

Research Article

# The Occurrence of Alloantibodies among Multitransfused Oncology Patients at Moi Teaching and Referral Hospital

Wapukha Zippy Bunoro<sup>1</sup>, Emonyi Wilfred Injera<sup>2</sup>, Tabitha Wanjau<sup>3</sup>

School of Health Sciences, Department of Applied Health Science, Kisii University, P.O. Box 408-40200

**Received:** October 7, 2021

**Accepted:** November 4, 2021

**Published:** November 20, 2021

**Abstract:** This study aimed at determining the presence and type of specific antibodies among multi-transfused oncology patients, that causes alloimmunization, the ABO and Rhesus blood group that is most affected by alloimmunization among multi transfused oncology patients, gender and age group that is most alloimmunized. The research study was conducted using experimental design. The sample size of the study was one hundred and sixty-two (162). Oncology patients were obtained through non-Probabilistic. The study used Non probabilistic and consecutive sampling which included all the subjects that were available. The one sixty-two (162) samples of multitransfused oncology patients who met the inclusion criteria were screened to determine the presence of alloantibodies. Out of 162 screened samples 152 had no alloantibodies, 10 were positive on antibody screening test resulting to Positivity rate of 10/162(6%). The findings of the identification of the type of alloantibodies in samples of multitransfused oncology patients, were as follows: out of ten (10) samples that had alloantibodies, five (5) samples had anti E, 5/10(50%), three (3) sample had anti K that is 3/10(30%) anti C, and anti D each had one alloantibody 1/10(10%). Alloimmunization are attributed to lack of proper management following potential sensitization events before and after blood transfusions. There is need to improve on the current practices of blood grouping and cross match in most of our Kenyan hospitals.

**Keywords:** Oncology patients, antibodies, blood transfusions.

## Introduction

Alloimmunization is an immune response to foreign antigens after exposure to genetically different cells or tissues. It is an undesirable outcome to blood transfusion or transplant from one person to another who is genetically different and also through repeated transfusion. When the body's immune system detects foreign antigens, it produces antibodies against them which can cause transfusion reactions in alloimmunized patients. Examples of human alloantibodies are anti E, anti jk<sup>a</sup>, anti C, anti fy<sup>a</sup> and anti k, commonly implicated in blood transfusion related alloimmunization (1).

Red cell alloimmunization is an effect that occurs with repeated transfusions of alloantigenic blood (2). Red blood cell antibodies such as E, JK<sup>a</sup>, c, FY<sup>a</sup> and K are commonly implicated in transfusion related alloimmunization (3). If these Rhesus antibodies are developed against red cell antigens, they can complicate transfusion therapy. It has been advocated that transfusion dependent patients should be given blood matched for antigens other than ABO and D, e.g. C, E, c, and K (4).

Alloimmunization in multi-transfused patients is a global problem and a challenge that requires intervention. It occurs in 15% of transfused dependent patients with myelodysplastic syndrome or chronic disease in myelomonocytic leukemia (5) and the incidence of alloimmunization increases with the number of transfusions (6). Alloimmunization causes morbidity and mortality, resulting to

inability and loss of life to people. Most of these people who are affected are adults, young people and children who require living quality life. Majority of the literature pertaining transfusion related alloimmunization involves patients with hemoglobinopathies (7).

Studies conducted on frequency of red blood cell alloimmunization in different population have rates of 1% to 6% in non-chronically transfused patients and up to 30% in multi-transfused patients. In Europe and United states, alloimmunization rates of 5% to 36% have been reported among sickle cell disease patients (8). Currently there are minimal data from Africa regarding transfusion dependent red blood cell alloimmunization with varied results. An investigation conducted in Egypt among Sickle cell patients reported an alloimmunization rate of 21.4% and among Tunisian thalassemia patients red blood cell alloimmunization was 7.7% (9). Studies conducted on thalassemia patients reported alloimmunization rate of 28% in Egypt (10).

