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Prevalence of hepatitis B and C in thalassemia major patients in south of Iran-Bandar Abbas

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Abstract. Thalassemia major is a genetic and blood disorder with a known defect in the hemoglobin. These patients require constant blood transfusions. This increases the risk of susceptibility to infectious diseases such as hepatitis in these patients. Given the importance of this infection and the mortality rates in patients with thalassemia, and as there are no reliable statistics available for these infections in this area, we decided to conduct this study. In this study, 120 patients with thalassemia major were evaluated within 3 years. Patients were selected voluntarily and randomly. Patient samples were examined for Anti HBs, HBs Ag and Anti HBc. Chi-square and Mann-Withney tests were used for data analysis. The results of the study showed that 17.0% of the patients with thalassemia major were infected with HCV and only one case was HBV positive. In this study, 65.0% of patients with hepatitis were men while 35.0% were women. However, only one more case was positive with PCR compared to ELISA. Safe blood transfusion for these patients are very important. Thalassemia major can affect the survival of these patients. The screening of blood donors and reducing these lethal infections in patients should be the main aim in the field of blood transfusion and health policies.

INTRODUCTION

Thalassemia major is one of the most common blood disorders with genetic source which creates many problems for the patients (Huang *et al.*, 2015). Patients with thalassemia major are dependent on frequent blood transfusion which is associated with excessive increase in iron leading to a wide range of complications including liver, heart and endocrine glands complications (Manisha *et al.*, 2015, Sadhukhan *et al.*, 2014, Shelton *et al.*, 2016). With increasing body iron, some will be deposited in the liver causing siderosis. However, chelators increase the body tolerance to iron to a large extent (Wu *et al.*, 2006, Neufeld 2010), but the effects of siderosis are inevitable due to liver fibrosis (Ardalan *et al.*, 2004). However, blood transfusion can improve survival rate and life of thalassemia patients, but it increases the risk of diseases such as viral infections including hepatitis B and C (Mirmomen *et al.*, 2006). Hepatitis C resulting from blood transfusion is a major concern for thalassemia patients (Lai *et al.*, 2013). Hepatitis C is also effective in liver fibrosis and increased mortality of thalassemia patients (Ataei *et al.*, 2012). The occurrence of hepatitis B can increase due to frequency of blood transfusions, which is dependent on conditions of donors (Singh *et al.*, 2003).

The high prevalence of thalassemia has been more commonly reported in tropical countries and some regions near tropics (Habibzadeh *et al.*, 1998), it is expected that the rate of thalassemia major would be greater in Iran especially areas nearer to the equator. Given the importance of blood transfusion thalassemia patients, sould be monitored for serious infections such as hepatitis B and C.

Since little is known about the prevalence of infectious diseases such as hepatitis B and C in patients with thalassemia major in southern regions of Iran that are somehow close to equator, the aim of this study was to investigate the rate of hepatitis B and C in these patients and the risk factors that could arise as a consequence.

METHOD

The present research is a descriptive study with a aim to determine the prevalence of Hepatisis B and C among the 120 patients including all thalassemia major patients referred to the Abu Rayhan centre in Shahid Mohammadi Hospital during year 2015-2016. A random sampling was conducted on those who participated in this study. Data were collected with the consent of patients. The Validity of the questionnaire was evaluated by 12 experts, and its reliability was assessed by Cronbach's alpha. Patients participation in this study was voluntary, and their names remained undisclosed.

A questionnaire was completed for each patient that included demographic information such as age, gender, history of hepatitis, intervals of blood transfusion, duration of blood transfusion, etc. Blood samples of the patient were taken and, analysed in the laboratory for HBV, HCV serological tests. They were examined for Anti-HBs, HBsAg, Anti-HBc.by ELISA tests; and the positive results were confirmed by RIBA test. Results of tests were recorded in the informational form of each patient, and the data obtained were analyzed using SPSS software. Chi-square and non-parametric Mann-Withney tests were conducted for categorical and quantitative variables, respectively, to find the significance of variables among patients' specifications and positive HBV and HCV. Multiple logistic regression model was performed to estimate odds ratio, and 95% confidence interval for the risk factors of positive HBV and HCV. All statistical tests were done with significance level of $P < 0.05$.

