

Hepatitis B, Hepatitis C, and Human Immunodeficiency Virus Infection in Multi-Transfused Thalassemic Patients, Kermanshah, Iran, 2015

Babak Sayad,^{1*} Maryam Foroughikia,¹ Reza Akramipour,² Alireza Farokhi,¹ Feizollah Mansouri,¹ Alireza Janbakhsh,¹ Mandana Afsharian,¹ Siavash Vaziri,¹ and Afshin Almasi³

¹Liver Diseases Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

²Department of Pediatrics, Kermanshah University of Medical Sciences, Kermanshah, Iran

³Department of Biostatistics and Epidemiology, School of Public Health, Kermanshah University of Medical Sciences, Kermanshah, Iran

*Corresponding author: Babak Sayad, Associate Professor in Infectious Diseases, Liver Diseases Research Center, Imam Reza Hospital, Sorkhe Lijeh Blvd., Kermanshah, Iran. Tel: +98-8334276342, Fax: +98-8338377734, E-mail: babaksayad@kums.ac.ir

Received 2017 February 02; Revised 2017 April 03; Accepted 2017 April 08.

Abstract

Background: Repeated blood transfusions in Thalassemic patients predispose them to blood-borne infections including Hepatitis B, Hepatitis C, and human immunodeficiency virus. These infections cause cirrhosis, portal hypertension, and acquired immunodeficiency syndrome.

Objectives: The current study aimed at determining the prevalence of these infections in Thalassemic patients of Kermanshah province, Iran.

Methods: Thalassemic patients registered at Mohammad Kermanshahi university hospital were included. Demographic data, history of blood transfusions, Hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (HBC Ab), Hepatitis B surface antibody (HBs Ab), Hepatitis C antibody, and Human immunodeficiency virus (HIV) antibody were extracted. Serologic tests were done using the third-generation enzyme linked immunosorbent assay (ELISA) and positive Hepatitis C virus (HCV) Ab and HIV Ab results was confirmed by Western Blotting.

Results: A total number of 232 patients were enrolled (111 females and 121 males), among whom HBsAg and HIV Ab were both negative. Positive HBS Ab was reported in 222 subjects (95.7%) and 19 cases (8.2%) had positive HBC Ab. Immunity to hepatitis B was the result of vaccination in 87.5% of cases. Hepatitis C antibody was positive in 14 cases (6%). Finally, a significant relationship was found between HCV infection and blood transfusion done before 1996.

Conclusions: High rate of hepatitis C was found to be due to the lack of screening for HCV Ab among blood donors before 1996. The negative HBS Ag can be justified by regular hepatitis B vaccination program in patients with thalassemia. The lack of HIV infection was concluded to be attributed to the low prevalence of this virus in the general population and blood donors as well as proper screening methods.

Keywords: Thalassemia, Hepatitis B, Hepatitis C, HIV, Iran

1. Background

Thalassemia is within the spectrum of genetic disorders with a prevalence of 15% to 30%. Considering how the globin chains are effected, the patients are categorized as minor, intermediate, or major subtypes (1). In major beta-thalassemia, blood transfusion is required from birth, owing to the severe anemia. During blood transfusion, patients are at the risk of blood-borne infections such as Hepatitis B virus (HBV), Hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infections (2). Hepatitis B and C infections can lead to serious liver diseases, including portal hypertension and cirrhosis, which complicate management of these patients (3).

In Iran, the prevalence of hepatitis B in the general

population is estimated between 1.7% to 2.14% in non-thalassemic individuals and 0% to 1.5% in patients with thalassemia (4, 5). In studies regarding the prevalence of HIV infection in patients with thalassemia, no case with this infection has been reported. As for hepatitis C, the rate of infection in the Iranian general population is less than 1%, yet, in patients with beta-thalassemia, this rate varies between 7.1% in East Azarbaijan to 55.5% in Kerman (6-9). Although routine vaccination and proper screening programs have been successfully applied in controlling the risk of HBV and HIV transmission, hepatitis C is still causing major post transfusion complications in multitransfused thalassemic patients and that is because preventing HCV infection is challenging and requires researchers

to promote and develop advanced screening methods for blood donors (10, 11).

2. Objectives

The objective of this study was to determine the prevalence of post transfusion complications, such as HBV, HCV, and HIV infections in patients with beta-thalassemia of Kermanshah province. It is believed that by making a fair estimate of these infections, we would be able to properly manage and prevent their high burden in the future.

