ORIGINAL ARTICLE

Blood Transfusion Reactions Among Multi-Transfused Thalassaemic Patients

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ABSTRACT

Objective: To determine the frequency of common blood transfusion reactions observed among multi-transfused thalassaemic patients in Sir Ganga Ram Hospital Lahore.

Methods: In this cross sectional comparative study, total of 122 thalassaemic patients attending Sir Ganga Ram Hospital Lahore were conveniently selected. Participants were interviewed about transfusion related reactions, using a pre-tested semi-structured questionnaire, after taking verbal informed consent. Patient's records were also reviewed for clinical manifestations, treatment modalities and laboratory investigations. Data was edited and analyzed using SPSS version -17. Information was described in terms of frequencies and percentages. Statistically significant difference in proportions was analyzed using Chi-Square test. A p-value of less than 0.05 was taken as significant.

Results: Of one hundred and twenty two thalassaemic patients, 99(81%) had thalassemia major and among them 62% required blood transfusions at least every fortnight. Proportions of males and females were 52% and 48% respectively. Mean age of these patients was 16 years with 47% and 29% belonged to B-positive and O-positive blood groups. Most commonly reported blood transfusion related reactions were fever (59.8%), rigors (43.5%), itching (25.4%), vomiting (28.7%), body aches (55.7%), back pain (59.8%), dyspnea (27.9%), lack of energy (55.7%), tachycardia (38.5%), cold extremities (50%), and abdominal pain (22.1%). No statistical difference was found between age and occurrence of these reactions, whereas symptoms of itching, back pain and tachycardia differ significantly ($p<0.05$) between Thalassemia major and Thalassemia intermedia patients. B positive and O positive patients had statistically significantly higher proportion of lack of energy and pain in side of back after blood transfusion ($p <0.05$).

Conclusion: Non-haemolytic reactions like fever, rigors and back pain are the most commonly occurring immediate complications among multiple-transfused thalassaemic patients. Blood transfusion reactions require immediate recognition, laboratory investigation, and clinical management among thalassemias.

Key Words: Thalassemia, Transfusion, Blood, Haemolytic reaction, febrile, multiple transfusions.

INTRODUCTION

Thalassaemias are a group of hereditary blood disorders characterized by anomalous production of hemoglobin, resulting in variable conditions ranging from clinically asymptomatic state to the development of profound anaemia, requiring multiple transfusions. Most thalassaemias are inherited as autosomal recessive trait and represents a situation in which there is defective synthesis of α and/or β globin chains, owing to mutations or deletions at chromosome 11 and 16 respectively.[1] Normally there is balanced (1:1) production of α and β chains, however, chromosomal defects lead to imbalanced globin chain production, which result in its precipitation within red cell precursors, ineffective erythropoiesis and haemolysis, with development of anemia.[1,2] In contrast to other types of α and β-thalassaemias, regular and multiple transfusions are required in β–Thalassemia major (Cooley's anaemia), in order to maintain the hemoglobin level in between 9.5-10.5 g/dl, to allow normal growth and development.

These transfusions may be required every 4-6 weeks.

This genetic blood disorder is prevalent in more than 60 countries with a carrier population of approximately 150 millions. In comparison to α-thalassemia, which is predominantly prevalent in African countries, β-thalassaemias are distributed mainly in Mediterranean countries, Middle East, Central Asia, India and Southern China.[2] Global incidence of symptomatic patients has estimated to be 1 in 100,000, whereas it is 1 in 10,000 in the European Union.[3] According to an estimate there are around 60,000 children suffering from thalassemia major in Pakistan and majority of them are transfusion dependent. In addition, every year, more than 4000 transfusion dependent beta thalassemia major cases are added.[4] This high proportion in this region may be due to widespread consanguineous marriages, high birth rate and large population size. Moreover, there is also a very high gene carrier rate (5.3%) in this part of the world, though variable in different regions (highest in province of Sindh, Khyber Pukhtunkhewa and Baluchistan).[4,5] There is also a historical parallel to this distribution since over hundreds of years; this region was inhabited by invaders from Middle East, central Asia, Iran, China and Mediterranean region.

