IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 12 Ver. IV (Dec. 2015), PP 137-141
www.iosrjournals.org

Red cell alloimmunization in blood transfusion dependent Patients with Sickle Cell Disease in El-Obied city, Sudan

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Abstract: *Blood transfusion remains a mainstay of management for patients with sickle cell disease. Transfusion in patients with sickle cell disease can result in the development of alloimmunization to red blood cell antigens. But also is one of effective therapy which use to decreasing morbidity and mortality in patients with sickle cell disease (SCD). The benefits of transfusion therapy, it is not without the risks of iron overload, Alloimmunization, and delayed hemolytic transfusion reactions. Development of anti red blood cell antibodies (both allo-and autoantibodies) remains a major problem among patients with sickle cell disease patients especially those who blood transfusion dependents. This study assessed the frequency of Alloimmunization to red cell antigens among sickle cell disease patients in El-Obied city, capital of north kordofan, Sudan.*
Objective: *We studied the frequency of red blood cell (RBC) Alloimmunization and autoimmunization among sickle cell disease (Hb SS) patients who received regular blood transfusions.*
Materials and Methods: *This study was conducted in Elobeyeid city capital of north kordofan between may2014 - April 2015.The study was carried out of 210 multiply transfused patients with HbSS. Clinical and transfusion records of all the patients were examined for age of patients (6 month –20 years), age at initiation of transfusion therapy, total number of blood units transfused (at least 2 unit's transfusions), transfusion interval and any health problem if observed likes status of splenectomy or other interventions. Then ABO, D, Alloantibody screening and identification was done for each patients.*
Results: *Anti-K was detected in five patients (2.4%) (, while anti-c in one (0.5%), anti-E were detected in two patients (1%), anti kidd in one patient (0.5% and anti leb in one patient (0.5%).O Rh + (34.7%), A Rh + (26.2%), B Rh + (14.8), AB Rh + (8.1%), AB Rh - (0.5%) B Rh – (4.3%), A Rh – (6.7%), O Rh – (5.2%).*
Conclusions: *In this study, we observed a low rate (4.3%) of Red blood cell alloimmunisation among patient with SCD. We recommended that there are many recent advances in blood group genotyping can be exploited to facilitate the identification of antigen-matched RBCs and improve transfusion support of patients with SCD.*
Keywords: *Alloimmunization, sickle cell disease, blood transfusion, Elobeyeid city*

I. Introduction:

Sickle cell disease is a chronic hemolytic disorder that is marked by tendency of hemoglobin molecules within red cells to polymerise and deform the red cell into a sickle (or crescent) shape resulting in characteristic vasoocclusive events and accelerated hemolysis [(1)]. Sickle cell disease affects millions of people throughout the world, and it is found to be the most common blood disorder among families whose ancestors came from SubSaharan Africa, South America, Cuba, Central America, Saudi Arabia, India, and the Mediterranean regions [(2)] .In Sudan, sickle cell anemia is the one of the major types of anemia especially in western Sudan where the sickle cell gene is frequent [(3)]. There's no cure for most people with sickle cell anemia. However, treatments can relieve pain and help prevent further problems associated with sickle cell anemia. Transfusions are another method of trying to deal with SCD complications and assisting with the prevention of strokes and acute chest syndrome and remain a major treatment in SCD management [(4)]. The purpose of red blood cell transfusion (RBC) is to increase oxygen distribution in the tissues and to replace the rigid sickle cell shaped RBCs with healthy deformable RBCs [(5)].Transfusions can lead to erythrocyte alloimmunization with serious complications for the patient. These antibodies are often directed against antigens expressed on RBCs of white persons, which represent the majority of donors in Western countries [(6)]. Alloimmunization consists of the induction of immunity in response to foreign antigens encountered through exposure to cells or tissues from a genetically different member of the same species [(7)].The major complications of regular blood transfusions in patients who

are chronically transfused. Blood group antigens can be immunogenic in individuals who lack the corresponding antigen on their red blood cells (RBCs). The most serious consequence of alloimmunization in SCD patients is the risk of developing a delayed hemolytic transfusion reaction (DHTR), which can be life-threatening [8]. Sensitization to Rh antigens (D, C, c, E, and e) and to K comprise the majority of the RBC antibodies encountered in SCD [9, 10]. This is a cross sectional descriptive study aimed to estimate the frequency of alloimmunization in SCD patients was conducted in Elobied teaching hospital and Elkowiety Children Hospital at North Kordfan State- Sudan because we observed that high prevalence of sickle cell disease among children presenting in health units in Kordfan State. We investigate to fulfill all causes and try to reflect the possible strategies which must be done to avoid the problem caused by immunization by incompatible cross matching in major or minor RH phenotype.

II. Materials and Method:

2.1. Study Population:

210 children with SCD (Were selected by Simple random method) followed in the Elobied teaching hospital and Elkowiety Children Hospital at North Kordfan State- Sudan from 2014 to 2015. Data collected used the questionnaire which filled for each of the children to collect demographic data, hematological characteristics and records monitoring transfusion.