3. Methods

The present study was a survey of existing data, which was performed after being confirmed by the ethics committee of Kermanshah University of Medical Sciences under the ethic code of 53252. All patients with intermediate and major beta-thalassemia, who had medical records at Dr. Kermanshahi hospital up to 30th of November 2015, were included in this study. This university hospital is a referral center for patients with beta-thalassemia residing in the Kermanshah province. At this center, serologic tests, including Hepatitis B Surface Antigen (HBS Ag), Hepatitis B core antibody (HBC Ab), Hepatitis C Virus Antibody (HCV Ab), and humane immunodeficiency virus antibody (HIV Ab) using the ELISA method (Pishtazteb Diagnostics®, Iran), and for HBS Ab, third generation ELISA (Dia, Pro Milano®, Italy) were routinely performed in the first instance of forming patients' files. Positive HCV Ab tests were confirmed by the Western blot method (MP Biomedical®, Germany). Primary screening lab tests were performed at 3- and 6-month intervals and were documented in the medical records of the patients. Demographic data, history of blood transfusions, and serum markers, including HBS Ag, HBC Ab, HBS Ab, HCV Ab, and HIV Ab, were collected by an observer. Having flaws or shortcomings in the patient's file was considered as the exclusion criteria.

The gathered data was analyzed with the STATA software v. 8.0. To express the data, qualitative variables, such as frequencies and percentages were used for nominal data. Mean and standard deviation were used for expressing quantitative variables. Also, to investigate the relationships between the variables, logistic regression was used. Significance level was set at 0.05.

4. Results

A total of 232 patients with beta-thalassemia were included in the study and since all files contained the required data, no patient was excluded. Among the included

subjects, 211 patients had major thalassemia and 21 had intermediate thalassemia. Patients aged between 4 to 48 years with a mean (SD) age of 22.62 (15.8) years. There were 111 females (47.8%) and 121 males (52.2%). Hepatitis B surface antigen test was negative in all patients. The HBS Ab was positive in 222 cases (95.7%). Among these, 19 subjects (8.2%) had simultaneous positive HBC Ab, reflecting a previous HBV infection. Logistic regression showed that as age increased, the likelihood of infection with HBV (i.e., positive HBC Ab) was also increased ($P = 0.011$, $OR = 0.08$, 95% $CI = 1.01$ to 1.15).

No case with positive HIV Ab was recognized. However, 14 cases (6%) had positive HCV Ab test results and they all had major beta-thalassemia. Table 1 shows characteristics of the patients based on HCV serology markers. As shown in Table 1, a significant relationship was found between infection with HCV and receiving blood transfusion before 1996. There was a significant relationship between age of more than 25 years and infection with HCV. According to the logistic regression, it was revealed that among those who received blood transfusion before 1996, with increasing age (in better words, higher number of blood transfusions), the likelihood of infection with HCV was also increased ($P = 0.045$, $OR = 1.11$). However, in those, who received blood transfusions after 1996, an increase in age was not associated with HCV infection ($P = 0.442$).

5. Discussion

Acquiring blood-borne infections in patients, who had received multiple blood transfusions depends on several factors, including the prevalence of particular infection in the general population, the prevalence of infection in blood donors, blood screening procedures, and vaccination status regarding preventable diseases (8-11). The prevalence of Hepatitis B in the Iranian general population and among Iranian blood donors ranges from 1.7% to 2.14% and 0.8% to 0.56%, respectively. This rate in Iranian patients with beta-thalassemia is estimated to be 0 to 1.5 (4, 5). In this study, no cases of HBV infection were found. About 95.7% of the studied sample had positive HBS Ab and 8.2% had positive HBC Ab. Therefore, 87.5% of the cases showed immunity to hepatitis B as a result of vaccination. This clearly demonstrated that vaccination against HBV in patients with beta-thalassemia, right after being diagnosed, has had a major role in preventing infection.

In the current study, no case of HIV infection was observed. The current estimates of HIV show a low prevalence of this infection in the general population of Iran (12). In a study on pregnant females, it was reported that of 5261 studied pregnant females, only 4 patients had HIV

