Original Article

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The Prevalence of Hepatitis B, Hepatitis C, and Human Immunodeficiency Virus Infections among β-thalassemia Major: A Multicenter Survey in Lorestan, West of Iran

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Abstract

Background: Although regular frequent blood transfusion improves overall survival of multi-transfused patients like β-thalassemic ones, it carries a definite risk of infection with blood-borne viruses such as viral hepatitis. This study was done to determine seropositivity of hepatitis B virus (HBV), hepatitis C virus (HCV), and Human Immunedeficiency Virus (HIV) infections among β-thalassemia major patients, and estimate the infection-associated risk factors among them.

Materials and Methods: In this cross-sectional study, serums of 143 patients with β-thalassemia major were collected from 2015 to 2016. Enzyme-linked immunosorbent assay (ELISA) was performed for the detection of antibodies to hepatitis C virus anti-HCV, hepatitis B surface antigen HBs Ag, hepatitis B core antigen (anti-HBC), and human immunodeficiency virus (anti-HIV). The positive anti-HCV and anti-HIV results were confirmed by RIBA assay and Western blot. Demographic information and risk factors were collected and analyzed.

Results: The findings showed that the prevalence rate of anti-HCV was 4.2%; while no patients were detected with HIV and HBV infections. Among the six anti-HCV positive patients, 5 (3.5%) were positive for anti-HCV using RIBA test. The prevalence of HCV seropositivity was higher in patients with sexual exposure risk (p= 0.04). There was no significant difference between sex and other risk factors such as history of splenectomy and different city with anti-HCV seropositivity (p=0.6 and 0.51, respectively). Moreover, the number of blood transfusions received by HCV positive thalassemia patients was significantly higher than that of negative anti-HCV thalassemia patients (p=0.001).

Conclusion: The prevalence of HCV infection was much higher among β-thalassemic patients comparing with HBV and HIV infection patients. Older age, blood transfusion, and sexual risk were associated with HCV seropositivity. Routine screening of donated blood for HCV is highly recommended. More study is needed to assess continuous screening of blood products for patients with risks of exposure to HCV.

Keywords: β –thalassemia, Hepatitis B, Hepatitis C, HIV infection

Introduction

β-thalassemia major syndrome represents a group of inherited blood disorders caused by reduced or absent synthesis of the beta chains of hemoglobin of red blood cells (1). This syndrome is more prevalent in regions such as the Middle East, South East Asia, Burma, and Indian subcontinent (2). Due to permanent use of blood products, the affected patients are more vulnerable to transmitted viruses by blood transfusion especially Hepatitis C virus (HCV), human immunodeficiency Virus (HIV), and Hepatitis B virus (HBV) (3).

The main cause of post-transfusion hepatitis (PTH) is hepatitis C virus which

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is considered as a main concern among β-thalassemia major patients (4, 5). Before initiating screening tests in donated bloods, 60-80% of the β-thalassemia major patients were infected by HCV (6). As the result of repeated transfusions, iron overload occurs in liver tissue of β-thalassemia major patients; thus simultaneous infection of HCV may result in liver fibrosis (7). Despite availability of an effective anti-hepatitis B vaccine and advanced therapy, infection of this virus is still a major health challenge throughout the world. In fact, 250 million people are chronically infected by HBV who are at the risk of liver disease progress (8). HIV prevalence in Iranian blood donors has followed a growing trend since 1990 (9) and the recipients- especially those affected by thalassemia and hemophilia are at a high risk of infection by this virus. Since there is no decisive vaccine or treatment for this virus, it is quite necessary to evaluate blood products.

Considering the importance of these three viruses in blood transfusion, the present study was conducted to evaluate their prevalence in β-thalassemia major patients in Lorestan province, west of Iran.

Materials and Methods

Study population

This cross-sectional study was carried out using patients with β-thalassemia major (n = 143) who were registered at the Coliz Unit of Blood Transfusion Organization in Lorestan, Iran, between September 2015 and February 2016. This study was approved by Ethical Committee of Lorest University of Medical Sciences (IR.TMI.REC.1395.028). Patients provided signed informed consent prior to enrollment. Information was collected by questionnaire that included demographical data, including age, gender, and marital status; socioeconomic characteristics such as educational level and region of residence; and risk factors, including splenectomy, sexual exposure risk, and transfusion. Patients were classified into the following four age groups: (1) group A: 1–10 years, (2) group B: 11–20 years, (3) group C: 21–30 years, and (4) group D: >30 years. The exclusion criteria consisted of patients with no history of HBV vaccination.

