Original Article *Iran J Ped Hematol Oncol. 2020, Vol 10, No 4, 250-256*

A Comparative Study of Transfusion Reactions in the Thalassemia Patients before and after Implementation of the Hemovigilance System in Yazd Province, Iran

Fatemeh Abbasinejad MD[1], Hayedeh Javadzadeh Shashshahani MD[2,3,*], Mahvash Akhavan Ghalibaf MD[3]

1. Ali Ebn Abitaleb (AS) School of Medicine, Islamic Azad University, Yazd Branch, Iran
2. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran
3. Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
*Corresponding author: Dr Hayedeh Javadzadeh Shashshahani, 2- Associate Professor and Faculty Member of Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran. Email: h.javadzadeh@tmi.ac.ir. ORCID ID: 0000-0003-4111-8622

Received: 02 June 2020 **Accepted:** 02 August 2020

Abstract

Background: Patients with thalassemia major require frequent blood transfusions. Blood transfusion can lead to the adverse reactions. Reporting and evaluating the transfusion reactions are among the goals of implementing the hemovigilance system to improve blood recipients' safety. This study aimed to compare the transfusion reactions in the thalassemia patients before and after implementation of the hemovigilance system in the Shahid Sadoughi Hospital in Yazd (Iran).

Materials and Methods: In this historical cohort study conducted in 2018, the data of 87 patients with thalassemia major including age, sex, the total number of blood transfusions before and after the implementation of hemovigilance system, information about the occurrence of blood transfusion reactions, type, and severity of each reaction were recorded in the questionnaire. Paired-Samples T-test and Chi-Square test were used for data analysis.

Results: The mean age of the participants was equal to 19.69±8.41 years old and 52% of them were male. The age of onset of transfusion was 14.3±16.62 months with a range of 2 - 96 months. The relative frequency of transfusion reactions in the thalassemia patients was 0.74% and 0.81%, respectively before and after implementation of the hemovigilance system. Allergic (54%) and non-hemolytic febrile reactions (23%) were the most frequent transfusion reactions. Severe and life-threatening reactions were reported more frequently after implementation of the hemovigilance system compared to pre-implementation (p=0.007). Totally, 8% of the reactions were hemolytic reactions and 7.5% of the patients had unexpected alloantibodies identified after implementation of the hemovigilance system.

Conclusion: Documentation and reporting of the transfusion reactions after implementation of the hemovigilance system have resulted in reporting of more severe reactions and determination of the clinically significant alloantibodies. Therefore, prevention of the subsequent reactions and increasing the safety of the blood transfusion for the thalassemia patients could be provided, emphasizing the continuation of the system.

Keywords: Blood Transfusion, Thalassemia, Transfusion Reactions.

[DOI: 10.18502/ijpho.v10i4.4408]

Introduction

Thalassemia major is the most common hereditary anemia in the world (1,2). Hematopoietic stem cell transplantation has cured the thalassemia in some patients, and researchers seek to explore new approaches including gene therapy to treat the thalassemia (3–8). However, not all the thalassemia patients are eligible for these therapies. Frequent blood transfusion is the main treatment for the patients with thalassemia major. Although, blood transfusion is vital for these patients, it can lead to the adverse reactions and some of them are life-threatening. Continuous exposure to the allogeneic antigens may trigger the formation of the alloantibodies against the red blood cell antigens leading to the hemolytic transfusion reactions in the subsequent blood transfusions (9).

The hemovigilance system was introduced for the first time in 1994 in France to protect the blood recipients against the

adverse effects of the blood transfusions. The effectiveness of the hemovigilance system depends on identifying, documenting, and reporting all the adverse reactions associated with the blood transfusions, leading to the analysis of complications and appropriate measures to prevent them from happening again (10).
Understanding these reactions and knowing their incidence will increase the readiness of the medical staff to deal with these reactions and reduce the adverse consequences of this life-saving treatment.
Therefore, this study was performed to compare different types of blood transfusion reaction in the patients with thalassemia major before (2007-2010) and after (2013-2016) implementation of the hemovigilance system in the Shahid Sadoughi Hospital in Yazd (Iran).

