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Trend in Prevalence of Hepatitis C Virus Infection among β-thalassemia Major Patients: 10 Years of Experience in Iran

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ABSTRACT

Background: Hepatitis C virus (HCV) is the leading cause of transfusion transmitted infections (TTIs) among patients with β-thalassemia major. A high prevalence of HCV was reported among these patients. The aim of this study is seeking the trend of the prevalence of HCV infection among the patients with β-thalassemia major in Guilan province, Northern Iran over a 10-year period.

Methods: A retrospective study was conducted on 1113 patients with β-thalassemia major in the Guilan province, northern Iran from 2002 to 2012, using multiple data sources. A blood sample was taken from each patient, and a questionnaire regarding demographic data and risk factors was completed for them. Enzyme-linked immunosorbent assay and recombinant immunoblot assay for HCV were performed in all cases. A stepwise forward logistic regression analysis was done.

Results: The prevalence of hepatitis C infection among β-thalassemia major patients was 13.6%. The risk of hepatitis C among β-thalassemia major patients was greater before screening program for HCV (odds ratio = 9.6, 95% confidence interval: 2.3–40.5). In addition, the prevalence of anti-HCV seropositivity was decreased dramatically among patients who have received transfusions after implementation of blood donor screening for HCV. There were no positive HCV cases in the patients younger than 10 years.

Conclusions: The risk of TTIs including HCV can be reduced by implementing screening program for healthy blood.

Keywords: Blood transfusion, hepatitis C, Iran, transfusion transmitted infections, β-thalassemia

INTRODUCTION

Patients with β-thalassemia major who regularly receive transfusions are at risk of developing posttransfusion hepatitis (PTH). Among these infections, hepatitis B and C are the most common.[1] It is well-known that hepatitis C virus (HCV) is a major cause of PTH infection, and it can lead to severe inflammation in liver with long-term problems such as disabling symptoms, cirrhosis, and hepatocellular carcinoma.[2] Due to lack of effective vaccine and inadequate infection control policies for HCV poses a significant and growing public health problem in low- and middle-income countries.[3]

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According to the World Health Organization, 170 million of people are infected by HCV in the world.[2] Over 21.3 million of them live in the eastern Mediterranean region.[4] A lot of studies among multi-transfused thalassemia patients reported the prevalence of HCV in β-thalassemia patients at a wide range of 3-67.3%.[5-9] However, under and over reporting trends have also been identified in the intra and inter countries in this region.[10] Mean age, duration, and mean amount of blood transfused have been associated with an increased risk of HCV infection in β-thalassemia patients. Saber-Firoozi *et al*. stated that the relative risk of HCV infection for each unit of blood transfusion is about 0.2%.[11] Study on thalassemia patients who regularly receive blood transfusion, could reflect the safety of blood products indirectly.

Iran is located in the middle of, what is called "the thalassemia belt." Thalassemia is an important health problem throughout Iran, particularly in the Guilan province, northern Iran. There are 1120 patients with thalassemia major in the Guilan province, and most of them had received blood transfusion before 1996, when routine blood screening for HCV infection started. The recent studies in Iran have shown that the prevalence of HCV infection in β-thalassemia patients are different from 2% to 32%.[12,13] In one of these studies, a very high prevalence of HCV among thalassemic and hemodialysis patients in Rasht (capital of the Guilan province) was reported (64%).[14] Regarding the controversies on the true prevalence of HCV infections, the objective of this study was to determine the actual rate of HCV infection in β-thalassemia patients in the Guilan province, northern Iran, in order to identify factors associated with HCV infection. This information could be used to develop more effective prevention strategies.

METHODS

Study design

This cross-sectional study was conducted in the Guilan province, one of the highest prevalent regions of thalassemia in Iran (about 10% of whole thalassemia population), during 2002–2012. Guilan province is located in northern Iran bordering the Caspian Sea with a population of about 2.5 million residents. The following administrative were assessed; including the noncommunicable disease centers, health centers, hospital records and clinics of hematology. A multi-stage sampling technique was applied during the study period to select a large, representative sample of sex and age group from all administrative to minimize refusals. Using a predesigned questionnaire, demographic data such as, age, gender, duration of receiving blood transfusion, residency, were obtained. A total of 1113 thalassemia patients were enrolled in this study. Blood sample of those patients who were frequently attending thalassemia clinics, were tested after obtaining written consent.

Laboratory process

The 2nd and 3rd generations of the immunoenzymatic test were used to screen β-thalassemia major patients during the study period. Positive case is defined as a patient who initial and duplicated (ELISA) test was positive. Samples were tested in accordance with manufacturer's specifications in duplicate to determine the percentage that was repeatedly reactive, confirmed by recombinant immunobloting assay test.

Statistical analysis

Records from different administrative were merged into a single file, using Excel 2012. Records were then sorted for cases that were reported in sources, using multiple screenings. Data analyses were conducted using the SPSS (version 18) 18)(SPSS Inc., Shicago IL). The Chi-square test was conducted to analyze significant associations between patient's characteristics and HCV positivity. A two-tailed $P < 0.05$ was considered as statistically significant. Variables history of blood transfusion and death were entered as predictors in a logistic regression model to calculate the adjusted odds ratio (OR) and 95% confidence interval where HCV seropositivity was the dependent variable.

This study proposal was reviewed, approved and sponsored by the Guilan Blood Transfusion Center and reviewed and approved by the Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran.