2.2. Study Design:

This is a cross sectional descriptive study aiming to determine frequency and characterization of alloimmunization among multiple transfused sickler patients in Elobeid North kordfan state.

2.3. Laboratory Investigation:

After consent obtained by children parents sample was obtained from each participant the **ABO grouping** besides the **Rhesues (D)** grouping and **Du method** for week Dantigen).**Alloantibody screening** and identification was done using cell panel. To detect autoantibodies. Select cells from available panels to exclude the following specificities: D, C, E, c, e, K, k, Fya, Fyb, Jka, Jkb, Lea, Leb, M, N , S, s . **For New Antibodies:** Immucor Panocell-10 and Panocell-10 Ficin Treated (if indicated) .Reagent red blood cell Panel Sheet or Master List corresponding to panel .**For Selected Cells:** Immucor Panocell-16, Immucor Panocell-20, Panoscreen I and II Reagent red blood cell Panel Sheet or Master List corresponding to panel . **Auto control** was carried out using polyspecific coombs (IgG + C3d) by tube method.

2.4. Statistical analysis:

Data were entered and analyzed by SPSS prograrmme (version 20). All demographic data of the study population were presented as mean ± SD in the text and Odds Ratio was used for detecting the power of relationship between the determinant and the outcome and 95% confidence interval was calculated.

2.5. Ethical consideration

Approval was taken from the ethical committee of faculty of Medicine and health science, University of kordofan, and both oral and written informed consent was obtained from patients or their guardians.

III. Result:

A total of 210 patients with SCD (HbSS) formed the study population. Table 1: shows distribution age group as fallow: Fifty nine patients were males (59%), and forty one were female (41%) . patient age between less than 2 years (34.8%) , 2 to5 years was (22.4%) , 6 to 12 years was (31%) and above 13 was (11.9). Table 2 &Fig 1: shows the rank order of blood group among subjects: O Rh + (34.7%), A Rh + (26.2%), B Rh + (14.8), AB Rh + (8.1%) , AB Rh - (0.5%) B Rh – (4.3%) ,A Rh – (6.7%) ,O Rh – (5.2%). Table III: show allo antibodies (4.3%) were detected among the 210 SCD (HbSS) patients who received transfusion. Anti-K was detected in five patients (2.4%) (, while anti-c in one (0.5%) ,anti-E were detected in two patients (1%), anti kidd in one patient(0.5% and anti leb in one patient.

Table 1. Show distribution of Age group of patients:

Age group	Frequency	Percent
less than 2 years	73	34.8%
2-5	47	22.4%
6-12	65	31.0%
Total	210	100%

Table 2. Show the frequency of ABO & RH group among patients

Blood group	Frequency	Percent
A + ve	55	26.2
A -ve	14	6.7
B +ve	31	14.8
B -ve	9	4.3
O +ve	72	34.3
O -ve	11	5.2
AB+e	17	8.1
AB-e	1	0.5
Total	210	100

Fig 1. Show the frequency of ABO & RH group among patients

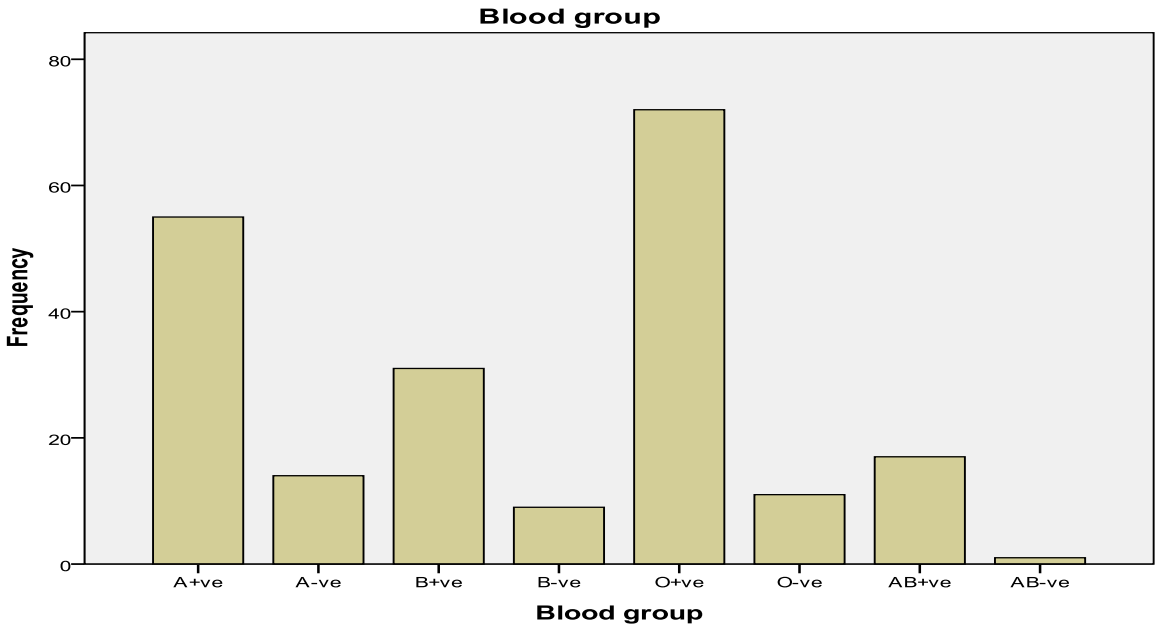

Table 3. Show Name and percent of antibodies identification:

