Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(1A):1-5 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com DOI: 10.36347/sjams.2016.v04i01.001

Original Research Article

Frequency of Rh D, C, c, E, e and Kell1 Antigens among Sudanese Patients with Sickle Cell Disease: A prospective Study from Khartoum, Sudan.

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Abstract: Sickle cell disease (SCD) is a group of haemoglobin disorders that increase the rate of morbidity and mortality. Blood transfusions have reduced morbidity and mortality for patients with SCD, but it can lead to erythrocyte alloimmunization the main aim in this descriptive analytical study, we determine the frequency of Rh antigens (C, D, c, E, and e) among sickle cell patients as well as to determine the frequency of kell1 antigen which will be useful in blood transfusion. The study was conducted during approximately eight months, followed informed consent, a total of 160 venous blood samples were collected from sickle cell patients in to 2.5 ml EDTA containers .All samples were tested for Rh D antigen using the slide agglutination techniques, and the same samples tested for Rh C, c, E, e, and kell1 antigens by immunodifusion gel technique. The results obtained showed that, the c antigen was most common frequency (100%), followed by D antigen occurred (90%), e antigen was found to be (82.5%), and least common were antigen C (67.5%), and E (80%).The kell1 antigen was the least frequency (10%).
Keywords: RBCs alloimmunization, Sickle cell disease, Kell1, Blood transfusion

INTRODUCTION:

Sickle cell diseaseis a group of haemoglobin disorders in which the sickle B-globin gene is inherited homozygous sickle cell anaemia (Hb SS), doubly heterozygote conditions of (Hb SC) and Hb SB thalassemia also because sickling disease [1]. The disease affects millions of people globally; the global incidence of diseases is approximately 4.5% [2]. Several medical issues will need to be addressed during the lifespan of the patient. These issues include the recurrent, painful sickle crises, the severe hemolytic anemia, organ damage from vaso occlusive disease, priapism in teenage males [3]. The Management of the SCD patients begins in the first year of life. The first line of SCD management is red blood cell transfusions which reduced morbidity and mortality for patients with SCD by reducing the number of sickle cells by one-third or more [4]. Transfusions can lead to erythrocyte alloimmunization, However, alloimmunization to red blood cell (RBC)blood group antigens remains a major complication for patients with SCD and often presents significant challenges in their medical management [5, 6, 7]. The incidence of alloimmunization in patient's with SCD ranges from 7% to 47%, dependent on age, RBC exposures, and extent of antigen matching for blood groups other than ABO and RhD [8, 9]. An estimated 4% to 11% of patients with SCD who receive transfusions develop overt delayed hemolytic transfusion reactions (DHTRs) [5, 10, 11], but mild DHTRs may be unrecognized. Erythrocytes alloimmunization involves multiple steps, starting with RBC antigen recognition, processing, and presentation of antigen by HLA class II to TCR, activation of CD4 helper T cells, interaction of T and B cells, and finally B-cell differentiation into plasma cells (Figure 1) [4]. However, with serious complications for the patient including life-threatening delayed hemolytic transfusion reactions and difficulty in finding compatible units, which can cause transfusion delays [12, 13]. An accurate knowledge of all the significant antibodies in a

patient serum, or history is the basic step that will allow proper unit selection after donor red cell to one or several antigen system before cross match [14]. Therefore in this studywe estimate the frequency of Rh (D, C, c, E, e) and Kell (K1) antigens as a risk factors alloimmunization among Sudanese SCD patients.

MATERIALS AND METHODS

This is cross-sectional, descriptive hospital based study conducted in Gaffer Ib no of Hospital; Khartoum state, Sudan. The study was conducted on 160 unrelated sickle cell patients 'volunteers also 60 healthy volunteers were used as control group.

Venous blood was collected from the anti cubital vein of both study and control group and subjected for RhD grouping method for determination of D antigen and Gel Immune Diffusion Technique to determine Rh C, c, E, e and Kell1.

Self-administered pre-coded questionnaire including all personal information including (name, age, race and some personal altitudes were collected from each patient, in order to facilitate the selection of patients on the basis of the disease.

Interpretation of results:

RhD grouping method: Positive reaction is indicated by clumping of cells (agglutination) where negative reaction shows no clumping and the red cells appear free and the preparation was homogeneous. Agglutination with anti-D anti-sera indicates the presence of the Rhesus antigen. Absence of reaction with anti-D anti-sera requires performing Du method; to confirm either the absence of Rhesus D antigen or the presence of weak D antigen.

Gel Immune Diffusion Technique: Agglutinated cells forming a red line on the surface of the gel or agglutinates dispersed in the gel indicates a positive reaction of ++++ to + which indicates the presence of corresponding antigen. A compact button of cells on the bottom of the micro- tube indicates a negative reaction i.e. the absence of the corresponding antigen.

