Incidence of Red Cell Alloantibody among the Transfusion Recipients of Universiti Kebangsaan Malaysia Medical Centre

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Abstract Red blood cell alloimmunization is a common complication among the transfusion recipients. In Malaysia, multiple ethnicity causes genetic heterogeneity among the population which in turn can cause a wide variation of antibody. The objective of this study was to analyse the red cell alloantibody detected during the pre-transfusion testing. This was a cross-sectional study done in the blood bank of Universiti Kebangsaan Malaysia Medical Centre during the period of January–December 2010. The data was retrieved from the hospital laboratory information system. A total of 24,263 patients' blood samples were subjected for pre-transfusion testing. Antibody screening was done using an indirect antiglobulin test method. The positive samples were further identified for antibody specificity. Antibody screening tests were positive in 184 patients out of 24,263 samples with the incidence of 0.76 %. Autoantibodies and alloantibodies were detected in 39/184 (21.2 %) and 140/184 (76.1 %) of the patients respectively. In five patients (2.7 %) the antibody specificity remained undetermined. Total 161 alloantibodies were identified. The suspected Anti-Mia alloantibody was observed most frequently (49/161, 30.4 %) followed by anti-E (30/161, 18.6 %) and anti-D (22/161, 13.7 %). Anti-E and anti-c were the most common combination of multiple alloantibodies. In view of the high incidence of suspected Anti-Mia antibodies, more efforts are needed to look into the techniques for confirmation of the Anti-Mia antibodies. Besides that, we suggested that all multiply

transfused patients should be phenotyped for the Rh system and to supply Rh phenotype specific blood in order to limit alloimmunization.

Keywords Red cell antibody · Alloimmunization · Transfusion recipient · Antibody specificity

Introduction

Red blood cell alloimmunization is a common complication among the transfusion recipients [1]. Immune response due to genetic difference between the blood donor and the recipient induces the formation of alloantibody. The other factors that influence alloantibody formation are the recipient's immune status as well as the dose, route of administration and the immunogenicity of the antigen [2–4]. The rate of RBC alloimmunization has been reported in the range of 5–30 % among the multiply transfused patients [5–7]. This red cell alloimmunization may lead to difficulty in finding compatible blood for transfusion or even can cause severe haemolytic transfusion reaction if the antibody titre remain weak, undetected or missed during pre-transfusion compatibility testing [8, 9].

Autoantibodies are directed against a patient's self antigen and presence of autoantibodies may mask the co-existing alloantibodies. In addition, autoantibodies can be associated with clinically significant warm autoimmune haemolytic anaemia [10].

Therefore, routine pre-transfusion testing is one of the important safety measures to detect the unexpected red cell antibody in the patient's serum to prevent the immediate and delayed haemolytic transfusion reaction [11]. Rh and Kell antibodies are most frequently found in alloimmunized patients in Western Europe and United States [12].

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In Malaysia, multiple ethnicity of the population has caused genetic heterogeneity among the population which in turn led to a wide variation of antibody specificity among the population. The objective of this study was to analyse the frequency and specificity of the red cell antibody detected during the pre-transfusion testing among the transfusion recipients of Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

Materials and Methods

This cross-sectional study was done in the Blood Bank Unit of UKM Medical Center by retrieving the data from the hospital laboratory information system as well as the hard copies of the pre-transfusion testing results performed from January 2010 to December 2010. We examined all patients with newly detected RBC antibodies. During this period, a total of 24,263 patients' blood samples were subjected for pre-transfusion testing. The pre-transfusion testing were done following the American Association of Blood Bank standard which consists of identification of the recipient and blood specimen collected, ABO and Rh D typing, antibody screening, antibody identification and comparison of the previous record and current results of the recipient, confirmation of the ABO and Rh D typing of the red cell components, selection of blood components of appropriate ABO and Rh D types and performing the crossmatching and labeling of the product with the recipients identifying information [13]. The antibody screening and crossmatching were done by indirect antiglobulin test, performed by gel agglutination technique using Diamed gel cards. For antibody screening, 3-cell screening panels (Diamed ID-Dia cell) were used. The positive results were then further identified for antibody specificity by the Diamed ID-Dia Panel (11 cell panel), including the use of enzyme treated cells (papain) at 37 °C and AHG phase.

