

## The frequency of Helicobacter Pylori infection in Beta Thalassaemia major Patients with recurrent abdominal pain

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### ABSTRACT

**Objective:** To determine the frequency of Helicobacter Pylori (HP) seroprevalence and infection in  $\beta$  Thalassaemia major(TM) patients and to compare between  $\beta$  TM patients and controls both presenting with recurrent abdominal pain (RAP).

**Methodology:** The study group included 62 TM and 41 healthy controls with RAP. Serum samples were examined for anti-HP antibody using an HPIgG ELISA. Urea-breath test was applied to patients with positive HPIgG by using <sup>14</sup>C. In 36 of TM patients (58.1%) and 20 of healthy children (48.8%) HPIgG (+) was stated.

**Results:** In terms of HPIgG frequency, no difference was found between TM and control groups (p=0.354). The Urea-breath test given to the TM patients and healthy children with HPIgG (+), test in 30 TM patient (48.4%) and 16 healthy children (39%) the Urea-breath test was found to be positive (p=0.34). With Urea-breath test of TM patients, statistically a significant relationships were found between ALT level, epigastric pain, periumbilical pain, splenectomy and age (respectively p=0.02, p=0.03, p=0.00, p=0.01).

**Conclusion:** Helicobacter Pylori in our developing country may be one of the causes of RAP in TM patients as well as healthy children.

**KEY WORDS:** Helicobacter Pylori, Thalassaemia Major, Recurrent Abdominal Pain.

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### INTRODUCTION

Beta thalassaemia syndromes are a group of hereditary disorders characterized by a genetic deficiency in the synthesis of beta-globin chains. In  $\beta$ -thalassaemia major (TM), the production of beta-globin chains is severely impaired because both beta-globin genes are mutated. This imbalance of globin-chain synthesis results in ineffective erythropoiesis and severe hypochromic microcytic anemia.<sup>1</sup>

Recurrent abdominal pain (RAP) is one of the most common complaints of childhood. RAP is defined as at least three episodic attacks of abdominal pain over at least three months that are severe enough to affect the usual activity of the child. The prevalence of RAP in children ranges between 10-20%.<sup>2,3</sup> In childhood period, it is still controversial that Helicobacter pylori(HP) infection play a role in the etiology of

RAP.<sup>4,6</sup> HP, is a gram-negative curved bacillus that colonizes gastric mucosa in humans. Its prevalence is 70% in developing countries.<sup>7</sup>

Epidemiological studies have demonstrated that the prevalence of HP infection increases with advancing age and is higher in developing countries and among population with low socioeconomic background, probably due to conditions that favour the acquisition of infection, such as poor hygiene, crowded living conditions, and absence or deficiency of sanitation.<sup>8</sup> RAP is one of the several gastrointestinal tract disturbances frequently seen in  $\beta$  TM patients with a great incidence.<sup>9</sup> However it is not proven that HP infection is one of the causes for RAP in  $\beta$  TM patients. There are very limited number of studies about this subject.<sup>10</sup>

The aim of the study was to determine the frequency of HP seroprevalence and infection in  $\beta$  TM patients and to compare between  $\beta$  TM patients and normal controls both presenting with RAP.

## METHODOLOGY

In this study, 62 patients with TM, who had RAP and were observed at Denizli Public Hospital, Thalassemia Centre and Adnan Menderes University, Faculty of Medicine, Department of Paediatric Haematology between October 2008 - October 2009 were taken. Forty one patients, whose ages and genders were compatible and who had RAP, but not a chronic illness, were included as a control group in the study. The study was approved by the institutional review board and the hospital's ethics committee. All participants/families gave written informed consent. RAP is defined by the presence of non-organic abdominal pain in children qualified by at least three episodes of abdominal pain, weekly episodes of abdominal pain, and/or symptom duration of at least 3 months used by Apley and Naish.<sup>2</sup> Detailed history was obtained from patients and the place and duration of pain was questioned. Abdominal pain was asked mothers and/or children. Detailed physical consultations of patients were done. Haemoglobin and leukocyte counts and liver and kidney function tests were measured for the purpose of definite diagnosis. Full urine examination and parasite investigation in urine culture and stools were done. Assessment of patients was done via Abdominal Ultrasonography. Cases with urinary tract infection, parasitosis, and infection, which may cause abdominal pain, were not included in the study in both groups.

