Association of *Helicobacter pylori* Infection with Clinical Characteristics and Steroid Response in Patients with Immune Thrombocytopenia: An Observational Study

Murtadha Salah Shyaa*, Manal Khalid Abdulridha*, Abdulhakim Mohammad Abdullah, Yaseen Mohyaldeen Taher***.**

Department of Clinical Pharmacy, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq

****Department of Clinical Pharmacy, College of Pharmacy, Hodeidah University,Al Hudaydah, Yemen.***

*****National Center of Hematology, College of Medicine, Mustansiriyah University, Baghdad, Iraq***

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Corresponding Author email:
Murtadha.salah95@gmail.com
Orcid: https://orcid.org/0009-0002-9387-0285

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Abstract:

Background: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by reduced platelet counts. Helicobacter pylori infection has been implicated in ITP pathogenesis, though its effect on clinical features and initial treatment response remains unclear.

Objective: To assess the impact of *H. pylori* infection on baseline characteristics, platelet counts, and corticosteroid response in adult ITP patients, including the role of ABO blood groups.

Methods: This observational comparative study included 100 adult primary ITP patients, equally divided into *H. pylori*-positive and negative groups based on stool antigen testing. Clinical and laboratory data were analyzed, and steroid response was evaluated using standard criteria. Statistical tests and logistic regression were applied to identify predictors of outcomes.

Results: Baseline characteristics and platelet counts were comparable between groups. Steroid response rates were similar (56% vs 54%, P=0.84). Among blood group Of patients, *H. pylori*-positive individuals had significantly lower platelet counts than negatives (P<0.001). In positive group, male sex predicted better steroid response, while higher BMI correlated with refractory disease. No independent predictors were identified in the negative group.

Conclusion: *H. pylori* infection does not affect baseline platelet levels or initial steroid response in ITP. However, interactions with host factors, particularly ABO blood group and sex, may influence disease severity and treatment outcomes.

Keywords: Immune thrombocytopenia; *Helicobacter pylori*; Corticosteroid response; ABO blood group; Autoimmune thrombocytopenia; Platelet count.

ارتباط عدوى الملوية البوابية بالخصائص السريرية والاستجابة للعلاج بالكورتيكوستيرويدات لدى مرضى فرفرية نقص الصفيحات المناعية: دراسة رصدية

مرتضى صلاح شياع*, منال خالد عبدالرضا*, عبد الحكيم محمد عبد الله, ياسين محي الدين طاهر*****.**
فرع الصيدلة السريرية، كلية الصيدلة، الجامعة المستنصرية، بغداد، العراق.
****فرع الصيدلة السريرية، كلية الصيدلة، جامعة الحديدة، الحديدة، اليمن.***
*****مركز امراض الدم، كلية الطب، الجامعة المستنصرية، بغداد، العراق.***

الخلاصة:

الخلفية: تُعدّ فرفرية نقص الصفيحات المناعية اضطرابًا مناعيًا ذاتيًا يتميز بانخفاض عدد الصفيحات. وقد ارتبطت عدوى الملوية البوابية بالمرض، إلا أن تأثيرها على العرض السريري والاستجابة العلاجية الأولية لا يزال غير واضح.

الهدف: تقييم تأثير عدوى الملوية البوابية على الخصائص السريرية، وعدد الصفيحات عند التشخيص، والاستجابة للكورتيكوستيرويدات، مع تحليل دور فصائل الدم.

الطرائق: شملت الدراسة 100 مريض بالغ مصاب بفرفرية نقص الصفيحات المناعية الأولية، قُسّموا بالتساوي إلى مجموعتين إيجابية وسلبية للعدوى. جُمعت البيانات السريرية، وتم تقييم الاستجابة للعلاج وفق المعايير الدولية، مع استخدام التحليل الإحصائي لتحديد العوامل المتنبئة.

النتائج: لم تُسجل فروق معنوية بين المجموعتين في عدد الصفيحات أو الاستجابة للعلاج (56% مقابل 54%). إلا أن المرضى الإيجابيين من فصيلة الدم O أظهروا انخفاضًا أكبر في عدد الصفيحات ($P<0.001$). كما ارتبط الجنس الذكري باستجابة أفضل للعلاج، وارتبط ارتفاع مؤشر كتلة الجسم بمسار مقاوم في مجموعة العدوى.

الاستنتاج: لا تؤثر العدوى على عدد الصفيحات الأساسي أو الاستجابة المبكرة للعلاج، لكنها قد تتفاعل مع عوامل المضيف مثل فصيلة الدم والجنس لتؤثر في شدة المرض ومساره.

الكلمات المفتاحية: فرفرية نقص الصفيحات المناعية؛ الملوية البوابية؛ الاستجابة للكورتيكوستيرويدات؛ فصائل الدم؛ عدد الصفيحات

Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia (platelet count $<100\times10^9$/L) resulting from autoantibody-mediated platelet destruction and impaired platelet production[1]. It has an incidence of approximately 2–5 per 100,000 adults per year, with a higher prevalence in females, especially during early to middle adulthood[1,2]. Clinical manifestations range from asymptomatic mild bruising to severe bleeding, but many patients present with mucocutaneous bleeding due to low platelet counts. According to the International Working Group criteria, ITP is classified by duration into newly diagnosed (<3 months), persistent (3–12 months), and chronic (>12 months) phases[3]. The pathogenesis of primary ITP is multifactorial and not completely understood; it involves loss of immune tolerance leading to autoantibodies (often IgG) against platelet surface glycoproteins (such as GPIIb/IIIa), as well as T-cell mediated platelet destruction[4,5]. These immune mechanisms are influenced by patient-related factors (such as genetic predispositions and hormonal milieu) and environmental triggers[4,6]. Women have a higher propensity for autoimmune diseases, potentially due to differences in sex hormones and immune regulation[6]. This may partly explain the female predominance in ITP and suggests that immunological triggers might have differential effects by sex[2,6]. One environmental factor implicated in ITP is chronic infection with *Helicobacter pylori*, a gram-negative bacterium. Since the initial reports by Japanese investigators linking *H. pylori* infection with platelet count

