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Original Research Article

Red Blood Cells (RBC) Alloantibodies in Multi-Transfused Chronic Kidney Disease (CKD) Patients

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Abstract:

Background: To determine the prevalence of Red Blood Cells (RBC) alloantibodies in multi-transfused chronic kidney disease (CKD) patients

Methods: Present study was conducted in the Department of Immuno-Haematology and Transfusion Medicine, S.P. Medical College and P.B.M. Associated Group of Hospitals, Bikaner.

Results: The distribution of alloantibodies across ABO blood groups revealed that the anti-C antibody was found in a patient with blood group A, while the anti-E antibody was detected in a patient with blood group O. No alloantibodies were observed in patients with blood groups B or AB, suggesting that the occurrence of alloimmunization was not confined to a specific blood group. Furthermore, the strength of the Indirect Antiglobulin Test (IAT) reactions indicated moderate (2+) reactivity for anti-C and stronger (3+) reactivity for anti-E, reflecting variable yet clinically significant immune responses.

Conclusion: The study highlights a middle-aged, male-dominated cohort of multi-transfused CKD patients, predominantly Rh-positive and with blood groups O and B being most common. Despite repeated transfusions, 2 cases of alloimmunization were observed, as evidenced ICT positive and all (100%) cases of DCT had negative results.

Keywords: CKD, ICT, DCT.

Introduction

The transfusion of blood and blood components has become an integral part of patient management in modern medicine. As a result, the blood transfusion services play an important role and are responsible for ensuring sufficient quality and safe blood supply. Blood transfusion is crucial for managing patients with hematologic disorders and malignancies, as they often need blood during their illness or over their lifetime [1].

Blood transfusion is an integral part of the management of patients with chronic kidney disease (CKD) as severe anaemia is a feature of the late stages [2]. Chronic Kidney disease (CKD) is defined either as kidney damage/injury for ≥ 3 months and/or glomerular filtration rate (GFR) <60ml/ min per 1.73m2 for ≥ 3 months with or without kidney damage. It is usually accompanied by features of uraemia, and a need for renal replacement therapy (which includes haemodialysis and/or kidney transplant) in its later stages [3-5]. Management of renal anaemia include the use of erythropoiesis-stimulating agents (ESAs), blood transfusion as well as replacement of iron and other nutritional supplements. The decision to treat a patient with either an ESAs or blood transfusion is made on the threshold for transfusion. A high threshold includes a low haemoglobin level, usually less than 10g/dl or the presence of cardiac decompensation [4,5]. In severe anaemia, immediate management may be blood transfusion to correct the anaemia in the short term. However, blood transfusion especially when given repeatedly may increase the risk of red cell alloimmunization [6].

CKD patients in need of RBC transfusions are preferential targets of post-transfusion alloimmunization. At each transfusion, the patient is exposed to new foreign antigens, eventually becoming alloimmunized against RBC antigens. Due to the presence of contaminating leukocytes in blood products, patients may also become sensitized to antigens of the human leukocyte antigen (HLA) system [7]. As a result, RBC alloimmunization may limit the availability of compatible blood for future transfusions, whereas the development of leukocyte

alloimmunization often makes it necessary to postpone transplantation [8].

Repeated Blood transfusion, common in CKD Patient increase the likehood of developing antibodies. Understanding the relationship between frequent transfusion and alloimmunization can guide better transfusion practices and protocols, potentially reduced the incidence of alloimunization. By identifying and addressing alloimmunization we can improve overall patient outcome. [9]

Alloimmunization is defined as the development of antibodies in response to alloantigen after exposure to genetically different cells or tissue. Many factors can influence the development of alloantibodies in the blood. Studies have shown that alloimmunization is influenced by the recipient's immune status, the dose of blood transfused, and the immunogenicity of the antigen [10].

Materials and Methods

Study Place: Department of Immuno-haematology and Transfusion Medicine Sardar Patel Medical College and Associated Groups of Hospitals, Bikaner, Rajasthan, India.

Study Design: Cross-sectional observational study.