Laboratory procedures

Blood samples of 3-ml were taken before the transfusion, collected into sterile tubes, allowed to clot at room temperature for 30 minutes, and centrifuged. Sera were separated, aliquoted, and stored at −20° C until used for assay. A third-generation commercial ELISA kit was used for the detection of antibodies against hepatitis C, anti-HCV (Dia.Pro Diagnostic BioProbesSrl, Italy), HBsAg (DiaSorin, Spain), anti-HBc (DiaSorin, Spain) according to the manufacturer's instructions. All sera were screened using anti-HCV assays with ELISA microplate kits (DIA.PRO, Italy) according to the manufacturer's instructions. All sera positive for HCV Ab were retested by the recombinant immunoblot assay (RIBA) kits (HCV blot 3.0; Genelabs Diagnostics, Redwood City, CA, USA). To verify HBV and HIV infection, ELISA kit was used to HBs Ag, anti-HBc and anti-HIV detection. For confirming test, positive samples were investigated by Western blot kit. The data then were analyzed according to sex, age, and other factors.

Statistical analysis

Data were analyzed using SPSS (version 22). The Chi-square test or Fisher's exact test were used for categorical variables. T-tests were also done whenever applicable. Statistical significance was established at P values of < 0.05.

Results

There were 106 (74.1%) males and 37 (25.9%) females. Demographic and clinical information of the patients are presented in Table I. Prevalence rate of anti-HCV was 4.2%; whilst none of the patients were detected with HIV and HBV infection. Among

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the six anti-HCV positive patients, 5 (3.5%) were positive for anti-HCV using RIBA test (Table II). A number of risk factors that could be potentially associated with HCV infection were compared between HCV-positive and HCV-negative patients (Table III). HCV seropositivity was significantly associated with patients aged 21-30 years (P=0.02) and sexual exposure risk (P=0.04). However, history of splenectomy and different city were not statistically significant with HCV seropositivity. In addition, the number of blood transfusions received by HCV positive thalassemia patients was significantly higher than that of negative anti-HCVthalassemia patients.

Table I.Demographic and Clinical data for the thalassemic patients

Variables[a]	NO/Mean	%
N	143	100
Gender		
Male	106	74.1
Female	37	25.9
Age		
1-10	18	12.6
11-20	58	40.6
21-30	58	40.6
>30	9	6.3
Education		
Illiterate	1	0.7
Primary &Secondary	74	51.7
High school	50	35
Literary Job	18	12.6
Marriage		
Married	6	4.2
single (never married)	137	95.8
Blood Transfusion (Units)	23±6	
Splenectomy		
Yes	52	36.6
No	91	63.4
City		
KhorramAbbad	49	34.3
Broojerd	40	28.0
Aligoodarz	16	11.2
Derood	15	10.5
Koohdasht	11	7.7
Alashtar	12	8.4
Sexual Exposure Risk		
Yes	5	5
No	138	95

[a] Data was expressed as Mean ± SD for quantitative measures and both number and percentage for categorized data

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Table II. HCV, HBV and HIV seropositivity results in thalassemic patients

Variables	Positive No (%)	Negative No (%)
Anti-HBC	0(0)	143 (100)
HBs Ag	0 (0)	143(100)
Anti-HCV	6(4.2)	137(95.8)
RIBA	5(3.5)	138(96.5)
Anti-HIV	0(0)	143(100)

HIV: Human immunodeficiency virus; HBV: Hepatitis B virus, HCV: Hepatitis C virus, RIBA: Recombinant ImmunoBlot Assay

Table III. Comparison of risk factors between HCV-positive and HCV-negative patients

