

Helicobacter pylori infection in chronic immune thrombocytopenic purpura patients in Malaysia

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SUMMARY

Helicobacter Pylori has been implicated with a possible link to immune thrombocytopenia purpura (ITP) and studies have shown contradicting results in platelet recovery after eradication of *H pylori* infection. **Objectives:** To determine the prevalence of *H pylori* infection in adult ITP patients in Malaysia and to examine the effect of eradication of *H pylori* infection in these patients.

Method: 50 ITP adult patients from haematology clinics were recruited. A 13C urea breath test for *H. pylori* infection was performed in all patients. Those with *H. pylori* infection were treated with standard eradication regimen. Platelet counts were monitored regularly after eradication therapy to assess response. Complete response (CR) was defined as the achievement of platelet counts of $>150 \times 10^9/L$ within 3 months after eradication therapy and partial response (PR) was defined as platelet count above $50 \times 10^9/L$ and/or at least doubling the baseline count.

Result : The median age of patients recruited was 50 years. The majority of patients were female (76%). Chinese was the largest ethnic groups (56%) followed by Malays (28%) and Indians (16%). 11 of the 50 patients (22%) were found to have *H. pylori* infection and all but one had eradication therapy. Overall, some response was observed in 3 patients (30%) with a CR seen in 2 patients and PR in one patient. However, all these patients had a drop in their platelet counts at 6th month follow up.

Conclusion: The prevalence of *H. pylori* infection is relatively low in our adult ITP patients (22%) and by eradicating the infection did not have any sustained effect in the platelet recovery.

KEY WORDS:

Immune thrombocytopenia purpura, helicobacter pylori infection

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a relatively common haematological disorder where there is persistent thrombocytopenia due to premature platelet destruction from autoantibodies and reduced megakaryopoiesis. Clinical features of ITP in adults are quite distinct compared with childhood acute ITP. Adult ITP usually has an insidious onset and does not resolve spontaneously. It is well documented that there is a link between ITP and *H. pylori* infection¹⁻⁴. According to Maastricht III consensus, ITP is one of the

extraintestinal diseases of *H. pylori* for which eradication therapy is indicated⁵. Eradication of the infection has been reported to produce increase in platelet counts in some studies but not in others. Initial reports from the Italian and Japanese studies showed that eradication of *H. pylori* infection improved platelet counts in ITP patients^{1-4,6-10}. However, there are also other conflicting studies which found no evidence of an association between *H. pylori* eradication and platelet recovery in ITP patients^{11,12}. A systematic review by Stasi et al found a complete response rate of 42.7% and overall response of 50.3%. However, all of the studies reviewed in that review article were from Europe and Japan¹³.

Malaysia is a multiethnic country where the three main ethnic groups are Malay (65%); Chinese (26%) and Indians (7.7%)¹⁴. The overall prevalence rate of *H. pylori* infection was previously reported to be 35.9% in Malaysia and it is well documented the prevalence rate differs in different geographical area within Malaysia¹⁵. It is also of interest that the Malay populations have the lowest prevalence of *H. pylori* infection (11-29%) compared to Indians (49-52.3%) and Chinese (26.7-57.5%)¹⁵. The prevalence rate in paediatric population in an urban area is reported to be lower than the adults at 10.3% , however the ethnic differences is found to be similar as the adult populations¹⁶. Within each geographical area in Malaysia, the difference in prevalence rate of *H. pylori* infection amongst the three ethnic groups is consistent.

There has not been any study which looked into the prevalence rate of *H. pylori* infection amongst the ITP patients in Malaysia or the South East Asia regions. We therefore performed a prospective study to determine the prevalence rate of *H. pylori* infection in adult ITP patients and to determine if eradication of the infection will improve the platelet counts.

MATERIALS AND METHODS

This is a prospective study where all adult patients with ITP in a local teaching institution were reviewed and recruited from June 2004 to December 2005 and again from July 2009 to January 2010.

The inclusion criteria includes patients more than 18 years of age, who had platelet counts persistently low ($<100 \times 10^9/l$) for more than 3 months and is otherwise well and do not have any active bleeding. Patients who were previously included were not recruited again. A bone marrow examination was performed in all patients to exclude other causes of

This article was accepted: 3 January 2013

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Table I: Patient Characteristics

	H pylori positive	H pylori negative	total
Median Age (range)	50 years (19-71)	49 years (18-79)	49.5 years (18-79)
Gender (M:F)	3:8	9:30	12:38
Race			
Chinese	25% (7)	75% (21)	56% (28)
Malays	7% (1)	93% (13)	28% (14)
Indians	37.5%(3)	62.5% (5)	16% (8)
Median years of diagnosis (months)	109 (36-216)	70 (3-336)	60 (3-336)
Platelet counts prior eradication x10 ⁹ /L (range)	24-100 (mean 58) Median 50	8-97 (mean 52) Median 49	8-100 (mean 53) 49.5 median

