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Evaluation of Transfusion-Related Infections in Patients with Beta Thalassemia Major in Southeast Turkey

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Abstract

Thalassemia is the most common monogenic disorder and the only curative treatment is stem cell transplantation. Patients must have a regular blood transfusion to maintain life. Multi-transfusion is a risk factor for transfusion-transmitted infections (TTIs). This study aims to assess the TTIs in pediatric thalassemia patients. This retrospective study was conducted between April 2015 and December 2016. In this study, 240 Beta-thalassemia children were enrolled. Enzyme-Linked Immunosorbent Assays test results for hepatitis B, C, human immunodeficiency virus (HIV) and reverse transcriptase-polymerase chain reaction results, hepatitis C virus (HCV) genotype results, serum ferritin and transaminase levels were obtained from medical records. The findings obtained in this study showed that the prevalence of HCV infection and hepatitis B virus infection was 5.4% and 0.8%, respectively, and there were no patients with HIV infection. The serum transaminase levels were higher in the patients with HCV infection. There was no difference in serum ferritin levels between hepatitis or non-hepatitis patients. The development of blood screening systems for TTIs is important for blood safety. Especially the patients, who live in places that have poor quality screening systems, are at high risk of TTIs.

Keywords: Beta Thalassemia, children, hepatitis, blood transfusions

Introduction

Thalassemia is the most common monogenic disorder.[1] It is related to mutations that may affect the synthesis of hemoglobin. Normal hemoglobins are tetramers of two alpha (α) and two beta (β) globin polypeptides. The down-regulation of β globin results in an increase at α globin chains that leads to hemolytic anemia. Beta thalassemia major is the most severe form of the disease.[2]

The only curative treatment of beta-thalassemia is stem cell transplantation. Until that time, the patients must have regular blood transfusions for survival. The aim of blood transfusion is to correct the anemia and prevent ineffective

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erythropoiesis. These multi-transfused patients may expose to various transfusion-related complications, such as infections and iron overload.[3,4] The main reason for mortality and morbidity in these patients are transfusion-related complications and iron overload.

Transfusion-related infections can be reduced by safe donor selection by reliable screening methods. This study was designed to evaluate the incidence of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections in thalassemia patients in our center.

Material and Method

A retrospective study was conducted from April 2015 to December 2016. In this study, 240 beta-thalassemia patients who had regular transfusion at Gaziantep Cengiz Gokcek Maternity and Children Hospital, Division of Pediatric Hematology, were included. Enzyme-Linked Immunosorbent Assays (ELISA) were performed for routine detection of hepatitis which detects circulating antibodies against HCV and HBV.

When a positive screening test was found, it was confirmed by reverse transcription-polymerase chain reaction (PCR). The COBAS® TaqMan® was used to measure PCR product accumulation through dual-labeled fluorogenic TaqMan® probes. HBV DNA was studied for hepatitis B and HCV-RNA was carried out for hepatitis C infection. The HCV genotype analysis was done for HCV RNA positive patients.

The serum ferritin and transaminase levels and, history of splenectomy were recorded for the patients who had positive serologic test results for hepatitis.

All of these findings were gathered retrospectively from the medical records of the patients. The ethics committee of Gaziantep University approved this study (approval number: 2018/161, date: 04.07.2018).

Statistical Analysis

Descriptive statistics for the continuous variables were presented as mean, standard deviation, minimum and maximum values while count and percentages for categorical variables. Mann-Whitney U test was used to compare two groups. Statistical significance level was considered as 5% and SPSS (ver: 13) statistical program was used for all statistical computations.

Results

In this study, 240 patients with beta-thalassemia were enrolled. One hundred and eighteen (49.2%) patients were female and 122 (50.8%) patients were male. Male to female ratio was 1.03. One hundred and forty-six (60.8%) of patients with beta-thalassemia were refugees from Syria and Iraq. The mean age at the time of this study was 74.6 months (range: 7 months - 18 years) (**Table 1**).