Antibodies name	Frequency	Percent
Anti K	5	2.4
Anti Kidd	1	0.5
Anti E	2	1.0
Anti Leb	1	0.5
Anti c	1	0.5
None	200	95.2
Total	210	100

IV. Discussion:

Alloimmunization to red cell antigens is an immune response usually stimulated by the transfusion of blood products and is one of the complications of RBC transfusions. Other than RBC alloimmunization, immunologic complications of repeated RBC transfusions include: Difficulties obtaining compatible blood, development of autoantibodies, acute or delayed hemolytic transfusion reactions and hemolytic disease of the newborn [(11)]. In this study we try to establish the incidence of the alloimmunization in this category in Elobeyeid city, Sudan. This study showed that the prevalence of red cell alloimmunization among multitransfused patients with sickle cell disease (Hb SS) was 4.3%. The prevalence of allo-immunization in our study is slightly found in this. Agree with several international and local studies presenting lower rates of alloimmunization frequencies in sickle cell disease, in Sudan 4% [(12)]. 6.1 % in Uganda, 2.6%, in Brazil [(13.14)], in Jamaica 2.0 % [(15)]. In Tunis 6% [(16)]. As general Alloimmunization to red blood cell antigens has been widely reported in patients with sickle cell disease living in industrialized countries, with a varying incidence from 8% to 50% [(17)]. prevalence of positive antibody screen in this present study as fallow: K (2.4%) E (1%) of the Rh system and to antigen were most commonly encountered. %) and c (0.5%), anti leb (0.5%). These alloantibodies have been the most commonly detected in many reports [(18, 19,20)]. Kell alloantibodies found in this study, as commonly reported in previous studies, is attributed to the high immunogenicity of the antigen. Kell antigens have been reported to be the third most potent, after ABO and Rhesus antigens 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, [21].The results from this study shows that blood antigen O predominate those of all other blood antigens and was found to be the most frequent (39.6%) among the study population, while blood group AB was least prevalent (8.6%). The prevalence of blood group A and B were 32.9 and 19.1%; respectively (Table 2).This finding was in agreement with many previous studies [22, 23, 24, 25]. Also our finding in frequency of blood group among sickler were not in consonance with some other studies that reported the frequencies of ABO blood system in the order other than our finding [26,27]. Most patients in our study were predominantly children aged age between less than 2 years (34.8%), 2 to5 years was (22.4%), 6 to 12 years was (31%) and above 13 was (11.9). Studies of paediatric patients have reported lower RBC alloimmunisation rates and concluded that children with SCD who were hypertransfused had a lower frequency of alloimmunisation as compared with adults [28, 29]. Another study involving 167 paediatric and 62 adult SCD patients supported this observation, where the rates of allo- and autoimmunization in children and adults were 29% and 8%; 47% and 9.7%, respectively [30]. The majority of our study patients were aged ≤ 5 years could have contributed to the low rate of RBC allo Ab formation that we observed. Finally the ability to react to alloantigen varies from person to person. Some individuals may not become immunized to any antigen despite repeated transfusions (no responders) whereas others will become immunized when transfused with any of the antigens they lack (responders) [31] .This was supported by our study which revealed that development of alloantibodies is generally not related to the number of units of blood received. Some patients who received 1 or 2 units of blood developed alloantibodies while some patients who had up to 5 or more units of blood transfusion did not develop alloantibodies. However, with improvements in health care, more SCD and patients are likely to receive a more intensive transfusion treatment, which could lead to an increased risk of RBC alloimmunisation. Therefore, further development of the healthcare system in Kenya will require a thorough reconsideration of the pre transfusion laboratory practice, in particular, if transfusion frequencies increase and/or donor groups change.

V. Conclusion:

In this study, we observed a low rate (4.3%) of Red blood cell alloimmunisation among patient with SCD.This low incidence of alloimmunization which detected may be agree with fact that development of alloimmunization is affected by many factors such as age of the patient, number of units of blood received and antigenic differences between the donor and recipient population [32,33,34].The majority of our study patients were aged ≤ 5 (57%) years could have contributed to the low rate of RBC allo Ab formation that we observed. Extended red blood cell grouping in sickle cell disease patients is recommended to prevent or reduce red blood cell alloimmunization in sickle cell disease population. We recommended that there are many recent advances in blood group genotyping can be exploited to facilitate the identification of antigen-matched RBCs and improve transfusion support of patients with SCD. Automated DNA extraction and the ability to test patients and donors on high throughput platforms, combined with database driven RBC matching, should make this possible in the near future.

Acknowledgments:

The authors wish to acknowledge the efforts and assistance given by staff of El-Obied teaching hospital and Elkowiety Children hospital for their help in recruiting patients and donors respectively.

Competing interests:
The author declares no competing financial interests

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