Blood transfusion is a life saving approach, however, it can become very hazardous and accompanied by fatal complications which may be infectious and non-infectious in nature. Problems may arise from inadvertent transfusion of incompatible blood. Although, modern era screening procedures have markedly minimized the risk of infectious agent transmission, yet this issue is still not resolved in developing countries like Pakistan. There is a higher risk of Hepatitis, HIV and Cytomegalovirus in patients who require multiple transfusions and rely on multiple donors from various sources. On the other hand, immunological complications, like alloimmunization which occurs due to transmission of foreign antigens present on red cells, leucocytes, platelets and plasma proteins, could place the transfused person at risk of severe reactions.[6,7] While, these does not cause problems with first transfusion, however with subsequent transfusions fatal reactions could put patient's life at risk. In addition, there may be delayed consequences like tissue graft rejection in transplants.[6] Haemolytic transfusion reactions can present as rigors, lumber pain, dyspnea, haemoglobinuria and renal failure.[1,2] Yet, non- haemolytic (febrile) transfusion reaction, characterized by flushing, tachycardia, fever >38 ℃, chills and rigors are more common among those with multiple transfusions. This is attributed to mechanism of alloimmunization.[7]

There is a lack of information about the reactions related to blood transfusion among the thalassaemic major patients, who are exposed to this procedure multiple times. Thalassemia center of Sir Ganga Ram Hospital Lahore is catering a substantial number of thalassaemic population of Lahore and surrounding regions, therefore status of its transfusion services should be continuously monitored and studied to ensure quality of care to attending thalassaemic children. Furthermore, the understanding about the frequency and types of blood transfusing reactions in these children may assist the attending physicians to take remedial actions to minimize this risk and also be vigilant regarding preventable factors. Purpose of this study is to assess the distribution of blood transfusion reactions and its types among children attending Sir Ganga Ram Hospital Lahore. Knowledge thus obtained not only identify high risk transfusion dependent thalassaemic patients for transfusion related reactions, but also provide a guideline for treating physician to devise a safe monitoring approach during this life saving procedure for thalassaemic children.

MATERIAL AND METHODS

This cross sectional comparative study was conducted in Thalassemia Day Care Centre of Sir Ganga Ram Hospital, Lahore. A total of 122 thalassaemic patients over the age of 5 years visiting regularly from 1st October 2011 to 31st December 2011 were selected using convenient sampling technique. Patients with acute illness or those who were hospitalized were excluded. Participants were interviewed about transfusion related reactions, using a pre-tested semi-structured questionnaire. Patient's records were also reviewed for clinical manifestations, treatment modalities and laboratory investigations. Sociodemographic characteristics were also recorded from patient's profile section. Responses were recorded on paper by investigators after explaining the purpose of study to respondents and taking their verbal consent. Confidentiality of information was maintained by codifying the subject's identity and contact details. Upon manually checking the interview forms, data was entered, cleaned, edited and analyzed using

Statistical Package for Social Sciences (SPSS) version 17. Further, data was classified based on Sociodemographic characteristics and types of blood groups. Numerical data was analyzed using mean ± SD, whereas categorical data were described in terms of frequencies and percentages. Statistically significant difference in proportions was computed using Chi-Square test and Fisher Exact test (where applicable). We used p-value of less than 0.05 as being statistically significant. Ethical approval for this study was obtained from ethical review committee of FJMC/Sir Ganga Ram Hospital Lahore.