RESULTS

During the study period from March 2002 (5 years after HCV screening) to March 2012, the data of 1113 β-thalassemia major patients were enrolled. These data also include the new cases (7%, 78 cases) and the number of patients that who died (3.3%, 36 cases) during the observation period. Of total cases, 48.1% were males and 51.9% were females, with female to male ratio 1.08:1. Mean age (±standard deviation [SD]) was 22.93 ± 8.37 years (range from 1 to 52 years). The age group 21–30 years, which included 522 (47%) of the cases was the largest group and the age group over the 40 years, which included 29 the (2.6%) of the cases was the smallest group. Demographic features are presented in Table 1.

Among 1113 thalassemia cases, 152 were found to be positive for anti-HCV, given an overall prevalence of HCV of 13.6%. The risk for being HCV positive was 1.5 time higher among males than females. The mean

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age (±SD) of positive cases was higher than that of negative cases (26.11 ± 5.3 vs. 22.5 ± 8.5). This study showed that prevalence of hepatitis C was found to be 12% in the age group less than 20, and almost 68% in the age group of 20–30 years, 20.5% in the age group of 30–40 and 0.01% in the age group of more than 40 years respectively, and the difference was statistically significant. However, there were no positive HCV cases in the patients younger than 10 years. This study also showed that there was no significant difference risk of infection according to blood groups [Table 2].

History of blood transfusion is main risk factors associated with anti-HCV seropositivity in our study population and had a significant univariate association with HCV seropositivity ($P < 0.0001$) [Table 2]. All 14.2% of positive anti-HCV cases have had a history of blood transfusion.

The majority of HCV positive patients have already received more than 150 times blood transfusion [Figure 1].

The multiple logistic regression test for variables gender, age group, blood group and history of blood transfusion demonstrated that, there is a strong significant relationship between history of blood transfusions with HCV infection before routine screening (1995), where the risk of blood transfusion before 1995 (OR 9.6, $P = 0.003$) with seropositivity of hepatitis C were predominant.

Table 1: Demographic characteristics of thalassemia patients in Guilan province during study period

Variables	*n* (%)
Gender	
Male	535 (48.1)
Female	578 (51.9)
Blood group	
A	361 (32.4)
B	239 (21.5)
AB	64 (5.7)
O	450 (40.4)
Age group	
Under 10	79 (7)
11-20	324 (29)
21-30	520 (47)
31-40	161 (14.4)
Above 40	29 (2.6)

Table 2: Univariate association between potential risk factors and HCV seropositivity

Variables	HCV antibody (%)		*P*
	Positive	Negative	
Gender			
Male	16.5	83.5	0.01
Female	11.1	88.9	
Blood group			
A	14.1	85.9	NS
B	13.8	86.2	
AB	14.9	85.1	
O	10.5	89.5	
Age group			
Under 10	0	100	<0.0001
11-20	11.84	88.16	
21-30	67.76	32.24	
31-40	20.39	79.61	
Above 40	0.01	99.9	
Residency			
Rural	16	84	0.02
Urban	11.2	88.8	
History of blood transfusion			
Yes	14.2	82.5	<0.0001
No	1.2	98.8	
Death			
Yes	38.7	61.3	<0.0001
No	12.7	87.3	

NS=Not significant, HCV=Hepatitis C virus

DISCUSSION

The current study shows that transfusion transmitted infections have always been a problem in thalassemia patients in last decade. The prevalence of HCV infection among patients with β-thalassemia major in our study (13.6%) was less than the reported rates in many other low- and middle-income countries.[5-10] The HCV prevalence among high-risk patients in other reports varies from 3% to 67.3% and similar results were found when looking at the rates in different parts of Iran, which ranged from 5.1% to 64%.[13-23] This discrepancy suggests that other factors are contributing to the relatively low rates of HCV infection in our study. One possible factor could be, using different laboratory tests with a wide range of validity for detecting HCV. Many reports were based on only ELISA tests without complementary and confirmation tests. However, some of those have used polymerase chain reaction as a confirmation test.

The second factor is that the prevalence of HCV infection in the general population in Iran is very low (<1%).[10]

The third factor is the policies that implement by blood transfusion organization, about screening of blood regarding the blood safety. In Iran, routine screening for blood borne diseases has been mainly conducted among blood and tissue donors since the 1996, and it seems that this policy reduced infection rate since that time. Furthermore, implementation of tests for screening of blood donors after 1995 in Iran has leaded to almost complete absence of any new HCV infected patients in the group age of <10 years of old. Also, the rate of

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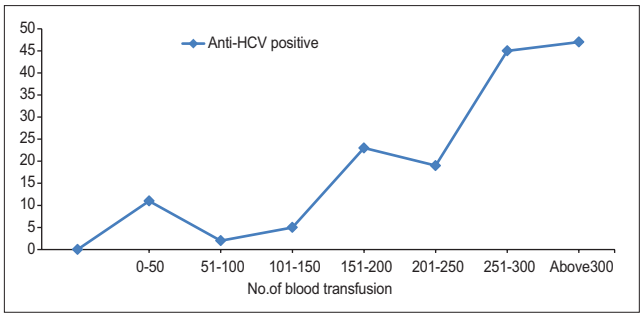

Figure 1: Number of blood transfusion status with thalassemia patients and HCV positive cases

infection in patients of 10–15 years old, who were at the beginning of this blood screening program was very low. This shows the importance of the blood donors screening program.

We think that previously reported high prevalence of HCV infection among high-risk patients (63.8%) in the Guilan province[14] has some bias including inappropriate sample size and unreliable laboratory tests.

Our study had a number of limitations. Because of the lack of information and missing data in records of patients, risk factors such as drug abuse, tattooing, and high-risk behaviors were not assessed in this study.

CONCLUSIONS

This study shows that blood donors screening program in regarding providing safe blood for the recipient was successful and prevent the risk of HCV infection among thalassemia patients. Finally, electronic data recording system for early detection of any infection in thalassemia patients is recommended.

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