PHARMACIA

Pharmacia 71: 1–6
DOI 10.3897/pharmacia.71.e136635

Research Note

Perioperative selection of blood and components for substitution: Immunohaematological assessment of immunization risk and methods for selection of optimally compatible blood

Maria Savcheva[1], Stefka Ivanova[2], Niya Semerdzhieva[3], Mariya Chaneva[3], Ventseslava Atanasova[4], Nikolay Bashev[3], Petar Atanasov[3]

1 *Transfusion Hematology Laboratory, Saint Sofia Medical Center, Sofia, Bulgaria*
2 *Bulgarian Pharmaceutical Science Society, Sofia, Bulgaria*
3 *Clinic of Internal Medicine, University Medicine Hospital "N. I. Pirogov", Sofia, Bulgaria*
4 *Bulgarian Pharmaceutical Union, Sofia, Bulgaria*

Corresponding author: Stefka Ivanova (ivanovastefka_pharm@yahoo.com)

Received 9 September 2024 ♦ **Accepted** 12 September 2024 ♦ **Published** 7 October 2024

Citation: Savcheva M, Ivanova S, Semerdzhieva N, Chaneva M, Atanasova V, Bashev N, Atanasov P (2024) Perioperative selection of blood and components for substitution: Immunohaematological assessment of immunization risk and methods for selection of optimally compatible blood. Pharmacia 71: 1–6. https://doi.org/10.3897/pharmacia.71.e136635

Abstract

The aim of this study is to assess the risk for immune and hematologic adverse events in perioperative transfusion of blood components. Our second goal is to propose methods for the selection of an optimally compatible donor in order to limit the negative impact of complications following blood component transfusion on the hospital outcome of patients admitted to clinics of general, gastrointestinal, thoracic, and vascular surgery.

The largest group of patients included in this study were patients with gastrointestinal disorders (614 patients; 31%) and patients with diseases of the organs of the blood and lymphatic system (589 patients; 30%). This was followed by patients with diseases of the skin and subcutaneous tissue (368 patients; 18%) and patients with benign and malignant neoplasms (365 patients; 18%). The remaining 65 patients (3%) were diagnosed with diseases of the endocrine system, trauma patients, and patients with genitourinary disorders.

The methods used for optimal selection of compatible blood components in this study are enzyme tests, Coombs tests, and tests in agglutinating medium.

The study shows that clinically significant antibodies, which could provoke a post-transfusion hemolytic reaction, were detected in 4.3% of the screened patients.

In the majority of patients, the specificity of antierythrocyte antibodies cannot be established. For those patients where the specificity of anti-erythrocyte antibodies could be established, the type of antibody and the antigen system to which it belonged were as follows (in descending order):

1. Anti-erythrocyte antibodies belonging to the Rh system: 37% (n = 17) of all screened patients (1.6% of all patients), including anti-E type (5 patients), anti-D (8 patients), anti-C-1, anti-C (2 patients), and anti-Cw (1 patient).
2. In 3 (6% or anti-erythrocyte antibodies belonging to other erythrocyte antigen systems—Kidd-1 patients, Lewis-2 patients—6% of the screened patients (0.3% of all patients).
3. In 57% (n = 26) of those screened (2.4% of all patients), alloantibodies without any known specificity were identified.

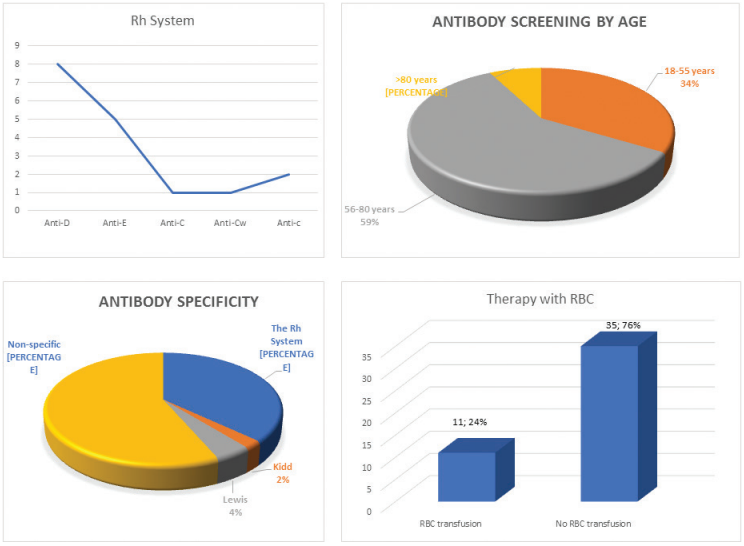
The largest number of identified antibodies were directed against the D antigen belonging to the Rh system.