Materials and Methods

This descriptive-analytical study was performed in 2018 using the historical cohort method. The total study population included 107 patients with thalassemia major who had received the blood at the Shahid Sadoughi Hospital (Yazd province, Iran). The study sample included 87 patients with thalassemia major who had received the blood during the intervals of 2007-2010 and 2013-2016 and their blood transfusion reactions had occurred in these periods of time. Thalassemia patients' records were reviewed by referring to the Thalassemia Center and Yazd Blood Transfusion Center. A questionnaire was used for entering the data. Information ,such as age, sex, age of onset of blood transfusion, intervals of blood transfusion, total number of blood transfusions before 2011 and after 2012, as well as information on the occurrence of blood transfusion reactions including reaction type and intensity, in each reaction was recorded in the questionnaire. The hemovigilance system was started in 2011 in Yazd province and during the years of 2011-2012, the physicians, nurses, and blood bank experts were provided with the necessary training on the system. Required statistics were collected from 2013 after the full establishment of the hemovigilance system. Data were entered into the SPSS software version 17 system and were analyzed using the Chi-Square test, and Paired-Samples t-test.
The study project was approved by the Ethics Committee of Islamic Azad University of Yazd with the code of IR.IAU.YAZD.REC.1396.34.

Results

Out of 107 studied thalassemia patients, 87 patients were present both before and after implementation of the hemovigilance system. Forty-five (52%) of the patients were male and 42 (48%) of them were female. The mean age of the cases was equal to 19.69±8.41 years old, with an age range of 0 - 47 years. The mean age of onset of transfusion was equal to 14.3±16.62 months, with a range of 2 - 96 months.
The total number of reactions recorded before 2011 (2007-2010) was obtained as 34. After implementation of the hemovigilance system (2013-2016), 36 reactions were reported. The total number of blood transfusions in the patients with thalassemia major was equal to 4582 cases before implementation of the hemovigilance system and it was equal to 4465 cases after the implementation. The frequency of reactions before 2011 was equal to 0.74% and it was equal to 0.81% after 2012. The mean relative frequency of transfusion reactions in the patients with thalassemia major was equal to 0.63% before implementation of the hemovigilance system and it was equal to 0.97% after the implementation. Although, the percentage of relative frequency of blood transfusion reactions was higher in these patients after 2012, it was not statistically significant. The mean relative frequency of blood transfusion reactions was equal to 0.84% before 2011 in the male patients with thalassemia major and it was equal to 1.07% after 2012, which was

[DOI: 10.18502/ijpho.v10i4.4408]

not statistically significant. In the female patients before 2011, it was equal to 0.39% and it was equal to 0.862% after 2012, and the difference was significant ($p<0.05$). Overall, the relative mean frequency of blood transfusion reactions was higher in the men than the women both before 2011 and after 2012 (Table I).

Table II shows the frequency of different types of blood transfusion reaction in the patients with thalassemia major. The most frequent reactions recorded at the time of study were allergic reaction (38 cases, 54%) and non-hemolytic febrile transfusion reaction (16 cases, 23%). Hemolytic transfusion reaction was reported only after implementation of the hemovigilance system and no case was reported before that. Five of the reported hemolytic reactions were due to the presence of alloantibodies in the plasma of thalassemia patients. The presence of anti-K and anti-C with anti-D was reported in 3 and 2 patients, respectively (Table II).

Table III shows the frequency of the severity of transfusion reactions in the patients with thalassemia major before and after implementation of the hemovigilance system. The severity of reactions was not the same in the two studied time periods. Prior to 2011, mild reactions were recorded in the patients' files and after 2012, severe and life-threatening reactions were reported more ($p<0.007$) (Table III).