Status	Anti HCV Positive No (%)	Anti HCV Negative No (%)	p^a
Age			0.028
1-10	0 (0)	18(100)	
11-20	1(1.7)	57(98.3)	
21-30	3(5.2)	55(94.8)	
>30	2(22.2)	7(77.8)	
Gender			1.00
Male	5(4.7)	101(95.3)	
Female	1(2.7)	36(97.3)	
Education			0.77
Illiterate	0(0)	1(100)	
Primary&Secondary	4(5.4)	70(94.6)	
High school	2(4)	48(96)	
Literary Job	0(0)	18(100)	
Marriage			1.00
Married	0(0)	6(100)	
Single	6(4.4)	131(95.6)	
Blood Transfusion	36±3	21±5	0.001
Splenectomy			0.6
Yes	3(5.8)	49(94.2)	
No	3(3.3)	88(96.7)	
City			0.51
Khooramabbad	2(4.1)	47(96.9)	
Broojerd	1(2.5)	39(97.5)	
Aligoodarz	2(12.5)	14(87.5)	
Derood	0(0)	15(100)	
Koohdasht	0(0)	11(100)	
Alashtar	0(0)	12(100)	
Sexual Exposure Risk	4(80)	1(20)	0.03

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Discussion

Despite availability of screening tests for HCV, HIV, and HBV infections before blood donation, these infectious agents are a major challenge for blood transfusion. The β-thalassemia major and hemophilia patients are at a high risk of infection by these viruses due to permanent need to blood products (10). In this study, the frequency of anti-HCV antibody positive cases was at low levels of 4.2% but none of these patients were positive for HBV and HIV. This is a relatively low percentage, keeping in mind that all the donated blood is regularly screened for HCV at all thalassemic centers in Lorestan.

The most common cause of post-transfusion hepatitis is HCV (11). According to the previous studies, the prevalence of HCV infection in thalassemic patient's eastern mediterranean countries was in ranged from 4% to 85%, in which also the general HCV prevalence was 18% among thalassemia patients in Iran (12). The reason for this wide range may be due to differences in the total prevalence amongst different population. In different parts of Iran, the prevalence of HCV infection in thalassemic patients differs: Mirmomen et al., reported the prevalence rate of anti-HCV and HBsAg as 19.3% and 1.5%; respectively; while no HIV-anti positive patient was observed which is similar to our study (4).

In other studies, the prevalence of anti-HCV in Bushehr, Zahedan, Shiraz, Yazd, and Isfahan was reported as 41.9%(9), 29.6%(13), 11.4%(14), 0%(15) and 9.4%(3) and 8%(5), respectively. This rate in various parts of the world in thalassemic patients differs: in Egypt, it is 40.5%(16), Pakistan49%(2), Iraq 13.5%(17), Oman 41%(18), and in Saudi Arabia, it is between 4.6% and 70%(19).There is a great difference concerning the prevalence rate of HCV in thalassemic patients among different regions of the world. In all these parts, the donor's blood is screened for HCV but thalassemic patients may acquire hepatitis C through the administration of HCV-infected blood collected during the donor window period.

In this study, anti-HCV antibody positivity was significantly higher with increased number of blood transfusion. This result was observed in other studies that the number of blood transfusions received by anti-HCV antibody positive thalassemia patients was significantly higher than that of anti-HCV antibody negative thalassemic patients (16, 20). The prevalence rate of seropositivity increases with the number of transfusions units. Therefore, it was indicated that blood transfusion was the main risk factor for HCV infection acquisition among thalassemic patients, especially through the administration of HCV-infected blood collected during the donor window period. Of course, the higher prevalence of HCV seropositivity in thalassemia patients with sexual exposure risk than patients without this risk, suggesting that transfusion of infected blood was not the main cause of this prevalence.

The results of this study showed that the mean age of positive HCV antibody was significantly higher than that of negative HCV antibody. This result had been expected due to more exposure to HCV infection in recurrent blood transfusion. It seems that HCV screening test had not been tested before 1976, thus this infection is more prevalent in older patients. Our observations strongly indicated blood transfusion as the main risk factor for HCV infection acquisition among thalassemic patients.

Conclusion

In conclusion, a low frequency of C infection has been seen in a cohort of β-thalassemia major patients undergoing regular transfusion in Coliz Unit of Blood

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Transfusion Organization in Lorestan. It is apparent that late diagnosis and frequent transfusion in peripheral centers contributed to HCV infection in these patients. The results suggested more studies to assess viral hepatitis and continuous screening of blood products to these patients that have a probable risk of exposure to HCV especially in higher years old. On the other hand, vaccination and screening test for HBVand HIV has been efficient in this province.

Conflicts of interest

The authors declare no conflict of interest.

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