Most of the anti-D alloantibodies found in Rhesus D (-) negative patients with no history of prior transfusion of D (+) positive red blood cell (RBC) concentrate possibly have resulted from prior Rh isoimmunization during pregnancy, provided that anti-D antibodies persist for a long time after birth—in some of the studied patients, 15–20 or more years.

A greater number of alloimmunizations were found in women—28 (61%), compared to men—18 (39%), due to previous sensitization with different blood group antigens during pregnancy.

This study shows that timely diagnosis is essential for the selection of appropriate RBC concentrate, for the avoidance of adverse reactions, and for the improvement of hematological parameters after transfusion of blood components.

Graphical abstract:



Keywords

transfusion reactions, antigens, alloantibodies, transfusion of blood components, host, donor, red blood cell concentrate

Introduction

Blood and blood component therapy are almost mandatory in surgical practice. In many cases, it is necessary for maintaining adequate circulation and tissue perfusion, making it life-saving. However, treatment with blood components also carries risks of complications.

The transfusion of allogeneic erythrocytes has been a life-saving measure for decades, particularly in patients with severe trauma or experiencing major blood loss from other etiologies.

In the last two decades, the safety of treatment with allogeneic blood components in terms of transmissible infections has significantly improved. However, the risk of immune hemolytic reactions remains possible and can be life-threatening. The factors contributing to the development of immune adverse events are related to differences in erythrocyte antigens between the donor and host, as well as the characteristics of the host's immune system and the immunomodulatory effect of the transfused blood component.

Repetitive blood cell transfusions can provoke the production of alloantibodies against one or more antigens present on the donor blood cells, including red blood cells. This complication can make subsequent transfusions more challenging.

Purpose

The aim of this study is to assess the risk of immune and hematologic adverse events in perioperative transfusion of blood components. Our second goal is to propose methods for the selection of an optimally compatible donor in order to limit the negative impact of complications following blood component transfusion on the hospital outcome of patients admitted to clinics of general, gastrointestinal, thoracic, and vascular surgery.

Materials and methods

The study included 2001 patients hospitalized in surgical departments—gastrointestinal and thoracic surgery (1222 patients; 61%), vascular surgery (553 patients; 28%), and general (septic) surgery (226 patients; 11%)—who underwent operative intervention. Diagnostic tests, specifically erythrocyte agglutination tests, were performed on all patients.

The degree of immunological risk was defined in advance in three levels of severity: mild, moderate, and severe. Patients with low risk underwent diagnostic tests in an agglutinating medium, and circulating antierythrocyte antibodies were not found (n = 927; 46%). Patients with moderate risk were defined as those having probable need or likely needing RBC transfusion (n = 1028; 52%); and patients with severe risk had both the need for RBC transfusion and detection of antierythrocyte antibodies (n = 46; 2.3%).

Routine and specific blood diagnostic methods were used, including agglutination, direct and indirect Coombs antiglobulin tests, and enzyme tests at temperature ranges of 4 °C, 18 °C, and 37 °C.

Results

A total of 2,001 blood samples obtained from patients admitted to general, gastrointestinal, thoracic, and vascular surgery and undergoing operative interventions were examined between 01 January 2023, and 31 December 2023. The samples were tested using the agglutinating method at 37 °C to determine the blood group type.

The largest share of patients suffered from gastrointestinal disorders (614 patients; 31%) and diseases of the organs of blood, lymphatic system, and arteries (589 patients; 30%). This was followed by patients with diseases of the skin and subcutaneous tissue (368 patients; 18%) and patients with benign and malignant neoplasms (365 patients; 18%). The remaining 65 patients (3%) were diagnosed with endocrine disorders, genitourinary disorders, or were trauma patients (Table 1, Fig. 1).

All patients included in the study were older than 18 years. The distribution of patients by age groups is presented in Fig. 2. The majority of patients—1103 patients (55%) were 56–80 years old, followed by 771 patients (39%) younger patients, 18–55 years old. The minority of patients were elderly (80 years and older)—127 patients (6%).