Table 1. Characteristics of Anti-Hepatitis C Virus-Positive and Negative Multi-Transfused Patients With Thalassemia

| | Variables Negative (No. %) | HCV-Ab Positive (No. %) | P Value |
|-------------------------|-------------------------------|----------------------------|---------|
| Gender | | | 0.584 |
| Female | 103 (92.8) | 8 (7.2) | |
| Male | 115 (95.1) | 6 (4.9) | |
| Age | | | 0.01 |
| < 25 | 138 (97.2) | 4 (2.8) | |
| ≥ 25 | 80 (88.9) | 10 (11.1) | |
| Thalassemia type | | | 0.622 |
| Major | 197 (93.4) | 14 (6.6) | |
| Intermedia | 21 (100) | 0 (0) | |
| Transfusion date | | | 0.021 |
| Before 1996 | 126 (91/3%) | 12 (8/7%) | |
| After 1996 | 92 (97/9%) | 2 (2/1%) | |

(0.07%). Also, in another study involving 6876 pregnant females studied between 2010 and 2013, only 1 patient (0.01%) had positive HIV Ab results. This rate is even lower in blood donors and is about 0.004% to 0.005% (12, 13). As observed in Table 2, in several studies performed in various provinces of Iran, no case of HIV infection was reported in patients with thalassemia (7, 9, 14-19). There is no doubt that the low prevalence of HIV infection in the general population as well as in blood donors and applying appropriate screening methods on donated blood by Iran Blood Transfusion Organization have been effective in protecting beta-thalassemia patients from HIV infection.

In contrast to HBV and HIV infections, prevalence of hepatitis C in the studied patients was as high as 14 patients (6%), which is lower than what has been reported in other provinces in Iran (Table 2). Among these 6%, 12 had a history of blood transfusion before 1996, which had a statistically significant association with hepatitis C infection. Interestingly, increasing age, which is reflected by higher numbers of blood transfusions, had a significant association with HCV infection in those, who received blood transfusions before 1996. The prevalence of hepatitis C in the general population of Iran is low (19). In a study that was conducted in 2006 in Kermanshah, the prevalence of hepatitis C in the general population was reported as 0.87% (20). This rate has been estimated as 0.1% among blood donors (21). The prevalence of hepatitis C in patients with thalassemia has been reported as low as 7.1% in East Azarbaijan and as high as 55.5% in Kerman (6, 9).

In a review article by Alavian et al. in East Mediterranean countries, published in 2010, the prevalence of HCV

infection in beta-thalassemia patients in Iran was reported as 18%. The risk of infection in those, who received blood transfusion before 1996, was 7.6 times higher than those, who received blood transfusion after this time since no screening for HCV was done before 1996 in Iran (8). It seems that this fact is the most important cause of high number of HCV infections that has been observed in the current study. After starting the use of third-generation ELISA by Iran Blood Transfusion organization, the rate of HCV infection in patients, who had received multiple blood transfusions, decreased markedly. In a study by Mirmomen et al. in 2006, the prevalence of hepatitis C in beta-thalassemia patients decreased from 22.8 in the pre-screening period to 2.6% after implementation of screening methods on donated blood samples (7).

In other countries, in a similar fashion, HCV infection in patients with beta-thalassemia showed a significant decrease by introducing screening methods on donated blood samples. In Eastern Mediterranean countries, the fact that first blood transfusion occurred before or after introduction of donated blood screening has been recognized as the most important factor in obtaining HCV infection among beta-thalassemia patients (8). In Kuwait and Jordan, all beta-thalassemia patients, who had HCV infection had a history of blood transfusion before introduction of screening methods (22, 23).

Since beta-thalassemia patients are at risk of blood-borne infections during their life, using modern and effective screening methods on donated blood samples has a crucial role in prevention of these infections. On the other hand, periodic assessment of patients for early detection

Table 2. Prevalence of Viral Seromarkers in Multi-transfused Patients of Different Regions of Iran

| Reference | Publication year | Region / City | Patients Group | Prevalence % | | | | |
|--------------------------------------|------------------|--|----------------------------|--------------|--------|--------|--------|--------|
| | | | | HBS-Ag | HBC-Ab | HBS-Ab | HCV-Ab | HIV-Ab |
| Kazemi Arababadi et al. (6) | 2008 | Kerman | Thalassemic | 0 | 33 | 40/7 | 55.5 | ND |
| Mirmomen Sh et al. (7) | 2006 | Tehran, Kerman, Qazvin, Semnan, Zanjan | Thalassemic | 1.5 | 13.6 | 55.2 | 19.6 | 0 |
| Torabi SE et al. (9) | 2005 | East Azarbaijan | Thalassemic | 0 | 6 | 37 | 7.1 | 0 |
| Alavian M et al. (14) | 2003 | Qazvin | Thalassemic | 1.1 | ND | ND | 24.1 | 0 |
| Mahdavi F et al. (15) | 2004 | Markazi | Thalassemic and Hemophilic | 0 | 29.8 | 81.5 | 7.2 | 0 |
| Javadzadeh Shahshahani H et al. (16) | 2006 | Yazd | Thalassemic and Hemophilic | 0 | ND | 89.4 | 9.4 | 0 |
| Assarehzadegan M et al. (17) | 2009 | Ahvaz | Hemophilic | 0 | ND | ND | 22.3 | 0 |
| Hariri M et al. (18) | 2006 | Isfahan | Thalassemic and Hemophilic | 0 | ND | ND | 10/9 | 0 |

Abbreviation: ND, Not Determined.

of blood-borne infections is effective and provides earlier management of such infections.