Table I: The relative mean frequency of blood transfusion reactions in thalassemia patients according to age before (2007-2010) and after (2013-2016) the hemovigilance system implementation

Sex	hemovigilance system implementation	No.	Transfusion reaction X± SD
Male	Before	45	1.18±0.84
	After	45	1.07±3.11
	P value		0.653
Female	Before	42	0.397±0.917
	After	42	0.862±1.42
	P value		0.046
Total	Before	87	0.626±1.07
	After	87	0.971±2.44
	P value		0.231

Table II: The frequency of different types of blood transfusion reactions in patients with thalassemia major before (2007-2010) and after (2013-2016) the hemovigilance implementation

Transfusion reaction	Before hemovigilance implementation		After hemovigilance implementation		Total	
	No	percent	No	percent	No	percent
Febrile non hemolytic reaction	8	50	8	50	16	100
Allergic reaction	19	51	19	49	38	100
Hemolytic transfusion reaction	0	0	7	100	7	100
Febrile non hemolytic reaction and Allergic reaction	3	100	0	0	3	100
Other	4	70	2	30	6	100
Total	34	48.6	36	51	70	100

P-Value=0.048

[DOI: 10.18502/ijpho.v10i4.4408]

Table III: Frequency of the severity of transfusion reactions in patients with major thalassemia before and after hemovigilance implementation

Transfusion reaction severity	Before hemovigilance implementation		After hemovigilance implementation		Total	
	No	percent	No	percent	No	percent
Mild to moderate	20	62.5	12	37.5	32	100
Severe	10	35.7	18	64.3	28	100
Life-threatening	4	40	6	60	10	100
Total	34	48.6	36	51.4	70	100

P-Value=0.007

Discussion

It is of crucial importance to report the transfusion reactions in the thalassemia patients. Blood transfusion reactions in the patients with thalassemia major have been recorded only in the files of thalassemia patients during the years before implementation of the hemovigilance system. After the implementation of this system, blood transfusion reactions are recorded in the adverse reaction forms and sent to the Blood Transfusion Center for follow-up. The hemovigilance system was first implemented in Yazd province in 2011. In this system, the physicians, nurses, and blood bank laboratory experts are trained on the blood transfusion indications, storage conditions of the blood components, pre- and post-transfusion care, investigation and treatment of the blood transfusion reactions in the transfusion-dependent patients, and recording and reporting of all the blood transfusion reactions. According to this plan, the reaction report form is first completed by the nurse and the hemovigilance practitioner of the health care center, with details about the severity and then, is sent to the Blood Transfusion Organization. Finally, reports on the blood transfusion reactions are reviewed and analyzed, and corrective and preventive action is taken to reduce the reactions and improve the safety of blood recipients. No complications have been reported before implementation of the hemovigilance system and transfusion reactions have only been recorded in the patient's file and have not been monitored or analyzed.

Kasraian et al., in a study reported that the incidence of blood transfusion reactions in the thalassemia patients was equal to 0.2% (11). Harvey found that the frequency of blood transfusion reactions was equal to 239 reactions in 100,000 transfused products (12). Dot et al., in a study conducted during 2015-2016 showed that the frequency of transfusion reactions was equal to 0.97% (13).

In the present study, allergic and febrile non-hemolytic transfusion reactions (FNHTR) were the most frequent reactions. Harvey et al., showed that 46.8% of the reactions were allergic reactions and 36.1% of them were FNHTRs (12). In the other studies, allergic reactions and FNHTRs have been shown to be more frequent (11,14-16).

In the present study, after implementation of the hemovigilance system, severe reactions were reported more frequently (Table III). In the study by the center for disease control (CDC), about 7% of the reported reactions have been reported to be severe and life-threatening (17). Results of a study in the Netherlands on the hemovigilance system showed that the majority of serious adverse reactions were related to the hematology ward (18). Harvey et al., found that 7.2% of the reactions were severe and life-threatening reactions and 0.1% of them were lethal

[DOI: 10.18502/ijpho.v10i4.4408]

reactions (12). In the present study, there was no case of lethal transfusion reaction.

In the thalassemia patients who had received the blood before screening of the donated blood for anti-HCV in 1996, 8 cases (7%) were reported to have hepatitis C but no cases of hepatitis B and HIV infection were reported. During the present study, no new cases of hepatitis B, C, and HIV were reported. Eshvandi et al., reported no HIV infection and hepatitis B cases but 22% of the cases had hepatitis C (14). Shamsian et al., in a study on the blood transfusion status in the patients with beta thalassemia major showed that about 9% of the patients had hepatitis C and 0.8% of them had hepatitis B (19).