Table 1. *The characteristics of beta-thalassemia patients with anti HCV (+)*

Patient No	Gender	Age (Month)	HBsAg	Anti- HCV	Anti- HIV	HBV DNA (copy/ml)	HCV RNA (IU/ml)
1	M	107	+	+	-	102569526	-
2	F	143	-	+	-	-	-
3	M	119	-	+	-	-	1411965
4	M	96	-	+	-	-	233097
5	M	192	-	+	-	-	-
6	M	121	-	+	-	-	-
7	M	41	-	+	-	-	-
8	F	179	-	+	-	-	1988192
9	M	119	-	+	-	-	8794834
10	F	204	-	+	-	-	-
11	F	180	-	+	-	-	-
12	F	216	-	+	-	-	-
13	F	83	+	+	-	1092	-
14	M	71	-	+	-	-	207458
15	M	197	-	+	-	-	2269469
16	F	150	-	+	-	-	250575
17	M	167	-	+	-	-	11403120
18	F	202	-	+	-	-	-
19	F	192	-	+	-	-	-
20	M	203	-	+	-	-	-
21	F	120	-	+	-	-	7310281
22	F	208	-	+	-	-	166825
23	F	155	-	+	-	-	1701014
24	M	171	-	+	-	-	-
25	F	180	-	+	-	-	-
26	M	61	-	+	-	-	4444
27	F	48	-	+	-	-	-
28	M	119	-	+	-	-	4544644

HBV: Hepatitis B virus, HBsAg: Hepatitis B surface antigen, HIV: Human immunodeficiency virus, HCV: Hepatitis C virus

At our center, we routinely screen patients with beta-thalassemia for hepatitis at admission and then every other three months. According to the medical records, 28 (11.7%) patients were anti-HCV positive. Male to female ratio was 1.0. HCV RNA was studied and, 13 (46.4%) of these patients were positive. Prevalence of hepatitis C infection was 5.4% among patients with beta-thalassemia at our center. HCV genotyping was performed and genotype 4 was determined as the most common type (46.2%). Genotype 4 and genotype 1 were determined at six (46.2%) and three patients (23.1%), respectively. We could not determine the HCV genotype in four patients (30.7%), who were anti HCV positive, despite recurrent studies with new blood samples. Two (0.8%) patients also had a positive test result for HBsAg and hepatitis B infection was confirmed by HBV DNA in these patients. One of these patients with hepatitis B infection, recovered from hepatitis C one year ago. All of these patients were refugees from Syria and Iraq. There were no cases that were positive for anti-HIV type 1 or type 2 (**Table 1**).

Highlights

- Transfusion transmitted infections are one of the reasons of morbidity and mortality in beta thalassemia patients.
- Hepatitis C infection is still a problem for thalassemia patients despite blood screening methods.
- A positive Anti-HCV result is not sufficient to determine HCV infection. PCR should be used for definitive diagnosis.

Serum ferritin levels and transaminase levels were evaluated for the patients who had positive HCV RNA test results. The mean serum ferritin, alanine aminotransferase and aspartate transaminase levels was 6.838 ng/mL (minimum: 3.688 ng/mL-maximum: 12.177 ng/mL), 296 U/L (minimum: 46 U/L-maximum: 1.032 U/L), and 227 U/L (minimum: 88 U/L-maximum: 705 U/L), respectively. The serum transaminase levels were higher in patients with hepatitis C infection. There was no difference in serum ferritin levels between the patients who had hepatitis or not (p>0.05) (**Table 2**).

Fourteen (50%) patients who were Anti-HCV positive had a history of splenectomy. Despite these patients had positive anti-HCV serology, only eight (28.5%) of them had positive HCV RNA test results. Depending on their past medical history, all of these patients had Hepatitis C infection before the surgery for splenectomy.

Discussion

Patients with beta-thalassemia need a regular blood transfusion to maintain life. Recurrent blood transfusions increase the risk of transfusion-transmitted infections (TTIs). Hepatitis C, B, and HIV-I/II are the main reasons for TTIs.[5] Especially in developing countries, TTIs are still high, as a result of poor screening programs.