improvement in ITP patients after eradication therapy, there has been considerable interest in this association[7,8]. *H. pylori* infection is common worldwide and especially in developing countries, and its prevalence among ITP patients varies geographically. In some cohorts a majority of ITP patients are infected, while in others a smaller fraction is infected[8]. Proposed mechanisms for *H. pylori*-associated ITP include molecular mimicry and chronic immune stimulation: antibodies against *H. pylori* (for example, against the CagA protein) may cross-react with platelet antigens, leading to platelet destruction[8,9]. Additionally, *H. pylori* can induce systemic immune alterations and chronic inflammation that might exacerbate autoimmunity[4]. Another interesting aspect is the role of host factors such as blood group. *H. pylori* expresses a blood-group antigen-binding adhesin (BabA) that facilitates attachment to the gastric mucosa by binding fucosylated Lewis^b and H antigens; individuals with blood group O (who universally express the H antigen) may therefore harbor *H. pylori* more readily or experience a more intense immune reaction to the infection[10]. Blood group O is also known to be associated with lower levels of von Willebrand factor and factor VIII, which could influence bleeding tendency and platelet kinetics[11,12]. These considerations raise the question of whether *H. pylori* infection might differentially affect ITP patients of certain blood groups or other demographic subsets.

Despite biologic plausibility, it remains unclear whether *H. pylori* infection alters the clinical course of ITP outside of the context of eradication therapy. Many studies, including systematic reviews, have found that eradication of *H. pylori* in infected ITP patients can lead to a platelet count increase in a subset of patients[7,13,14]. However, prior to therapy, infected and uninfected ITP patients often show similar baseline platelet counts and disease severity[15,16]. . For instance, a recent study by Dogan *et al.* reported no significant difference in baseline platelet count or initial bleeding severity between *H. pylori*-positive and -negative ITP patients[15]. Moreover, current treatment guidelines do not recommend altering first-line ITP therapy based on *H. pylori* status, although testing and treating for *H. pylori* is suggested, given the potential for benefit and low risk of therapy[5,8]. In Iraq and the Middle East region, both ITP and *H. pylori* infection are prevalent, yet data on their interplay are limited. Given the potential implications for patient management, we conducted an observational study to compare *H. pylori*-infected and uninfected ITP patients in terms of their clinical and laboratory features and responses to standard therapy. In particular, we examined whether *H. pylori* infection is associated with differences in baseline platelet count, steroid responsiveness, or overall disease outcome, and whether host factors such as sex, age, body mass index (BMI), or ABO blood group modulate these relationships. aim of the study is to clarify if *H. pylori* infection identifies a distinct subset of ITP patients with different clinical behavior, which could inform tailored management strategies.

Materials and Methods

Trial registration: This study was registered on ClinicalTrials.gov (Identifier: NCT07150286).

Study Design and Patients: This study was designed as an observational screening study that enrolled adult patients confirmed for diagnosis with primary ITP who tested either *H. pylori* positive or *H. pylori* negative distributed equally, in two hematology centers. We enrolled a total of 100 ITP patients from National Center of Hematology of Al-Mustansiriyah University and the

Hematology and Bone Marrow Transplantation Center of the Medical City Teaching Directorate in Baghdad, Iraq, between September 2024 and March 2025. Patients were included if they met standard diagnostic criteria for primary ITP (platelet count 100 × 10^9/L), with no other causes of thrombocytopenia[5]. Exclusion criteria included secondary causes of thrombocytopenia such as connective tissue diseases, lymphoproliferative disorders, active viral infections (HIV, hepatitis B/C, etc.), or previous *H. pylori* eradication therapy. All patients provided informed consent for *H. pylori* testing and participation in the study, and the study protocol was approved by the institutional ethical committee.

***Helicobacter pylori* Testing:** Detection of *Helicobacter pylori* infection was performed using a rapid stool antigen immunochromatographic assay (ICT) (HMBIO, China). This qualitative lateral flow assay is based on monoclonal antibody–mediated detection of *H. pylori* antigens in stool samples.

Fresh stool specimens were collected in sterile stool containers provided with the test kit. The sampling stick attached to the cap was inserted into the fecal sample to fill the grooved tip with stool material. The stick was then returned to the extraction tube containing the assay buffer. The container was shaken vigorously several times to ensure proper homogenization and antigen extraction.After sample preparation, the dropper cap was removed, and the first one to two drops were discarded. Subsequently, three drops (approximately 110 µL) of the processed sample were dispensed into the sample well of the test cassette. The test device was kept at room temperature (15–30°C) and interpreted within 3–10 minutes. Results were considered positive when both the control line and the test line appeared, and negative when only the control line was visible. Tests without a visible control line were considered invalid and repeated.According to the manufacturer's specifications, the assay demonstrates high diagnostic performance for active *H. pylori* infection, with reported sensitivity and specificity exceeding 90%.

Patients were classified as *H. pylori*-positive if the test result was positive and as *H. pylori*-negative if the result was negative.

Data Collection: Baseline demographic and clinical data were recorded for each patient, including age, sex, and body mass index (BMI). The duration of ITP at presentation was noted and categorized into three phases according to the International Working Group (IWG) criteria[3]: newly diagnosed (<3 months since diagnosis), persistent (3–12 months), or chronic (>12 months). We also recorded any family history of ITP or other autoimmune diseases. ABO/Rh blood group was determined from hospital records or by standard hemagglutination testing, as part of the patient's routine blood typing.

Baseline laboratory investigations included a complete blood count with peripheral smear review to confirm isolated thrombocytopenia and assess platelet morphology. Bone marrow examination results were available for a subset of patients (those who were older than 60 years or had atypical features, in line with guideline recommendations[5]; bone marrow findings when done were classified as either consistent with ITP (normal or increased megakaryocytes with no other pathology) or other, and this was noted for correlation analyses.