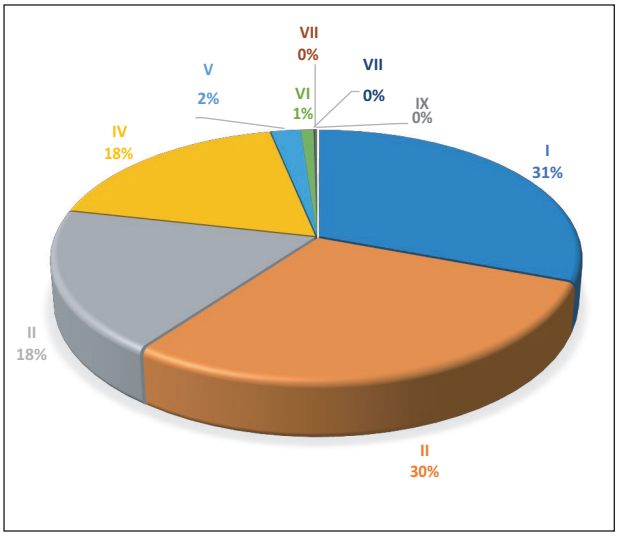


Figure 1. Distribution of admitted hospital patients according to system localization of the disorder.

Table 1. Distribution of patients undergoing surgical treatment according to diagnoses.

	Diagnosis	Number of patients
I	Diseases of the digestive system	614
II	Diseases of the organs of blood and lymphatic system	589
II	Diseases of the skin and subcutaneous tissue	368
IV	Neoplasms - benign and malignant	365
V	Diseases of the endocrine system	42
VI	Injuries, poisonings	18
VII	Diseases of the genitourinary system	2
VII	Factors affecting the health status of the population	2
IX	Diseases of the musculoskeletal system	1

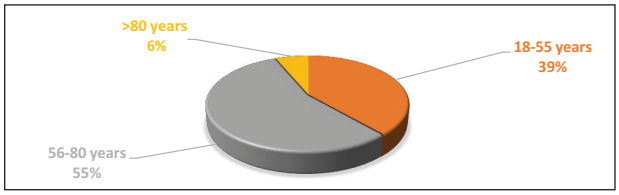


Figure 2. Distribution of patients by age.

The testing for anti-erythrocyte antibodies was conducted on 1074 patients using Coombs' immune agglutination test in enzyme medium at 37 °C. The distribution by age groups is as follows: 18–55 years old: 362 patients (34% or 18% of the total number of patients); 56–80 years old: 630 patients (59% or 35% of the total number of patients); and older than 80 years: 82 patients (7% or 4% of the total number of patients) (Fig. 3).

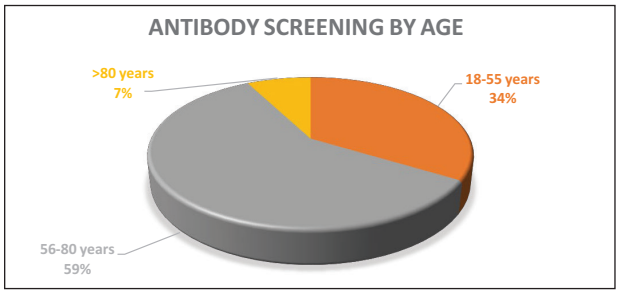


Figure 3. Distribution by age of patients screened for antierythrocyte antibodies.

In 46 (4.3%) of patients screened, antibodies against erythrocyte antigens were found. The distribution by age groups is from 18–55 years -9 (1%), from 56–80.

Years: 34 (3%) and over 80 years: 3 (0.3%). The antibodies found were further characterized as specific antibodies: 20 (2%), antibodies with undetermined specificity: 26 (2.3%).

Our results show that in 4.3% of the screened patients, clinically significant antibodies are detected, which can provoke a post-transfusion hemolytic reaction. When identifying the antibody specificity, we found that the majority of antierythrocyte alloantibodies were of established specificity. In the rest of the cases, the antibody specificity cannot be established. The major antibody types and the antigen system to which it belonged were as follows (descending order):

1. Anti-erythrocyte antibodies belonging to the Rh system: 37% (n = 17) of all screened patients (1.6% of all patients), including anti-E type (5 patients), anti-D (8 patients), anti-C-1, anti-C (2 patients), and anti-Cw (1 patient).
2. In 3 (6% or anti-erythrocyte antibodies belonging to other erythrocyte antigen systems—Kidd-1 patients, Lewis-2 patients6% of the screened patients (0.3% of all patients).
3. In 57% (n = 26) of those screened (2.4% of all patients), alloantibodies without any known specificity were identified (Table 2, Fig. 4).