In conclusion, the findings that indicated HBS antigen and HIV antibody were negative in patients with thalassemia in Kermanshah province and also the low frequency of infection in hepatitis C in these patients are strengths of this study, while it still seems necessary to evaluate the possibility of Occult Hepatitis B infection (OBI) with molecular methods (24, 25). The latter issue could be further studied through a prospective study.

Acknowledgments

The authors thank the personnel of Dr. Mohammad Kermanshahi hospital for their cooperation in this study and also Miss Fatemeh Norooznezhad for her contribution in grammatical editing.

Footnotes

Authors' Contribution: Study concept and design: Babak Sayad, Maryam Foroughikia, and Reza Akramipour; acquisition of data: Maryam Foroughikia; data analysis: Afshin Almasi; drafting of the manuscript: Babak Sayad and Maryam Foroughikia; administrative, technical, and material support: Alireza Farokhi; study supervision, Feizollah Mansouri, Alireza Janbakhsh, Mandana Afsharian, and Siavash Vaziri; Final revision: Babak Sayad.

Conflict of Interests: Authors claim no conflict of interest regarding this article.

Funding/Support: The research reported in this article was financially supported by Kermanshah University of Medical Sciences. The terms of this arrangement have been reviewed and approved by Kermanshah University of Medical Sciences in accordance with its policy on objectivity in research.

References

- Mcpherson R, Pincus M, Henry S. Clinical diagnosis and management by laboratory methods. 22nd ed. Philadelphia: Elsevier Saunders; 2011.
- Kliegman R, Behrman R, Jenson H, Stanton B. Nelson text book of pediatrics. 19th ed. Philadelphia: Elsevier Saunders; 2011.
- Mandell GL, Bennett JE, Dolin R. Principles and practice of infectious disease. 7th ed. Philadelphia: Churchill Livingstone; 2010.
- Poorolajal J, Majdzadeh R. Prevalence of chronic hepatitis B infection in Iran: a review article. *J Res Med Sci.* 2009;14(4):249-58. [PubMed: 21772891].
- Alavian M, Hajarizadeh B, Ahmadzad-Asl M, Kabir A, Bagheri-Lankarani K. Hepatitis B virus infection in iran: A systematic review. *Hepat Mon.* 2008;8(4):281-94.
- Arababadi MK, Hassanshahi, Yousefi H, Zarandi ER, Moradi M, Mahmoodi M. No detected Hepatitis B virus-DNA in thalassemic patients infected by Hepatitis C Virus in Kerman province of Iran. *Pakistan J Bio Sci.* 2008;11(13):1738-41. doi: 10.3923/pjbs.2008.1738.1741.
- Mirmomen S, Alavian SM, Hajarizadeh B, Kafaee J, Yektaparast B, Zahedi MJ, et al. Epidemiology of hepatitis B, hepatitis C, and human immunodeficiency virus infections in patients with beta-thalassemia in Iran: a multicenter study. *Arch Iran Med.* 2006;9(4):319-23. [PubMed: 17061602].
- Alavian SM, Tabatabaei SV, Lankarani KB. Epidemiology of HCV infection among thalassemia patients in eastern mediterranean countries: A quantitative review of literature. *Iran Red Crescent Med J.* 2010;12(4):365-76.

