

Characteristics of Seropositive Hepatitis B and C Thalassemia Major Patients in South-East of Iran

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Received 2015 December 21; Revised 2016 January 26; Accepted 2016 February 21.

Abstract

Background: Hepatitis is a serious blood born infection in patients with β -thalassemia major (β -TM). There was no previous report on hepatitis prevalence in patients with β -TM in Zabol, Iran.

Objectives: The current study aimed to evaluate characteristics of hepatitis in patients with β -TM visiting Imam Khomeini Hospital of Zabol, in Sistan and Baluchistan province of Iran.

Patients and Methods: There were 90 patients with β -TM. General demographic and laboratory results were obtained by interviews and reviewing clinical and laboratory histories. Data for anti-HCV, HBs antigen and anti-HBs were extracted from latest archived records, and analyzed using SPSS ver. 19.

Results: Males and females comprised 51% and 49% of the patients, respectively. Mean age of the patients was 14.8 ± 7.4 years old. Anti-HCV and HBs antigen were detected in 10% and 3.3% of the patients, respectively. Significant difference was found between the mean age of anti-HCV positive (20.1 ± 3.6 , 95% CI: 17.3 - 22.9) and negative (14.2 ± 7.5 , 95% CI: 12.5 - 15.9) patients ($P = 0.02$). Mean ferritin value was measured 4702 ± 2743 ng/mL. A significant correlation was observed between serum ferritin level and age ($r = 0.3$, $P = 0.01$). Hepatic enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) had mean levels of 51.8 ± 32.8 IU/L and 58.8 ± 59 IU/L, respectively. No significant association was identified between hepatitis status and either ferritin or hepatic enzymes levels.

Conclusions: Results demonstrated the relatively high prevalence of HCV infection in the patients. Applying sensitive methods to screen blood units is recommended to minimize the risk of transfusion associated hepatitis.

Keywords: β -Thalassemia Major, Anti-HCV, HBs Antigen, Anti-HBs, Ferritin

1. Background

Thalassemia constitutes a major general-health problem in Iran (1, 2), and β -thalassemia major (β -TM) is the most common cause of thalassemia major in Iranians. In addition to psychological and financial burdens, encountering adverse effects of transfusion therapy represents a dilemma for patients with β -TM and their families. Accordingly, transmission of hepatitis infections renders as concerning sequel of repeated transfusions in patients with β -TM (3). In fact, hepatitis is responsible for a large spectrum of liver dysfunctions including hepatic enzymes abnormalities, hepatic fibrosis and cirrhosis (4, 5).

Relatively high frequencies of both β -TM and hepatitis are reported in Sistan and Baluchistan province (2, 6). Therefore, patients with β -TM are at significantly high risk of being infected with hepatitis through transfusion of donated blood units. Despite this fact, there is no report on frequency and features of hepatitis infection in transfusion dependent patients with β -TM in Zabol.

2. Objectives

The current study aimed to evaluate the seroepidemiology and clinical significance of anti-HCV, HBs antigen and anti-HBs in patients with β -TM seeking medical care in Imam Khomeini Hospital of Zabol.

3. Materials and Methods

This descriptive cross-sectional study was carried out in 2014. Consent form was signed by the patients or their parents before entering into the study. Authors interviewed and checked clinical records of 90 patients with β -TM regularly visiting Imam Khomeini hospital of Zabol to obtain demographic and general laboratory data.

Positivity for anti-HCV, HBs antigen and anti-HBs were determined using latest clinical records of the patients. Subsequently, data were transferred into SPSS ver.19 software; and then descriptive and inferential statistical analyses were carried out using Chi-square test, standard inde-

pendent sample t-test, one-way ANOVA and logistic regression for the intended variables.

4. Results

Distribution of two genders in the selected sample was 51% males and 49% females. Mean age of the patients was 14.8 ± 7.4 years old. Mean ferritin value was 4702 ± 2743 ng/mL; while mean serum values of aspartate transaminase (AST) and alanine transaminase (ALT) enzymes were measured 51.8 ± 32.8 IU/L and 58.8 ± 59 IU/L, respectively. Table 1 shows general features of the studied population including age groups and health status of spleen and liver.

