MULTIPLE TRANSFUSION ASSOCIATED ALLOIMMUNIZATION IN CHRONIC KIDNEY DISEASE PATIENTS AT STATE SPECIALIST HOSPITAL MAIDUGURI, NIGERIA

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ABSTRACT

Background: Red blood cell (RBC) alloimmunization is a common complication in blood in patients receiving multiple transfusion. chronic kidney disease (CKD) develop anemia, which requires regular blood transfusions as part of routine management, these exposes patients to different donors' antigens and they developed RBC antibodies and complicates subsequent process making it difficult to selects suitable blood for transfusions.

Aim: The study aimed to determine the prevalence of red cell alloimmunization among multiply transfused CKD patients.

Methods: this is a cross-sectional study of 100 subjects with CKD, who passed inclusion criteria and consented to participate in the study. An interviewer-administered questionnaire was used to obtain demographic data. Four millilitres (4 ml) of blood was collected by aseptic venepuncture technique into a plain container. The ABO, Rh blood groups and indirect coombs test (ICT) were done by using standard tube technique.

Results: Out of 100 participants, 54 were males (54%) and 46 were females (46%), within the age range of 20–79years, with an overall mean age of 46.45 ± 11.67years. The blood types O, B, and A Rh positive are more prevalent, accounting for 34%, 26%, and 19%, respectively. While AB Rh negative was the least in prevalence (1%). The CKD subjects who receive 6–8 units of blood were higher in prevalence (42.2%), while those who receive 15–17 was the least (2.3%). The overall prevalence of red cell alloimmunization was 9% among the study participants

Conclusion: The results of the present study have demonstrated that the blood type O Rh positive are more prevalent in the study and account for high CKD individuals which is also appear to be the most prevalent blood group phenotype in this region, the rate of red cell alloimmunization has shown to be depend on number of unit of blood transfused .This indicate that the more the number of transfusion the more red cells alloimmunization and the chance of transfusion reaction related complications

Key: CKD, red blood cells, alloimmunization, ICT

INTRODUCTION

Red cell alloimmunization, in which the recipient's immune system produces allo-immunoglobulin by reacting to deficient antigens, this effect is one of the major setbacks in transfusion science (Hythum, *et al.*, 2014). Alloimmunization is defined as the development of antibodies in response to alloantigen following exposure to genetically different cells or tissue, several factors influence the development of alloantibodies include immune status of the patients, immunogenicity of the antigens, and the dose of blood transfused (Yusoff, *et al.,* 2020).

Genetic differences lead to alloimmunization to red blood cell antigens (Bhuva and Vachhani, 2017). Also, alloimmunization may be transfusion defendant and may vary with the number of transfusions (Pathak *et al*., 2011). The kidney plays a crucial excretory role in maintaining acid-base balance, sensing hypoxia, the synthesis and release of erythropoietin which triggers erythropoiesis (Freiz *et al.,* 2020). In disease state, these activities are impaired, resulting in varying degrees of complications, with refractory anemia being the leading challenge prompting lifesaving maneuvers (CDC, 2016). Chronic renal disease is a progressive and irreversible loss of renal functions, it is a worldwide phenomenon affecting all ages, sexes, and races with diverse outcomes (CDC, 2023). The prevalence of the disease is rising, particularly in Africa, with Nigeria having the highest burden (Chukwuonye *et al.,* 2018).

The disease has no affordable care, most of which patients rely on routine managements (erythropoietin therapy, hemodialysis, and blood transfusion) to enhance their quality of life. Blood transfusions is associated with many risks such as transfusion-transmitted infection, transfusion immunomodulation, and alloimmunization (Bajpai *et al.,* 2016). Common complications include hemolytic transfusion reactions and hemolytic disease of the fetus and new born (Gardner *et al.,* 2015). Alloimmunization in repeated transfused CKD patients may interfere with patients care through exposure to a variety of antigens (Rashmi, 2013), causing difficulties in selecting suitable blood for transfusion (Isam *et al*., 2019). Studies have shown that antibodies to Rhesus and Kell blood group antigens comprise almost 75% or more of clinically significant non-D alloantibodies followed by those of other blood groups including Duffy, Kidd, and MNS, (Pahuja *et al.,* 2010). The study aimed to determine the prevalence of red cell alloimmunization among multiply transfused CKD patients. Therefore, assessed the prevalence of alloimmunization in relation to the number of transfusions received with hope that our data may provide clue to better understand and assist in minimizing transfusion-related complications.