RESULTS

Of one hundred and twenty two thalassaemic patients, 99(81%) had thalassemia major and among them 62% required blood transfusions at least every fortnight. Proportions of males and females were 52% and 48% respectively. Mean age of these patients was 16 years with 47% and 29% belonged to B-positive and O-positive blood groups; while proportion of other blood groups ranged between 0.8% - 8.2% (Table 1). Out of ninety-nine (81%) thalassemia major patients, 66% were receiving both blood transfusion and iron chelating therapy, whereas 34% were getting blood transfusion only. The Haemoglobin (Hb) level of most of the patients (48%) was ranging between 7-9g/dl. Ferritin levels were measured only among 81(66%) of these patients over the period of last two years. Among these, 19% had less than 1000 g/d, 42% between 1000-2500 g/d, 32% had between 2500-5000 g/d and only few (7%) had more than 5000 g/dl ferritin levels. Public hospitals were the main source of blood supply (63%) to these patients (Table 2).

Most commonly reported blood transfusion related reactions were fever (59.8%), rigors (43.5%), vomiting (28.7%), bleeding from different sites of body (20%), itching (25.4%), body aches (55.7%), back pain (54.1%), joint pains (32.8%) and abdominal pain (22.1%) (Figure 1). Cardiac symptoms observed in these patients included dyspnea (27.9%), lack of energy (55.7%), cold extremities (50%), tachycardia (38.5%), irregular heart beat (36%) - self reported, shortness of breath (27.9%), and flushing (33.6%) (Figure 2).

No statistically significant difference was found among age groups and occurrence of these reactions, whereas symptoms of itching, back pain, and tachycardia differ significantly ($p<0.05$) between Thalassemia major and Thalassemia intermedia patients. Upon comparison among different blood groups and occurrence of blood transfusion reactions, on the basis of ABO compatibility it was found that back pain was reported most commonly by subjects of AB and A blood groups, whereas body aches, skin rashes, itching, and rigor were seen in A, and B blood groups. Loss of consciousness and vomiting were experienced by patients having O blood groups. Similarly, excessive bleeding and fever were observed more frequently in patients of A, B blood groups (Figure 3). And on the basis of Rh compatibility it was found that back pain, body aches, excessive bleeding, and skin rashes were reported most commonly by subjects of negative blood groups, whereas loss of consciousness, vomiting, itching, rigor, and fever were more frequently reported by subjects of positive blood groups (Figure 4). Yet, these differences were not found significant ($p<0.05$).

Table 1: Distribution of Blood Group Types among Thalassaemia Patients Attending Thalassaemia Center at Sir Ganga Ram Hospital Lahore (N=122).

Blood Type	Frequency	%
A Positive	10	8.2
A Negative	03	2.5
B Positive	57	46.7
B Negative	01	0.8
AB Positive	10	8.2
AB Negative	02	1.6
O Positive	35	28.7
O Negative	04	3.3

Appearance of cardiac symptoms after blood transfusion; swelling in legs, flushing, cold extremities, tachycardia, and lack of energy were most frequently reported by O blood groups patients, whereas abdominal pain, irregular heartbeat, and shortness of breath were reported by patients of A blood groups (Figure 5). Rh compatible blood grouping showed swelling in legs, cold extremities, tachycardia, and lack of energy were most frequently reported by patients having negative blood groups, whereas abdominal pain, flushing, and shortness of breath were reported by patients of positive blood groups (Figure 6). Furthermore, no statistically significant difference was observed among different age groups or type of β-thalassemia as regard to various blood transfusion reactions like shortness of breath, lack of energy, tachycardia, redness and

warmth, abdominal pain and pain on the side of back (p>0.05). However, significant association did exist between lack of energy and back pain among different blood groups (p<0.05).

Table 2: Hemoglobin and Serum Ferritin levels, and Blood Transfusion among Thalassaemia Patients (N=122).