Treatment and Definitions of Response: All patients were managed with first-line ITP therapy according to standard practice guidelines[5]. This typically consisted of corticosteroid therapy (prednisone or an equivalent, ~1 mg/kg/day for 2–4 weeks,

with tapering thereafter). Some patients, particularly those with very low platelets or bleeding, also received intravenous immunoglobulin (IVIG) in addition to steroids as per treating physician's discretion. No patient received *H. pylori* eradication treatment during the initial observation phase of this study,for the *H. pylori*-positive group, eradication therapy was planned as part of a subsequent interventional phase).

We evaluated the initial response to steroid therapy about 4 weeks after treatment initiation or at the end of first-line therapy if it was given for a shorter or longer duration in certain cases. Treatment responses were defined according to international consensus criteria[3]: a **complete response (CR)** was defined as a platelet count ≥100×10⁹/L and absence of bleeding; a **partial response (R)** was a platelet count ≥30×10⁹/L and at least doubling of baseline count, with no significant bleeding; **no response (NR)** was platelet count <30×10⁹/L or less than doubling of baseline, or bleeding symptoms persistence. For the purposes of analysis, we often combined CR and R into a single **responder** category (achievement of at least a partial response), versus **non-responder** (no response).

Patients were monitored subsequently for maintenance of platelet response. **Remission** was defined as the maintenance of a platelet count ≥100×10⁹/L for at least 6 months without the need for any ongoing ITP therapy. Patients who lost their initial response or required additional treatment were considered **relapsed**, while those who never achieved a meaningful response or required second-line therapies (such as splenectomy or thrombopoietin-receptor agonists) were categorized as **refractory**[17,18]. For analysis, we grouped patients into **remission** vs **relapsed/refractory** outcomes based on their status at last follow-up in this observational phase, with a median follow-up of 6 months for newly diagnosed cases and longer for persistent/chronic cases.

Statistical Analysis: The Anderson–Darling test was performed to assess whether continuous variables followed a normal distribution. Normally distributed variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median with interquartile range (IQR, 25th–75th percentile). Discrete variables were summarized as frequencies and percentages. Comparisons between two groups were conducted using the two-sample t-test for normally distributed variables without significant outliers, or the Mann–Whitney U test for non-normally distributed variables. Binary logistic regression analysis was used to calculate odds ratios (OR) with their corresponding 95% confidence intervals (CI) for categorical outcomes. Linear regression analysis was applied to assess relationships between continuous variables, while Spearman's rank correlation was used when assumptions of normality were not met.

Results

A total of 100 patients with ITP were included, with 50 categorized *as H. pylori*-negative and 50 as *H. pylori*-positive. All patients were of middle age (42.56 ± 15.21 vs 39.1 ± 13.76 years), primarily female (52% vs 76%). The average BMI was within the normal range (26.22±6.04 vs 26.99±6.26 kg/m²), respectively. The median duration of ITP was 6 months compared to 5 months, predominantly associated with a negative family history and the O positive blood group phenotype. The response to standard steroid treatment was noted in only 54.0% of patients compared to 56.0%, while the remission rate success was found in 48% versus 52% of patients, respectively (Table 1).

Table 1 Sociodemographic and disease characteristics of participants

Variable		***H. pylori*-negative n=50**	***H. pylori*-positive n=50**	**P - Value**
Age (years) #	Mean ± SD	42.56 ± 15.21	39.24 ± 13.76	P< 0.05
Sex▽	Female	26 (52%)	38 (76%)	P< 0.05
	Male	24 (48%)	12 (24%)	P< 0.05
		P≥ 0.05	P< 0.001	
BMI (kg/m2) #	Mean ±SD	26.22±6.04	26.99±6.26	P≥ 0.05 (t-test)
BMI groups	Underweight <18.5	4	4	P≥ 0.05
	Normal 18.5-24.99	20	16	
	Overweight 25-29.99	14	16	
	Obese Class I 30-34.99	9	9	
	Class II 35-39.99	2	3	
	Class III ≥ 40	1	2	
ITP duration (months) ø	Median (IQR)			
	Newly diagnosed (0 -<3) months 1 month	18 (36%)	17 (34%)	P≥ 0.05
	Persistent (3 to 12) months 6 months	19 (38%)	24 (48%)	P≥ 0.05
	Chronic: >12 months 60 months	13 (26%)	9 (18%)	P≥ 0.05
Family History▽	Positive	3 (6%)	1(2%)	P≥ 0.05
	Negative	47 (94%)	49 (98%)	
Steroidal responsiveness▽	Responder	27 (54%)	28 (56%)	P≥0.05
	Non-responder	23 (46%)	22 (44%)	P≥0.05
		P≥0.05	P≥0.05	
ABO phenotypes▽	A	10 (20%)	5 (10%)	P ≥0.05
	B	7 (14%)	12 (24%)	
	AB	7 (14%)	3 (6%)	
	O	26 (52%)	30 (60%)	
ITP treatment outcome▽	Relapsed/ Refractory	26 (52%)	24 (48%)	P≥0.05
	Remission	24 (48%)	26 (52%)	

Continuous data presented based on normality test either as Mean ± standard deviation, or median and range median (interquartile range), categorical data presented as frequency and percentage number (percentage), P value ≥ 0.05 is considered non-significant. P value < 0.05 is considered significant.

Baseline Laboratory Measurements

The baseline haematological evaluation compared platelet counts between 50 *H. pylori* positive patients and 50 *H. pylori* negative patients. Statistical analysis revealed that the mean baseline platelet count for *H. pylori* positive individuals was 39.56±18.24×10^9/L, while the *H. pylori* negative group exhibited a mean platelet count of 42.12±20.15×10^9/L. The average difference between the two groups was −2.56×10^9/L (P≥0.05) as illustrated in table 2 Table 2.

