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Original Article

Helicobacter Pylori in Patients with Chronic Immune Thrombocytopenic Purpura: A Pilot Study

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Abstract:
Background: Chronic immune thrombocytopenic purpura (ITP) is an autoimmune disorder. Children with chronic ITP were reported to be at higher risk of associated *Helicobacter pylori* (*H. pylori*) infection.
Aim of the work: To identify the frequency of *H. pylori* infection among children with chronic ITP.
Subjects and Methods: This cross-sectional observational study included 70 children with chronic ITP and a control group consisted of healthy 60 children of similar age and sex. They all underwent enzymatic immunoassay (EIA) stool antigen test (SAT) for H. pylori.
Results: The group with chronic ITP included 40 (57.1%) males and 30 (42.9%) females, while the control group included 30 (50%) males and 30 (50%) females (p=0.47). The mean ± SD age of the cases and control group was 10.5 ± 6.5 years and 10.3 ± 4.2years (p=0.44). The mean ± SD duration of ITP was 15.8 ± 5.6 months. All patients were on corticosteroid therapy. Only 10 (14.3%) of the cases with ITP underwent splenectomy. There was no statistical difference in the rates of *H. pylori* among those with ITP and the control group. Among the 70 children with a chronic ITP, 20 (28.6 %) had *H. pylori*, compared to 11 (19%) of the control group (p=0.172). The rate of *H. pylori* infection correlated with longer duration of ITP (p-value = 0.03).
Conclusion: Despite an apparent increase in rate of *H. pylori* among those with chronic ITP compared to the control group, it did not mount to statistical significance. Children with chronic ITP do not seem to be more vulnerable than their healthy peers to *H. pylori*. Further studies of the effect of *H. pylori* treatment on chronic ITP are recommended.

Keywords: chronic immune thrombocytopenic purpura; *Helicobacter pylori*
Abbreviations: *H. pylori*: *Helicobacter pylori*; ITP: immune thrombocytopenic purpura

Introduction

Chronic idiopathic thrombocytopenic purpura (ITP) is an immunological disorder of the hematological system, with the standard clinical feature of isolated low platelet count (less than 100,000/µL), known as thrombocytopenia. The anti-platelet antibodies cause a dual pathology, they destroy the platelets during circulation and inhibit the function of the megakaryocyte is why the count reduces (*1*)**.** It is becoming apparent that chronic ITP is a multi-factorial disorder (*2*)**.** ITP in children frequently appears as an acute self-limited condition that lasts weeks and often several months, but almost 25-30% become chronic. About 50% will do so after a number of years (*3*)**.** The comorbidities present a considerable hurdle in chronic ITP, especially in those with more than one thrombocytopenic episode or those with more than one treatment modality. It is logical that the approach to manage these comorbidities would help enhance the quality of life and life expectancy of ITP patients (*4*).

Of the various comorbidities reported with ITP, *Helicobacter pylori* infection has received a lot of attention due to its relationship with autoimmune diseases. This gram-negative bacterium, which is primarily active in the stomach and is implicated in the pathogenesis of peptic ulcers and gastric carcinoma, and may have a role in the pathogenesis of ITP (*5*). The first link of *H. pylori* infection with ITP was observed in Japan, where an improvement in platelet count was noted in a few patients after they underwent *H. pylori* eradication therapy (*6*). Nonetheless, the elimination treatment has not worked in all regions, with significant differences in success rates among populations (*7*). This variation questioned the role of *H. pylori* infection as a contributor of increased in platelet destruction as well as the potential benefit of eradication therapy in managing chronic ITP. Hence, a unified protocol of eradication therapy is not supported (*8*).

Moreover, children with chronic ITP receive different immune suppressive treatment modalities that may increase their susceptivity to *H. pylori* and other infections (*9*).

The present study aimed to identify the frequency of *H. pylori* infection among children with chronic ITP.

Subjects and Methods

This pilot study was conducted at The Pediatric Department, Ahmed Maher Teaching Hospital in Cairo and Pediatric Hematology Unit, Damanhour Teaching Hospital in Damanhour, Egypt. It was conducted over 12 months between May 2022 and May 2023. The parents/care givers consented to the study**.** The study was approved by Research Ethical Committee of The General Organization for Teaching Hospitals and Institutes Committee, Egypt. The study complied with the Helsinki Declaration ethical principles for research of human subjects (*10*). All personal information was coded to secure confidentiality of the enrolled subjects. The trial registration number (HAM00085).

Participants

The study included children and adolescents with chronic ITP, which was defined as having a platelet count of below 100,000/mm^3 for more than 12 months. Those suffering from secondary forms of thrombocytopenia due to leukaemia, systemic lupus erythematosus, aplastic bone marrow and metabolic causes were excluded. Those with acute or drug induced thrombocytopenia were also excluded. The control group consisted of children with no gastrointestinal or hematological manifestations. The participants were recruited during scheduled visits or admitted to the pediatric unit.

Methods

The following data were collected and analyzed: duration of ITP and progression of the disease, age at onset, and treatment history and complications, history of undergoing splenectomy, were collected as well as family history. Both cases and control group underwent: 1) clinical examination: including the evaluation of purpura bleeding tendencies, jaundice, growth and development, chest, abdominal, neurological system, cardiovascular system, joints, rashes, and other physical characteristics. 2) The results of laboratory tests: complete blood count (CBC), manual platelet counts, and coagulation profile. *H. pylori* was tested using a stool antigen assay by ELISA (*H. pylori* Ag ELISA test system, Monocent, Inc., USA) (*11*).