Table 1. Clinical and Laboratory Characteristics of Patients With β -Thalassemia Major

Characteristics	Gender		Total
	Male (N = 46)	Female (N = 44)	
Age groups, y			
< 10	12	22	34 (37.8)
10 - 20	25	17	42 (46.7)
> 20	9	5	14 (15.6)
Spleen status			
Normal	15	18	33 (36.6)
Splenectomy	18	12	30 (33.3)
Splenomegaly	13	14	27 (30)
Liver status			
Normal	39	39	78 (86.6)
Hepatomegaly	7	5	12 (13)
AST, IU/L			
Normal (5 - 40)	17	23	40 (44.4)
Abnormal low (< 5)	0	0	0
Abnormal high (> 40)	29	21	50 (55.6)
ALT, IU/L			
Normal (5 - 40)	25	20	45 (50)
Abnormal low (< 5)	0	1	1 (1.1)
Abnormal high (> 40)	21	23	44 (48.9)

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase.

Anti-HCV was identified in nine out of 90 patients (10%), and HBs antigen was positive in three (3.3%) patients. Regarding anti-HBs, 68 (75.6%) subjects were immune (antibody titer > 10 IU), 14 (15.6%) were non-immune (antibody titer 2 - 10 IU), and 8 (8.9%) had negative results (antibody

titer < 2 IU). Significant association was observed between anti-HCV positivity and both age and spleen condition of the patients (respective p values of 0.01 and 0.05, Table 2).

Table 2. Clinical and Laboratory Features in Anti-HCV Positive and Negative Patients With β -Thalassemia Major^a

Characteristics	Anti-HCV Antibody		P Value
	Positive (N = 9)	Negative (N = 81)	
Gender			
Male	3 (6.5)	43 (93.5)	0.2
Female	6 (13.6)	38 (86.4)	
Age group, y			
< 10	0	34 (100)	0.01
10 - 20	5 (11.9)	37 (88.1)	
> 20	4 (28.6)	10 (71.4)	
Spleen status			
Normal	0	33 (100)	0.05
Splenectomy	5 (16.7)	25 (83.3)	
Splenomegaly	4 (14.8)	23 (85.2)	
Liver status			
Normal	7 (9)	71 (91)	0.4
Hepatomegaly	2 (16.7)	10 (83.3)	
AST (IU/L)			
Normal (5 - 40)	4 (10)	36 (90)	1
Abnormal low (< 5)	0	0	
Abnormal high (> 40)	5 (10)	45 (90)	
ALT, IU/L			
Normal (5 - 40)	3 (6.7)	42 (93.3)	0.5
Abnormal low (< 5)	0	1 (100)	
Abnormal high (> 40)	6 (13.6)	38 (86.4)	

Abbreviations: ALT, alanine transaminase; Anti-HCV1, anti-hepatitis C virus; AST, aspartate transaminase.

^aValues are expressed as No. (%).

Mean age of anti-HCV positive patients was higher (20.1 ± 3.6) than negative individuals (14.2 ± 7.5 , $P = 0.02$, Table 3). Although mean serum levels of AST and ALT hepatic enzymes were also higher in anti-HCV positive patients, the difference was not statistically significant. Moreover, no association was observed between anti-HBs or HBs antigen status and demographical or clinical parameters.

Furthermore, serum ferritin level was significantly correlated with age of the patients ($P = 0.01$). Mean value of ferritin was significantly higher in patients > 10 years old

Table 3. Mean Values of Age, Ferritin and Hepatic Enzymes Respective to Anti-HCV1 Positivity or Negativity and Different Age Groups

Characteristics	Anti-HCV Antibody		P Value	Age Groups, y			P Value
	Positive (N = 9)	Negative (N = 81)		< 10 (N = 34)	10 - 20 (N = 42)	> 20 (N = 14)	
Age, y			0.02				0.001
Mean	20.1 ± 3.6	14.2 ± 7.5		7 ± 2.9	17.7 ± 4.2	24.9 ± 2.8	
95% CI	17.3 - 22.9	12.5-15.9		6 - 8.1	16.4 - 19	23.3 - 26.5	
Ferritin, ng/mL			0.4				0.01
Mean	5353 ± 2464	4630 ± 2777		3317 ± 357	5501 ± 353	5673 ± 1063	
95% CI	3459 - 7248	4016 - 5245		2590 - 4045	4787 - 6215	3376 - 7971	
AST, IU/L			0.2				0.6
Mean	63.3 ± 4.1	50.5 ± 3.1		55.5 ± 7.3	49.1 ± 3.6	50.5 ± 8.1	
95% CI	31.2 - 95.4	43.4 - 57.5		40.6 - 70.4	41.7 - 56.5	32.9 - 68.2	
ALT, IU/L			0.9				0.6
Mean	60.5 ± 3.9	58.6 ± 6		64.9 ± 12.3	58 ± 8.4	46.7 ± 7.9	
95% CI	29.9 - 91.2	45.2 - 72.1		39.7 - 90	40.9 - 75.1	29.6 - 63.8	

