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Original Research Article

Red Cell Alloimmunization in Sickle Cell Anemia Patients: An Institutional Study

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Abstract

Western part of Odisha is a region where prevalence of sickle cell disease patients is much high. The prevalence of sickle cell disease in Odisha is about 21-40%. Most of these patients suffer from different types of crises & require frequent blood transfusion. As a result they develop alloantibody resulting in hemolysis in vivo at the time of subsequent blood transfusion. Till now no study has been done in this part of Odisha regarding the prevalence of alloantibody in these patients. In general population, the prevalence of alloantibody is 5%- 8%. So, in our medical college which is a tertiary care center, a prospective study has been done to find out the prevalence of alloantibody in these groups of patients. All diagnosed Sickle Cell Disease patients by HPLC method of different age groups who have received Blood Transfusion were taken for study with their grouping & Rh typing. Then by semi automatic method, three panel antibody screening was done for each sample & DAT was also done for all cases. Out of 90 no. of Sickle Cell Disease patient's alloantibody was detected in 11 samples. Direct Antiglobulin test was positive in all these cases. In Sickle Cell Disease, who received Blood transfusion, alloantibody formation in these patients is a probability in some cases leading to Delayed Hemolytic Transfusion Reactions. In these patients corresponding antigen negative blood transfusion should be given.
Keywords: Sickle Cell Anemia, Alloantibody, DHTR: Delayed Hemolytic Transfusion reaction.

INTRODUCTION

In spite of good results with HYDROXYUREA administration, Blood transfusion still remain a key management modality to reduce morbidity and mortality during last decade. This is more so, due to increased availability of erythrocytarpheresis & better oral chelating drugs to treat transfusion induced iron overload.

Sickle cell anemia patients require frequent packed cell (Red blood cell transfusions), especially to prevent sequestration crises & aplastic crises [1, 2]. Transfusion therapy is also needed at the time of accidents/ surgery in these patients [3, 1].

The red cell transfusion in these patients is always necessary to minimize morbidity & mortality. But on the contrary, such type of transfusion in these patients results in formation of alloantibody & other transfusion related complications. The prevalence of alloantibody in SCA patients rages from 8%-50% in comparison to 2-5% of all transfused recipients [1]. The probability of development of alloimmunisation in SCD patients depends on number & frequency of transfusion, antigenecity, recipient's immunoresponse, antigenic pattern difference between donors & recipients. So, choosing a compatible blood unit for these patients is always a problem on the part of physician, otherwise there is a chance of delayed Hemolytic Transfusion Reactions (DHTRs).

The most common alloantibodies reported to be detected include in higher to lower frequency anti-E, anti-C, anti-K followed by anti-F-y, anti-JK, anti-S & anti-D. Some patients also develop multiple alloantibodies. Some of these antibodies may not be detected during pre transfusion testing & may cause DHTR. The incidence of DHTR is reported to be 11% [4, 5]. Sometimes, the signs & symptoms of DHTR mimic that of SCA patients with vaso-occlusive crises & hemolytic crises.

Racial mismatch is believed to be one of the reasons for the high level of alloantibody in SCA patients. So, it is always advisable to issue antigen-matched blood for these groups of patients [3].

The objective of this prospective study is to find out prevalence of alloantibody in these groups of

SCA patients over a period of one year, to sensitize regarding pre-transfusion antibody screening of patient's samples before X-match for safe transfusion practice & to find out incidence of RBC alloantibodies in repeatedly transfused patients.

MATERIALS AND METHODS

A prospective analysis of all the SCA patients diagnosed with HPLC, who came to the department of transfusion Medicine for receiving blood over a period from July 2017 to JUNE 2018 were taken into consideration. The age of these patients ranged from one year to twenty five years, who have received at least one unit of blood / packed cell (ABO& D matched) in the Transfusion Medicine Department of VIMSAR, Burla. Patients with multiple transfusions due to other hemoglobinopathies or sickle Anemia with no history of transfusion were excluded from this study.

Laboratory investigation

After ABO & Rh blood grouping was done by the standard tube method, for every- sample, the following protocol was followed:-

(A) **Antibody screening:** Before transfusion every serum sample was tested for presence of alloantibody using a 3 cell Panel by gel card method. (Tulip Diagnostics). Auto control was done for each sample.