Table 2 Baseline Platelet count among ITP patients in both study groups

Variable	***H.pylori* Positive (n=50)**	***H.pylori* Negative (n=50)**	**Mean Difference**	**P-value**
Baseline Platelet Count (times10^9/L)	39.56 ± 18.24	42.12 ± 20.15	-2.56	P≥0.05

Data presented as mean ± standard deviation, P-value was calculated using an independent t-test, P value ≥ 0.05 is considered non-significant

Assessment of Steroid Responsiveness among *H. Pylori*-Negative and *H. Pylori* - Positive ITP Patients

To evaluate the impact of *H. pylori* infection on the efficacy of first-line steroid treatment. The comparative analysis (Figure 3.1) revealed response rates of 54% in the *H. pylori* negative cohort and 56% in the *H. pylori* positive cohort. The Chi-square test indicated that this difference was not statistically significant (p=0.84).

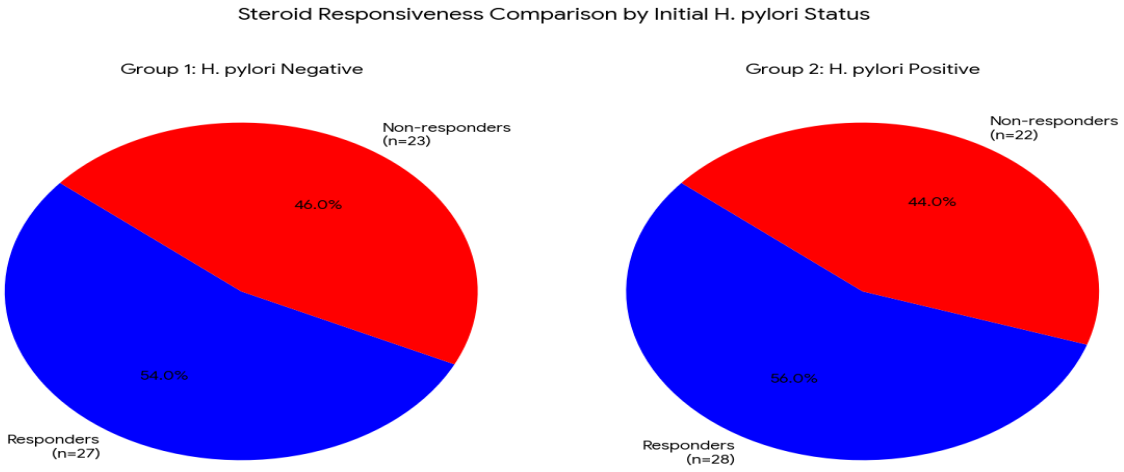

Figure 1: Correlation Between *H. Pylori* Status and Corticosteroid Response in ITP Patients
Distribution of Platelet Count according to ABO Phenotypes

Baseline platelet counts were evaluated among ABO blood groups to compare patients positive and negative for *H. pylori*. A statistically significant difference was seen in Blood Group O, where H. pylori negative individuals exhibited higher mean baseline platelet counts compared to *H. pylori* positive patients (56.9 vs 37.2; P < 0.001). No statistically significant differences in baseline platelet counts were noted for Blood Groups A (p=0.329), B (p=0.141), or AB (p=0.794) as shown in figure (2).

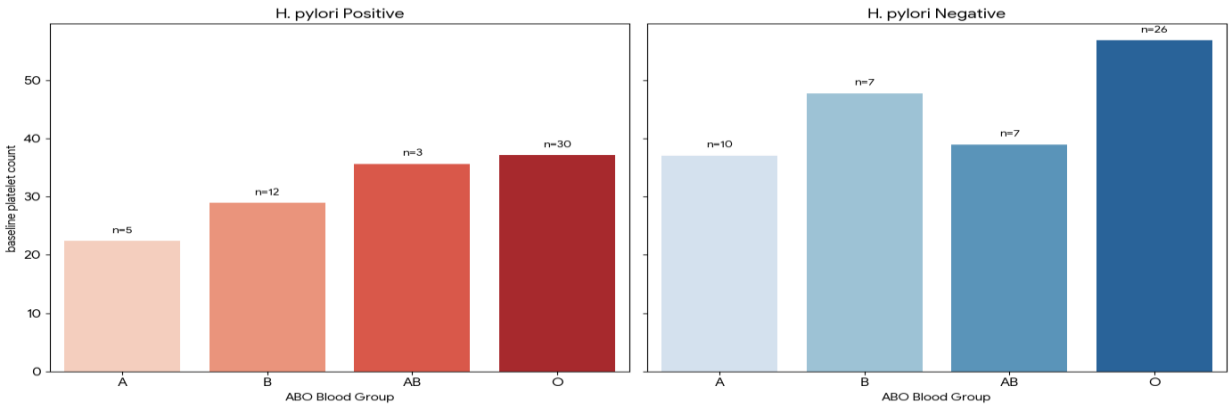

Figure 2: The Impact of *H. pylori* Infection on Baseline Platelet Counts Across Different ABO Blood Groups in ITP Patients

Correlation Between Platelet Count and Disease Characteristics.

Spearman correlation analysis was performed separately in *H. pylori*-negative and *H. pylori*-positive ITP patients to evaluate the relationships between baseline platelet count and clinical variables (Figures 3 and 4; Tables 3 and 4).

In the *H. pylori*-negative group, baseline platelet count showed no significant correlation with age (P=0.210), sex (P=0.450), body mass index (BMI) (P=0.812), duration of ITP (P=0.610), family history (P=0.880), or bone marrow findings (P=0.412).However, strong statistically significant associations were identified between disease status (relapsed/refractory) and both steroid responsiveness (P<0.001) and duration of ITP (P<0.001). Patients with longer disease duration and poor steroid response were significantly more likely to develop a relapsed or refractory course. Additionally, steroid responsiveness was significantly associated with disease duration (P<0.001), indicating that chronicity of ITP negatively influenced treatment response. These findings suggest that in infection-negative ITP, disease behavior is primarily driven by intrinsic disease chronicity and therapeutic response rather than demographic or baseline biological characteristics.