### **Factors that influence occurrence of alloimmunization**

Evidence shows that low rate of alloimmunization occurs when there is homogeneity of red blood cells antigens between donors and recipients. Immune compromised patients have been proved to have a low risk to develop alloantibodies such as those reported in some D negative AIDS patients receiving D positive Red blood cells transfusions and in multiple transfusions AIDS patients AZT associated anaemia (11) due to immunosuppression in this patients. According to several studies, haematological malignancies such as leukemia and lymphoproliferative disease have been shown to have a low risk to red blood cell alloimmunization in terms of their ability to produce blood group alloantibodies. This can be attributed to lymphocytes dysfunction by concomitant chemotherapy and radio therapy as well as suppression of the immune response that is characterized by an inspired immunological response and therefore alloimmunization to Red blood cell antigens following multiple transfusions is less common (12). However there have been reports that this is not the case in patients with myelo-proliferative disorders since antibodies develop more easily probably because of their chronic inflammatory state (13). Other unexpected risk factors have been found such as diabetes and solid tumor which have considerably an increased risk.

### **Red blood cells alloimmunization pathology**

Alloimmunization occur as a result of antigenic difference between the donor and the recipients red blood cells (14). Alloimmunization to red blood cells involves a series of steps which involves; red blood cells recognition and presentation of antigen by human leukocyte antigen (HLA) Class II to T cell Receptor (TCR). Immune system consists of innate and adaptive immune response that recognizes a foreign antigen.

The main mechanism for alloimmunization involves presentation of donor antigens by antigen presenting cell (APC) to T cells receptor (TCR) on recipients' CD4 T cells which may involve direct and indirect pathway of allo-recognition. In direct recognition, the donor HLA class II antigens expressed in donor antigen presenting cells (APCs) are directly recognized by recipients CD4 T cells (15). However mature red blood cells lack human leukocyte antigen (HLA) class II antigens and therefore direct antigen presentation will not occur.

### **Effects of alloimmunization**

Studies reveal that the impact of alloimmunization can be significant; it increases the complexity of finding compatible blood for multi-transfused patients (16) resulting in added costs to health care system and inconvenience to patients. Acute hemolytic reactions are usually the result of blood group incompatibility between the donor and the recipient of the blood product. In some patients these reactions are not associated with signs and symptoms; where as in other patients' morbidity can range from mild to severe. Symptoms include fever, chills, hemoglobinuria, and less commonly renal failure, dyspnea, and disseminated intravascular coagulation. Delayed transfusion reactions occur at the rate of 1 in 6,715 units of red blood cells transfused. This reaction results from alloantibody formation 3 days to 2 weeks after transfusion (1).

Alloimmunization in sickle cell is as high as 29% in children, 47% in adults in Egypt (17) and 37% in Taiwan (18). Transfusion of red cells may induce alloantibodies potentially causing many problems in chronically transfused patients such as those with myelodysplastic syndromes (19). Although clinical factors that affect the rate of alloimmunization have been suggested, predicting which patients will form one or more alloantibodies after each red cell transfusion is not possible (20).