Statistical Analysis

The data gathered during the research was analyzed using Statistical Package for the Social Sciences software (SPSS, version 20, IBM, Armonk, USA). For descriptive purposes, continuous variables such as age and platelet counts were described using measures of central tendency and dispersion such as the mean, median, and standard deviation. The presence of *H. pylori* infections, and other infections were presented as percentage. Chi-square or Fisher's exact tests were also employed. A p-value of less than 0.05 was considered statistically significant. In relation to this study's cross-sectional design, participants were not examined longitudinally; therefore, the statistical analysis has been directed towards correlation and not causation. The logistic regression analysis should be interpreted with care since the duration of the *H. pylori* infection is unknown. To examine the order of ITP and *H. pylori* infection, a longitudinal study would be necessary.

Results

The demographic and clinical features of the study subjects are illustrated in Table 1. None of the studied cases or control group had abdominal pain, heartburn, nausea, vomiting, bloating, burping, loss of appetite, or unexplained weight loss. Both chronic ITP and control group had statistically comparable rates of *H. pylori* infection (p=0. 172). *H. pylori*-positive patients with chronic ITP had a mean age of 11.3 ± 2.8 years comparable to those with negative *H. pylori* of 10.1 ± 3.4 years (p = 0.18), and their mean ± SD platelet count was also comparable being 65 +/- 20 x 10^3/µL and 72 +/- 27 x 10^3/µL (p= 0.25). Yet, the mean ± SD duration of chronic ITP in patients with *H. pylori* infection, was longer among those without *H. pylori* (18.2 ± 4.05 months and 14.7 +/- 5.08 respectively) (p = 0.03). *H. pylori* was encountered among 6 (60%) of those who underwent splenectomy, and among 4 (23%) who retained their spleen (p=0.027). Longer duration of disease was associated with 2.75 folds increase in *H. pylori* infection (odds ratio (OR) of 2.75) (95% CI: 1.12-6.75, p = 0.02). All patients were on corticosteroids brief courses (prednisone 5–10 mg/day).

Table 1. Demographic, Clinical and laboratory data of the Study Population

	Children with Chronic ITP (Number=80)		Control group (Number= 60)		P value
	Number	Percentage	Number	Percentage	
Sex					
- Male	40	57.1	30	50	0.09
- Female	30	42.9	30	50	
Splenectomy Status					
- Yes	10	14.3	0	0	0.001
- No	60	85.7	60	100	
	Mean ±SD	Median (IQR)	Mean ±SD	Median (IQR)	
Age (years)	10.5 ± 6.5	14 (8–16)	10.3 ± 4.2	11 (8–13)	0.4
ITP Duration (months)	15.8 ± 5.6	16 (12–20)			
Platelet Count (×10³/µL)	70 ± 25	65 (50–90)	250 ± 22	190 ± 20	0.001
	Number	Percentage	Number	Percentage	
H. pylori Infection					
- Yes	20	28.6	11	19	0.172
- No	50	72.4	49	81	

ITP: Idiopathic thrombocytopenic purpura

Table 2. Platelet counts and duration of Cases with chronic ITP and *H. pylori* infection

	H. pylori positive Number= 20	*H. pylori* negative Number=50	P value
	Mean ± SD	Mean ± SD	
Platelet Count (×10³/µL)	65 ± 20	72 ± 27	0.25
Duration of ITP (months)	18.2 ± 4.5	14.7 ± 5.8	0.03

Discussion

Both chronic ITP and control group had statistically comparable rates of *H. pylori* infection (p=0.05). All those with *H. pylori* infection were asymptomatic. Children with chronic ITP are reported to have increased risk of infection because they have immune dysregulation, defective regulatory T and B cells (*12*), and because of the immune suppressive medications they receive (*13*). The *H. pylori* infection was incriminated in the pathogenesis of chronic ITP, yet evidence to support generalization of such an assumption is lacking (*8*). Our study did not aim to verify the incrimination of *H. pylori* in the pathogenesis of chronic ITP, but rather to study if those with chronic ITP are more susceptible to *H. pylori*. Our study provides evidence that those with chronic ITP are not more susceptible to *H. pylori* despite being on immune-suppression.

All those with *H. pylori* in the control were asymptomatic, and all the cases with *H. pylori* among those with chronic ITP were also asymptomatic which suggests that We did not study the specific *H. pylori* strains among those with chronic ITP and the control group, we did not study any of *H. pylori* virulence factors, the CagA protein intracellular delivery of host and the vacuolating cytotoxin A (VacA) that disrupts cell membranes, causing vacuolation and ends in cell death (*14*) as it was not within the scope of our study. Chronic ITP is associated with higher levels of IL-12 and IL-23 (*15*), which are capable of eliminating *H. pylori* among the immune competent subjects (*16*). Hence, it seems that chronic ITP immune dysregulation does not compromise the ability to eliminate *H. pylori*.

It is interesting that children with chronic ITP and *H. pylori* had no symptoms. We did not study the *H. pylori* genotypes (*17*), hence we do not know if the *H. pylori* strains among our studied cohort were pathogenic or merely colonizers/commensals (*18*). In view of the recent evidence that *H. pylori* suppresses other gastric potentially proinflammatory and/or pro-carcinogenic bacteria, it may have a protective role among children with chronic ITP. This is further supported by our finding that *H. pylori* was commoner among those who underwent splenectomy (p=0.027), and was also asymptomatic.

It seems that the mere presence of *H. pylori* in children with chronic ITP may not be an indication for treatment or eradication. There is a gap of knowledge to support the decision when or when not to treat or eradicate *H. pylori* among children with chronic ITP.

Conclusion

Despite an apparent increase in rate of *H. pylori* among those with chronic ITP compared to the control group, it did not mount to statistical significance. Children with chronic ITP do not

seem to be more vulnerable than their healthy peers to *H. pylori*. Further studies of the effect of *H. pylori* treatment on chronic ITP are recommended.

Author Contributions

All authors shared equally in the study. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study.

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