In the *H. pylori*-positive group, baseline platelet count similarly showed no statistically significant association with age (P=0.139), sex (P=0.336), BMI (P=0.643), duration of ITP (P=0.560), family history (P=0.778), or bone marrow findings (P=0.211).As observed in the negative group, disease status (relapsed/refractory) was strongly associated with steroid responsiveness (P<0.001) and duration of ITP (P<0.001).Notably, BMI demonstrated a statistically significant correlation with relapsed/refractory disease status (P=0.038), suggesting that higher BMI may contribute to a less favorable disease course in infected patients. Furthermore, sex showed a significant association with bone marrow findings (P=0.004), and male sex demonstrated a clinically meaningful trend toward improved steroid responsiveness, later confirmed by logistic regression analysis. Overall, while platelet count at presentation was not significantly influenced by demographic variables in either group, disease chronicity and steroid response consistently emerged as the strongest determinants of disease outcome. In *H. pylori*-positive patients, additional host-related factors—particularly BMI and sex—appeared to exert a modifying influence on disease progression.

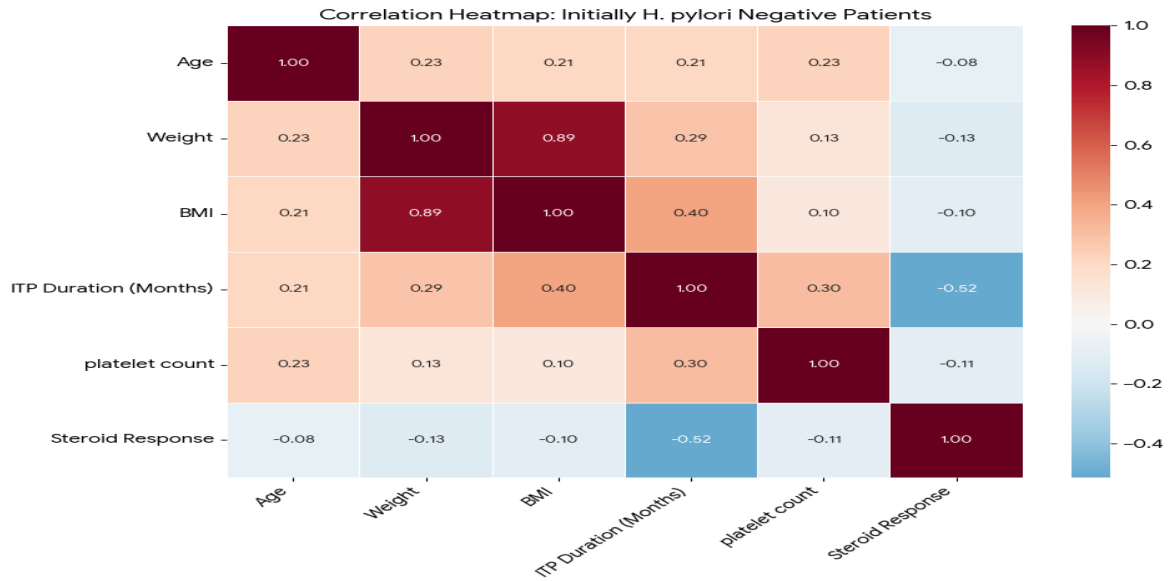

Figure 3: Spearman correlation matrix heat map between various variables with platelet count for *H. Pylori*-negative ITP patients.

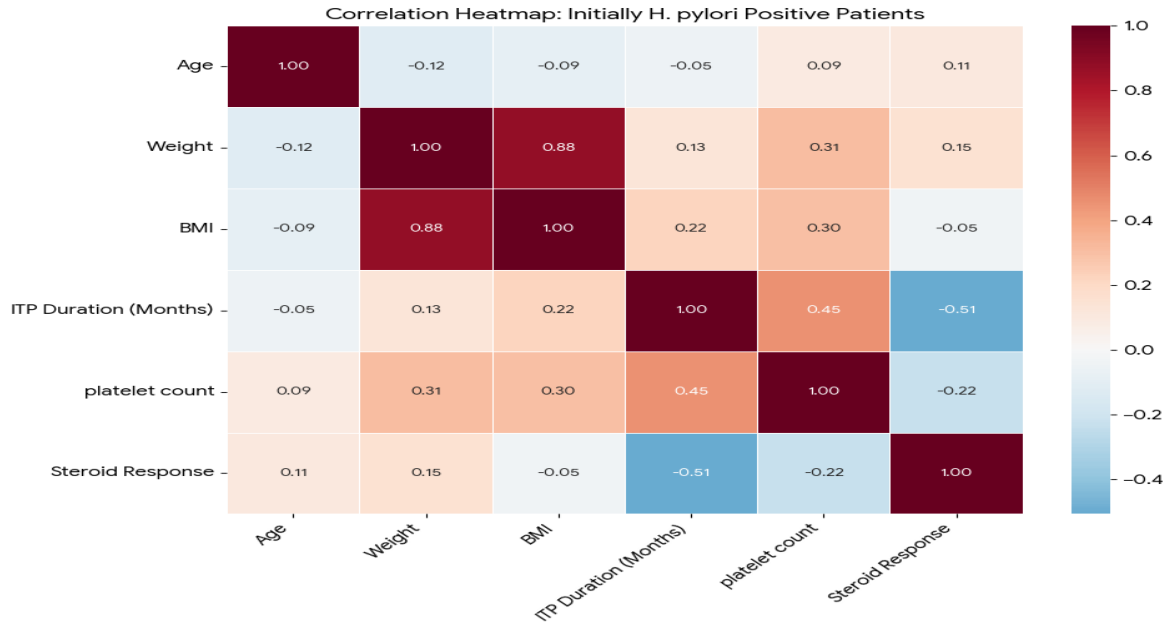

Figure 4: Spearman correlation matrix heat map between various variables with platelet count for *H. Pylori*-positive ITP patients.