Despite blood screening programs, hepatitis C infection is still a problem in patients with transfusion-dependent thalassemia. The prevalence of HCV among multi-transfused patients differs from region to region. The highest prevalence reported in Egypt, in which 75% of patients with β-thalassemia infected with HCV infection.[6-8] The prevalence of HCV infection was reported between 11-40.5% in different studies.[9] In our country, Canatan[10] found HCV prevalence 18%, and Ocak et al.[11] found 4.5%. In this study, we found the prevalence of HCV infection by 5.4% in patients with thalassemia that were confirmed by HCV RNA. Only 46.4% of the anti-HCV positive patients were HCV RNA positive in this study. We realized that most of the studies performed only anti-HCV to determine the HCV infection. Thus, the findings suggest that unless HCV RNA is performed; patients can be overdiagnosed with HCV infection.

The prevalence of HBV infection has been reduced by the effects of vaccination programs worldwide, so hepatitis B infection is less common than HCV in patients with thalassemia. Mirmomen et al.[12] and Vidja et al.[13] found the prevalence of hepatitis B among patients with beta-thalassemia at 1.5% and 2.0%, respectively. The prevalence of hepatitis B in this current study was 0. 8%. In our country, Ocak et al.[11] found this prevalence at 0.75%. The literature data support our finding.

The prevalence of HBV and HCV infections among refugee patients were 0.8% and 5.4% respectively. Yazal Erdem et al.[14] found hepatitis B antigenemia 0.6% and antihepatitis C 5.3% among 299 refugee patients. This data is in accordance with our immigrant patients.

Human immunodeficiency virus infections can be related to drug abuse, contact between broken skin, wounds, or mucous membranes and HIV-infected blood or blood-contaminated body fluids. The prevalence of HIV among blood donors is different in various parts of the world. In patients with beta-thalassemia, the prevalence of HIV infection is generally found negative in studies.[15,16] On the other hand, Manisha et al.[17] and Vidja et al.[13] found HIV prevalence 1.5%, 3.0%, respectively. In our study, none of the patients were diagnosed with HIV.

Table 2. *The comparision of serum AST, ALT and ferritin levels among anti-HCV (+) patients*

	HCV RNA (+) (n=13)			HCV RNA (-) (n=15)			P values
	Mean ± SD	Min	Max	Mean ± SD	Min	Max	
Serum ferritin (ng/mL)	6839±2225.5	3.688	12.177	6.502±2994.3	1.310	10.931	p=0.742
AST (U/L)	Median 164	Min 88	Max 705	Median 68	Min 20	Max 179	p=0.000
ALT (U/L)	194	46	1.032	54	20	157	p=0.000

SD: Standart deviation, AST: Aspartate transferase, ALT: Alanine aminotransferase, HCV: Hepatitis C virus

In patients with thalassemia, measuring serum ferritin level is not the gold standard procedure to point iron overload, but it is a practical predictor for this. We try to maintain serum ferritin level below 1000 ng/mL in patients with thalassemia to minimalize the risk of iron toxicity. In our study, we found high ferritin levels (1.310 ng/mL-12.177 ng/mL) in patients with beta-thalassemia. We compared the serum ferritin levels between the patients with or without hepatitis and did not find a significant difference. Ameli et al.[18] found the mean serum iron level higher in anti-HCV positive versus negative patients.

The liver is one of the targeted organs for iron toxicity in patients with thalassemia. Both irregular use of oral iron chelation treatment and the presence of hepatitis can give damage to the liver. Elevated serum transaminase levels are related to liver damage. In our study, we determined high transaminase levels in patients with hepatitis. This finding is similar to the literature. Salama et al.[19] and Ameli et al.[18] found higher serum transaminase levels in patients with hepatitis.

Conclusion

In conclusion, in this study we found the prevelance of HCV and HBV infection 5.4% and 0.8%, respectively, and there were no cases of HIV infection. Sometimes ELISA cannot be enough to determine the infection, in this condition PCR should be used to confirm the exact diagnosis unless the infections can be overdiagnosed.

Ethical Approval: The ethics committee of Gaziantep University approved this study (approval number: 2018/161, date: 04.07.2018).

Informed Consent: Because the study was designed retrospectively no written informed consent form was obtained from the patients.

Author Contributions: Pekpak Şahinoğlu E: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Literature Search, Writing.; Karakoyun M: Analysis or Interpretation, Writing.

Conflict of Interest: The authors have no conflicts of interest to declare.

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