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Alloimmunization in Sudanese Leukemic Patients with Multiple Blood Transfusions

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Abstract
Background: *Blood transfusion is one of effective treatments which used to decrease morbidity and mortality rate in leukemia patients, but it can results in development of alloimmunization to red blood cell antigens, which often results in difficulties in finding compatible blood and a higher risk of delayed hemolytic transfusion reactions.*
Objective*: The current study aimed to determine the frequency of allo antibodies among Sudanese multiply blood transfused leukemic patients in Khartoum state, the study also aimed to correlate between the frequency of alloimmunization and duration of blood transfusion therapy.*
Materials and Methods: *This study was conducted in Khartoum state between August 2015 and January 2016. 176 multiply transfused leukemic patients were included in this study . previous blood transfusion and clinical data of all the patients were obtained including age of patients, duration of transfusion and other health problems, Blood samples were collected from each participant, Then ABO, RhD grouping was checked, Alloantibody screening and identification was done for each patients.*
Results*: we found that 13 patients (7.3%) had RBC alloantibodies. Anti-K was detected in four patients (2.2%), while anti-c in one (0.56% anti-E was detected in three patients (1.7%), anti C in one patient (0.56%) and anti Fya in two patient (1.13%). O blood group was found to be the most frequent (38.5%) among the alloimmunized patients, whereas blood group AB was least frequency (7.7%). The prevalence of blood group A and B were 30.7% and 23.1% respectively*
Pearson's correlation has shown significant positive correlation between alloimmunization and duration of blood transfusion therapy (r = 0.343, P-value 0.001).
Conclusions*: we observed that 7.3% of study population were alloimmunized against RBCs antigens. The majority of detected antibodies were against Kell and Rh blood group systems and the Incidence of allo-immunization increases with duration of transfusion therapy. Multiply transfused leukemic patients should be screened regularly before blood transfusion against red cell alloantibodies to reduce the rate of RBC alloimmunization and hemolytic transfusion reactions.*
Key words: *Alloimmunization, screening test, leukemia, Sudanese.*

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I. Introduction

Alloantibodies are produced after exposure to genetically different or non self antigens of the same species, such as different RBC antigen after transfusion. Transfused component may elicit the formation of alloantibodies against antigens (red cell, white cell and platelets) not present in the recipient. Auto antibodies are produced in response to self antigen. They can cause reaction in the recipient if they have specificity that is common to the transfused blood.

Hemolytic transfusion reaction is any unfavorable transfusion-related event occurring in patient during or after transfusion of blood components, may be immediate or delayed [1]. Immediate reaction associated with the massive intravascular hemolysis is the result of complement- activating antibodies of IgM or IgG classes usually with ABO specificity.

Leukemias are a group of disorders characterize by the accumulation of malignant white blood cell in bone marrow and blood [2]. Generally leukemia classified into four types: Acute and chronic leukemias, which are further subdivided into lymphoid and myeloid [3].

Leukemic patients usually received blood as part of the treatment protocol due to repeated anaemias [4]. Complication of blood transfusion in leukemic patients may cause consequence abnormality that worsening the underlying disease. However, reaction can occur with any blood component, the patients make antibodies to the donor's blood; some patients may produce antibodies against certain antigens in transfused blood, although blood is typed for the most important antigen that presented on the red cell. The medical term for this

phenomenon is alloimmunization. This effect does not necessarily cause immediate symptoms but is important if subsequent transfusions are needed. Alloimmunization increase the time required for cross matching and may delay treatment in addition to increasing the chance of transfusion reaction. For that reasons a routine screening test should be performed at the time of blood transfusion especially in patients who received more than two units of blood within 72hr [5]. Accordingly this study has aimed to determine the frequency of alloantibodies in Sudanese leukemic patients, and to identify the types of the screened antibodies which will certainly help to reduce the rates of RBC alloimmunization and hemolytic transfusion reactions.