Attribute	Frequency	Percentage
Type of thalassaemia diagnosed		
Thalassaemeia major	99	81.1
Thalassaemeia intermedia	23	18.9
Type of therapy		
Blood transfusion therapy	42	34.4
Both (blood transfusion and chelation therapy)	80	65.6
HB level		
<7 g/dl	56	45.9
7-9 g/dl	58	47.5
>9 g/dl	8	6.6
Serum ferritin (N=81)		
<1000 ng/ml	15	18.5
1000-2500 ng/ml	34	42.0
2500-5000 ng/ml	26	32.1
5000-10,000 ng/ml	6	7.4
From where do you get the blood for transfusion?		
From blood bank	18	14.8
Govt. hospital	77	63.1
From relative	11	9.0
Other	16	13.1
How often do you get blood transfusion?		
<15 days	75	61.5
16-30 days	43	35.2
31-60 days	4	3.3
How many blood transfusions have you receive till one month?		
Once a month	41	33.6
Twice a month	63	51.6
Thrice a month	9	7.4
4 times a month	9	7.4
Serum ferritin (N=81)		
Adequately chelated	15	18.5
Inadequately chelated	66	81.5

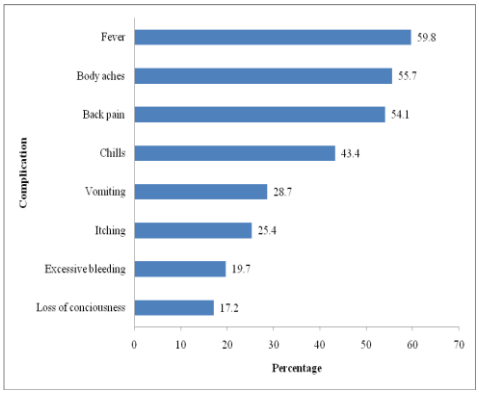

Figure 1: Immediate Complications after Blood Transfusion among Thalassaemia Patients (N=122).

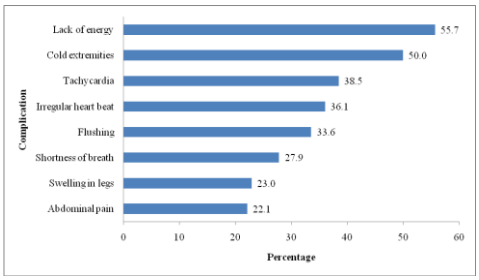

Figure 2: Cardiac Complications after Blood Transfusion among Thalassaemia Patients (N=122).

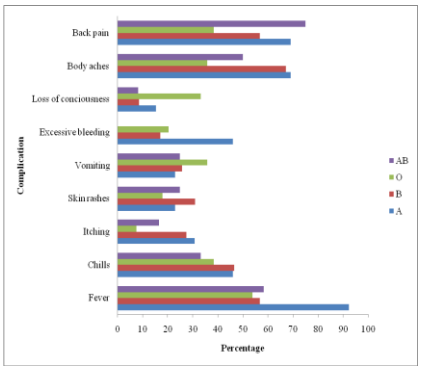

Figure 3: Immediate Complications after Blood Transfusion among Thalassaemia Patients by ABO Compatibility (N=122).

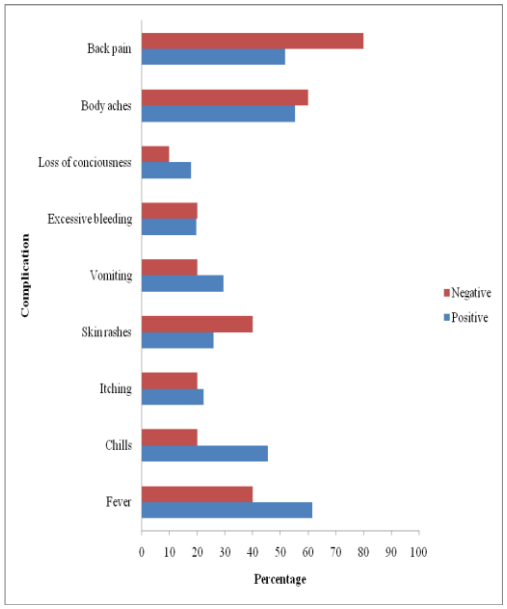

Figure 4: Immediate Complications after Blood Transfusion among Thalassaemia Patients by Rh Compatibility (N=122).