The largest number of identified antibodies were directed against the D antigen belonging to the Rh system.

Table 2. Number of patients with antierythrocyte antibodies—and according to the individual antibody type and the system of interacting erythrocyte antigens.

Specificity		Number of patients
The Rh system		17
	– Anti-D	8
	– Anti-E	5
	– Anti-C	1
	– Anti-c	2
	– Anti-Cw	1
Kidd		1
Lewis		2
Non-specific		26

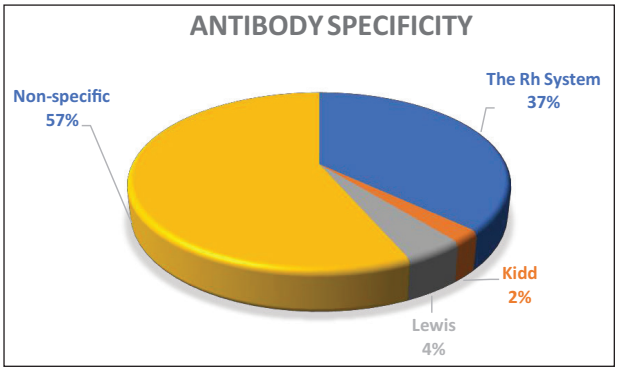


Figure 4. Identification of antibodies.

The largest number of identified antibodies interacted with RBC antigens attributed to the Rh system. Most of those antibodies were directed against the D antigen (Fig. 5) (Reverberi 2008).

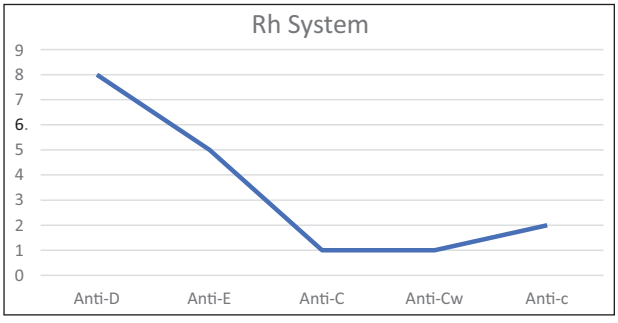


Figure 5. Specificities of the Rh system.

A greater number of alloimmunizations were found in women—28 (61%), compared to men—18 (39%) (Table 3, Fig. 6).

Table 3. Difference by gender of the patients with established alloantibodies.

Patients with anti-erythrocyte antibodies	N	%
Female patients	28	61%
Male patients	18	39%

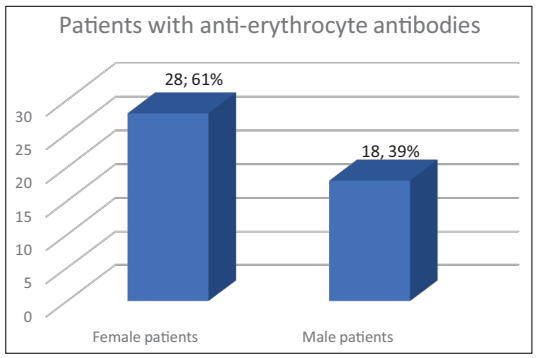


Figure 6. Men versus women distribution of the alloimmunized patients.

Red blood cell transfusion received 11 (24%) of the patients with antierythrocyte alloantibodies. All these patients underwent in vitro compatibility tests between donor erythrocytes and patient serum. Not proceeding with transfusion was the adopted strategy in 35 (76%) patients based on decision after analysis of the chance of harm compared to effect (Table 4, Fig. 7).

Table 4. Rate of RBC transfusion to patients with antierythrocyte alloantibodies.