In the present study, 7 cases of hemolytic transfusion reaction were reported after implementation of the hemovigilance system, and no case was reported before the system implementation. In these cases, after investigating the cause of reaction, the patient's blood sample is checked for the unexpected antibodies at the blood transfusion center. If the unexpected antibodies have caused the hemolytic transfusion reaction, these antibodies are identified in the patient's plasma/serum sample. Then, the blood units that lack the related antigens are selected for the subsequent transfusions. If the reaction is caused by a personnel error, retraining of the personnel is carried out to prevent the reaction from occurring again. The training courses include identifying the patient, the blood sample, and the blood bag during the blood transfusion process. Failure to report the hemolytic transfusion reactions prior to implementation of the hemovigilance system may be due to the lack of familiarity of the laboratory and medical personnel with these reactions and follow-up to determine their cause. Azarkeivan et al., in a study on the thalassemia patients in Tehran showed that the hemolytic reactions occurred in 1.6% of the patients (20). Salimi et al., showed that 0.5 cases of the acute hemolytic reaction occurred per 1,000 blood transfusions (21). Raja demonstrated that the anti-E and anti-D were the most common unexpected antibodies in the hemolytic transfusion reactions (22). In the study by the CDC, 19% of the thalassemia patients had the unexpected antibodies, and anti-K, anti-C, and anti-E alloantibodies were the most common antibodies in those patients (17). In the present study, 5% of the thalassemia patients had an unexpected antibody. Unexpected antibodies that led to the reaction included anti-K, anti-C, and anti-D. The Yazd Blood Transfusion Center has provided the D-negative, K-negative, and C-negative blood units for these patients. Previously, thalassemia patients only had received ABO/D compatible blood units. Currently, all the thalassemia patients receive the K-compatible blood units in addition to ABO/D matched blood units. However, there is a need for continuous communication through the hemovigilance system between the health care centers and blood transfusion centers so that, the reactions are regularly reported and followed up. Previous studies have indicated that implementation of the hemovigilance system is associated with an increased reporting of the blood transfusion reactions. The causes of these reactions have been studied and identified, leading to an increase in the transfusion safety of the patients receiving the blood units (18, 20).

Conclusion

In general, the blood transfusion reactions in the patients with thalassemia major have been reported more frequently after implementation of the hemovigilance system. Implementation of the hemovigilance system has provided an opportunity for documentation and reporting of the severe reactions, determination of the alloantibodies, and the possibility of following up and preventing the recurrence of the blood transfusion reactions in the patients. Thus, our findings highly emphasize on

[DOI: 10.18502/ijpho.v10i4.4408]

continuing the process of hemovigilance system.

Acknowledgement

This article is part of a thesis entitled " Comparison of the types of transfusion reactions in thalassemia patients before and after the implementation of the hemovigilance system in Shahid Sadoughi Hospital, Yazd." and supported by the Ali Ebn Abitaleb School of Medicine(AS), Islamic Azad University of Yazd. The authors would like to thank the staff of Thalassemia Center of Shahid Sadoughi Hospital and Yazd Blood Transfusion Center who helped in the study.

Conflict of interest

The authors declare no conflict of interest.