For those 57 cases that were positive for the Mia antigen positive cell in the Diamed ID-Dia 3-cell screening panels, but negative for the Diamed ID-Dia 11-cells identification panel, the cases were subjected to further antibody identification using the CSL antibody identification panels which consist of cells positive for MUT and Mur antigens. The antibody was labeled as suspected Anti-Mia only if the antibody identification using the CSL panel cells showed negative results.

In some cases, tests were performed at 4 and 22 °C in suspected cold antibody cases depending on clinical information and other laboratory findings. Direct Coombs' test was performed using polyspecific AHG on the patient's red cell followed by monospecific test in the positive cases. Elution and adsorption methods were commenced in patients with suspected autoantibodies to specify the autoantibody and to look for possible underlying alloantibody specificity.

For any unresolved antibody and also all the cases of suspected Anti-Mia antibody, the samples were also sent to the reference laboratory at National Blood Centre for further identification.

We analysed all the red cell antibodies and calculated the incidence of clinically significant red cell alloantibodies.

Results

During the study period, a total of 184 patients were presented with 206 irregular antibodies out of total 24,263 patients' samples with the incidence of 0.76 %. Table 1 describes the different types of the unexpected antibody among the 184 patients. Direct Coombs' test was positive in 39/184 (21.2 %) of the patients, auto IgG and cold agglutinin were identified either alone or in combination were seen in 37/184 (20.1 %). Red cell alloantibodies were detected in 140/184 (76.1 %) of the patients and a combination of auto and alloantibodies were identified in 2/184 (1.1 %) patients. The total numbers of autoantibodies and alloantibodies identified from these 184 patients were 40 and 161 respectively. In five patients, their antibodies remained undetermined (2.7 %) where no specificity was identified.

Table 2 describes the specificity of the unexpected antibody among the 184 patients. 165 patients (89.7 %) had developed single red cell antibody, 16 patients (8.7 %) had a mixture of two antibodies and three patients (1.6 %) had three antibodies. Among the single red cell antibodies identified, Anti-Mia was the most common alloantibody detected (48/165, 29.1 %) followed by anti-D (21/165, 12.8 %) and anti-E (19/165, 11.5 %). By using the CSL antibody identification panel, we have identified 7/165 (4.2 %) of anti-MUT and 1/165 (0.6 %) of anti-Mur. Anti-P1 (6/165, 3.6 %) was the most common cold alloantibody identified followed by anti-M (3/165, 1.8 %). Of the multiple antibodies detected, anti-E and anti-c were the most common combination found. Among the autoantibodies detected, warm reactive auto IgG antibodies (15.2 %) were most common followed by cold agglutinins (6.5 %). Majority of the autoantibodies detected were single antibody except for one case where auto IgG and cold agglutinin were detected and in another two cases, auto IgG and also anti-E antibody were identified.

Table 3 is showing the specificities of the alloantibodies in 140 patients and there relationship with blood transfusion. For those patients with single alloantibody, the suspected Anti-Mia alloantibody was the most frequently identified (48/140, 34.3 %) followed by anti-D (21/140, 15 %) and anti-E (19/140, 13.6 %). The confirmed anti-MUT and anti-Mur constituted 5 % and 0.7 % of the single alloantibodies identified. The other clinically significant

Table 1 Distribution of 206 unexpected antibodies among 184 patients

Unexpected antibody	Total patient		Total antibody	
	Number	Percent	Number	Percent
Autoantibody only				
Single	36	19.6	36	17.5
Two	01	0.5	02	1.0
Alloantibody only				
Single	124	67.4	124	60.2
Two	13	7.1	26	12.6
Three	03	1.6	09	4.4
Mixed auto and alloantibody				
Two	2	1.1	4	1.9
No specificity				
Single	5	2.7	05	2.4
Total	184	100	206	100

alloantibodies were listed in Table 3. As for the multiple alloantibodies cases, 13 patients were identified with two alloantibodies and 3 patients with 3 alloantibodies. Combination of anti-E and anti-c was the most frequent multiple alloantibodies identified with 5.0 % followed by anti-Le^a and anti-Le^b of 1.4 %. Of these 140 patients, 68 (48.6 %) have previous histories of blood transfusion, 56 (40.0 %) without history of transfusion and no information available

for the remaining 16 (11.4 %). As for the patients without the history of transfusion, 48 (34.3 %) are female patients.