Gel column method

Material and reagent required

- Coombs-card or Neutral cards
- Card centrifuge
- Incubator of 37^0C
- Pipettes (10µl, 25µl, 50µl)
- isotonic saline solution) with pH 7.2

(B) **Direct antiglobin test (DAT):** the test was done by AHG Gel Card (TULIP)

RESULTS

Out of ninety no of Sickle Cell Anemia patients screened for alloantibody, eleven no. of patients showed alloantibody (Table-1). Out of ninety no. of sickle cell anemia patiens, 49 were males & 41 were females (Table-2).

The age distribution of sickle cell Anemia patients has been depicted in bar diagram. The most common blood groups of these patients were in rank order O+ (n=36 patients), A+ (n=16 patients), B+ (n=28 patients) AB+ (n=10 patients). This distribution has been shown in Table-3 and Pie Chart-2.

Table-1 shows the presence of alloantibody. The gender wise distribution of these patients showing alloantibody has been shown in pie diagram-1. Two patients have both alloantibody & autoantibody.

DAT was positive in all these patients.

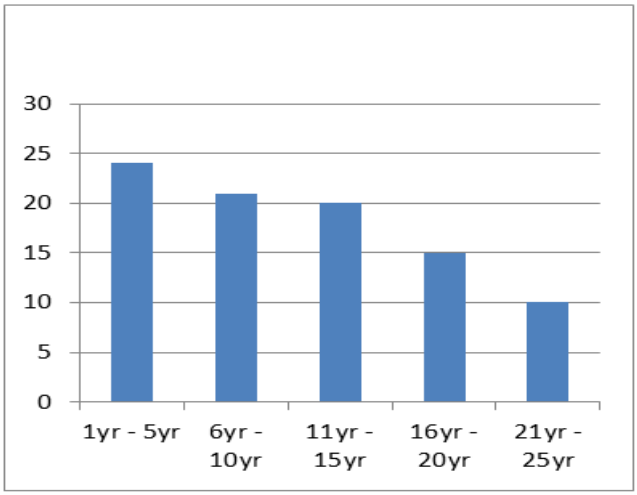
Table-1:

Gender	Presence of alloantibody	Absence of alloantibody	%
Male	6	43	12.24%
Female	5	36	12.19%
Total	11	79	12.22%

Table-2: Demographic data of sickle cell Anemia patients who received regular blood transfusion

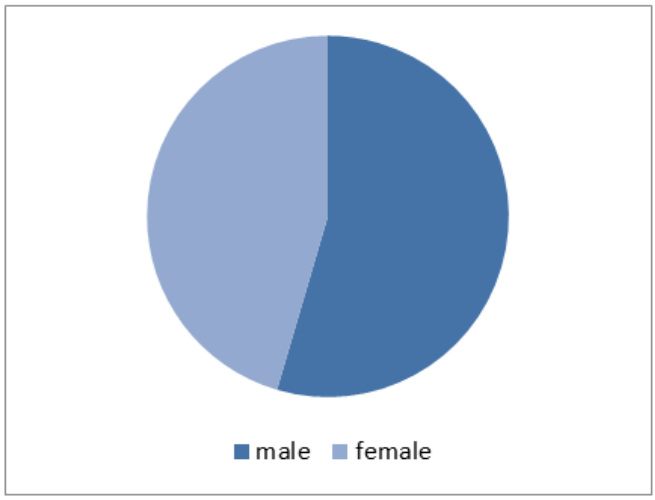
Demographic data	No of patients	%
Total patients	90	
Diagnosis		
Sickle cell disease	90	100%
Gender		
Male	49	54.4%
Female	41	45.5%

