an elevated incidence of gastrointestinal complications among patients with immune thrombocytopenia (ITP) [21].

In the present study, the investigators also calculated the odds ratio and 95% confidence interval (CI) in order to evaluate the association between H. pylori infection and ITP. A chances ratio of 13.07 (95% CI; 4.29-39.80) suggests a strong association between H. pylori infection and ITP. This finding aligns with other research that has similarly shown a limited correlation between H. pylori infection and ITP[22].

Overall, the findings of this research add to the growing body of evidence suggesting a potential correlation between H. pylori infection and ITP. However, more investigation is required to validate this correlation and get into the underlying processes. Furthermore, further research is required to examine the possible influence of gastrointestinal disorders and genetic variables on the pathogenesis of immune thrombocytopenia (ITP). Healthcare providers may enhance their management and treatment of immune thrombocytopenia (ITP) in patients by gaining a comprehensive grasp of the possible correlations among these factors.

**Study Limitation**

The limited sample size of the current study is one drawback, which may restrict the generalizability of the results. Furthermore, patients from a single hospital were included in the study, which may not be typical of the total community. To corroborate the conclusions of this research, bigger sample numbers and more varied populations are required in future investigations.

## CONCLUSION

The present study provides support for a potential association between H pylori infection and ITP. The research emphasizes the need of healthcare providers considering the possible impact of gastric disorders and hereditary variables in the development of ITP. Healthcare workers may better monitor and treat ITP in patients by recognizing these possible links.

## REFERENCES

1. Nugent D, McMillan R, Nichol JL, Slichter SJ. Pathogenesis of chronic immune thrombocytopenia: increased platelet destruction and/or decreased platelet production. British journal of haematology. 2009 Sep;146(6):585-96.
2. Kusters JG, Van Vliet AH, Kuipers EJ. Pathogenesis of Helicobacter pylori infection. Clinical microbiology reviews. 2006 Jul;19(3):449-90.
3. Wen H, Luo J, Li J, Li X. Helicobacter pylori infection in rheumatic diseases. Arthritis research & therapy. 2012 Jan 1;14(Suppl 1):P74.
4. Bravo D, Hoare A, Soto C, Valenzuela MA, Quest AF. Helicobacter pylori in human health and disease: Mechanisms for local gastric and systemic effects. World journal of gastroenterology. 2018 Jul 7;24(28):3071.
5. Testerman TL, Morris J. Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. World journal of gastroenterology: WJG. 2014 Sep 9;20(36):12781.
6. Marques AR, Sousa L, Mendes M, Apolinário I. Immune thrombocytopenia associated with Helicobacter pylori - unclear associative mechanisms. Hematol Transfus Cell Ther. 2019 Jul-Sep;41(3):272-274.

7. White JR, Winter JA, Robinson K. Differential inflammatory response to Helicobacter pylori infection: etiology and clinical outcomes. Journal of inflammation research. 2015 Aug 13:137-47.
8. Chmiela M, Gonciarz W. Molecular mimicry in Helicobacter pylori infections. World journal of gastroenterology. 2017 Jun 6;23(22):3964.
9. Swinkels M, Rijkers M, Voorberg J, Vidarsson G, Leebeek FW, Jansen AG. Emerging concepts in immune thrombocytopenia. Frontiers in immunology. 2018 Apr 30;9:880.
10. Chmiela M, Karwowska Z, Gonciarz W, Allushi B, Stączek P. Host pathogen interactions in Helicobacter pylori related gastric cancer. World journal of gastroenterology. 2017 Mar 3;23(9):1521.
11. Hagymási K, Tulassay Z. Helicobacter pylori infection: new pathogenetic and clinical aspects. World journal of gastroenterology: WJG. 2014 Jun 6;20(21):6386.
12. Testerman TL, Morris J. Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. World journal of gastroenterology: WJG. 2014 Sep 9;20(36):12781.
13. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of Helicobacter pylori infection. Official journal of the American College of Gastroenterology| ACG. 2017 Feb 1;112(2):212-39.
14. Negrini R, Lisato L, Zanella I, Cavazzini L, Gullini S, Villanacci V, Poiesi C, Albertini A, Ghielmi S. Helicobacter pylori infection induces antibodies cross-reacting with human gastric mucosa. Gastroenterology. 1991 Aug;101(2):437-45.
15. Kuwana M. Helicobacter pylori-associated immune thrombocytopenia: clinical features and pathogenic mechanisms. World Journal of Gastroenterology: WJG. 2014 Jan 1;20(3):714.
16. Psaila B, Bussel JB. Refractory immune thrombocytopenic purpura: current strategies for investigation and management. British journal of haematology. 2008 Oct;143(1):16-26.
17. Al-Outaibi GT. Association between Helicobacter pylori infection and rheumatic heart disease (Doctoral dissertation, KING ABDULAZIZ UNIVERSITY JEDDAH).
18. Stasi R, Rossi Z, Stipa E, Amadori S, Newland AC, Provan D. Helicobacter pylori eradication in the management of patients with idiopathic thrombocytopenic purpura. The American journal of medicine. 2005 Apr 1;118(4):414-9.
19. Emilia G, Luppi M, Zucchini P, Morselli M, 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, The Journal of the American Society of Hematology. 2007 Dec 1;110(12):3833-41.
20. Cines DB, Bussel JB, Liebman HA, Luning Prak ET. The ITP syndrome: pathogenic and clinical diversity. Blood, The Journal of the American Society of Hematology. 2009 Jun 25;113(26):6511-21.
21. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, Cuker A, Despotovic JM, George JN, Grace RF, Kühne T, Kuter DJ, Lim W, McCrae KR, Pruitt B, Shimanek H, Vesely SK. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019 Dec 10;3(23):3829-3866.
22. Barbosa AM, Ribeiro RA, Silva CÍ, Cruz FW, Azevedo O, Pitombeira M. Platelet count response to Helicobacter pylori eradication for idiopathic thrombocytopenic purpura in northeastern Brazil. Rev Bras Hematol Hemoter. 2018;40(1):12–17.