Discussion

This cross-sectional study was undertaken to determine the prevalence and specificity of RBC alloantibodies among the transfusion recipients of UKMMC. Alloantibodies arise in the patient's blood after exposure to foreign red cells by pregnancy, transfusion or transplantation. Red cell alloantibody formation complicates the transfusion therapy in which corresponding antigen negative matched blood is required for safer transfusion. Sometimes these alloantibodies may become undetectable over time and endanger the future transfusion in which these patients can develop delayed haemolytic transfusion reaction due to anamnestic antibody production after blood transfusion. [3, 8].

Here the positive antibody screening results were found in 0.76 % (184/24,263) of pre-transfusion samples. Previous study in Malaysia by Nadarajan et al. showed that the incidence of antibody screening positive cases was 1.4 % of pre-transfusion samples [14]. In their study, 1,297 antibody positive screening results were detected out of 89,629 pre-transfusion samples. Our study findings are relatively low. Comparatively smaller sample size could be the reason for this low frequency. The antibody prevalence

Table 2 Distribution of specificity of unexpected antibody among 184 alloimmunized patients

Single antibody specificity		Two antibody specificity		Multiple antibody specificity	
Name	Number	Name	Number	Name	Number
Suspected Anti-Mia	48	Anti-E+c	7	Anti-E+c+N	1
Anti-D	21	Anti-E+Jk ^a	1	Anti-D+C+Jk ^a	1
Anti-E	19	Anti-E+IgG	2	Anti-L ^a + ^b +P1	1
Anti-c	01	Anti-C+e	1		
Anti-Jk ^a	07	Anti-Le ^a +Le ^b	2		
Anti-MUT	07	Auto IgG+cold agglutinin	1		
Anti-S	04				
Anti-Jk ^b	01	Anti-Mia+Di ^a	1		
Anti-e	01	Anti-Jk ^a +P ₁	1		
Anti-Fy ^b	01				
Anti-P1	06				
Anti-M	03				
Anti-N	02				
Anti-Le ^a	02				
Anti-Mur	01				
Auto IgG	25				
Cold auto agglutinin	11				
No specificity	05				
Total	165 (89.7%)		16 (8.7%)		03 (1.6%)

Table 3 Transfusion history and gender distribution of 140 patients with alloantibody (n = 140)

Antibody specificity	Frequency n (%)	Transfusion history (n)								
		Yes			No			NA		
		M	F	Total	M	F	Total	M	F	Total
Single										
Anti-Mia	48 (34.3)	10(7.1)	14(10)	24(17.1)	5(3.6)	14(10)	19(13.6)	02(1.4)	03(2.2)	05(3.6)
Anti-MUT	07 (5.0)	01(0.7)	04(2.9)	05(3.6)	0	0	0	0	02(1.4)	02(1.4)
Anti-Mur	01 (0.7)	01(0.7)	0	01(0.7)	0	0	0	0	0	0
Anti-E	19 (13.6)	06(4.3)	08(5.7)	14(10.0)	0	05(3.6)	05(3.6)	0	0	0
Anti-D	21 (15.0)	0	01(0.7)	01(0.7)	0	20(14.3)	20(14.3)	0	0	0
Anti-c	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Anti-Jk ^a	07 (5.0)	01(0.7)	02(1.4)	03(2.2)	0	0	0	01(0.7)	03(2.2)	04(2.9)
Anti-P1	06 (4.3)	0	02(1.4)	02(1.4)	01(0.7)	02(1.4)	03(2.2)	01(0.7)	0	01(0.7)
Anti-S	04 (2.9)	01(0.7)	01(0.7)	02(1.4)	0	01(0.7)	01(0.7)	0	01(0.7)	01(0.7)
Anti-jkb	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Anti-e	01 (0.7)	0	0	0	0	01(0.7)	01(0.7)	0	0	0
Anti-Le ^a	02 (1.4)	0	01(0.7)	01(0.7)	0	01(0.7)	01(0.7)	0	0	0
Anti-M	03 (2.2)	0	01(0.7)	01(0.7)	0	0	0	01(0.7)	01(0.7)	02(1.4)
Anti-N	02 (1.4)	01(0.7)	0	01(0.7)	01(0.7)	0	01(0.7)	0	0	0
Anti-Fy ^b	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Two										
Anti-E+c	07 (5.0)	02(1.4)	02(1.4)	04(2.9)	0	03(2.2)	03(2.2)	0	0	0
Anti-Le ^a +Le ^b	02 (1.4)	0	01(0.7)	01(0.7)	0	01(0.7)	01(0.7)	0	0	0
Anti-Mia+Anti-Di ^a	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Anti-E+Jk ^a	01 (0.7)	0	0	0	0	0	0	01(0.7)	0	01(0.7)
Anti-C+e	01 (0.7)	01(0.7)	0	01(0.7)	0	0	0	0	0	0
Anti-Jk ^a +P1	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Three										
Anti-E+c+N	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Anti-D+C+Jk ^a	01 (0.7)	0	01(0.7)	01(0.7)	0	0	0	0	0	0
Anti-Le ^a + ^b +P1	01 (0.7)	0	0	0	01(0.7)	0	01(0.7)	0	0	0
Total	140 (100)	24(17.1)	44(31.4)	68(48.6)	08(5.7)	48(34.3)	56(40.0)	06(4.3)	10(7.1)	16(11.4)

