ORIGINAL ARTICLE

EFFECT OF ERADICATION OF *HELICOBACTER PYLORI* INFECTION ON THE PLATELET COUNTS IN PATIENTS PRESENTING WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Background: Idiopathic thrombocytopenic purpura (ITP) is a rare autoimmune disease characterized by the platelet destruction that is autoantibody mediated, and there is suboptimal platelet production in the absence of a known cause, this leads to decreased peripheral blood platelet counts or thrombocytopenia and *Helicobacter pylori* has direct association with ITP. The aim of this study was to see the platelet recovery in patients of ITP after the *H. pylori* infection eradication. **Methods:** This was a case control study and 120 ITP patients who tested positive for *H. pylori* (divided into age and sex matched treatment and the control groups) were enrolled from the outdoor patients (OPD) of Sheikh Zayed Medical Complex. Stool antigen (HpSA) enzyme immunoassay method (EIA) method was used for *H. pylori* detection. **Results:** The response of the platelet count in the treatment group was a 'complete response' in 35 (60.3%) patients, a partial response in 16 (27.6%) patients and no response was found in 7 (12.1%) cases. However, no remarkable change was seen in the platelet counts of the patients in the control group. **Conclusion:** Complete eradication of *H. pylori* helps in the recovery of *H. pylori* induced platelet reduction and detection and eradication of *H. pylori* infection should be considered in the work-up of patients with ITP.

Keywords: Eradication therapy, *H. pylori*, Idiopathic Thrombocytopenic Purpura, Platelet counts Thrombocytopenia

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INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is a rare autoimmune disease characterized by the platelet destruction that is autoantibody mediated, and this leads to decreased peripheral blood platelet counts ($<150\times10^9$/L) or thrombocytopenia. The disease typically runs a chronic (>6 months) course in adults.[1,2] Approximately one-fourth of the patients are asymptomatic at the time of diagnosis, however, petechia, purpura and mucosal bleeds may be seen.[3]

A considerable association has been detected between the *H. pylori* infection and thrombocytopenia in patients with ITP. About 50% of the world's population is affected by *H. pylori* infection. WHO has designated *H. pylori* as a class-1 carcinogen as it acts as a co-factor in the development of both adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphomas.[4,5]

Search for *H. pylori* infection must be attempted in ITP patients at the time of diagnosis for setting a better and effective treatment plan for these patients. The aim of the present study was to see the platelet recovery in patients of ITP after the *H. pylori* infection eradication.

MATERIAL AND METHODS

This case control study conducted in the Department of Haematology, Sheikh Zayed Medical Complex, Lahore and Lab One Lahore from Dec 2012 to Dec 2013. Patients aged 18 years or older from either sex, having persistent or chronic ITP (defined by the International Working Group[4]) with concomitant *H. pylori* infection, confirmed by using stool antigen testing were included in the study. Patients who had *H. pylori* eradication treatment previously (last 3 months), or suffering from comorbid conditions like some form of active bleeding or with history of potentially adverse effects associated with penicillin or those reporting other debilitating illness, e.g., cancer were excluded from the study.

After taking written informed consent, patients fulfilling the inclusion criteria were enrolled through the Haematology Out-patient Department of Sheikh Zayed Hospital, Lahore. Total 120 patients were enrolled by convenient sampling and randomly allocated to either the treatment group or the control group. The initial platelet counts in both groups were noted. Sixty patients falling in the treatment group were given the bacterial eradication therapy for two weeks and were reassessed after a period of 4 weeks and any change in their platelet counts was noted.

Standard antibiotic therapy for bacterial eradication comprising of Omeprazole 20 mg PO BD, Clarithromycin 200 mg PO BD and Amoxicillin 750 mg PO BD. This therapy was taken for 14 days. Eradication or persistence of *H. pylori* infection was

determined by another *H. pylori* stool antigen test after the completion of four weeks. *H. pylori* infection status of the ITP patients was determined by the *H. pylori* stool antigen (HpSA) an enzyme immunoassay (EIA) based method. The WHO recommended kit used for this test is Premier Platinum HpSA kit (Meridian Diagnostic, Cincinnati, Ohio).

The outcome measure was to look for the improvement in the patient's platelet counts after *H. pylori* eradication. The Guidelines Developed for the American Society of Haematology[3] were followed according to which 'a complete remission (CR) was defined as a platelet count higher than 150×10^9/L, while partial remission (PR) is a platelet count between 50 and 149×10^9/L, or an increase of more than 30×10^9/L with respect to the pre-treatment value'.

RESULTS

This study was conducted on 120 *H. pylori* positive ITP patients. These patients were divided into two groups of 60 patients each. One group was labelled as 'Treatment group' or group A. It included 60 patients (at random) who were exposed to the *H. pylori* infection eradication treatment for two weeks, along with the conventional treatment they were getting for ITP. The second group was labelled as 'Control Group' or Group B and it also included 60 patients who were given only the routine ITP treatment. Two of the 60 patients in group A (Treatment group), dropped out of study due to complications, i.e., one patient developed vomiting and diarrhoea while the other denied participation after counselling. There were 21 (35.0%) males and 39 (65.0%) females in each group. The age of males in group A was 56.1±12.76 years and for group B was 55.33±12.47 years. The age of females in group A was 48.33±11.89 years and in group B it was 49.56±11.23 years. Age of group A, overall, was 51.05±12.66 years and for group B it was 51.58±11.90 years.

The average duration of illness was 10.17±6.73 months for group A and 10.28±6.06 months for group B. The difference was not significant (p=0.931). Haematologic parameters were noted and recorded on Day 1 in both groups.