Study Population: All multi transfused CKD patients who are admitted in Department of Medicine and Nephrology required blood transfusion including Inclusion and exclusion criteria.

Sample Size: All multi-transfused CKD patients who are admitted in Department of Medicine and Nephrology requiring blood transfusion. During the study period which 1st January 2024 to 31st December 2024, a total of 200 patients were screened.

Inclusion Criteria

- CKD Patients admitted in Department of Medicine and Nephrology and receiving at least more than one unit of PRBC transfusion.
- Patients who gave consent to participate in this study.

Exclusion Criteria

- Patients not meeting the above inclusion criteria.
- Who didn't give consent.

Data Analysis: Collected data were entered into Microsoft Excel were presented in the form of tables, figures, graphs, diagrams. Appropriate statistical tests wherever necessary was applied using SPSS software for statistical analysis version 26.00.

Observations: The study population consists of 200 cases, divided into four distinct age groups. The majority of participants fall within the 41–60 years age bracket, accounting for 81 cases (40.5%), indicating this age range is the most affected or represented in the sample. The 21–40 years group follows with 65 cases (32.5%), suggesting a significant proportion of middle-aged adults. Individuals aged over 60 years represent 47 cases (23.5%), reflecting a notable elderly population in the study. The youngest age group (<20 years) includes only 7 cases (3.5%), indicating minimal representation of adolescents or young adults. The gender-wise distribution of the study population reveals a marked male predominance. Out of the total 200 cases, 128 (64.0%) were male and 72 (36.0%) were female. This indicates that nearly two-thirds of the participants were male, with a male-to-female ratio of approximately 1.78:1. All 200 participants (100.0%) had a history of previous blood transfusion, indicating that this was a common factor among the entire study population. This uniformity suggests that blood transfusion may be a key inclusion criterion or a significant common risk factor in the context of the study. Regarding the history of dialysis, 165 cases (82.5%) had undergone dialysis, while 35 cases (17.5%) had not. This highlights that a large majority of the participants were on dialysis, which may reflect the severity or chronicity of the underlying condition. The predominance of dialysis among participants suggests that renal impairment could be a major comorbidity or clinical focus in this population. The most common blood group observed was O, found in 70 cases (35.0%), followed by blood group B, which was present in 61 cases (30.5%). Blood group A was noted in 51 participants (25.5%), while blood group AB was the least common, seen in 18 cases (9.0%). The Rh status distribution among the 200 participants reveals a clear predominance of Rh-positive individuals, accounting for 183 cases (91.5%). In contrast, Rh-negative status was observed in only 17 cases (8.5%).

Table 1: Distribution of Cases according to IAT

IAT	No. of Cases	Percentage
Positive	2	1.0
Negative	198	99.0
Total	200	100

The Indirect Antiglobulin Test (IAT) results for the 200 study participants show that 198 (99%) tested negative, while only 2(1%) were positive cases reported.

This finding indicates the absence of detectable alloantibodies in the participants' serum at the time of testing. A negative IAT suggests that there is no immune sensitization against red blood cell antigens, which is particularly relevant in contexts such as blood transfusion compatibility, pregnancy-related Rh incompatibility, or immune-mediated hemolytic conditions. The uniform negativity across the cohort may also reflect effective screening and transfusion practices.

Table 2: Frequency of Alloimmunization in CKD Patients

Status	No. of cases	Percentage
Positive (3-cell screening)	2	1.0
Negative (3- cell screening)	198	99.0
Total	200	100

Out of these, only 2 cases (1.0%) tested positive for irregular antibodies, indicating the presence of alloantibodies detected by the 3-cell screening method. The remaining 198 cases, accounting for 99.0% of the total, showed negative results, suggesting no detectable alloantibodies in those samples. This distribution highlights the low prevalence of alloimmunization in the studied population based on this screening method.

