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Original Research Article

Red cell alloimmunization in multitransfused chronic renal patients on haemodialysis in a tertiary care centre of Jammu region

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ABSTRACT

Background: There is a high incidence of alloimunization in many patients with diseases that require repetitive blood transfusions. One such group is chronic renal failure patients as majority of them have severe anemia due to deficiency of erythropoietin. As many such patients are unable to afford erythropoietin, they are treated with blood transfusions. This study was thus undertaken to study alloimunization in such patients at our center.
Methods: A total of 96 patients found eligible were enrolled in this cross-sectional study that was carried out from June 2016 to august 2016. After detailed history, antibody screening was done by using Immucor Panoscreen three vial set and if screening came out to be positive antibody identification was then done by using Immucor Panocell-10.
Results: 96 patients including 76 male and 20 female patients recieved a total of 912 transfusions. Alloantibodies were detected in a total of 12 patients (12.5%). Of these 12 patients 8 patients had a single antibody whereas 4 patients developed two antibodies. The antibodies developed at a rate of 1.8% per transfusion (16/912). On alloantibody type identification, the most common type found was anti E (4/16) followed by both anti D and anti C in 3 patients each.
Conclusions: Alloimmunization to minor erythrocyte antigens occurs in many patients of chronic renal failure. This results in frequent pre-and post-transfusion complications. Inclusion of antibody screening test in routine pretransfusion testing protocol for the patients who are at higher risk of alloimmunization and require long-term transfusion dependence is desirable.

Keywords: Alloimunization, Anemia, Renal failure

INTRODUCTION

Anemia is one of the major complications present in patients of chronic renal failure and occurs in almost 80% of such patients.[1] Most chronic renal disease patients continue to remain anemic during the course of their treatment involving repeated dialysis. The etiology of the anemia is multifactorial but primarily due to the reduction in production and activity of erythropoietin.[2] Although anemia in chronic renal disease responds well to injection erythropoietin or its substitutes, it is still a common practice to transfuse packed red blood cells (RBC'S) in resource limited settings. Repeated blood transfusions may be associated with some complications such as iron overload, platelet and RBC alloimmunization.[3-5] Repetition of transfusions exposes patients to various RBC antigens which provoke the patient's immune system to produce anti-erythrocyte antibodies (alloantibody and/or autoantibody).[6] Erythrocyte autoantibodies appear less frequently, but they can result in clinical hemolysis and in difficulty in cross-matching blood. Alloimmunization against red blood cell antigens

increases the need for transfusion and can significantly complicate transfusion therapy. Red blood cell alloantibodies can develop in approximately 6-36% of patients who receive repeated transfusion.[7,8] Various factors influence alloantibody formation in our body including the number and frequency of the transfusions as well as the recipient's sex, age, immune status and underlying disease.[9-11] The antibodies thus formed result in difficulty in cross matching, various types of transfusion reactions, haemolysis and other potentially life-threatening events.[12]

Various studies in the past have demonstrated the presence of alloantibodies in multi transfused patients including thalassemia, sickle cell disease and chronic renal disease patients. The reports have demonstrated varying percentages in different population groups and different diseases.[7,8,13,14] Keeping in view this disparity this study was planned and conducted to identify alloantibodies in patients of chronic renal failure undergoing dialysis at a tertiary care center in northern India.

METHODS

This study was approved by ethical committee Government medical college Jammu and an informed consent was obtained from the patients after explaining the purpose of the study. Patients suffering from chronic renal failure as defined by national kidney foundation as kidney damage or glomerular filtration rate (GFR) of less than 60ml per minute per 1.73m^2 (body surface area) for three months or more and having received more than 2 transfusions in the past were included in this study 15. Patients on immunosuppressive agents were excluded. A total of 96 patients found eligible were enrolled in this cross-sectional study that was carried out from June 2016 to august 2016. A detailed history including details of previous transfusions and any transfusion reactions was noted. Blood samples were obtained in EDTA vacutanners for detection of red cell alloantibodies and the serum was separated as per manufacturer's directions. Antibody screening was done by using ImmucorPanoscreen three vial set and if screening came out to be positive antibody identification was then done by using Immucor Panocell-10. Quality control of saline, screening cells was performed every time samples were screened for irregular antibodies. These tests were performed in accordance to the manufacturer's instructions. Validity of the test was checked by using Ig G coated check cells. Results were recorded in the antigrams provided with reagent cells according to the presence and dosage of antigens in reagent red cells. Results were interpreted as per manufacturer's instructions.

Statistical analysis

The results were expressed in percentages and proportions.

RESULTS

A total of 96 patients were included in the study and screened for the presence of any antibodies. This included 76 males and 20 female patients. The patients were between 31 to 62years of age with a mean age of 48.5 years. Number of blood units transfused per patient ranged from 3 to 13 with a total of 912 transfusions and an average of 9.5 units per patient. Alloantibodies were detected in 12 out of 96 patients i.e. 12.5% of total patients (Figure 1). The mean age of patients with alloantibodies was 51.5years. There were 10 males and 2 female patients with alloantibodies. Of the total 12 patients 8 patients had a single antibody whereas 4 patients developed two antibodies. Thus, a total of 16 antibodies were found in 12 out of a total of 96 patients. The details of patients with alloimunization is depicted in Table 1. The antibodies developed at a rate of 1.8 % per transfusion (16/912). On alloantibody type identification, the most common type found was anti E (4/16) followed by both anti D and anti C in 3 patients each, as shown in Figure 2.