rate is variable among different population. It is approximately 0.8 % in the blood donors and 1–2 % in hospital based patients [15].

In this study, single alloantibody was found most frequently. The Anti-Mia has been observed with the greatest frequency (48/165, 29.1 %) among these alloantibodies. Recent study in Taiwan also showed similar result where Anti-Mia was the most frequently occurring alloantibody [9]. In Caucasians, this phenotype is very rare with the incidence of less than 0.01 % [16] but the incidence ranging from 2 to 88 % in East Asian populations [17]. Prathiba et al. [18] showed that Anti-Mia antibodies were the third most commonly occurring antibody detected in general and antenatal patients in Malaysia. They have identified 77 Anti-Mia antibodies out of 33,716 specimens. The significance of Anti-Mia could not be underestimated as there have been reports of clinically significant

Haemolytic Transfusion Reaction and Haemolytic Disease of Foetus and Newborn by IgG class antibodies against these vMNS antigens [19, 20]. All these studies insisted the necessity of proper detection of vMNS antibody in the antenatal cases or during pre-transfusion testing.

The second most common alloantibody detected in this study was anti-E and this result is consistent with other studies. Study in Eastern Taiwan and Greece showed that anti-E was the second most common alloantibody [9, 21]. In Malaysia, study by Nadarajan et al. and Haslina MNN et al. also showed similar findings [14, 22].

Total of 19 patients were identified as having a multiple antibodies including 16 patients with a mixture of two antibodies and 3 patients with three antibodies. Anti-E and anti-c were found to be the most common combination of multiple alloantibodies. This result is similar to the results of other studies [9, 23, 24]. It was reported that in

alloimmunized patients, the probability of additional antibody formation increases approximately three fold [25]. This report alerts us that the multiply transfused patients with single alloantibody are at risk of developing multiple alloantibodies in further course of time.

When we investigated the relationship between transfusion and the alloimmunization, we found that 68 (48.6 %) patients out of 140 have previous history of transfusion of one or more units of red cell which most likely be the cause of the red cell alloimmunization. In 56 patients (40 %), there were no previous history of transfusion, however, 48 of these patients (34.3 %) are females whom might have been sensitized during the pregnancies, and the remaining 16 patients (11.4 %), the history of transfusion were not known. Tormey CA et al. [15] showed that the frequency of alloantibody is higher among the transfusion recipients of one or more units of red cell transfusion, approximately 2–9 % forms new alloantibody. The highest alloimmunization rate is approximately 9–30 % which is among the patients receiving chronic transfusion therapy such as thalassaemia patients, haematological malignancy patients or sickle cell anaemia patients. Haslina MNN [22] showed that the rate of alloimmunization among the Malay thalassaemia patients were 8.6 % while in Iran it was documented as 5.7 % and in Taiwan it was as high as 37 % [7]. Heterogeneity among the population and sensitivity of the test method can cause a variation of alloimmunization rate.