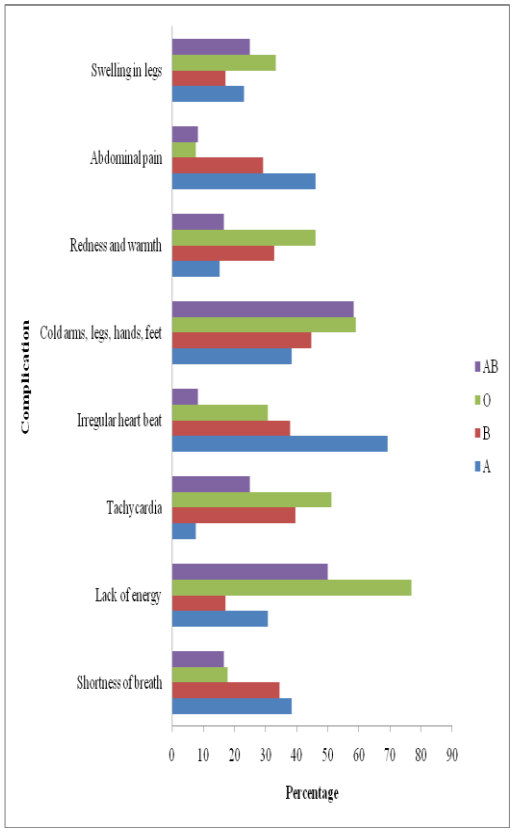

Figure 5: Cardiac Complications after Blood Transfusion among Thalassaemia Patients by ABO Compatibility (N=122).

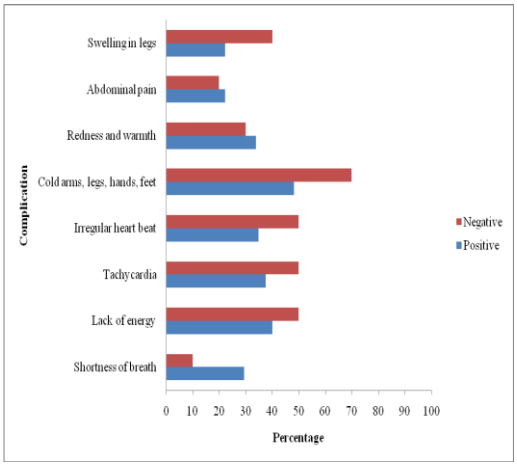

Figure 6: Cardiac Complications after Blood Transfusion among Thalassaemia Patients by Rh Compatibility (N=122).

DISCUSSION

Immediate blood transfusion reactions like fever and chills are thought to be caused by recipient antibodies reacting with white cell antigens, white cell fragments in blood products and cytokines which accumulate in the blood product during storage. The majority of haemolytic reactions i.e. chills, fever, pain in back and chest, hypotension, dark urine and uncontrolled bleeding are caused by transfusion of ABO incompatible blood. However, most haemolytic reactions are the result of human error such as the transfusion of properly labeled blood to the wrong patient, or improper identification of pre-transfusion blood samples. Very high fever, rigors, profound hypotension, nausea and/or diarrhea may be occur due to bacterial infection introduced into the pack at the time of blood collection from sources such as donor skin, donor bacteremia or equipment used during blood collection or processing.

Cardiac symptoms following blood transfusions i.e. shortness of breath, lack of energy, tachycardia, irregular heartbeat, cold arms, legs, hand, feet, pain in joints, redness, abdominal pain, swelling in legs, weight loss, side back pain were found in about quarter of our patients. Similar findings were reported by Ragab et al.[8] in Egypt and shah et al.[9] however, urticaria and itching were more pronounced in these studies. No statistically significant difference among different age groups were seen regarding various immediate blood transfusion reactions like fever, chills, itching, skin rashes, vomiting, excessive bleeding, loss of consciousness, weight loss, body

aches and back pain and as regard to shortness of breath, lack of energy, racing heart, irregular heartbeat, cold arms, hands, legs, feet, joints pain, redness and warmth, abdominal pain, swelling in legs, weight loss, side back pain.