II. Materials and Methods

This is a cross-sectional descriptive hospital based study; it was carried out to determine the RBCs alloimmunization among multiply blood transfused leukemic patients in Radiation and Isotopes Center of Khartoum (RICK) in Khartoum state during the period from August 2015 to January 2016. 176 Sudanese leukemic patients, 34.2% of them were diagnosed as AML, 5.3% CLL, 9.2% AML and 48.7% CML, from different age, gender and ethnic groups were recruited for this study. Immune compromised patients, pregnant ladies and patients who receive radiotherapy were excluded from this study. EDTA blood samples (2.5ml) were collected from each participant, then antibody detected in patient's plasma by indirect coomb's test, which performed using polyclonal anti IgG as screening test aimed to detect unexpected antibody, in parallel with determining the ABO and Rh -D grouping in all patients to exclude the A and B antibodies. Antibody identification then performed using the plasma samples under investigation, it was tested against a panel of eight or more group O red cell samples of known antigen composition(phenotype); 10 test tubes were labeled as 1, 2, 3…..10 ; Then in each tube the panel cells were added according to labeling, mixed with patient`s serum and incubated at 37ċ for 15 minutes, then the tubes were centrifuged for 10 minutes and results were interpreted and recorded [6].

Ethical consideration

This study was approved by the ethical committee of Al-Neelain University, faculty of Medical Laboratory Sciences, written and oral informed consents were obtained from each participant or their relatives, and approval also was taken from the hospital administration.

Statistical analysis

Data were analyzed using SPSS Software version 20. Descriptive statistics on subject demographics were calculated, Odds Ratio was used for detecting the relationship between determinant and the outcome and 95% confidence interval was calculated. Pearson's correlation was applied to correlate between alloimmunization and duration of transfusion therapy.

III. Results

The percentage (%) showed equality of gender among study participants (49% females and 51% males) 37% of them between 1 – 20 years old while 13% are more than 60 years old. The results showed that 13 patients (7.3%) had RBC alloantibodies, anti-K was detected in four patients (2.2%), while anti-c in one (0.56%) anti-E was detected in three patients (1.7%), anti C in one patient (0.56%) and anti Fya in two patient (1.13%) which presented in table 3.3 and figure 3.1. In table 3.2 O blood group is the most frequent (38.5%) among the alloimmunized patients, whereas blood group AB is least frequent (7.7%). The prevalence of blood groups A and B are 30.7% and 23.1% respectively. Pearson's correlation has shown significant positive correlation between alloimmunization and duration of blood transfusion therapy (r = 0.343, P-value 0.001) which is presented in fig 3.2.

Table 3.1: Distribution of age in study participants

Age	Frequency (n)	Percent (%)
1 – 20	65	37.0
21 – 40	44	25.0
41 – 60	44	25.0
61+	23	13.0
Total	176	100.0

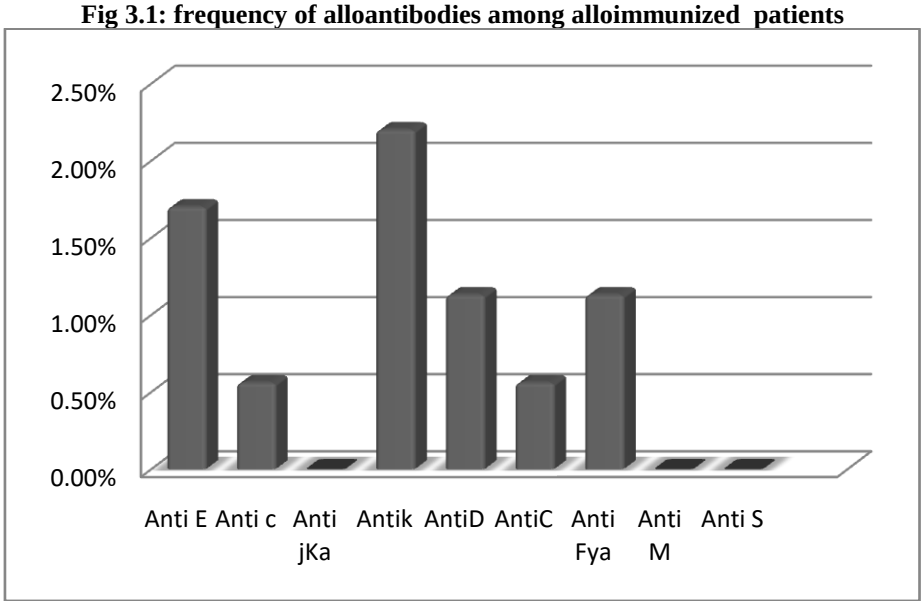
Table 3. 2: ABO and Rh blood groups frequency in alloimmunized patients