Schonewille H [23] suggested in a previous study to match the red cell phenotype other than ABO and D (e.g C, E, c and K) among the transfusion dependent patients in an attempt to prevent alloimmunization. However, the cost effectiveness of this red cell phenotype and the doubt whether this truly adds benefit to the patient made this policy a matter of debate. One study by Singer et al. stated that patients who received blood matched for Rhesus and Kell system from their first transfusion, have relatively lower rate of alloimmunization among them [2]. In western countries, 10 % of Caucasian population has K antigen which causes Kell antibodies as a frequently detected antibodies besides Rh antibodies [26]. So, the strategy to match Rh and Kell system could be effective for them. It is reported that in East Asian countries, more than 99 % populations are Kell negative [27]. Hence, the chance of formation of this antibody is very low in Malaysia. Our study also did not detect any anti-K antibody which is consistent with this report. So Kell antigen matching will not be cost-effective here. Due to greater prevalence of anti-E, we would like to suggest to phenotype those multiply transfused patients for Rh phenotype and transfuse them with blood matched with the Rh system in addition to ABO and D antigen.

Frequency of anti-D detected in our study was 13.7 % (22/161) and all of them are female patients. Most of the anti-D (n = 20) detected were due to passive immunization by anti-D prophylaxis given routinely during antenatal period to Rh D negative mothers. Only two patients detected to have alloanti-D. In Malaysia, it is a standard practice to phenotype the Rhesus system and supply phenotype compatible RBC for Rh D negative patients, so anti-D formation as a consequence of blood transfusion is rare. For pregnant women, anti-D immunoglobulin prophylaxis is routinely given at antenatal and at postnatal period. All these factors have caused the decline in alloanti-D formation in our population. However, antenatal anti-D prophylaxis has led to increase in positive antibody screening tests and without detailed information provided by the clinicians, this has led to more work load and delay in blood supply for the patients.

The least common clinically significant alloantibody detected in our study was anti-Jk^b, anti-Fy^b, anti-C, and anti-e. The specificity of the cold antibodies detected was against antigens P1, Lewis, MN blood group system.

Conclusion

This study demonstrated that suspected Anti-Mia was the most frequently detected alloantibody followed by anti-E, anti-D, anti-Jk^a and anti-c antibody among the transfusion recipients in UKMMC. In view of the high incidence of detecting these suspected Anti-Mia antibodies, more efforts are needed to look into developing the simple methods for confirmation of anti-vMNS antibodies as well as to phenotype the vMNS antigen. Furthermore, we would like to recommend that all multiply transfused patients must be phenotyped for the Rh system and be supplied with Rh phenotype specific blood for transfusion in order to limit the Rhesus system alloimmunization.

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References

1. Walker RH, Lin DT, Hatrick MB (1989) Alloimmunization following blood transfusion. *Arch Pathol Lab Med* 113:254–261
2. Singer ST, Wu V, Mignacca R, Kuypers FA, Morel P, Vichinsky EP (2000) Alloimmunization and erythrocyte autoimmunization in transfusion dependent thalassemia patients of predominantly asian descent. *Blood* 96:3369–3373
3. Bilwani F, Kakepoto GN, Adil SN, Usman M, Hassan F, Khurshid M (2005) Frequency of irregular red cell alloantibodies in patients with thalassemia major: a bicenter study. *J Pak Med Assoc* 55:563–565