Table 3 P-value of the matrix showing the association significant levels between various variables with platelet count for *H. Pylori*-negative ITP patients.

Variable	Baseline PLT	Age	Sex	BMI	Relapsed/ Refractory	Steroid Responsive	Duration of ITP	Family History	Bone Marrow Study
Baseline PLT	-	0.210	0.450	0.812	0.510	0.320	0.610	0.880	0.412
Age	-	-	0.620	0.410	0.380	0.590	0.910	0.120	0.750
Sex	-	-	-	0.490	0.820	0.310	0.410	0.110	0.005*
BMI	-	-	-	-	0.120	0.750	0.380	0.210	0.610
Relapsed/ Refractory	-	-	-	-	-	<0.001*	<0.001*	0.580	0.910
Steroid Responsive	-	-	-	-	-	-	<0.001*	0.510	0.820
Duration of ITP	-	-	-	-	-	-	-	0.850	1.000
Family History	-	-	-	-	-	-	-	-	0.310

*Significant at $p < 0.05$

Table 4 P-value of the matrix showing the association significant levels between various variables with platelet count for *H. Pylori*-positive ITP patients.

Variable	Baseline PLT	Age	Sex	BMI	Relapsed/ Refractory	Steroid Responsive	Duration of ITP	Family History	Bone Marrow Study
Baseline PLT	-	0.139	0.336	0.643	0.591	0.242	0.560	0.778	0.211
Age	-	-	0.559	0.340	0.426	0.673	0.998	0.094	0.822
Sex	-	-	-	0.527	0.791	0.256	0.424	0.065	0.004*
BMI	-	-	-	-	0.038*	0.840	0.469	0.149	0.594
Relapsed/ Refractory	-	-	-	-	-	<0.001*	<0.001*	0.609	0.850
Steroid Responsive	-	-	-	-	-	-	<0.001*	0.469	0.704
Duration of ITP	-	-	-	-	-	-	-	0.904	1.000
Family History	-	-	-	-	-	-	-	-	0.229

*Significant at $p < 0.05$

Figure (5) displays forest plots illustrating the results of a logistic regression analysis aimed at identifying potential predictors of illness outcomes within the research population. The odds ratio (OR) serves as the measure of effect, with an OR of 1.0 (shown by the red

dashed line) denoting no connection. The horizontal black lines represent the 95% confidence intervals (CI), and if a CI intersects the OR = 1.0 line, the result is deemed statistically insignificant. Figure (5 A) demonstrates that none of the examined variables, such as age, sex, BMI, family history, or bone marrow testing results, serve as credible predictors of relapsed or refractory disease status in this dataset. The results depicted in Figure (5 B) corroborate the conclusion drawn from Figure (5A). None of the examined variables, including age, sex, BMI, familial history, or bone marrow analysis, emerged as statistically significant predictors of the outcome in this investigation.

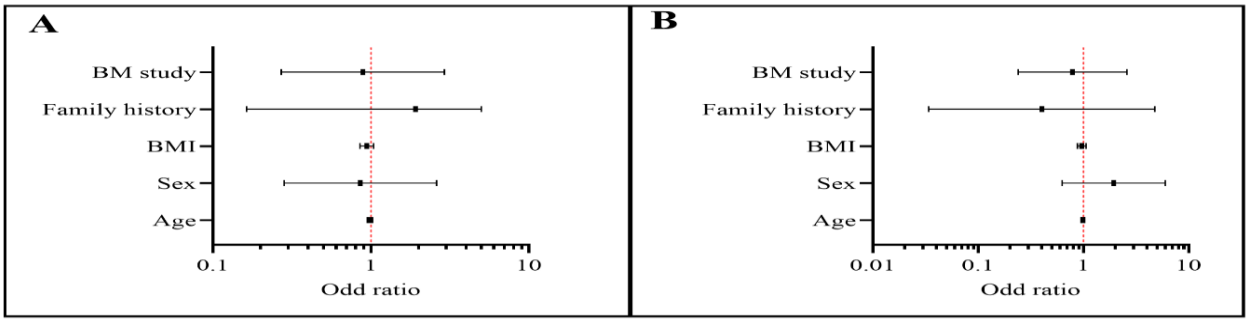

Figure 5: Forest plot for *H. Pylori*-negative ITP patients of A) predictors of disease status (Relapsed/Refractory), B) predictors of Steroid Responsive (binary logistic regression analysis)

Figure (6) presents the forest plots for the *H.pylori*-positive patients. Multivariate binary logistic regression analysis was conducted to identify factors associated with disease outcome and treatment response.

A) Predictors of Disease Status (Relapsed/Refractory)

In individuals with positive infections, none of the clinical markers achieved statistical significance in forecasting a relapsed or refractory disease status. Age and BMI exhibited Odds Ratios (OR) close to the null effect line, signifying no significant influence on disease status. Males had reduced odds of relapse/refractory status in comparison to females.

B) Predictors of Steroid Response

The examination of steroid responsiveness indicated a clear trend related to gender. Male patients exhibited a considerably higher likelihood of being steroid-responsive than female patients (95% CI: 3.25 – 179.18). Additional Variables: Age and BMI did not significantly affect the probability of steroid response. Family History: Although the odds ratio for family history was elevated, the extensive confidence interval indicates the low occurrence of positive family history within this cohort, rendering it an unreliable independent predictor in this model.