RESULT:

In this study venous blood samples were collected from 160 sickle cell patients (116 males & 44 females) (Figure 2), with age ranged from (2-13) years old. This study showed that the most frequent antigen was Rh c antigen which represent (100%) followed by Rh D and Rh e with positivity and negativity of (90%), (82.5%) and (10%), (18.5%)respectively. On other hand of 160 study subjects only (32.5%) were positive for Rh C antigen, while the remaining were (67.5%) were negative. In this study Rh E antigen and kell1 antigen had the lowest frequencies. Rh antigen E was positive in only (20%) of our study subject while the remaining (80%) were negative. The kell1 antigen was occurred only in (10%) of our study subject, while the remaining (90%) were negative as showed in (Figure 3).

In contrast, as showed in table1, 100% of control group were positive for Rh c antigen, followed by Rh D antigen which represent (93%) positivity. While the lowest positivity were observed with Rh Kell1, E, C and e antigen which were occurred in 7%, 7%, 13% and 47% of our control group respectively.

Table 1: Showed the frequency of studied antigens among patient's and control group.

		Groups	
		Patients(n=160)	**Control(n=60)**
C	+	52(32.5%)	8(13%)
	-	108(67.5%)	52(87%)
c	+	160(100%)	60(100%)
	-	0(0%)	0(0%)
D	+	144(90%)	56(93%)
	-	16(10%)	4(7%)
E	+	32(20%)	4(7%)
	-	128(80%)	56(93%)
e	+	132(82.5%)	28(47%)
	-	28(17.5%)	32(53%)
Kell1	+	16(10%)	4(7%)
	-	144(90%)	56(93%)

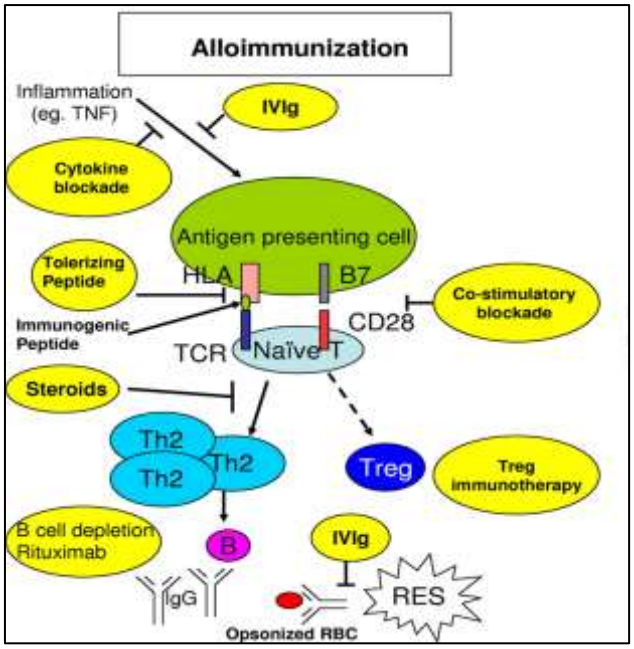

Fig-1: Immune response to RBC antigens in alloimmunized patients [4].