Table 3: Antibody specificities of alloimmunised CKD patients

Antibody	No. of Cases	% of total population studied (n=200)
Anti-C	1	0.5%
Anti-E	1	0.5%
Total	2	1.0%

Two distinct antibodies were detected. One case (0.5%) was positive for anti-C, and another case (0.5%) was positive for anti-E. Together, these accounted for a total of 2 cases, representing 1.0% of the total study population. This finding indicates that alloimmunization was infrequent in the studied group, with each detected antibody occurring in only a single individual.

Table 4: Blood group and antibody specificity

Blood Group	Anti-C	Anti-E
A	1	0
B	0	0
O	0	1
AB	0	0

The distribution of specific alloantibodies—anti-C and anti-E—according to the ABO blood groups among the study population. One individual with blood group A was found to have anti-C antibody, while one individual with blood group O had anti-E antibody. No alloantibodies were detected in individuals with blood groups B and AB. This suggests that the occurrence of alloantibodies in this study was limited and showed no significant clustering within any particular blood group, with isolated cases observed in groups A and O only.

Table 5: IAT Strength and antibody correlation (Gel Card)

IAT Strength	Anti C	Anti E
2+	1	0
3+	0	1
4+	0	0
Total	1	1

presents the strength of Indirect Antiglobulin Test (IAT) reactions for the detected alloantibodies—anti-C and anti-E. The anti-C antibody showed a reaction strength of 2+ in one case, indicating a moderate level of antibody-antigen interaction. On the other hand, the anti-E antibody demonstrated a stronger reaction with an IAT strength of 3+ in one case. No cases were observed with a reaction strength of 4+. Overall, each antibody was identified in one case, with varying reaction intensities, reflecting individual variability in immune response.

Discussion

Present study was conducted in the Department of Immuno-Haematology and Transfusion Medicine, S.P. Medical College and P.B.M Associated Group of Hospitals, Bikaner.

In present study, the bulk of multi-transfused chronic kidney disease (CKD) patients were aged 41–60 years (40.5%), followed by 21–40 years (32.5%), those >60 years (23.5%), and a small minority under 20 years (3.5%). This distribution

underscores CKD's prominence in middle-aged and older adults, likely due to prolonged exposure to chronic conditions like hypertension and diabetes.

A comparable retrospective study of hemodialysis patients found an alloimmunization prevalence of 9.8% among 81 multi-transfused CKD patients (mean ~8.5 units transfused), further noting that alloantibodies mostly belonged to Rhesus and Kell groups, corroborating the middle-aged patient profile [27]. Similarly, a systematic review and meta-analysis of 44 Indian studies reported an overall alloimmunization rate of 4.8% among multi-transfused patients, with anti-E and anti-c as the most prevalent antibodies [11]. Another cross-sectional analysis from Nigeria, though in a different setting, registered a 3.2% alloimmunization rate among 124 multi-transfused CKD patients, echoing the antigen-specific pattern (anti-E) noted in Indian cohorts [12].

In this study of 200 CKD patients, the alloimmunization rate was 1.0%, with one case each of anti-C and anti-E detected via 3-cell antibody screening. Both belong to the highly immunogenic Rh system, which is frequently implicated in red cell alloimmunization. This low prevalence is in line with findings among multi-transfused patient populations in India. For example, a retrospective study of 200 multi-transfused patients reported a 5.5% overall alloimmunization rate, with roughly 73% of antibodies targeting Rh antigens [13]. Likewise, a study at a Western India tertiary care center found the majority of alloantibodies among multi-transfused patients also belonged to the Rh system [14]. These observations reinforce the consistency of our antibody profile—centered on the Rh system—across varied transfusion-dependent cohorts.

The comparatively lower alloimmunization rate in our CKD population versus broader multi-transfused groups likely reflects a lower overall transfusion burden and perhaps more homogeneous antigen exposure. Nonetheless, the detection of clinically significant antibodies such as anti-C and anti-E underscores their potential to complicate transfusion therapy if not identified. Accordingly, our results support implementing routine antibody screening and extended Rh-Kell phenotyping in CKD patients who require recurrent transfusion. This strategy may help minimize alloimmunization and enhance transfusion safety in this vulnerable group.