Serum samples were examined for anti-HP antibody using HPIgG ELISA (Chorus, Diesse, Italy). Samples were considered positive for HP infection when anti-

body levels were >12 UA/ml and negative when they were <12 UA/ml. Urea-breath test was applied to patients with positive HPIgG by using <sup>14</sup>C. After 4-6 hour hunger period, 37 kBg<sup>14</sup> C-Urea capsules with 50 ml water were given to drink. Breath samples were collected with dry system cartridge (Breathcard) in the 10<sup>th</sup> minute. Patients were made to insufflate into the mouthpiece for 1-4 minutes until the colour of indicator membrane turning to yellow from orange. The cartridge, which is ready to assessment, was made to read in the analyzer (Heliprobe-Analyzer, Sweden), and the result was taken after 250 seconds. Grade 0= Uninfected, Grade 1= Suspected, Grade 2= Infected were evaluated as like. In the case of Grade 1, the reading process was made to repeat in analyzer.

*Statistical Analysis:* The SPSS 16.00 program was used in the evaluation of the data. In parametrical data (measuremental) "t" test, in evaluations with the number of group "30" and over "importance of difference between two median" test and in evaluations with the number of group under "30" "Man Whitney U" test were used. "ki-square analysis" was used in non-parametric (qualitative) data. p<0.05 was accepted as significant. "Correlation analysis" of data was done to understand whether there is a relationship between two or more variables. If the correlation factor is between 0.0-0.50, the relation was accepted as weak, if between 0.50-1.0 as strong.

## RESULTS

Sixty two TM patients were observed because of RAP, whose average age was 11.8±5.2 (4-21), 35 females (56.5%) and 27 males (43.5%), were included in this study. In 62 patients included in the study, RAP with less than six months was found in the rate of 87.1% and RAP in proportion to 53.2% was in Epigastrium localization. The features of RAP in TM patients are shown in Table-I. 41 healthy children, who are RAP, whose genders and ages are compatible; whose average age is 8.2±3.2 (4-15), 21 females (51.2%) and 20 males (48.8%), were included as control group.

Table-I: The features of pain in TM patients.

	N	%
Pain Span		
>6 month	8	12.9
< 6 month	54	87.1
Pain Localization		
Epigastrium	33	53.1
Periumblical	29	46.8

Table-II: Comparison of HPIgG(+) and Urea-Breath Test Results in TM and Healthy Children.

	TM(n=62)	%	Control(n=41)	%	p
HPIgG (+)	36	58.1	20	48.8	0.35
Urea-Breath Test (+)	30	48.4	16	39	0.34

p<0.05

In 36 of TM patients (58.1%) and 20 of healthy children (48.8%) HPIgG (+) was stated. In terms of HPIgG frequency, no difference was found between TM and control groups (p=0.354). There was no significant relationship found statistically (p>0.05) between positive HPIgG and AST, ALT, ferritin levels, splenectomy, gender and periumbilical pain. However, a significant relationship was stated between positive HPIgG and epigastric pain, pain span and age (respectively p=0.043, p=0.015, p=0.012). While AST and ALT levels of HPIgG (+) stated TM patients were found higher in respect of HPIgG (-) TM patients (respectively p=0.003, p=0.00), there was no a significant difference found (p=0.484) between the levels of ferritin. When HPIgG (+) TM patients and HPIgG (+) healthy children compared no difference was found in terms of AST, ALT, pain place, age and gender, however, it was seen that there was a significant difference in terms of pain span in both groups (p=0.015). In respect of this, pains till six months were seen much more in HPIgG (+) TM patients. The Urea-breath test was made to do to the TM and healthy children with HPIgG (+), and in 30 TM patient (48.4%) and 16 healthy children (39%) the Urea-breath test was stated as positive (p=0.34) (Table-II). With Urea-breath test, which was done to TM patients, statistically a significant relationship was found between ALT level, epigastric pain, periumbilical pain, splenectomy and age (respectively p=0.02, p=0.03, p=0.00, p=0.01) (Table-III). TM patients with positive Urea-breath test were not compared statistically with the healthy children, whose test was positive, because of inadequacy in number.