The normal range of platelet counts, i.e., 150–400×10^9/L was taken as standard. The mean platelet counts just before the eradication therapy, i.e., Day 1, were similar in both groups. The mean counts were $47.97\pm25.70\times10^9$/L in group A, and $42.82\pm23.36\times10^9$/L in group B (p=0.253). (Table-1)

The mean platelet counts in both groups were compared after giving eradication therapy for *H. pylori* infection to group A patients, keeping it as Day 28 (end of eradication therapy). The mean platelet counts in group A were $175.59\pm97.90\times10^9$/L and those recorded in group B were $83.30\pm23.20\times10^9$/L with statistically significant differences (p<0.001). (Table-2)

The comparison of platelet counts at Day 28 between group A and group B according to the baseline platelet counts was made. It was observed that among the patients with initial platelet counts $\leq30\times10^9$/L, there were 7 patients in group A, out of which 2 (28.6%) showed complete response, 3 (42.9%) showed partial response and 2 (28.6%) showed no response.

In group B (control group) out of 7 patients, 3 (42.9%) showed a partial response and 4(57.1%) had no response (p=0.592). The cases with initial platelets in range of 31–60×10^9/L at Day 1 showed 15 patients in group A, out of which 9 (60.0%) showed a complete response and 6 (40.0%) showed a partial response. Out of 18 patients in group B, 7 (38.9%) had partial response and 11 (61.1%) showed no response (p<0.001). The cases with initial platelet count $\geq60\times10^9$/L were taken as 36 patients in group A. Out of these, 24 (66.7%) showed complete response, 7 (19.4%) showed a partial response and 5 (13.9%) showed no response. Among 35 patients of group B, 4 (11.4%) showed partial response, whereas, 31 (88.6%) showed no response (p<0.001).

Fifty-eight cases were taken in the treatment group. Platelet counts before eradication were $47.97\pm25.70\times10^9$/L and $175.59\pm97.9\times10^9$/L after eradication therapy. This showed a complete response of 35 (60.3%), partial response of 16 (27.6%) and no response in 7 (12.1%) cases. (Table-3)

Table-1: ITP patients at day 1 (at the start of treatment)

	Group A		Group B		
Parameter	**Mean±SD**	**Range**	**Mean±SD**	**Range**	***p***
Hb (g/dl)	13.39±2.3	9.50–17.50	13.86±2.00	9.50–18.00	0.292
MCV (fl)	87.70±6.14	75.00–95.00	86.50±7.35	72.00–95.00	0.334
TLC ($n\times10^9$/L)	7.41±2.59	3.50–12.50	6.20±2.23	3.50–11.00	0.28
PLT ($n\times10^9$/L)	47.97±25.70	5.00–90.00	42.82±23.36	5.00–85.00	0.253

Table-2: Comparison of platelet counts among two groups of ITP patients at day 28 (end of eradication treatment)

	Group A		Group B		
Parameter	**Mean±SD**	**Range**	**Mean± SD**	**Range**	***p***
Platelet count ($n\times10^9$/L)	175.59±97.9	15.00–581.00	83.30±23.20	35–120	<0.001

Table-3: Comparison of platelet counts at day 28 (after treatment) between Group 'A' & 'B' according to base-line platelet counts [n (%)]

Platelet count at day 1	Group	Total patients	Platelet count response at day 28			*p*
			Complete response	Partial response	No response	
≤30.0×10^9/L	A	7	2 (28.6)	3 (42.9)	2 (86.6)	0.592
	B	7	0	3 (42.9)	4 (57.1)	
31.0–60.0×10^9/L	A	15	9 (60.0)	6 (40.0)	0	<0.001
	B	18	0	7 (38.9)	11 (61.1)	
>60×10^9/L	A	36	24 (66.7)	7 (19.4)	5 (13.9)	<0.001
	B	35	0	4 (11.4)	31 (88.6)	

DISCUSSION

In this study, 58 cases were taken in the treatment group. Platelet counts before eradication were 47.97±25.70×10^9/L and after eradication therapy they improved to 175.59±97.9×10^9/L. This showed a complete response in 35 (60.3%), partial response in 16 (27.6%) and no response in 7 (12.1%) cases. According to Michael[6] and Francine[7], it was demonstrated that prevalence of *H. pylori* infection in the general population increases with increasing age. Regarding our study, *H. pylori* infected patients of ITP were found to be significantly older, i.e., of mean age 55 years. Hence, this finding was in uniformity with the international studies cited earlier.

Inaba *et al*[8] and Emilia *et al*[9] reported a significant improvement of the platelet counts in ITP patients after eradication of *H. pylori* infection. In our study, a complete response in 35 (60.3%) was seen after eradication of *H. pylori* infection (p<0.001). These results were comparable to those of previous studies which were done in the Asian countries, such as Japan[10] and South Korea[11]. In general, the prevalence of *H. pylori* infection varies according to the geographic location and in Asian countries like Pakistan, is too high.[12] In our study the improvement in the platelet counts was observed as a better improvement in those patients having slightly higher base-line platelet counts, i.e., ≥30×10^9/L whereas, poor response in the platelet counts was seen in ITP patients with severe thrombocytopenia (platelets≤30×10^9/L). These results show that the chance of obtaining a response by *H. pylori* eradication treatment is lower in patients with severe thrombocytopenia.

CONCLUSION

Eradication of *H. pylori* infection led to a good platelet response in ITP patients. Considering the low costs, the non-invasiveness of diagnostic method, and much less toxicity and hazards of the eradication therapy compared to the standard ITP therapy (steroids or splenectomy) the assessment of *H. pylori* infection and the use of its eradication therapy should be attempted in ITP patients. This will allow a good non-immunosuppressive option in a significant number of patients.

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