Abbreviations: ALT, alanine transaminase; Anti-HCV1, anti-hepatitis C virus; AST, aspartate transaminase.

compared to that of the patients < 10 years old; however, the differences of mean values of hepatic enzymes were not of statistically significant in different age groups (Table 3). In addition, significant difference of mean ferritin value was noticed regarding spleen status (Table 4). In contrast, mean levels of hepatic enzymes were not statistically different regarding either spleen or liver conditions. Tables 3 and 4 represent stratified description of mean age, ferritin and hepatic enzymes regarding anti-HCV status, and spleen or liver conditions.

5. Discussion

Successive long-term transfusions expose patients with β -TM to the risk of infections with a wide range of pathogens including hepatitis. In recent decade, effective vaccination and screening procedures resulted in remarkable reduction in hepatitis B virus (HBV) transmission through blood products. However, hepatitis C virus (HCV) is still encountered in a relatively high ratio of blood recipients (7). HCV is responsible for 90% of transfusion related non-A and non-B hepatitis infections worldwide (8). It is estimated that 3% of the world population are exposed to HCV virus (9). Furthermore, HCV infection may cause a complicated situation in patients with β -TM through aggravation of iron-induced organ damage (10). It is mentioned that some current anti-viral treatments against HCV infection can induce RBC hemolysis, which accentuate iron overload (11). On the other hand, HCV

infection and iron toxicity may cooperate to accelerate development of chronic liver abnormalities such as fibrosis and cirrhosis in patients with β -TM (8, 10, 12).

Anti-HCV was detected in 10% of the patients with β -TM in the current study. It was lower than the ratio described in some previous studies in North of the country (13, 14), but similar to the rate obtained in the study performed on Iranian patients by Tamaddoni et al. (15). Higher incidence of HCV infection in the northern regions may be partly due to high ratio of individuals with HCV infection harboring in general population of the areas (16). Furthermore, positivity for anti-HCV was as high as 33% in studies conducted on Iranian patients with thalassemia major before 2000; however, this ratio was reported to have decreased to 15% - 19% in recent years (6). In other studies on Iranian patients, anti-HCV was described in range of 6% - 8% in patients with thalassemia (17, 18). Moreover, in the studies carried out in Thailand (8) and Jordan (19), anti-HCV frequencies were 20% and 40% respectively in patients with thalassemia. Collectively, these results indicate the efficiency of blood donor screening programs in decreasing transmission of HCV infection over the past decade in Iran. However, more sophisticated strategies should be implemented to minimize the risk of transmission of infections by blood transfusion.

In the current study, anti-HCV positivity was significantly associated both with age and spleen condition of the patients (Table 1). Patients with positive results for anti-HCV were older than the ones with negative results by a mean difference of six years (Table 2, P = 0.02). A pre-

Table 4. Mean Values of Age, Ferritin and Hepatic Enzymes Respective to Liver or Spleen Clinical Status