Table 1: Chart representing details of alloimmunized Patients.

Age/sex	Total blood transfusion	Antibody	Agglutination level
62/M	13	Anti E	3+
43/M	7	Anti C	3+
52/F	8	Anti K	2+
55/M	10	Anti E	3+
51/M	10	Anti D, Anti N	2+
49/F	8	Anti D, Fy^a	4+
50/M	11	Anti E	3+
46/M	7	Anti D, Fy^a	2+
59/M	12	Anti E	3+
44/M	9	Anti K	2+
58/M	12	Anti C, Anti N	2+
46/M	8	Anti C	3+

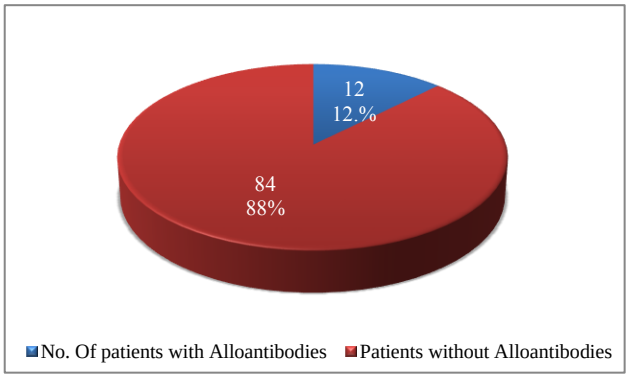

Figure 1: Frequency of patients with alloimmunization.

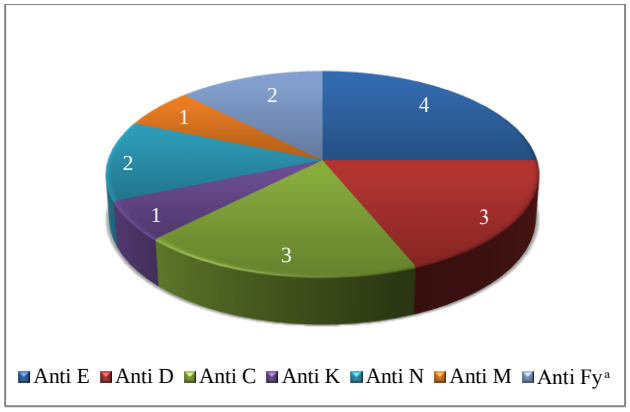

Figure 2: Frequency of different types of alloantibodies.

DISCUSSION

The present study was undertaken to investigate the presence of alloantibodies in chronic renal failure patients as any patient requiring repeated transfusions is exposed to an array of antigens and any disparity between donor and recipient may thus lead to antibody formation. This becomes clinically relevant as Red cell alloantibody formation leads to mismatch and other complications unless corresponding antigen negative matched blood is transfused.[10] There have been a few studies from different parts of world that have demonstrated the presence of alloantibodies in thalassemia patients, Sickle cell disease patients, and also chronic renal disease patients.[7,8,14] This study was undertaken to determine the frequency and specificity of RBC alloantibodies among the chronic renal failure patients of Jammu region which have not been previously described.

In our study a total of 12 out of 96 patients developed alloantibodies with alloimmunization rate of approximately 12.5%. This rate is almost similar to that reported in some earlier studies viz frequency of 8.2% reported by Patel J et al, 9.9 % reported by Shukla JS et al, 13.1% reported by Babiker HAM et al.[7,16,17] Spanos T et al in demonstrated that for patients of thalassemia who received blood matched for the AB0, rhesus and Kell systems had a much lower alloimunization rates (3.7%) as compared to those who received blood matched only for the AB0 and Rh-D antigens (15.7%, $p < 0.001$).

There is some disparity in the reported incidence of alloimunization in chronic renal disease patients receiving multiple transfusions. While the rate of alloimmunization in such patients was as high as 14% in the study of Blumberg et al, on the other hand Agarwal et al in their study in 2016 could not identify alloantibody even in a single patient out of a total 47 such patients included in their study.[11,18] Therefore it is desirable to conduct more such studies in different population groups and identify the frequency and type of alloantibodies in multitransfused patients specific to that area.

Similar to previous studies, in the present study the most common type of alloantibody found were anti Rh including anti E (4/16) followed by both anti D and anti C in 3 patients each. Anti kell and anti-duffy antibodies were found in two patients each.[13,17]

The calculated risk of alloimunization per unit transfusion was found to be 1.8% which is slightly higher than rate of alloimunization in general population. This finding along with a much lesser rate of alloimmunization of close to 5% found in multitransfused thalassemia patients suggests that chronic renal disease patients may be at a higher risk of alloimunization as compared to other multitransfused population groups. A possible explanation could be the fact that exposure to antigens at an earlier age may be better tolerated as compared to an exposure to antigens at a later age as happens in most cases of chronic renal disease patients.[13]

CONCLUSION

Alloimmunization to minor erythrocyte antigens in multitransfused patients with anemia of different etiologies is now well documented. This results in frequent pre-and post-transfusion complications. Inclusion of antibody screening test in routine pretransfusion testing protocol for the patients who are at higher risk of alloimmunization and require long-term transfusion dependence should ideally be practiced. But being an expensive test, it may not be feasible for multitransfused patients who have to incur multiple other expenses during the course of their treatment. It is though desirable that we are aware of the prevalence of different alloantibodies and their subtypes in different types of multitransfused patients and where possible offer extended red cell phenotyping during pretransfusion testing or alternate treatment options including erythropoietin.

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