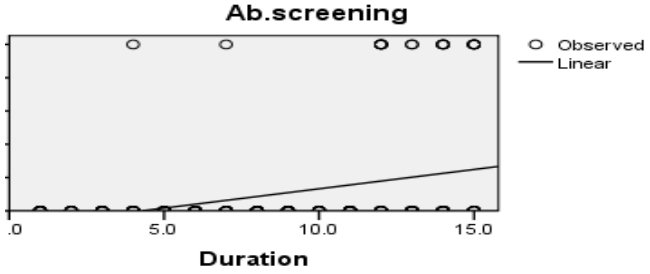
		ABO				Total
		A	B	AB	O	
Rh	Rh +ve	3	3	1	4	11
	Rh -ve	1	0	0	1	2
Total		4	3	1	5	13
percent		30.7	23.1	7.7	38.5	100

Table 3.3: frequency of alloantibodies in alloimmunized leukemic patients

Antibody type	Frequency(N)	Percent (%)
Anti E	3	1.70
Anti c	1	0.56
Anti JKa	0	0
Anti K	4	2.20
Anti D	2	1.13
Anti C	1	0.56
Anti Fya	2	1.13
Anti M	0	0
Anti S	0	0
None	163	92.7
Total	13	7.3

Fig 3.1: frequency of alloantibodies among alloimmunized patients





r = 0.343,
P-value0.001

Fig 3.2: Correlation between alloimmunization and duration of transfusion/months

R=positive or negative correlation, p-value indicate strength of correlation

IV. Discussion

The prevalence of anemia in cancer patients at different stages of disease and treatment is around 40%[7]. Transfusions of red cells are treatment of choice in cancer related anemia in order to elevate their Hemoglobin level to tolerate the chemotherapy especially in the children [8, 9]. Allo-antibodies that arise from the transfusion can lead to serious clinical consequences and logistic problems [10]. Reports from previous Studies observed that the incidence of RBCs allo-immunization ranges between 1 and 6% in occasionally transfused and up to 30% in poly-transfused patients [11, 12].

In this study the overall prevalence of allo-antibodies in multiply transfused leukemic patients was observed to be 7.3%, this finding is in agreement with previous study report by Schonewille on patients with malignant disorders which concluded that the overall immunization rate about 9% [13]. In other studies allo-immunization to RBCs was observed in 7.4% of patients in Iran, 22% in Saudi Arabia, 6.1% in Uganda in patients who received multiple blood transfusions with different diseases [14, 15, 16].

In the present study prevalence of positive antibody screening as follow: K (2.2%) E (1.7%) C (0.56%), c (0.56%), D (1.13%) and Fya (1.13%), These alloantibodies have been the most commonly detected in many reports in different multiply transfused patients [17, 18, 19]. as commonly reported in previous reports Kell alloantibodies was found to be most frequent antibodies among alloimmunized patients detected in this study and this result is probably attributed to the high immunogenicity of the antigen. After ABO and Rhesus antigens Kell antigens have been reported to be the third most potent at triggering an immune reaction. Antibodies produced against Kell antigens are usually IgG type, does not bind complement and hemolysis is usually extra vascular in nature [20]. Since alloimmunization against these minor blood groups antigens can affect the effectiveness and frequency of blood transfusions, selection of compatible blood in term of these blood groups especially for Rh(E) and kell is particularly important.

The results also has shown that blood group O was found to be the most frequent (38.5%) among the alloimmunized patients, whereas blood group AB was least frequency (7.7%). The prevalence of blood group A and B were 30.7% and 23.1% respectively (Table 3.2).This finding is also in agreement with many previous studies [21, 22, 23].

Similar to other authors, in this study Pearson's correlation revealed that there was strong positive correlation between duration of transfusion therapy and red cells alloimmunization ($r = 0.337$ p- value 0.001), this finding also in accordance with previous study conducted by Shahida Mohsin which concluded that the allo immunization increases with the number of transfusions and donor exposure to the recipients, also Vitor Mendonça Alves in his prospective study which concluded that there was a higher occurrence of allo immunization in individuals with history of transfusions [12, 24].

V. Conclusion

The study has concluded that the overall prevalence of RBC allo-antibodies among Sudanese multiply transfused leukemic patients was 7.3%. The majority of detected antibodies were against Kell and Rh blood group systems, also the occurrence of alloimmunization is increased with duration of blood transfusion therapy, hence We recommended to perform phenotyping, antibody screening and identification before blood transfusions for leukemia patients especially in case of ordinary blood transfusion to reduce the risk of alloimmunization against minor blood groups antigens which in turn affect the efficiency of frequent blood transfusion.

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