Association between alloantibody and gender of sickle cell disease patients

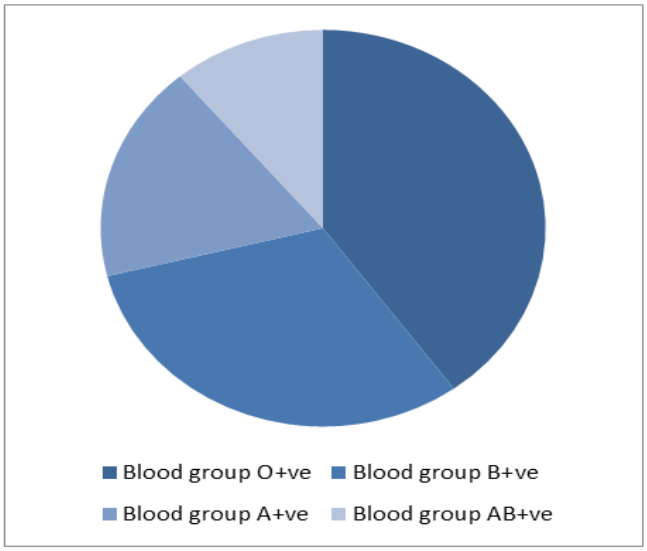


Number of patients according to age (Bar diagram)

Distribution of presence of alloantibody in these patients



Pie Chart-1: According to gender



Pie Chart-2: Distribution of patients according to blood groups

Table-3: Distribution of patients according to blood groups

Blood groups	No of patients	% from total
O+ve	36	40%
B+ve	28	31%
A+ve	16	18%
AB+ve	10	11%

DISCUSSION

Alloimmunisation to red blood cell antigen due to genetic disparity between donor & recipient is one of the risk factors in SCD patients receiving blood transfusion. Repeated blood transfusion can result in production of alloantibody against one / more- blood cell antigens. Alloantibodies can interfere in the x-matching tests & then can create problem in selecting a compatible blood unit & also sometimes gives rise to delayed Hemolytic Transfusion Reaction (SHTR).

Another serious consequence of alloantibodies in SCD patients is the development of DHTR. In many cases of DHTR in SCD patients, patient's Hb level falls below the pre transfusion level, thereby suggesting that, in addition to hemolysis of transfused RBC, patient's own RBCs are lysed. This is due to formation of Alloantibody which once formed stimulates autoantibody formation.

For SICKLE CELL ANEMIA patients, blood transfusion therapy is one of the vital modalities of treatment. In most of the blood banks in Odisha, there is no clear cut policy regarding selection of proper blood unit for these patients. As most of these SCD patients develop alloantibody in course of their transfusion, it becomes very difficult at times to select a compatible blood donor for these patients.

In our study out of Ninety SCA patients, eleven developed clinically significant alloantibody. Genomic analysis such as admixture mapping could indentify molecular markers which could be used to indentify immune responders to transfusion.

International society of Blood transfusion (ISBT) has diagnosed 30 blood group systems out of which 9 blood group systems like ABO, Rhesus, Kell, Kidd, Duffy, MNS, P, Lewis & Lutheran are thought to be clinically significant as incompatibility of these blood group antigens may lead to serious hemolytic transfusion reaction [5].

Very often it is advocated that, partial red cell matching for at least Rh & Kell antigen should be done to reduce the rate of alloimmunisation, however the risk of alloimmunisation to unmatched antigen still exists.

Routinely RBC antigen matching should be done. But, cost, time and labor are the constraints.

The development of alloantibody due to frequent blood transfusion is a fact known since many years.

Some experts advocate issue of leukocyte–depleted blood, because when blood is stored at 2-8^{0}C, it will induce apoptosis of WBC leading to release of immunostimulatory agents & soluble biologic mediators from dying cells which may lead to autoantibody formation.

Alloantibody to WBC and Platelet antigens can occur in SCA patients So, in SCA patients, as far as possible, leukocyte reduced blood & transfusion of red cells matched for the main Rh antigens & Kell antigen may be given.

All of our SCA patients have received Packed cell Transfusion and due to non availability for specific identification of alloantibody, all were referred to higher centers for the same. But, these patients could not be followed up.

L.A. M Bashawari of King Fahd hospital of the university, Saudi Arabia found 13.7% sickle cell patients who developed alloantibody.

CONCLUSION

In areas where prevalence of SCA patients is very high and when they depend on blood transfusion, it is always wise to screen for alloantibody and give them corresponding antigen negative blood.

The production of unnecessary antibodies in sickle cell patients due to transfusion can be avoided. The hemolytic transfusion reaction (acute or delayed) due to alloantibody can be prevented.

Confilct of Interest - Nil

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