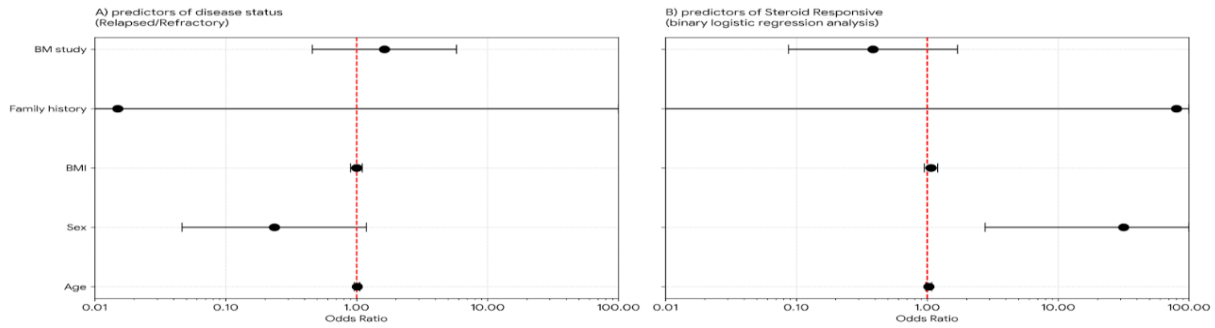

Figure (6) Forest plot for *H. Pylori*-positive ITP patients of A) predictors of disease status (Relapsed/Refractory), B) predictors of Steroid Responsive (binary logistic regression analysis)

A multivariate interaction test was performed to evaluate prediction models (forest plots) between *H. pylori*-positive and *H. pylori*-negative groups. Concerning steroid responsiveness (Plot B), the clinical predictive profiles exhibited a marginally significant difference between the groups (p=0.062), suggesting an increased probability of response among males in the *H. pylori*-positive category. Conversely, regarding disease status (Plot A), the predicted patterns exhibited no significant differences across the groups (p=0.385).

Discussion

Patients Demographics and Disease Characteristics

In the study cohort, the majority of enrolled patients (n=100) were in their early 40s, with a notable predominance of females, particularly in the *H. pylori*-positive group. These findings align with the published epidemiological statistics on primary ITP, indicating a greater frequency among adult females.[1,2]. While immunological thrombocytopenia (ITP) mostly impacts females, current data suggests that the inflammatory response triggered by *H. pylori* may find a more vulnerable environment inside the female immune system.[19], which is more susceptible to autoimmunity triggered by molecular mimicry[9]. The study cohorts comprised individuals of normal weight, predominantly with a negative familial history. The median duration of ITP in the current study was 1 month for newly diagnosed cases, 6 months for persistent cases, and 5 years (60 months) for chronic cases, as per the International Working Group (IWG) on ITP Consensus Report.[7]. All patients received standard treatment in accordance with practice guidelines; nevertheless, approximately half exhibited inadequate steroid response and failed to achieve remission. Prior research indicated a comparable mean age of ITP patients, around 41 years (range 19–71), in Iran.[20], among ITP patients in Pakistan the mean age was 43.18±12.5 years [21]. The duration of ITP disease in the later study was of a median of 61 months for chronic patients[21], while other study from France reported a median of 3.3 months for persistent patients[22], meanwhile newly diagnosed ITP patient of (2.2) months was reported from Australia[23].

Baseline Platelet Count and Distribution of Platelet Count according to ABO Phenotypes

The platelet count is a crucial indicator of illness state; the current data indicated no difference in baseline platelet counts between *H. pylori*-positive and *H. pylori*-negative groups, with all patients presenting values < 50×10^9/L. A comparable lack of substantial baseline variance has been documented in the existing research. Dogan et al. observed

similar findings in their evaluation of ITP patients, showing no statistically significant variation in baseline platelet counts irrespective of infection status (p=0.354).[15]. The data suggest that while *H. pylori* may serve as a significant catalyst for the autoimmune response, presumably via molecular mimicry of the CagA protein, it does not dictate the degree of platelet destruction upon diagnosis.[16].

Moreover, several systematic reviews (Stasi et al.) and clinical studies (Franchini et al.) corroborated that *H. pylori* acts as an independent variable in the initial manifestation of the disease.[14]. Studies corroborate this baseline parity, highlighting that the bacterium's harmful involvement is primarily revealed with the response to eradication therapy rather than in the first haematological assessment [7, 13]. These data corroborate the Two-Hit concept of ITP, wherein the bacteria triggers autoantibody synthesis, while the subsequent platelet clearance rate aligns with the general ITP population.[24].

The observed baseline homogeneity in this investigation enhances internal validity and establishes a reliable basis for assessing the therapeutic effects of bacterial eradication in Phase II.

The current findings revealed a significant variation in platelet count specifically among patients with blood group O positive. Patients negative for *H. pylori* demonstrated elevated platelet counts relative to those positive for *H. pylori*. No notable changes were detected in other ABO phenotypes. It has been previously observed that blood group O+ is consistently linked to reduced circulating levels of von Willebrand factor and factor VIII in comparison to non-O blood groups. These variations may affect platelet longevity and elimination dynamics in immune-mediated thrombocytopenia. Although immune-mediated platelet destruction is the principal mechanism in ITP, diminished von Willebrand factor levels in persons with blood group O+ may exacerbate the clinical consequences of immunological activation. This decrease may lead to more pronounced thrombocytopenia in the presence of viral triggers like *H. pylori*.[11,12]. ABO antigens are found on both platelets and endothelial cells and may affect immune recognition. Molecular mimicry between *H. pylori* antigens and host glycoproteins has been suggested as a pathogenic mechanism in *H. pylori*–associated ITP.[7]. The pathogenicity of *H. pylori* is somewhat facilitated by BabA (Blood group antigen-binding adhesin), which acts as a crucial link for bacterial adhesion. *H. pylori* employs BabA to attach to the H-antigen receptor on the stomach mucosa, demonstrating the greatest binding affinity for the H-antigen, a characteristic trait of the O blood type.[10].

The absence of a significant difference in platelet counts among blood groups A, B, and AB reinforces the notion that ABO-related influences on ITP are phenotype-specific rather than universal. This discovery corresponds with the heterogeneity observed in prior ITP groups.[4,5].