9. Torabi SE, Abed Ashtiani K, Dehkhoda R, Moghadam AN, Sorkhabi R, Bahram MK, et al. Prevalence of hepatitis B and C in thalassemic patients of East Azarbaijan in 2003 (Persian). *Sci J Iran Blood Transfus Organ*. 2005;2(4):115-22.
10. Alavian SM, Adibi P, Zali MR. Hepatitis C virus in Iran: Epidemiology of an emerging infection. *Arch Iran Med*. 2005;8:84-90.
11. Ansari SH, Shamsi TS, Khan MT, Perveen K, Farzana T, Erum S, et al. Seropositivity of hepatitis C, hepatitis B and HIV in chronically transfused beta-thalassaemia major patients. *J Coll Physicians Surg Pak*. 2012;22(9):610-1. doi: [10.2012/JCPSP.610611](https://doi.org/10.2012/JCPSP.610611). [PubMed: [22980623](https://pubmed.ncbi.nlm.nih.gov/22980623/)].
12. Islamic Republic of Iran AIDS Progress Report: On Monitoring of the United Nations General Assembly Special Session on HIV and AIDS. National AIDS Committee Secretariat, Ministry of Health and Medical Education; 2015. .
13. National Commitments and Policies Instrument (NCPI). UNAIDS. Iran (Islamic Republic of) Report; 2014-2015. .
14. Alavian SM, Kafaei J, Yektaparast B, Hajarizadeh B, Kamali A, Sadri M. The prevalence of Hepatitis B and C among Thalassemia major patients in Qazvin (Persian). *Kowasr Med J*. 2003;4:319-25.
15. Mahdavian F, Saremi S, Rafiee M. Prevalence of hepatitis B, C and HIV infection in thalassemic and hemophilic patients of Markazi province in 2004 (Persian). *Sci J Iran Blood Transfus Organ*. 2008;4:313-22.
16. Javadzadeh-Shahshahani H, Attar M, Yavari MT, Savabieh S. Study of the prevalence of Hepatitis B, C and HIV infection in Hemophilia and Thalassemia population of Yazd in 2003 (Persian). *Sci J Iran Blood Transfus Organ*. 2006;2(315-22).
17. Assarehzadegan MA, Ghafourian Boroujerdnia M, Zandian K. Prevalence of hepatitis B and C infections and HCV genotypes among haemophilia patients in ahvaz, southwest iran. *Iran Red Crescent Med J*. 2012;14(8):470-4. [PubMed: [23105982](https://pubmed.ncbi.nlm.nih.gov/23105982/)].
18. Hariri MM, Akbari N, Yavari FM, Javadi E, Javer SH. Prevalence of Hepatitis B, C and HIV markers in Thalassemic and Hemophilic patients in Isfahan 2004 (in Persian). *Sci J Iran Blood Transfus Organ*. 2006;2:201-4.
19. Mirminachi B, Mohammadi Z, Merat S, Neishabouri A, Sharifi AH, Alavian SH, et al. Update on the prevalence of hepatitis c virus infection among iranian general population: A systematic review and meta-analysis. *Hepatit Month*. 2017;17(2) doi: [10.5812/hepatmon.42291](https://doi.org/10.5812/hepatmon.42291).
20. Sayad B, Shamsedin SF, Keyvani H, Rezaii M, Asadi T, Siavash V. Seroepidemiology of Hepatitis C in Kermanshah (West of Iran, 2006). *Hepat Mon*. 2008;8(2):141-6.
21. Khedmat H, Alavian S. M. , Miri SM, Amini M, Abolghasemi H, Hajibeigi B. Seroprevalence of Hepatitis B, Hepatitis C, HIV, and syphilis infections in Iranian blood donors from 2003 to 2005. *Hepat Mon*. 2009;9(1):24-8.
22. al-Fuzae L, Aboolbacker KC, al-Saleh Q. beta-Thalassaemia major in Kuwait. *J Trop Pediatr*. 1998;44(5):311-2. [PubMed: [9819498](https://pubmed.ncbi.nlm.nih.gov/9819498/)].
23. Al-Sheyyab M, Batieha A, El-Khateeb M. The prevalence of hepatitis B, hepatitis C and human immune deficiency virus markers in multi-transfused patients. *J Trop Pediatr*. 2001;47(4):239-42. [PubMed: [11523766](https://pubmed.ncbi.nlm.nih.gov/11523766/)].
24. Singh H, Pradhan M, Singh RL, Phadke S, Naik SR, Aggarwal R, et al. High frequency of hepatitis B virus infection in patients with beta-thalassemia receiving multiple transfusions. *Vox Sang*. 2003;84(4):292-9. [PubMed: [12757503](https://pubmed.ncbi.nlm.nih.gov/12757503/)].
25. Shaker O, Ahmed A, Abdel Satar I, El Ahl H, Shousha W, Doss W. Occult hepatitis B in Egyptian thalassemic children. *J Infect Dev Ctries*. 2012;6(4):340-6. [PubMed: [22505444](https://pubmed.ncbi.nlm.nih.gov/22505444/)].