## **Materials and Methods**

### **Research Design**

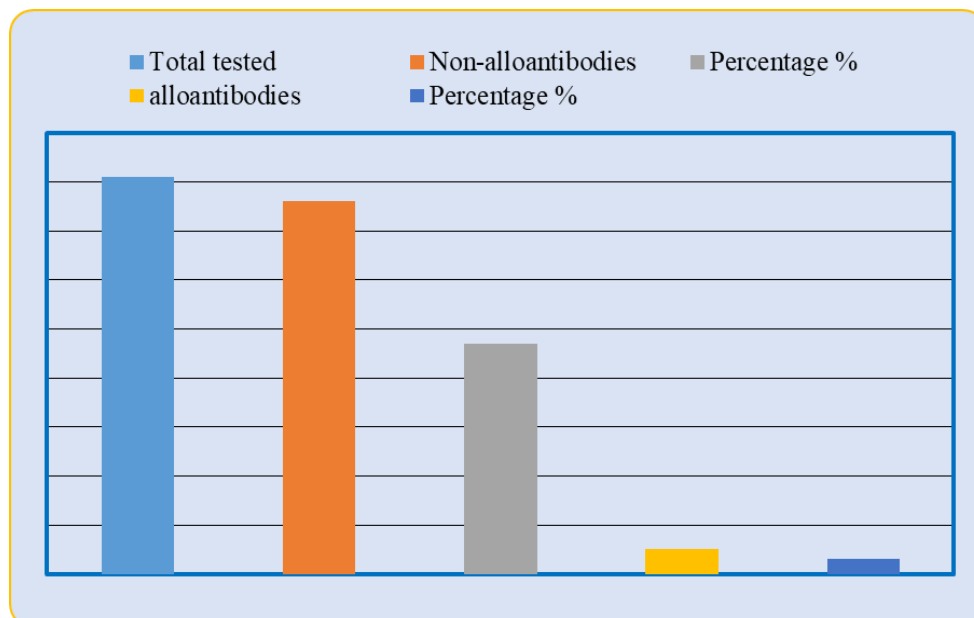
The research study was conducted using experimental research design whereby Venous blood sample from multitransfused oncology patients, that were already collected and available in blood transfusion laboratory for grouping and cross match in red top vacutainer tubes, were centrifuged to separate serum. Pooled O positive cells were prepared and Antibody screening tests was carried out appropriately. Target population comprised of 600 oncology patients whose samples were done grouping and cross-matching at Moi teaching and referral hospital. The study used a sample of 162 patients. Direct coombs test was performed to detect the sensitized red blood cells with antibodies *invivo*. The technique is used to detect the presence or absence of antibodies coated onto the red cells *invivo* (auto antibodies). Patient's Red blood cells were washed in normal saline three times. The normal saline was poured off at the third wash. Two (2) drops of antihuman globulin were added mixed and centrifuged at 1000 RPM for 2 minutes. Results are scored as haemolysis or agglutination macroscopically or microscopically which is an indication of sensitized cells *invivo*. Agglutination indicates weak D<sup>u</sup> antigen and therefore Rh-positive blood group. Haemolysis shows the presence of autoantibodies in patient's serum. Non agglutination result an indication of Negative blood group. The ungrouped frequencies antibody screening test, antibody identification test and blood group results that were obtained were subjected to descriptive statistics, in which tables and Bar graphs were derived.

## **Key Findings**

### **Descriptive Analysis**

The first objective was to determine the presence of alloantibodies among multitransfused oncology patients. Out of 162 samples from oncology patients screened 152/162 (93.8%) had no alloantibodies, 10/162 (6%) were positive on antibody screening test resulting to 6% Positivity Rate.

### **Non-alloimmunized, alloimmunized and their percentage**



**Figure 1. Non-alloimmunized, alloimmunized and their percentage**

## **Discussion**

The overall results yielded by this study were: 10/162(6%) alloantibodies present among multitransfused oncology patients at Moi teaching and referral hospital. Similar results were reported on patients with malignant disorder whose overall immunization rate was reported as 9% (21). In other studies, alloimmunization to red blood cells was positive in 7.4% of patients in Iran. Transfusion therapy is frequently complicated by alloimmunization in the Saudi study, the development of alloantibodies was determined in 68 multi-transfused patients (thalassemia, n = 38) and sickle cell anemia, n = 30). Thirteen patients received blood from the same ethnic group (Arab) and none developed alloantibodies, while of 47 patients who received multi-ethnic blood, 10 developed alloantibodies. (22) Studied frequency of red blood cells alloimmunization in sickle cell disease patients in Uganda where pre-transfusion screening for Alloantibodies is not practiced. The study reported twenty-six patients 26 (6.1%) possessed red blood cells alloantibodies and 21 (80.7%) of whom had received up to 10 transfusions. Five of the 26 alloimmunized patients had multiple antibodies. This study in Uganda concurs with the current study in the findings of the presence of alloantibodies in multitransfused patients which resulted in 10/162(6%) in multitransfused oncology patients at Moi teaching and referral hospital. It is true that several transfusions result into development of alloantibodies although the Uganda study focused more on the sickle cell disease patients while this study focused on oncology patients.