MATERIALS AND METHODS

Study Area

The study was carried out among patient with chronic renal disease at kidney centre within State Specialist Hospital Maiduguri the Borno State capital North-eastern Nigeria. The centre operates routinely on 24hrs per 7 days to ensure proper managements of the patients.

Study design and participant

It was a cross-sectional study involving subjects with chronic kidney disease receiving therapy at the state specialist hospital in Maiduguri.

Sample size determination

The sample size for the study was determined using a standard formula for calculating the minimum sample size for prevalence study by (Pourhoseingholi *et al.,* 2013). Recent findings on the mean prevalence of red cell alloimmunization of in CKD at 5.2%by (CDC, 2022) was used to determine the sample size for this study.

$N=z^2 P(1-P)/d^2$.

Where n=minimum sample size, Z= Desired level of significance at 95% (1.96), P= expected prevalence obtained in previous study 5.2% (0.052), d= precision corresponding to effect size 5%=0.05

N= 3.8416x 0.052(0.948)/0.0025

N=75.8, which was roundup to 100 samples size.

Ethical consideration

Ethical approval was obtained from the Ethics and Research Committee of the state specialist hospital, Maiduguri with reference number SSH/GEN/641/Vol. 1.

Inclusion criteria

Subjects diagnosed to have Chronic kidney disease on treatments and had received more than two units of blood and consented to participate in the study.

Exclusion criteria

Chronic renal disease patients who decline blood transfusion and did not consent to participate in the study were excluded

Data collection

An interviewer questionnaire was used to obtain demographic data, while that of the laboratory was obtained following sample collection and analysis.

Samples Collection

A convenient sampling method was employed for the study and 4 ml of blood sample was collected, from each subject aseptically by standard venepuncture as described by Decie and Lewis (2011) and transferred into plain vacutainer bottle.

Laboratory procedures

ABO and Rh blood group was determine via standard tube method as described by Li and Guo, (2022). The indirect antihuman globulin test using standard tube method involving patient's serum and reagents cells as described by Hamilton (2019).

Statistical Analysis

The data obtained from the study were analysed using the statistical package for social science (SPSS) version 20.0. The results were presented as frequency and percentage.

RESULTS

The study consists of 100 participants with chronic renal disease within the age range of 20 to greater than 79 years who have been transfused with three or more units of blood at different time, out of which 54 (54%) were males and 46 (46%) were females. Table 1. shows the socio-demographic data of the study participants comprising of 54 (54%) males and 46 (46%) females, respectively. The age of the study participants ranges from 20 to 79 years, which were within the age groups: 20–39 years (45%), 40–59 years (45%), and 60–79 years (10%).

Table 1 shows the socio-demographic data of study participants.

Variables		**n**	**%**
Gender	Female	46	46
	Male	54	54
Age (years)	20-39	45	45
	40-59	45	45
	60-79	10	10
Mean Age(years)	46.45 ±11.67		

Legend: n – number, % - percentage

Table 2 shows the frequency distribution of the ABO and Rhesus blood groups among multi-transfused CKD subjects. With A Rh positive having a frequency of 19(19%), A Rh negative 5(5%), B Rh positive 26(26%), B Rh negative 3(3%), AB Rh positive 10(10%), AB Rh negative 1(1%), O Rh positive 34(34%), and O Rh negative 2(2%), respectively.

Table 2: Distribution of ABO and Rhesus blood groups among multi-transfused CKD patients

ABO / Rh blood groups	**N**	**%**
A-	5	5
A+	19	19
AB-	1	1
AB+	10	10
B-	3	3
B+	26	26
O-	2	2
O+	34	34
Total	**100**	**100**

Legend: n – number, %- percentage CKD=Chronic Kidney Disease, $^{-}$ - negative, $^{+}$ positive Rh - Rhesus

Table 3 shows the number of units transfused, frequency, and percentage among study participants. The units of blood transfused range from 3–17 and have a total of 662 (100%) transfusions. Patients transfused with 3-5 units have a frequency of 145 (21.9%), those transfused with 6–8 units have a frequency of 279 (42.2%), patients transfused with 9–11 units have a frequency of 137 (20.7%), patients transfused with 12–14 units have a frequency of 86 (12.9%), and patients transfused with 15–17 units have a frequency of 15(2.3%), respectively

Table 3 shows distribution of multi-transfused CKD patients based on number of transfusions received

Number of transfusions	n	%
3-5	145	21.9
6-8	279	42.2
9-11	137	20.7
12-14	86	12.9
15-17	15	2.3
Total	**662**	**100%**

Legend: CKD - Chronic kidney, n – number, % - percentage

Table 4 shows the frequency of positive and negative results of indirect Coomb's test (ICT) among multi-transfused CKD patients. The ICT positive has a frequency and percentage of 9(9%) while that of ICT negative 91(91%) respectively.