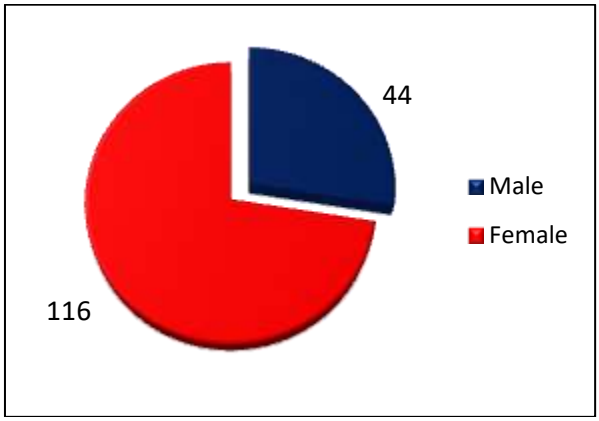

Fig-2: Distribution of study population by gender

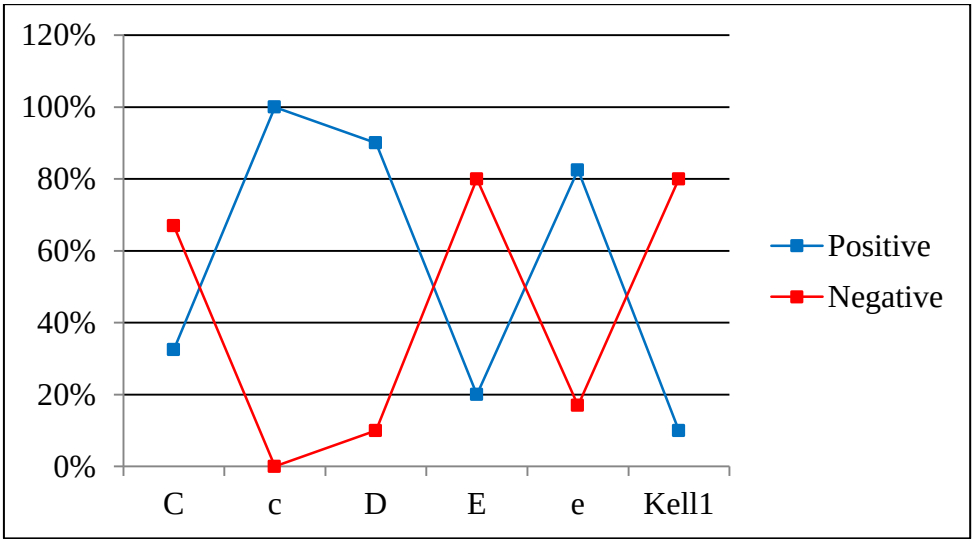

Fig-3: Distribution of positive and negative result among study population.

DISCUSSION

In this cross sectional, descriptive study 160 samples were collected from patients with sickle cell anemia to determine the frequencies of five antigens of Rhesus blood group system have. These have clinical significant in blood transfusion, those antigens were D, C, c, E and e. The study also determines the frequency of kell antigen (Kell1) in sickle cell patients.

In addition to 160 samples, fifteen additional samples were collected randomly from healthy volunteers and compared as control for the test samples. This study showed that there were significant differences between the frequencies of Rhesus antigens D,C ,c, E, and e among sickle cell patients, Rh c was found to be have the highest frequency (100%) followed by Rh D which was found to be (90%), but lower than that reported in Rh E(80%). The frequency of Rh C was found to be (32.5%) while Rh e recorded (82.5%). Although most sickle cell patients in Sudan die by hemolytic crises, no previous study was done in Sudan in the frequency of Rhesus antigens and Kell antigens specially kell1 which was found to be (10%). Transfusion of patients with sickle cell disease (SCD) represents a significant challenge in clinical transfusion medicine with red blood cell (RBC) alloimmunization a primary and serious complication of transfusions. A major cause of alloimmunizationin patients with SCD is the disparate distribution of red cellantigens between donors, who are primarily of European ancestry, and patients with SCD, who are primarily of African ancestry.

Management of alloimmunization in SCD has been the subject of much debate, and currently there is no standard approach. Over two thirds of alloantibodies formed by patients with SCD have Rh blood group specificities. Many programs transfuse patients with SCD with RBCs that are phenotype-matched for D, C/c, E/e, and K, and some also supply RBCs from African-American donors when possible. Although these approaches reduce the incidence of alloantibody production, patients still become alloimmunized. Genetic analysis of patients who develop antibodies in the face of conventional antigen matching has revealed that these patients carry altered RH alleles [15].

Kell is the most important blood group system after ABO and Rh because all frequently occurring Kell-specific antibodies must be considered clinically significant. The highly immunogenic Kell antigens are usually involved in red cell (RBC) alloimmunization that can cause either hemolytic transfusion reactions or perinatalhemolytic disease. Patients with hemoglobinopathies such as sickle cell disease (SCD) require frequent blood transfusions. Therefore, they often become alloimmunized and produce antibodies to low-prevalence Kell antigens, especially KELL1 [16].

Eighteen patients with sickle-cell disease underwent partial exchange transfusion. Three developed delayed hemolytic reactions, with selective disappearance of transfused cells. All reactions occurred within 6 days of transfusion, and patients presented with the clinical features of painful crises. The two most severe reactions were associated with antibodies to Jk^a. These patients developed fever, arthritis, and a clinical course suggesting serum sickness. In both patients, other alloantibodies had previously been seen. A fourth patient developed multiple alloantibodies, accelerated destruction of transfused cells, but milder illness. Such reactions may be commoner than is appreciated and should be suspected when patients have recurrent or severe sickle crises after transfusion. Blood that is non-immunogenic in antigen systems frequently associated with delayed hemolytic reactions (Rh, Kell, Duffy, and Kidd) is preferred for sickle-cell patients who lack these antigens, especially if these patients have previously demonstrated capability to form erythrocyte alloantibody [17].

CONCLUSION

Rhesus blood group antigen c was the commonest antigen among Sudanese patient with SCD as well as Rhesus blood group antigen D has the second frequency among SCD patients in Sudan. In contrast kell1 antigen has the least frequency among Sudanese patients with SCD.

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