Therapy of patients with antierythrocyte alloantibodies	N	%
RBC transfusion	11	24%
No RBC transfusion	35	76%

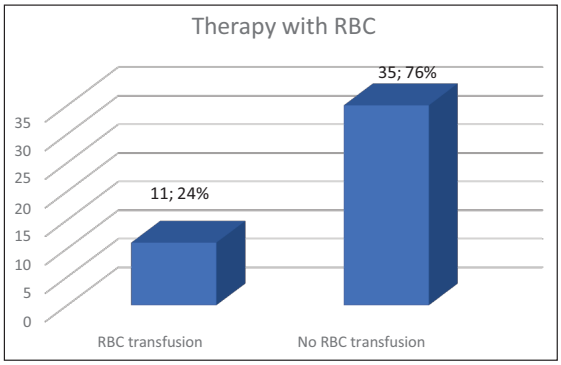


Figure 7. Patients with alloantibodies treated with RBC.

Nine of the transfused patients were diagnosed with embolism and thrombosis of arteries—iliac, arteries of lower and upper limbs. Three patients had skin and subcutaneous tissue infections.

Blood not containing the corresponding antigen was selected for patients with identified antibodies. For patients with non-specific antibodies in serum, an erythrocyte con-

centrate with a negative or weakly positive reaction was selected. They received preventive therapy with corticosteroids and antihistamines. In this way, post-transfusion complications were brought down to zero, and the desired therapeutic effect of blood transfusion was achieved.

Discussion

Alloimmunization after transfusion of blood and blood components is the most common immune system complication. It is associated with delay in treatment initiation due to the need for selection of matched blood components and the insufficient supply of blood component products of certain blood types. The increased risk of adverse effects due to incompatible RBC transfusion (hemolysis, shock, acute renal failure) and of adverse effects of the therapy of complications of incompatible transfusion, such as immunosuppression or ineffectiveness of transfusions, are among other reported problems.

The safety of blood products is linked to the unique antigen array of a specific blood component. The use of screening for anti-erythrocyte antibodies in a patient whenever repeated transfusions of blood components are needed (e.g., perioperatively) reduces the risk of developing hemolytic immune reactions.

The screening and identification of antierythrocyte antibodies and the selection of blood that does not contain the corresponding antigens to which the antibodies are directed have a significant role in improving the safety of blood component transfusion.

Our results show that in 4.3% of the screened patients, clinically significant antibodies are detected, which can provoke a post-transfusion hemolytic reaction. The rate of alloimmunization found in our study is consistent with data published by other authors (Ansari et al. 2008; Usman et al. 2011; Sood et al. 2013). When identifying the antibody specificity, we found that the majority of antierythrocyte alloantibodies were of established specificity. In the rest of the cases, the antibody specificity cannot be established. Those antibodies, in which specificity could be established, belonged to the Rh system (Shukla and Chaudhary 1999; Achargui et al. 2017; Pons et al. 2023).

Anti-D alloantibodies in plasma of Rhesus D (-) negative patients were the prevalent type alloantibodies found in the patients screened before blood component transfusion in our study. Most of the anti-D alloantibodies found in Rhesus D (-) negative patients with no history of prior transfusion of D (+) positive red blood cell (RBC) concentrate. This is possibly a result of prior Rh isoimmunization during pregnancy, provided that anti-D antibodies persist for a long time after birth—in some of the studied patients, 15–20 or more years (Reverberi 2008; Hauser et al. 2020). The difference in the rate of alloimmunization between men and women in our study is probably due to previous sensitization with different blood group antigens during pregnancy, as found by other investigators (Roopam et al. 2009; Politou et al. 2020; Lackovic et al. 2023).

Laboratories in hospital care facilities that have included a screening test to identify antibodies ensure safe blood transfusions. Patients with anti-erythrocyte antibodies can be entered into a single database, thereby quickly and easily providing an appropriate erythrocyte concentrate according to the patient's phenotype at the next hospital admission in any hospital with access to this database.

Of course, the promising solution is a wider application of mini-invasive and robotic methods, enabling a one-step surgical intervention with minimal perioperative blood loss. The robotization of variably complex surgical interventions is already being applied increasingly in many surgical subspecialties, including in emergency conditions (Atanassov et al. 2023).

Conclusions

The alloimmunization against erythrocyte antigens should not be a neglected complication of therapy with blood components. Alloimmunization almost invariably leads to the development of a post-transfusion hemolytic reaction during a subsequent blood transfusion. In many cases, "another blood transfusion" can be life-saving.

In the setting of alloimmunization, provision of compatible blood and blood components is often impossible. In these cases, replacement with blood and blood components of compatible blood cell type is necessary for avoiding complications. Antierythrocyte antibodies should be tested in patients undergoing surgery. A positive screening should identify the relevant antibodies, and the patient should receive an appropriate antigen-negative RBC concentrate, which will minimize the hemolytic risk.