Table II: Platelet counts in patients who were tested positive with H Pylori

Patient	Ethnic	Platelet counts before treatment (10 ⁹ /l)	Platelet counts 2 weeks after treatment (10 ⁹ /l)	Platelet counts 4 weeks after treatment (10 ⁹ /l)	Platelet counts 8th week after treatment (10 ⁹ /l)	Platelet counts 12th week after treatment (10 ⁹ /l)	Platelet counts 6 months after treatment (10 ⁹ /l)
1	C	56	78	62	88	59	35
2	I	46	64	64	70	56	56
3	I	56	79	71	63	71	96
4	C	50	52	38	39	42	50
5*	C	100	152	--	82	164	114
6*	C	92	119	107	125	186	144
7*	C	35	47	40	85	75	12
8	C	48	97	133	66	94	50
9	I	24	12	6	63	152	67
10	M	39	33	40	41	36	50

Patient 8 and 9 was on high dose of prednisolone.

thrombocytopenia. Patients were not eligible if they had prior treatment for *H. pylori* infection or have been treated with a proton pump inhibitor or antibiotic within 4 weeks of recruitment. Informed consents were obtained from all patients and the study was approved with the local institute ethic committee.

H. pylori infection was assessed by 13C urea breath test. Those found to have *H. pylori* infection will be treated with eradication therapy. The eradication regimen comprised amoxicillin 1g twice daily, clarithromycin 250mg 3 times daily and pantoprazole 40mg twice daily for 7 days. Platelet counts were monitored every 2 weeks for 4 weeks and monthly for the next 2 months and reassess again at 6th month after the end of treatment. Success of eradication of *H. pylori* infection was assessed by repeat urease breath test 4 weeks after treatment.

A complete response (CR) was defined as the achievement of platelet counts of >150x10⁹/L within 3 months after eradication therapy and partial response was defined as platelet count above 50x10⁹/L and/or at least doubling the baseline count. Patient who required dose changes of their treatment during the 3 months period were considered as non responders.

Statistical analysis

Difference between *H. pylori* positive and *H. pylori* negative patients were analysed using non-parametric test. The

response rate after *H. pylori* eradication in patients who are *H. pylori* positive is compared using chi-square analysis. A p value of <0.05 was considered significant.

RESULTS

A total of 50 patients were recruited. 20 patients were recruited during the year 2004 and another 30 patients in 2009. The median age was 50 years (ranges from 18-79). The majority of patients were female (76%). Chinese was the largest ethnic groups (56%) followed by Malays (28%) and Indians (16%). The patients' characteristic is shown in Table I. One patients passed away due to severe sepsis 3 months after recruitment. He was not found to have *H. pylori* infection. There was no significant difference between *H. pylori* positive and negative patients in terms of age, gender, ethnic groups, initial platelet counts and duration of ITP.

11 of the 50 patients (22%) had a positive breath test. All but one patient had eradication regimen. That one patient was lost to follow up. Repeat breath test 4 weeks after treatment showed all had achieved successful eradication of *H. pylori* infection. Platelet counts were followed up in these remaining 10 patients for a total of 6 months and the platelet response is documented in Table II. The overall response was observed in 30% (3) patients; CR in 2 patients and PR in one patient. However, all patients relapsed at 6th month follow up. There was no significant correlation of the existing platelet counts, duration of ITP with response rate.

DISCUSSION

The prevalence of *H. pylori* infection is different in different countries where higher rate is seen in Japan (73%) and Italy (51%) compared to 18-22% in Northern America¹⁷.

The prevalence rate of 22% in our patient cohort is quite similar to those reported in Northern America and is much lower compared to that of the Japanese and Italian population^{12,13,17,18}. Although the prevalence rate of ITP patients in this study is lower than the reported prevalence rate of 35.9% within Malaysia, it is consistent when the same geographical area i.e. Klang Valley is considered (26.4%)¹⁵. The prevalence rate of *H. pylori* infection in the three different ethnic groups is also consistent with the general population in Malaysia where the Malays has the lowest infection rate (7%) compared to Indians and Chinese, 37.5% and 25% respectively¹⁵.

In a review by Stasi *et al*, the overall response was reported to be 50.3% after *H. pylori* eradication with a complete response rate of 42.7%¹³. The review reported a correlation between infection rate and platelet response rate whereby the response rate is higher in countries with higher prevalence rate of *H. pylori* infection and patients with milder thrombocytopenia. This explained the higher reported response rate seen in studies performed in Japan and Italy where the prevalence rate of *H. pylori* infection is more than 50%¹⁷. In contrast, studies in North America revealed contradictory results where there was no sustainable platelet response after *H. pylori* eradication^{12,19}. Similar findings is also found in Australia where there was no demonstrable sustained platelet response after *H. pylori* infection eradication²⁰. In this study, the reported overall response rate was 30% and this is similar to those reported in America but lower compared to studies done in Japan and Europe. Our study had also showed no sustainable platelet recovery in patients who had demonstrated initial response.

The limitation of this study was the lack of controls and the small sample size which may have affected the results.

In conclusion, the prevalence of *H. pylori* infection in our ITP patients is 22 % and this is comparable to the general population from the same geographical area in Malaysia. The result of this study showed no evidence that *H. pylori* infections is associated with chronic ITP patients in our population and by eradicating the infection will have any sustained effect in the platelet recovery. Perhaps a future study with larger sample size with control groups will be able to confirm this finding.

ACKNOWLEDGEMENT

This study was supported by research grant from University Malaya F0350/2004A and postgraduate research grant 2009

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