In a study on the prevalence of allo-and auto antibodies in transfused sickle cell disease (23) the study was similar to the current study in that it studied on alloimmunization among multitransfused cancer patients. The study reported alloimmunization rates of 2.6% in sickle cell disease and 2.2% in malignant or cancer patients. The current study findings had prevalence rate of (6%) may be explained by previous reports showing that cancer patients have higher rates of alloimmunization to red blood cells antigens because of several transfusions (24). Studies have shown that sensitization was higher in patients who received more than ten transfusions (25) despite the fact that there is individual predisposition, possibly of an inherited nature, which is present in the first exposures to foreign antigens (26). It has also demonstrated that alloimmunization is poorly correlated with the number of transfusions, with strong evidence of a subgroup of patients who present an increased risk of developing alloantibodies (27). The study of red blood cells alloimmunization increases with the number of transfusions and the number of donor exposures (28). This was the case in alloimmunized patients in the current study, whereby according to the records of cross matches in blood transfusion unit, among oncology patients who were done cross matches blood unit at Moi teaching and referral hospital, where majority of oncology patients who were transfused, several times were direct antiglobulin test (DAT) positive. In the current study none of the oncology patients' samples with hematological malignancy e.g., leukemia was DAT positive, an indication of absence of alloantibodies. It has been previously that found out that lymph proliferative diseases and leukemia have lower risk of alloimmunization attributed to lymphocyte dysfunction leading to lack of immune response (24). This has been to attributed lymphocytic leukemia may be characterized by a lack of immunologic response.

## **Conclusion**

Oncology patients receive intensive transfusion treatment leading to an increased risk of alloimmunization. In this study the overall prevalence of alloantibodies among multitransfused oncology patients was 6%, there was slightly lower prevalence of alloantibodies according to samples carried out and this may be explained by previous reports showing that cancer patients have lower rates of alloimmunization to red blood cells antigens because they are immune suppressed and may not manifest any evidence of prior-alloimmunization.

## **Recommendations**

Oncology patients receive intensive transfusion treatment leading to an increased risk of alloimmunization. In this study the overall prevalence of alloantibodies among multitransfused oncology patients was 6%, there was slightly lower prevalence of alloantibodies according to

samples carried out and this may be explained by previous reports showing that cancer patients have lower rates of alloimmunization to red blood cells antigens because they are immune suppressed and may not manifest any evidence of prior-alloimmunization.

### **Conflicts of interest**

The authors declare no conflicts of interest.

### **References**

1. Callum JL, Lin Y, Pinkerton PH. *Bloody Easy 3: Blood Transfusions, Blood Alternatives and Transfusion Reactions, a Guide to Transfusion Medicine*. 3rd ed. Canada: Ontario Regional Blood Coordinating Network. 2011.
2. Natukunda B, Schonewille H, Van De Watering L, Brand A. Prevalence and specificities of red blood cell alloantibodies in transfused Ugandans with different diseases. *Vox Sanguis*. 2010;98(2):167-71.
3. Calverley D, Haley L, Ballem P. Red blood cell alloimmunization in transfused patients on AZT. *Br. J. Haematol*. 1991;78(2):248-50.
4. LaSalle-Williams M, Nuss R, Le T, Cole L, Hassell K, Murphy JR, Ambruso DR. Extended red blood cell antigen matching for transfusions in sickle cell disease: a review of a 14-year experience from a single center (CME). *Transf*. 2011;51(8):1732-9.
5. Sanz C, Nomdedeu M, Belkaid M, Martinez I, Nomdedeu B, Pereira A. Red blood cell alloimmunization in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukemia. *Transf*. 2013;53(4):710-5.
6. Stiegler G, Sperr W, Lorber C, Fabrizii V, Höcker P, Panzer S. Red cell antibodies in frequently transfused patients with myelodysplastic syndrome. *Ann Hematol*. 2001;80(6):330-3.
7. Azarkeivan A, Ansari S, Ahmadi MH, Hajibeigy B, Maghsudlu M, Nasizadeh S, Shaigan M, Toolabi A, Salahmand M. Blood transfusion and alloimmunization in patients with thalassemia: multicenter study. *Pediat Hematol Oncol*. 2011;28(6):479-85.
8. Talano JA, Hillery CA, Gottschall JL, Baylerian DM, Scott JP. Delayed hemolytic transfusion reaction/hyperhemolysis syndrome in children with sickle cell disease. *Pediat*. 2003;111(6):e661-5.
9. Aly R, El-sharnoby MR, Hagag AA. Frequency of red cell alloimmunization in patients with sickle cell anemia in an Egyptian referral hospital. *Transf Apher Sci*. 2012;47(3):253-7.
10. O'Suoji C, Liem RI, Mack AK, Kingsberry P, Ramsey G, Thompson AA. Alloimmunization in sickle cell anemia in the era of extended red cell typing. *Pediat Blood Cancer*. 2013;60(9):1487-91.
11. Calverley D, Haley L, Ballem P. Red blood cell alloimmunization in transfused patients on AZT. *Br J Haematol*. 1991;78(2):248-50.
12. Fluit CR, Kunst VA, Drenthe-Schonk AM. Incidence of red cell antibodies after multiple blood transfusion. *Transf*. 1990;30(6):532-5.
13. 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.
14. Yazdanbakhsh K, Ware RE, Noizat-Pirenne F. Red blood cell alloimmunization in sickle cell disease: pathophysiology, risk factors, and transfusion management. *Blood*. 2012;120(3):528-37.
15. Fast LD. Recipient elimination of allogeneic lymphoid cells: donor CD4+ cells are effective alloantigen-presenting cells. *Blood*. 2000;96(3):1144-9.