Various factors contribute to the development of alloimmunization: population heterogeneity, age at the first antigenic stimulus, antigenic difference between the donor and the recipient, the immune status of the recipient, the immunomodulatory effect of allogeneic blood transfusion on the immune status of the recipient, even possible splenectomy. The likelihood of alloimmunization is directly related to the number and frequency of transfusions, the immunogenicity of the antigen, and the immune response of the recipient.

References

Achargui S, Zidouh A, Abirou S, Merhfour FZ, Monsif S, Amahrouch S, El Ghobre A, El Halhali M, Temmara H, El Hryfy A, Motqi M, Satty A, Kandili M, Aghri M, Hajjout K, Benajiba M (2017) Identification of alloantibodies and their associations: Balance sheet of 3 years at the Regional Center of Blood Transfusion in Rabat/Morocco and difficult in transfusion management. Clinical Biology 24(4): 422–430. https://doi.org/10.1016/j.tracli.2017.04.006

Ansari S, Voosogh P, Mosthaghian S (2008) Assessment of frequency of allo immunization and erythrocyte alloimmunisation in transfusion dependent thalassemia patients. Acta Medica Iranica 46: 137–140.

Atanassov T, Todorova K, Tsvetanov A (2023) First case of robotic-assisted bariatric surgery in Bulgaria – Robotic-assisted sleeve gastrectomy. Bulgarian Society of Medical Sciences Journal 3(3): 233–240.

Hauser RG, Esserman D, Karafin MS, Tan S, Balbuena-Merle R, Spencer BR, Roubinian NH, Wu Y, Triulzi DJ, Kleinman S, Gottschall JL, Hendrickson JE, Tormey CA (2020) [for the NHLBI Recipient Epidemiology and Donor Evaluation Study-III (REDS-III)] The evanescence and persistence of RBC alloantibodies in blood donors. Transfusion 60(4): 831–839. https://doi.org/10.1111/trf.15718 [Epub 2020 Feb 15. PMID: 32061102]

Lackovic SJ, Custendil SD, Zabic A, Mahmutovic AS, Smajic SC, Husni AO (2023) Significance of Detecting Antierythrocyte Antibodies in Pretransfusion Testing. Acta Informatica Medica 31(2): 121–125. https://doi.org/10.5455/aim.2023.31.121-125

Politou M, Valsami S, Dryllis G, Christodoulaki M, Cheropoulou C, Pouliakis A, Baka M, Stamoulis K (2020) Retrospective Study on Prevalence, Specificity, Sex, and Age Distribution of Alloimmunization in Two General Hospitals in Athens. Turkish Journal of Haematology 37(3): 154–166. https://doi.org/10.4274/tjh.galenos.2020.2019.0459

Pons S, Poirrier L, Fleuriot E, Martinaud C (2023) Prevalence of red blood cell alloantibodies among blood donors in the French Military Blood Institute: A 10-year retrospective study First published. Vox Sanguinis 118(12): 1100–1104. https://doi.org/10.1111/vox.13537

Reverberi R (2008) The persistence of red cell alloantibodies. Blood Transfusion 6(4): 225–234. https://doi.org/10.2450/2008.0021-08 [PMID: 19112738; PMCID: PMC2626905]

Roopam J, Perkins J, Susan JT, Choudhury NA (2009) A prospective study for detection and identification of red cell allo-antibodies in multiply transfused thalassemia major patients: 34th National Congress of Indian Society of Blood Transfusion and Immunohaematology, 20–22.

Shukla JS, Chaudhary RK (1999) Red cell alloimmunization in multi-transfused chronic renal failure patients undergoing hemodialysis. Indian Journal of Pathology & Microbiology 42: 299–302.

Sood R, Makroo RN, Riana V, Rosamma NL (2013) Detection of alloimmunization to ensure safer transfusion practice. Asian Journal of Transfusion Science 7: 135–139. https://doi.org/10.4103/0973-6247.115577

Usman M, Moin S, Moinuddin M, Saeed A, Perveen R, Azmi MA (2011) Frequency of red cell alloimmunization among patients with transfusion dependent beta thalassemia in Pakistan. International Journal of Hematologic Oncology 21: 166–169.