No statistically significant differences were found among various blood groups regarding various immediate transfusion reactions. While there was significant association present for lack of energy and side back pain regarding symptoms of heart complication among different blood group types. Mismatched blood may be the one of the major risk factor of adverse reaction (transfusion reaction). Transfusion reaction may also occur when antibodies in the recipient's blood react to foreign blood cells by the transfusion. This tends to be seen more commonly in patients requiring frequent blood transfusions. The development of hemolytic alloantibody and erythrocyte auto antibodies complicates transfusion therapy in thalassemia patients[7, 10] and observed reactions may be attributed to this phenomenon. On the other hand, not all individuals develop the hypersensitivity to foreign antigen as described by Azarkeivan et al.[11] in their study of 835 patients, in which 74.1% had no history of transfusion reactions, whereas only 2.5% developed hemolytic complications, out of which 9.3% showed allergic symptoms and 14% reported febrile reactions during transfusion.[11]

Results of this study should be interpreted considering that study population was restricted to patients attending one specialized center only. Results might lack external validity and might not be applicable to other patients attending other transfusion centers. Furthermore, we collected data at one point in time and the reactions experienced by these respondents during previous occasions may not be totally recalled and highlighted during the interview. Many of the reported reactions were non- specific and might not be related to transfusion. It is suggested that a follow-up study may be conducted on this particular cohort to identify immediate and delayed reactions with more precision and accuracy.

CONCLUSION

Non-haemolytic reactions like fever, rigors and back pain are the most commonly occurring immediate complications among multiple-transfused thalassaemic patients, while cold extremities, joint pains, tachycardia and skin rashes were reported as the most frequently occurring delayed reactions.

REFERENCES

1. Kumar P, Clark M. Clinical Medicine, Fifth edition. W.B Saunders, Elsevier Science limited. 2002.
2. Galanello R, Origa R. Beta-Thalassemia. Orphanet journal of rare diseases. 2010; 5(11):2-15.
3. Vichinsky EP. Changing patterns of thalassemia worldwide. Ann N Y Acad Sci. 2005; 1054:18-24.
4. Ahmed S, Saleem M, Sultana N, Raashid Y. Prenatal diagnosis of β-thalassemia in Pakistan: experience in a Muslim country. Prenat diagn. 2000; 20:378-83.
5. Sengupta M. Thalassemia among tribal communities of India. Int J Biol Anthro. 2008; 1(8):445-7.
6. Alter HJ, Klein HG. The hazards of blood transfusion in historical perspective. Blood. 2008; 112(7):2617-26.
7. Q Ain, Ahmed L, Hassan M, Rana SM, Jabeen F. Prevalence of β-thalassaemic patients associated with consanguinity and Anti-HCV antibody positivity- A cross sectional study. Pakistan J Zool. 2011; 43(1):29-36.
8. Ragab LA, Hamdy MM, Shaheen IA, Yassin RN. Blood transfusion among thalassemia patients: A single Egyptian center experience. Asian J Transfus Sci. 2013; 7:33-6.
9. Shah N, Mishra A, Chauhan D, Vora C. Study on effectiveness of transfusion program in thalassemia major patients receiving multiple blood transfusions at a transfusion centre in Western India. Asian J Transfus Sci. 2010; 4:94-8.
10. Singer ST, Wu V, Mignacca R, Kuypers FA, Morel P, Vichinsky EP. Alloimmunization and erythrocyte autoimmunization in transfusion-dependent thalassemia patients of predominantly Asian descent. Blood. 2000; 96(10):3369-73.
11. Azarkeivan A, Ansari S, Ahmadi MH, Hajibeigy B, Maghsudlu M, Nasizadeh S, Shaigan M, et al. Blood transfusion and alloimmunization in patients with thalassemia: multicenter study. Pediatr Hematol Oncol. 2011; 28(6):479-85.