16. Santos FW, Magalhães SM, Mota RM, Pitombeira MH. Post-transfusion red cell alloimmunisation in patients with acute disorders and medical emergencies. *Rev Bras Hematol Hemoter.* 2007;29(4):369-72.
17. Harm SK, Yazer MH, Monis GF, Triulzi DJ, AuBuchon JP, Delaney M. A centralized recipient database enhances the serologic safety of RBC transfusions for patients with sickle cell disease. *Am J Clin Pathol.* 2014;141(2):256-61.
18. Saied DA, Kaddah AM, Eldin RM, Mohaseb SS. Alloimmunization and erythrocyte autoimmunization in transfusion-dependent Egyptian thalassemic patients. *J Pediat Hematol/Oncol.* 2011;33(6):409-14.
19. Heal JM, Phipps RP, Blumberg N. One big unhappy family: transfusion alloimmunization, thrombosis, and immune modulation/inflammation. *Transf.* 2009;49(6):1032-1036.
20. Bauer MP, Wiersum-Osselton J, Schipperus M, Vandenbroucke JP, Briët E. Clinical predictors of alloimmunization after red blood cell transfusion. *Transf.* 2007;47(11):2066-71.
21. Schonewille H, Haak HL, Van Zijl AM. Alloimmunization after blood transfusion in patients with hematologic and oncologic diseases. *Transf.* 1999;39(7):763-71.
22. Natukunda B, Schonewille H, Ndugwa C, Brand A. Red blood cell alloimmunization in sickle cell disease patients in Uganda. *Transf.* 2010;50(1):20-25.
23. Mangare C, Mbugua A, Maturi P, Rajab J, Blasczyk R, Heuft HG. Red cell allo- and autoimmunisation in transfused sickle cell and cancer patients in Kenyatta National Hospital, Nairobi, Kenya. *Afr J Laborat Med.* 2015;4(1):1-7.
24. Ibanez IM, Casas AA, Martinez OC, Aguado JE, Mateos MM. Humoral immunity in pediatric patients with acute lymphoblastic leukaemia. *Allergol Immunopathol.* 2003;31(6):303-10.
25. Alves VM, Martins PR, Soares S, Araújo G, Schmidt LC, Costa SS, Langhi DM, Moraes-Souza H. Alloimmunization screening after transfusion of red blood cells in a prospective study. *Rev Bras Hematol Hemoter.* 2012;34(3):206-11.
26. Novaretti MC. Investigação Laboratorial em Pacientes com Anticorpos Eritrocitários. In: Bordin JO, Langhi Júnior DM, Covas DT, editors. *Hemoterapia: Fundamentos e Prática.* São Paulo: Editora Atheneu; 2007.
27. Higgins JM, Sloan SR. Stochastic modeling of human RBC alloimmunization: evidence for a distinct population of immunologic responders. *Blood.* 2008;112(6):2546-53.
28. Sanz C, Nomdedeu M, Belkaid M, Martinez I, Nomdedeu B, Pereira A. Red blood cell alloimmunization in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukemia. *Transf.* 2013;53(4):710-5.

**Citation:** Bunoro WZ, Injera EW, Wanjau T. The Occurrence of Alloantibodies among Multitransfused Oncology Patients at Moi Teaching and Referral Hospital. *Int J Rec Innov Med Clin Res.* 2021;3(4):13-18.

**Copyright:** ©2021 Bunoro WZ, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.