## DISCUSSION

Recurrent abdominal pain is one of the most frequent reasons of consulting to paediatric clinic. The role of HP was disputable in aetiology of RAP in children.<sup>4-7</sup> In literature, HP frequency in children with RAP was stated in the rate of 40%-54%.<sup>11-13</sup> This ratio in the studies that were done in our country was between 56.3%-72.4%.<sup>14-16</sup> Gunel et al<sup>16</sup> stated HPIgG (+) in the rate of 72.4% in children with RAP, and they showed that there were no relation between RAP and HP infection when compared to healthy children. The studies done about HP were restricted in number in

Thalassemia patients. In a study, HPIgG antibody scan was done in TM patients and no difference was found between healthy children and those<sup>17</sup> In another study, much more HP infection was found in TM patients with RAP in respect of healthy children with RAP, however, the difference was not statistically significant.<sup>10</sup> In our study, HPIgG (+) was stated in the rate of 58.1% in TM patients with RAP and 48.8% in healthy children with RAP.

HPIgG (+) was found in a higher ratio in TM patients, however, the difference between healthy children was not statistically significant (p>0.05). Seroprevalence levels stated in this study were found to be compatible with the data of our country and world. Serologic tests were used for seroprevalence in the diagnosis of HP in epidemiologic studies. As active infection indicator, Urea-breath test was shown as an alternative because of its being non-invasive in endoscopic examinations.<sup>18,19</sup> In our study, positive urea-breath test in higher ratio (48.4%) was stated in TM patients in respect of healthy children, however, the difference again was not stated statistically significant. When compared to endoscopic biopsy results, positive urea-breath test was found in a low ratio in both TM patients and healthy children<sup>14</sup> We connect this change to high socio-economic and

Table-III: Comparison of HPIgG(+) and Urea-Breath Test(+) results with some relevant parameters in TM Patients.

	HPIgG(+)P	Urea-Breath Test(+)P
Age	0.012	0.001
Gender	0.814	0.46
Pain Span	0.015	0.71
Pain Localization		
Epigastrium	0.16	0.02
Periumbilical	0.04	0.035
ALT(U/L)	0.16	0.02
AST(U/L)	0.2	0.03
Splenectomy	0.64	0.00

P<0.05

cultural level of our region and gradually developing environmental conditions of Turkey.

The frequency of HP infection increases with the age process.<sup>20,21</sup> Both seroprevalence and active infection increase with the age in TM patients.<sup>10,17</sup> In literature, different results are indicated about gender.<sup>17,21</sup> In this study, seroprevalence and active infection results were increasing with the age are compatible with the literature. No relationship about gender was indentified.

In our study, though different from literature no relationship between seroprevalence and splenectomy was found, however, a strong relationship between active infection and splenectomy was found.<sup>17</sup> This result makes us think that immune response, which can change after splenectomy, affects active HP infection. In HP infection, the pain localized frequently to Epigastrium. There was no relationship found between HP infection with place of pain and localization in TM patients.<sup>10</sup> In our study, increasing of HPIgG seroprevalence in epigastric pains till the 6<sup>th</sup> month, because of there were epigastric and periumbilical pains independent from time in active infection, it was needed to think HP infection in repeating abdominal pain in TM patients, as well.

As a result, HP in our developing country may be one of the causes of RAP in TM patients as well as healthy children. With active infection, splenectomy and AST rise, HP infection was seen more frequently. We recommend that HP infection should be ruled out in TM with RAP.

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