RESULTS

Information of 120 patients including 78 (65.0%) male and 42 (35.0%) female with an average age of 26.09 ± 6.80 years (ranging from 7 to 39 years), was statistically analyzed for to evaluate the prevalence of hepatitis B and C in patients with thalassemia major. The average age of initial blood trunsfusion was 17.98 ± 28.85 months (from 1 to 120 months), and the average age of last blood reception was 17.95 ± 7.54 days (from 1 to 60 days). Average ferritin blood level was 3179.54 ± 1621.72 (161 to 8345). The average number of years patients received blood transfusion was 24.59 ± 7.37 years, with a minimum of 4 years and a maximum of 38 years. The average number of blood transfusion received per month was 1.52 ± 0.76, at least once, and at most four times a moth. The average number of blood transfusion per month in HCV PCR positive individuals was 1.61 ± 0.84, while in HCV PCR negative it was 1.50 ± 0.75.The difference between the two types was not statistically significant (P-value = 0.701). In 3 patients, (2.5%) PCR for HBsAg and HBV were positiveAnd it was positive for HCV.Ab in 17 (14.2%) patients, while PCR and HCV were positive in 18 (15.0%) patients (HCV.Ab was negative only in one case, while PCR was positive). In none of the patients HBsAg and HCV.Ab were simultaneously positive. But in one case, HBsAg (or PCR, HBV) and PCR, HCV were positive which were not statistically significant corelated (P=0.389) (Table 1). The relationship between gender and hepatitis-related tests is presented in Table 2.

Table 1. Hepatitis-related tests

Test	Sub-group	HBsAg (or PCR, HBV) test			P-value
		Positive	Negative	Total	
HCV. Ab	Positive	0(0.0%)	17(100%)	17(100%)	
	Negative	3(9.2%)	100(97.1%)	103(100%)	–
	Total	3(2.5%)	117(97.5%)	120(100%)	
PCR, HCV	Positive	1(5.6%)	17(94.4%)	18(100%)	
	Negative	2(2.0%)	100(98.0%)	102(100%)	0.389
	Total	3(2.5%)	117(97.5%)	120(100%)	

Table 2. The relation between gender and hepatitis-related tests

Test	Sub-group	HBsAg (or PCR, HBV) test			P-value	OR	CI95%
		Male	Female	Total			
HbsAg (PCR, HBV)	Positive	1(33.3%)	2(66.7%)	3(100%)			
	Negative	77(65.8%)	40(34.2%)	117(100%)	0.280	–	–
	Total	78(65.0%)	42(35.0%)	120(100%)			
HCV. Ab	Positive	9(52.9%)	8(47.1%)	17(100%)			
	Negative	69(67.0%)	34(33.0%)	103(100%)	0.261	1.804	0.639–5.089
	Total	78(65.0%)	42(35.0%)	120(100%)			
PCR, HCV	Positive	9(50.0%)	9(50.0%)	18(100%)			
	Negative	69(67.6%)	33(32.4%)	102(100%)	0.148	2.091	0.759–5.757
	Total	78(65.0%)	42(35.0%)	120(100%)			

Table 3. The relationship between the average age of patients and the results of hepatitis-related tests

Test	Sub-group	Number	Average age	P-value
HbsAg (PCR, HBV)	Positive	3	31±2.64	0.123
	Negative	117	25.96±6.83	
HCV. Ab	Positive	17	28.11±5.77	0.183
	Negative	103	25.75±6.92	
PCR, HCV	Positive	18	28.33±5.67	0.111
	Negative	102	25.69±6.93	

To investigate the relationship between age and ferritin level, Spearman correlation coefficient was obtained to be 0.032 (indirect and very weak), but it was not statistically significant (0.725).

The average age difference in patients with positive and negative hepatitis tests was evaluated; and there were no statistically significant differences (Table 3).