Characteristics	Liver		P	Spleen			P
	Normal (N = 78)	Hepatomegaly (N = 12)		Normal (N = 33)	Splenectomy (N = 30)	Splenomegaly (N = 27)	
Age, y			0.04				0.01
Mean	14.2 ± 7.6	18.8 ± 4.5		10.5 ± 8.4	19.5 ± 3.5	14.8 ± 6.2	
95% CI	24.4 - 15.9	15.9 - 21.7		7.5 - 13.5	18.2 - 20.8	12.3 - 17.2	
Ferritin, ng/mL			0.2				0.01
Mean	4567 ± 2780	5587 ± 2403		3579 ± 2124	5270 ± 2266	5445 ± 3453	
95% CI	3940 - 5194	4060 - 7115		2826 - 4333	4424 - 6117	4079 - 6811	
AST, IU/L			0.9				0.8
Mean	51.3 ± 3.4	54.5 ± 2.4		51.7 ± 3.1	54.2 ± 2.8	49.1 ± 3.9	
95% CI	43.7 - 59	38.7 - 70.2		40.4 - 62.9	43.5 - 64.9	33.6 - 64.6	
ALT, IU/L			0.7				0.6
Mean	59.1 ± 6.1	56.9 ± 4.1		55 ± 4.2	55.3 ± 3.5	67.5 ± 9	
95% CI	45.3 - 73	30.4 - 83.4		40.1 - 69.9	41.9 - 68.6	31.6-103.3	

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase.

vious study in Iran also demonstrated that anti-HCV positive patients were significantly older compared to anti-HCV negative ones (20). Similarly, patients who had anti-HCV-positive results were significantly older than anti-HCV-negative ones in a study carried out in Oman (21). In addition, previous studies suggested the HCV infection as a strongly age dependent complication in patients with β -TM (22). Therefore, it is beneficial to consider performing regular occasional screenings for HCV infection especially in older patients with β -TM.

In addition, spleen condition is suggested as a risk factor associated with HCV infection in patients with β -TM. Results of the current study also supported this hypothesis since a significant relationship was observed between spleen status and anti-HCV positivity. On the contrary, Ahmad Akbari et al. found no association between spleen state and HCV positivity in a study on the Iranian patients with thalassemia major and intermediate (23). Nevertheless, it seems that splenectomy may potentially boost the risk of HCV infection in higher ages; therefore, it is recommended to postpone this procedure as long as possible in patients with β -TM.

Additionally, it was also observed that serum ferritin level was higher in anti-HCV positive patients with β -TM (Table 2); however, the difference was not statistically significant ($P > 0.05$). In parallel, serum ferritin level was significantly higher in anti-HCV positive patients with β -TM in a systemic multivariate analysis in Iran (7). Nevertheless, ferritin value is also highly dependent on different factors including efficacy of chelation therapy which should

be considered when studying the effects of HCV infection on ferritin level.

It is established that HCV infection also contributes in liver dysfunction and deranged levels of hepatic enzymes. Although mean levels of hepatic enzymes were higher in anti-HCV positive patients in the current study (Table 2), the difference was statistically insignificant. In another study in Iran, also no association was detected between the level of hepatic enzymes and HCV infection (14). In comparison, anti-HCV positive patients had significantly higher AST and ALT levels in a study on Thai patients (8). Considering intercalated relationships between hepatic function and both HCV infection and iron-burden of liver; more studies are necessitated in order to establish the role of these factors in pathogenesis of liver dysfunction in β -TM.

Frequency of HBs antigen positivity was 3.3% in the current study. This was higher than the results recorded by Wanachiwanawin et al. (8) and Karimi et al. (24). On the other hand, the current study results showed lower prevalence in comparison to a study carried out on Indian patients (25). Regardless of the above mentioned facts, high prevalence of HBs antigen positivity in the current study highlights requirements for more intense screening procedures to minimize the ratio as much as possible. Reactivity for anti-HBs occurred in a high proportion (91%) of the patients evaluated in the present study. Accordingly, negative HBs antigen results and also lack of previous vaccination in majority of anti-HBs positive patients raise the challenges regarding the source of these antibodies. It is suggested that these antibodies may be passively transmit-

ted from immunized blood donors. This phenomenon is plausible because of the vaccination programs performed on normal Iranian populations in past years (26).

5.1. Conclusions

Considering the high rate of HCV infection in the present study, it is recommended to screen the patients with appropriate tests on a routine basis. Regarding the lower rate of HBs antigen positivity, it seems that reactivity of anti-HBs, especially in younger patients, originates from passively transmitted antibodies rather than true infection; however, cautious vaccination is appropriate in such patients.

Footnote

Authors' Contribution: Ali Bazi: design of the study, acquisition of data, analysis of data, preparing and editing the manuscript; Ebrahim Mirimoghaddam: data analysis and editing the manuscript; Daryoush Rostami: study concept preparing and developing, analysis of data; Mansour Dabirzadeh: conceptual participation to the study and editing the manuscript.

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