Present international guidelines ignore ABO blood group from standard ITP risk classification. These data suggest that patients with blood group O infected with *H. pylori* may represent a unique subgroup exhibiting more severe baseline thrombocytopenia, necessitating more rigorous clinical evaluation.[25].

Steroid Responsiveness among *H. Pylori*-Negative and *H. Pylori* -Positive ITP Patients

The present investigation found no difference in the immediate therapeutic response to first-line corticosteroid therapy between *H. pylori*-positive and *H. pylori*-negative ITP patients, as all patients received conventional treatment for ITP. The data suggest that baseline *H. pylori* infection status did not

influence the rapid response to steroid therapy in this study cohort, indicating that *H. pylori* infection likely has no significant effect on short-term steroid responsiveness during the initial phase of ITP management. Corticosteroids largely exert their therapeutic impact in ITP by inhibiting autoantibody synthesis, diminishing Fc receptor-mediated platelet destruction, and modifying T-cell-mediated immunological dysregulation.[26]. Rather than through pathways that glucocorticoids directly target, these processes operate independently of infectious triggers like *H. pylori*, which are thought to contribute to ITP through molecular mimicry, persistent immunological activation, and dysregulated host–pathogen immune interactions.[4]. Therefore, it is biologically possible that there was no difference in steroid response between *H. pylori*-positive and negative patients in this investigation. This is consistent with corticosteroids' immunomodulatory impact rather than their antibacterial effect.

Crucially, recent global recommendations, such as those issued by the American Society of Haematology[5], Because there is little evidence to indicate a link between *H. pylori* infection and the effectiveness of first-line steroid therapy, beginning corticosteroid medication should not be stratified based on *H. pylori* infection status. Rather than improving the immediate response to immunosuppressive medication, *H. pylori* eradication is seen as a supplemental technique meant to achieve delayed or prolonged platelet recovery in specific patients.

Correlation Between Platelet Count and Disease Characteristics

Clinical correlations in *H. Pylori*-negative patients often follow "standard" primary ITP patterns, frequently demonstrating higher associations between treatment resistance and chronicity. Age, sex, body mass index, family history, and bone marrow results do not significantly correlate with baseline platelet count. This implies that in infection-negative cases, the degree of thrombocytopenia at presentation is mostly unrelated to constitutional or demographic factors. These results lend credence to the idea that immune-mediated processes, not patient-related baseline features, are the main drivers of primary ITP.[5,25].

However, steroid responsiveness and ITP duration were found to be strongly inversely significant in connection to relapsed or refractory illness state. The correlation between steroid responsiveness and recurrence is consistent with known clinical trends in ITP, where patients who have insufficient immunosuppressive response are more likely to have chronic or recurrent illness.[25,27]. Furthermore, the established progression from newly diagnosed to chronic ITP, which is marked by immune memory formation, persistent autoantibody production, and decreased treatment responsiveness, is supported by the strong correlation between longer disease duration and relapsed or refractory status.[3]. The total duration of ITP and steroid responsiveness have been found to be correlated, which highlights the impact of persistent immunological dysregulation on treatment results. Steroid resistance in primary ITP is a result of T-cell imbalance, compromised regulatory T-cell function, and epitope spreading, all of which are associated with longer disease duration.[3,27].

According to current guidelines, bone marrow examination does not reliably predict disease severity or treatment response in typical ITP presentations5. The current study's bone marrow test result showed no correlation with baseline platelet count or disease outcomes. Additionally, the heat map for *Helicobacter pylori*-negative patients shows a disease model primarily influenced by intrinsic immune mechanisms, suggesting

that immune behaviour and disease chronicity, rather than external modifying factors, are the primary determinants of clinical course and treatment response.[5].

The current study's *H. pylori*-positive immune thrombocytopenia (ITP) patients showed similar results to those of non-infected ITP patients. This emphasises how immunological persistence and treatment resistance, regardless of infection status, play a crucial role in influencing the course of disease.[25]. Additionally, bolster the idea that *H. pylori* infection contributes to ITP by altering the disease rather than causing it.[8,25].

In the current investigation, male patients with *H. pylori*-positive status were more likely to be steroid-responsive and had lower probabilities of relapse or refractory status than female patients. A multivariate interaction test further supported this sex-specificity, showing that males in the *H. pylori*-positive category were more likely to respond. This could be the result of interactions between sex-related immunomodulatory variations and infection-induced immunological activation. According to earlier research, male patients have unique Th1/Th2 immune profiles and cytokine responses, which could increase steroid sensitivity when exposed to long-term infectious stimuli like *H. pylori*.**[6,28].**

Additionally, a possible connection between metabolic and immunological variables is suggested by the strong correlation between body mass index and relapsed or refractory status in the *H. pylori*-positive population. Immune dysregulation in infection-associated ITP may be made worse by obesity, which is linked to chronic low-grade inflammation, altered macrophage polarisation, and decreased glucocorticoid response.[28,29].

Overall, the *H. pylori*-positive heatmap depicts a more complicated, multidimensional illness model wherein host biological factors—specifically, sex and metabolic condition—interact with infection status to affect the course of the disease and responsiveness to therapy.

Conclusion

In conclusion, *Helicobacter pylori* infection does not affect baseline platelet counts or short-term corticosteroid responsiveness in primary immune thrombocytopenia patients. However, certain host variables modulate disease expression in infected people. Those with blood group O and *H. pylori* positivity had more severe baseline thrombocytopenia, suggesting a phenotype-specific interplay between infection status and host biology. Male sex and higher BMI also affected treatment response and disease course in *H. pylori*–positive patients, indicating a more complex disease model. These results confirm existing guidelines that do not stratify first-line ITP care by *H. pylori* status, but they suggest that host-infection interactions may improve risk assessment and therapeutic techniques.

Other Consideration

Conflict of interest

The authors have declared that no competing interests exist.

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