References

1. Aydinok Y. Thalassemia. Hematology 2012;17:S28-S31.
2. Pinto VM, Poggi M, Russo R, Giusti A, Forni GL. Management of the aging beta-thalassemia transfusion-dependent population - The Italian experience. Blood Rev 2019;38:100594-100596.
3. Borgna-Pignatti C, Cappellini MD, De Stefano P, Del Vecchio GC, Forni GL, Gamberini MR, et al. Survival and complications in thalassemia. Ann N Y Acad Sci 2005;1054: 40–47.
4. Mettananda S, Gibbons RJ, Higgs DR: Understanding α-globin gene regulation and implications for the treatment of β-thalassemia. Ann N Y Acad Sci 2016;1368(1):16–24.
5. Guo S, Aghajan M, Casu C, Gardenghi S, Booten S, Rivella S, et al. Targeting TMPRSS6 using antisense technology for the treatment of Beta-Thalassemia. Blood 2015;126(23):753-759.
6. Hudecova I, Chiu RW. Non-invasive prenatal diagnosis of thalassemias using maternal plasma cell free DNA. Best Pract Res Clin Obstet Gynaecol 2017;39:63–73.
7. Mohanan EP, Panetta JC, Royan SSB, Abraham A, Edison ES, Lakshmi KM, et al. Population Pharmacokinetics of Fludarabine and Treosulfan in Patients with Thalassemia Undergoing Hematopoietic Stem Cell Transplantation. Blood 2015; 126(23):3120-3125.
8. Cao A, Moi P, Galanello R. Recent advances in β-thalassemias. Pediatr Rep 2011; 3(2):e17-e19.
9. Sahu S, Hemlata, Verma A. Adverse events related to blood transfusion. Indian J Anaesth 2014;58(5):543–551.
10. Siegenthaler MA, Schneider P, Vu DH, Tissot JD. Haemovigilance in a general university hospital: Need for a more comprehensive classification and a codification of transfusion related events. Vox Sang 2005; 88(1):2–30.
11. Kasraian L, Karimi MH. The Incidence rate of acute transfusion reactions in thalassemia patients referred to the Shiraz Thalassemia Centre, Shiraz, Iran, before and after the establishment of the hemovigilance system. Int J Hemoglobin Re 2015; 39(4): 274–280.
12. Harvey AR, Basavaraju SV, Chung KW, Kuehnert MJ. Transfusion-related adverse reactions reported to the National Healthcare Safety Network Hemovigilance Module, United States, 2010 to 2012. Transfusion 2015;5 5(4):709-718.
13. Dutt N, Sidhu M, Sharma S, Parihar R, Kumar D. Effectiveness of buffy coat leukoreduced packed red blood cells in decreasing febrile non-hemolytic transfusion reactions in thalassemic patients. Int J Res Med Sci 2017; 5: 1756-1759.
14. Ashvandi KH, Bakhsh M. Evaluation of transfusion reactions in thalassemia patients in hospitals of Hamadan. Sci J nursery obstetric Hamadan 2010; 17: 53-57. [In Persian]
15. Teimuri H, Imani F, Maghsudlu M, Kia Daliri K, Fallah Tafti M. Prevalence of acute blood transfusion reactions in 11 hospitals of Tehran and Mazandaran province. Sci J Iran Blood Transfus Organ 2007; 4(1): 19-24. [In Persian]

[DOI: 10.18502/ijpho.v10i4.4408]

16. Savage WJ. Transfusion reactions. Hematol Oncol Clin North Am. 2016; 30(3):619-634.
17. Vichinsky E, Neumayr L, Trimble S, Giardina PJ, Cohen AR, Coates T, et al. Transfusion complications in thalassemia patients: a report from the Centers for Disease Control and Prevention (CME). Transfusion 2014; 54(4):972–979.
18. Vries R, Faber J, Strengers P. Haemovigilance: an effective tool for improving transfusion practice. Vox Sang 2011;100: 60–67.
19. Shamsian Sh, Arzanian M, Shamshiri A.R, Alavi S, Khojasteh O. Blood transfusion status in beta major thalassemia patients in Mofid Children Hospital in Tehran. Sci J Iran Blood Transfus Organ 2008; 4(4): 253-258. [In Persian]
20. AzarKeyvan A, Ahmadi MH, Hajibeygi B, Gharehbaghian A, Shabehpour Z, Maghsoudlu M. Evaluation of transfusion reactions in thalassemic patients referred to the Tehran Adult Thalassemia Clinic. J Zanjan Univ Med Sci Health Services 2008; 16(62):57–66. [In Persian]
21. Salimi S, Feizi A, Vanabadi N. Incidence rate of acute reactions in transfusion of blood and its products prepared by Urumia Blood Refinery Center. Adv Nurs Midwifery 2009; 19:8-13. [In Persian]
22. Makroo RN, Bhatia A, Hegde V, Chowdhry M, Thakur UK, Rosamma NL. Antibody screening & identification in the general patient population at a tertiary care hospital in New Delhi, India. Indian J Med Res 2014; 140(3): 401–405.

[DOI: 10.18502/ijpho.v10i4.4408]