Table 4 Shows the frequency distribution and percentage of ICT among multi-transfused CKD patients

ICT	n	%
Negative	91	91
Positive	9	9
Total	**100**	**100**

Legend: ICT= Indirect Coombs Test, CKD= Chronic Kidney Disease, n number, %- percent

Table 5. shows the percentage distribution of red cell alloimmunization in multi-transfused patients observed in different studies

Previous studies	No. of participants (n)	Overall red cell alloimmunization (%)	Year of the publications	location
Handa *et al.,*	100	7	2020	Africa
Wapukha *et al.,*	162	7.5	2023	Africa
Philip *et al.,*	200	5.5	2014	Asia
Bajpai *et al.,*	842	5.22	2016	Asia
Wilson *et al.,*	200	11	2023	Africa
Ugwu *et al.,*	145	9.3	2015	Africa
Current study	100	9	-	Africa

Key: %= percentage

DISCUSSION

The findings of the present study have shown that CKD is more prevalent among male individuals than their female counterparts. The current finding is contrary to the report of Handa *et al. (*2020) the difference observed may be due to higher female participation in their study than their male counterparts. On the other hand, the disease is more common among the middle and old age groups. Though, subjects older than 60 years account for a lower prevalence, the lower prevalence in older age may be attributed to age-related complications and CKD-associated mortality among the study participants. Previously, Obi *et al.* (2018) reported similar findings. The prevalence of chronic renal disease in relation to ABO and Rhesus blood groups, group O Rh D positive, appears to be more prevalent in the present study, while AB Rh D negative had the least prevalent in the study area. These findings may be due to high prevalence of blood group O and the low prevalence of AB in this region. Similar findings were reported by Legese *et al.* (2021) and Debele *et al.* (2023). On the basis of multiple transfusions, chronic kidney disease patients who received 6–8 units of blood account for the highest prevalence and percentage, while participants that received the highest units of blood appeared to be the least prevalent. The lower percentage recorded among patients transfused with the highest units of blood in the present study may be associated with CKD-associated morbidity, mortality, and its related complications leading to the patient's death, accounting for their least frequency. These findings are in conformity with the report of Gill *et al.* (2013).

The prevalence of red cell alloimmunization among CKD patients in the current study was similar to the reports of Patel *et al.* (2009); Shukla and Chaudhary (1999) respectively. On the contrary, Babiker and Elsayed (2013) reported a prevalence higher than that of the present study. The variation in the prevalence rate may be due to the continued rise of the disease, as other literature has suggested.

Comparing the results of the present study, the overall prevalence of 9% agrees with that of Ugwu *et al*. (2015) Handa *et al*. (2020), and Wapukha *et al.* (2023) respectively. On the other hand, Wilson *et al.* (2023) reported a higher prevalence of red cell alloimmunization compared to that of the present study; the difference observed may be attributed to the larger sample size used in their study. The close relation in the overall prevalence on the African continent may be associated with genetic homogeneity and the least antigenic variant compared to those of another continent. On the other hand, Philip *et al.* (2014) and Bajpai *et al*. (2016) recorded low prevalence on the Asian continent compared to the present study. The lower prevalence recorded in their study may be attributed to the year of the study and restriction on transfusions of only the same ABO and Rhesus blood types from suitably qualified donors to recipients.

CONCLUSION

Based on the findings of the present study, we concluded that alloimmunization occur in multiple transfused chronic kidney disease patients, and this may cause difficulty in selecting blood for these patients. Therefore, to minimize the risk of alloimmunization, emphases should be placed on proper compatibility testing, transfusion of matched ABO, Rhesus, other blood group systems with clinically significant antibodies, transfusion of antigen-negative blood, and routine antibodies screening may go a long way in reducing transfusion-related complications and may provide a better management strategies for these patients.

Conflicts of interest

There are no conflicts of interest to declare.

Sources of funds

No sources of funds to declare

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