4. Schonewille H, van de Watering LMG, Loomans DSE, Brand A (2006) Red blood cell alloantibodies after transfusion: factors influencing incidence and specificity. *Transfusion* 46:250–256
5. Blumberg N, Peth K, Ross K, Avila E (1983) Immune response to chronic red blood cell transfusion. *Vox Sang* 44:212–217
6. Fluit CRMG, Kunst VA, Drenthe-Schonk AM (1990) Incidence of red cell antibodies after multiple blood transfusions. *Transfusion* 30:530–535
7. Natukunda B, Schonewille H, van de Watering L, Brand A (2010) Prevalence and specificities of red blood cell alloantibodies in transfused Ugandans with different diseases. *Vox Sang* 98:167–171
8. Lee CK, Ma ESK, Tang M, Lam CCK, Lin CK, Chan LC (2003) Prevalence and specificity of clinically significant red cell alloantibodies in Chinese women during pregnancy—a review of cases from 1997 to 2001. *Transfus Med* 13:227–231
9. Jan RH, Yu LC, Wen SH, Tsai SS, Lin TY (2009) Incidence of alloantibodies in transfused patients in Eastern Taiwan. *Tzu Chi Med J* 21:66–69
10. McNerney ME, Baron BW, Volcheboum SL, Papari M, Keith M, Williams K, Richa E (2010) Development of warm auto and alloantibodies in a 3-year old boy with Sick cell haemoglobinopathy following his first transfusion of a single unit of red blood cells. *Blood Transfus* 8:126–128
11. Makarovsk-Bojadzieva T (2004) Blood group antibodies that cause problems in pretransfusion testing. *Blood Banking Transfus Med* 2:89–93
12. Redman M, Regan F, Contreras M (1996) A prospective study of the incidence of red cell alloimmunization following transfusion. *Vox Sang* 71:216–220
13. Downes KA, Shulman IA (2008) Pre transfusion testing. In: Roback JD, Rae Combs M, Grossman BJ, Hillyer CD (eds) American association of blood banks technical manual, 16th edn. Bethesda, Maryland, pp 437–438
14. Nadarajan SN, Hlaing AA, Maung TH, Jeyajoti I, Kyu TN, Ranjana KJ, Myint AA (2007) Incidence of red cell alloantibodies in a multi-ethnic hospital patient population. *Vox Sang* 93:63–64
15. Tormey CA, Fisk J, Stack G (2008) Red blood cell alloantibody frequency, specificity and properties in a population of male military veterans. *Transfusion* 48:2069–2076
16. Wu KH, Chang JG, Lin M, Shih MC, Lin HC, Lee C, Peng T, Tsai CH (2002) Hydrops foetalis caused by anti-Mur in first pregnancy—a case report. *Transfus Med* 12:325–327
17. Heathcote DJ, Carroll T, Wang JJ, Flower R, Rodionov I, Tuzikov A, Bovin N, Henry S (2010) Novel antibody screening cells, MUT+Mur codeocytes, created by attaching peptides onto red blood cells. *Transfusion* 50:635–641
18. Prathiba R, Lopez CG, Usin FM (2002) The prevalence of GP Mur and anti-“Mia” in a tertiary hospital in peninsular Malaysia. *Malays J Pathol* 24:95–98
19. Broadberry RE, Lin M (1994) The incidence and significance of anti-“Mia” in Taiwan. *Transfusion* 34:349–352
20. Lin CK, Mak KH, Szeto SC, Poon KH, Yuen CMY, Chan NK, Liu HW, Ng CP (1996) First case of haemolytic disease of the newborn due to anti-Mur in Hong Kong. *Clin Lab Haematol* 18:19–22
21. Bezirgiannidou Z, Martinis G, Theodoridis M, Terzoude V, Nannou S, Paganiani K (2005) Retrospective review of alloimmunization frequency in the patients of north eastern Greece. *Vox Sang* 89:140
22. Haslina MNN, Ariffin N, Hayati II, Rosline H (2006) Red cell immunization in multiply transfused Malay thalassemic patients. *Southeast Asian J Trop Med Public Health* 37:1015–1020
23. Schonewille H, Haak HL, van Ziji AM (1999) Alloimmunization after blood transfusion in patients with hematologic and oncologic diseases. *Transfusion* 39:763–771
24. Lin-Chu M, Broadberry RE, Chang FJ (1988) The distribution of blood group antigens and alloantibodies among Chinese in Taiwan. *Transfusion* 28:350–352
25. Guastafierro S, Sessa F, Cuomo C, Tirelli A (2004) Delayed hemolytic transfusion reaction due to anti-S antibody in patient with anti-Jk^a autoantibody and multiple alloantibodies. *Ann Hematol* 83:307–308
26. Patel J, Shukla R, Gupte S (2009) Red cell alloimmunization in multitransfused patients and multiparous women. *Indian J Hematol Blood Transfus* 25:49–52
27. Reid ME, Lomas-Francis C (2007) Blood group antigens and antibodies. A guide to clinical relevance and technical tips SBB Books, New York