Average ferritin level in males and females were respectively 3326.88 ± 1271.44 and 2905.90 ± 2116.46, which had significant statistical difference (0.026). However there were no significant differences between the average age of males (26.45 ± 6.58 years) and females (25.38 ± 7.28 years) (0.444). In addition, the average ages of onset of blood reception in males (13.24 ± 20.31 months)

Table 4. Average ferritin level in patients with positive and negative hepatitis tests

Test	Sub-group	Number	Average level of ferritin	P-value
HbsAg (PCR, HBV)	Positive	3	2640.66±1129.60	0.608
	Negative	117	3193.35±1633.49	
HCV. Ab	Positive	17	2638.58±1357.59	0.174
	Negative	103	3268.82±1649.96	
PCR, HCV	Positive	18	2629.77±1317.59	0.152
	Negative	102	3276.55±1656.24	

Table 5. Average age of onset of blood transfusion in patients with positive and negative hepatitis tests

Test	Sub-group	Number	Average level of ferritin	P-value
HbsAg (PCR, HBV)	Positive	3	10±3.46	0.552
	Negative	117	18.18±29.18	
HCV. Ab	Positive	17	12.11±7.03	0.142
	Negative	103	18.95±30.92	
PCR, HCV	Positive	18	11.77±7.03	0.238
	Negative	102	19.07±31.05	

and females (26.75 ± 38.96 months) were not significantly different (0.134).

The difference of average ferritin level in patients was evaluated by positive and negative hepatitis tests that showed there were no statistically significant differences (Table 4).

The difference of the average age of initial blood transfusion in patients was evaluated with positive and negative hepatitis tests; and there were no statistically significant differences (Table 5).

DISCUSSION

β thalassemia major is a hereditary blood disorder caused by a defect in the β hemoglobin chains. These patients need frequent blood transfusions and are associated with the risk of acquiring infectious diseases such as hepatitis and AIDS that can increase mortality in these patients compared to normal population (Lee *et al.*, 2005). Transmission of hepatitis infection in thalassemia patients can be largely prevented by safe blood transfusion and vaccination. Hepatitis infection is one of the most common risk factors for thalassemia patients because of blood transfusion, and thus, they are at high risk for infections. The current study showed that blood transfusion is a risk factor for hepatitis in thalassemia patient indicating that screening must be considered seriously in blood donors.

The present study was conducted to determine the prevalence of hepatitis B and C in thalassemia patients. According to studies conducted in Iran, the rate of hepatitis C in thalassemia patients has been reported to be 13.6% (Jafroodi *et al.*, 2015). However, the prevalence rate differs in various places of Iran. The rates of hepatitis C in thalassemia patients in the provinces of Markazi and Isfahan and in the city of Zabol was 5.1% (Samimi-rad & Shahbaz 2007), 8.0% (Ataei *et al.*, 2012), and 8.5% (Yousefi *et al.*, 2017), respectively. In this study, we showed that 17.0% of patients were HCV positive, while only one case of HBV was observed in these patients which was confirmed by PCR test. In our study, HBsAg and HCV.Ab were not reported to be present simultaneously. The rate of HbsAg in the current study was 3.0%

which was in the range of the Iranian population (2.5–3.5%) (Zali 1996). In other studies conducted (Manisha *et al.*, 2015, Sanei *et al.*, 2004), like our study, HCV was more prevalent than HBV which had a lower prevalence. In addition, no positive HIV was reported in the present study which may be due to HIV control in donors.

Compared with HBV, HCV is associated with higher risk for developing chronic liver diseases (Younus *et al.*, 2004). The HCV infection was relatively higher in our study. According to WHO guidelines, serological care in first-time blood donors is the best tool to estimate the prevalence of HBV among the adult populations (Poorolajal & Majdzadeh 2009). However, one of the problems in the studies conducted, was the lack of considering a careful analysis of blood donors in Iran. In this study, ferritin blood level of participantswas high, emphasizing that there is a need to take precautions before and during blood transfusions in order to reduce hepatitis infection.

There is a need to train thalassemia patients to be made aware of transmission infections including HBV and HCV, which are of great importance. Since HCV and HBV infections are increasing in communities, appropriate measures must be taken to reduce the transmission of these infections. This study tries to evaluate variables such as ferritin level, age of onset of blood reception, gender, and age. By hepatitis genotypic analysis we can achieve greater and stronger understanding of hepatitis prevalence rate in the patients. It is believed that if studies are performed in larger sizes, better results will be obtained.

CONCLUSION

Given the potential importance of infectious diseases in blood transfer, constant training must be provided for these patients. Furthermore, it is necessary for medical and blood transfusion centers to examine and monitor the donors regarding any incident of infection. By implementing the comprehensive and effective policies, we can eliminate the risk of infectious diseases such as hepatitis in thalassemia patients and also expand their life span. Complications due to repetitive transfers can also be eliminated or reduced.

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