The present study also examined the distribution of red cell alloantibodies according to the ABO blood groups among the 200 chronic kidney disease (CKD) patients. It was observed that the anti-C antibody was detected in one patient with blood group A, while the anti-E antibody was found in one patient with blood group O. No alloantibodies were detected among patients with blood groups B or AB.

Although the number of alloimmunized cases was low, the presence of antibodies exclusively in individuals with blood groups A and O aligns with findings from other Indian studies, where the majority of alloantibodies are often observed in patients with these more common blood groups. A study by Datta et al [15] reported similar trends, with most alloimmunized individuals having blood group O or A, likely due to their higher population frequency and greater exposure to transfusions.

Importantly, the identification of Rh system antibodies (anti-C and anti-E) in these patients—regardless of ABO group—reinforces the immunogenicity of Rh antigens and their potential to cause complications such as hemolytic transfusion reactions. These findings further emphasize the importance of not only ABO compatibility but also extended antigen matching, particularly for Rh antigens, in transfusion-dependent CKD patients to reduce the risk of alloimmunization.

In the current study, the strength of the Indirect Antiglobulin Test (IAT) reactions for the detected alloantibodies was also assessed to evaluate the clinical significance of the immune response. Among the two positive cases, the anti-C antibody showed an IAT strength of 2+, indicating a moderate reaction, while the anti-E antibody demonstrated a stronger 3+ reaction, suggesting a more robust immune response. No reactions were observed at 4+ strength.

The variation in reaction strengths reflects differences in antibody titers and potential immunogenicity. A 2+ strength generally corresponds to a moderate presence of antibody that may not cause severe hemolytic transfusion reactions but still warrants clinical attention. In contrast, a 3+ strength, as seen with the anti-E antibody in this study, is considered clinically significant and may pose a risk of hemolysis if incompatible blood is transfused.

These findings are in line with previous literature indicating that anti-E antibodies often present with moderate to strong agglutination strength due to their high immunogenic potential within the Rh blood group system. For instance, Makroo et al[58] also reported anti-E as one of the most frequent and clinically significant antibodies with strong IAT reactivity in multi-transfused patients. Monitoring the strength of antibody reactions can guide transfusion decisions, particularly in selecting antigen-negative units for alloimmunized patients.

Table: 6 Comparison of alloimmunization rate reported from India

Study	Country	Year of Study	Sample Size	Alloimmunization Rate (%)
Shukla & Choudhary [16]	Lucknow, India	1999	81	9.8%
Thakral et al [17]	North India	2008	531	3.4%
Mathur et al [18]	North+South India	2012	258	2.71%
Gamit et al [19]	Bhavnagar, India	2015	50	10%
Bhuva & Vachhani [20]	Jamnagar, India	2017	300	3%
Present study	Bikaner, Raj India	2025	200	1%

Table 7: Comparison of alloimmunization rate reported internationally

Study	Country	Year of Study	Sample Size	Alloimmunization Rate (%)
Baby et al [21]	Bamako, Mali	2010	78	1.28
Da Silva etal [22]	Northeastern Brazil	2013	393	33.6
Makarovska-Bojadzieva et al [23]	Skopje, Republic of Macedonia	2017	36000	0.5
Present study	Bikaner, Raj India	2025	200	1%

Conclusion

The study highlights a middle-aged, male-dominated cohort of multi-transfused CKD patients, predominantly Rh-positive and with blood groups O and B being most common. Despite repeated transfusions, 2 cases of alloimmunization were observed, as evidenced ICT positive and all (100%) cases of DCT had negative results. These findings suggest that current transfusion practices may be effective in preventing alloimmunization, although continued vigilance through routine screening and extended antigen matching is warranted. The results also underscore the need for tailored transfusion strategies in high-risk populations like CKD patients undergoing dialysis.

Although the prevalence is low, the presence of such antibodies—especially in patients who may require multiple transfusions over time—highlights the need for routine antibody screening and extended red cell phenotyping. Implementing such practices in transfusion protocols for CKD patients can help prevent hemolytic transfusion reactions and improve transfusion safety.

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