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# CLINICAL OUTCOME OF ALLOANTIBODY IN THALASSEMIA PATIENT

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**ABSTRACT**

**ORIGINAL RESEARCH ARTICLE**

**Background:** Thalassemia is a common hemoglobin ailment in Bangladesh and one of the major public health complications. Although blood transfusions are lifesavers for thalassemia patients, they may be associated with some complications especially erythrocyte alloimmunization. The development of alloantibodies may complicate the management of patients with thalassemia. An extended antigenic matching may decrease the risk of alloimmunization.
**Objective:** The aim of the study was to evaluate the outcome of alloantibody in thalassemia patient.
**Methods:** This is an observational study. This study was carried out on 105 population including male and female patients in the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University, Chittagong Medical College Hospital and MH Samorita Hospital & Medical College, Bangladesh. The duration of the period from January 2022 to December 2022. The period from Data was entered in MS Excel and Statistical analysis was done using SPSS-24.
**Results:** The total study population was 105 patients aged 10 – 30 years, 49(46.67%) were ≤10 years, 19(18.09%) were 11-19 years, 20(19.04%) were 20-29 years and 17(16.19%) were ≥30years. And sex distribution of the population where, 28(26.66%) were male and 77(73.33%) were Female.
**Conclusion:** Thalassemia patients may benefit from receiving red blood

cells (RBC) transfusions based on extended antigen matching as demonstrated by the lack of new alloantibodies. There is relatively high rate of alloimmunization in the patients and red cell alloimmunization should not be overlooked in patients receiving regular blood transfusions.

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## INTRODUCTION

Thalassemia is a frequent hemoglobin disease and one of the primary public health problems. Thalassemia is a group of inherited conditions brought on by means of genetic lesions leading to reduced synthesis of one or extra of the globin subunits. [1] The globin chains that are produced in relative excess can injury the red cells or their precursors. As a result, there is an ordinary deficit of hemoglobin tetramers in the red blood cells (RBC) and the mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) are reduced. [2] Thalassemia is regarded the most frequent genetic ailment worldwide. It happens with an especially high frequency in a large belt extending from the Mediterranean basin through the Middle East, India and Southeast Asia. According to data collected from the Hereditary Disease Program of the World Health Organization (WHO) and based totally on nearby surveys and reports through visiting experts, the carriers of hemoglobin issues in the world are estimated to be 269 million. [3] The only countries where a thalassemia register is maintained for surveillance functions are Iran and Oman. [4]

Symptoms of the disorder commonly appear in the first year of life, as fetal hemoglobin (HbF) synthesis diminishes. Pallor is generally the first sign, accompanied by way of splenomegaly of various severity, fever, and failure to thrive. Affected children fail to strengthen and develop normally. Conventional treatment of beta thalassemia major is primarily based on regular blood transfusion from early childhood, which improves the anemia and reduces the skeletal deformities related with immoderate erythropoiesis. [5] Although blood transfusion is a lifesaver for thalassemia patients, it might also be related with some issues such as iron overload, platelet and RBC alloimmunization. [6] Repetition of transfusions for the cure of thalassemia main provokes the patient's immune system and produces anti-erythrocyte antibodies. Erythrocyte autoantibodies appear less frequently; however, they can result in medical hemolysis and in concern in cross-matching blood. Alloimmunization in opposition to red blood cell antigens will increase the need for transfusion and can be appreciably complicated transfusion therapy. Some alloantibodies are hemolytic and can also cause hemolytic transfusion reactions and limit the availability of similarly secure transfusion. Others are clinically insignificant. [7]

Appropriate and regular red cell transfusion remains the important treatment desire for a massive quantity of patients with thalassemia major. These patients who are maintained on hypertranfusion schedule can develop various complications due to multiple transfusions, one of them being allosensitization to red cell antigens. As blood is automatically matched with admire to major blood group antigens i.e., ABO and Rh D antigen, there is an excessive probability that the donor will have minor blood group antigens no longer current in the recipients which will result in alloimmunization. Alloimmunization appreciably worries the Rhesus, Kell, Duffy and Kidd system which are clinically significant. [9] They can cause, not perpetually hemolytic transfusion reactions and limit the potential of safer transfusion while, others are clinically insignificant. [10]

Factors for immunization are complicated and contain at least three important contributing elements. This consists of RBC antigenic distinction between the blood donor and the recipient, the recipient's immune status and immunomodulatory impact of the allogenic blood transfusions on the recipient's immune system. [11]

In thalassemia major, red cell alloantibody manufacturing typically happens after the age of 6 years after multiple transfusions. Perhaps this is due to immune tolerance developed through periodic blood transfusion started out in early age. [13] The relation between the quantity of blood transfused and antibody formation is unknown in thalassemia major however it is an essential component for improved alloimmunization. However, it has been said that the earliest sensitization if any, appears frequently after ten transfusions. [14]

**METHODOLOGY**

This is an observational study. This study was carried out on 105 population including male and female patients in the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University, Chittagong Medical College Hospital and MH Samorita Hospital & Medical College, Bangladesh. The duration of the period from January 2022 to December 2022. After collection, the data were checked and cleaned, followed by editing, compiling, coding and categorizing according to the objectives and variable to detect errors and to maintain consistency, relevancy and quality control. The choice of treatment was made by the patient after a full discussion with the multidisciplinary team consisting of haematologist and transfusion medicine specialist. The data for this study about had been accumulated from patients' medical information. Statistical evaluation of the results used to be got via the use of a window-based computer software program devised with Statistical Packages for Social Sciences (SPSS-24).

**RESULTS**

**Table 1:** Distribution of patients according to age

| Age Group | n=105 | % |
|---|---|---|
| **≤10** | 49 | 46.67 |
| **11-19** | 19 | 18.09 |
| **20-29** | 20 | 19.04 |
| **≥30** | 17 | 16.19 |

Table 1 shows that age distribution of the population, where 49(46.67%) were ≤10 years, 19(18.09%) were 11-19 years, 20(19.04%) were 20-29 years and 17(16.19%) were ≥30years.

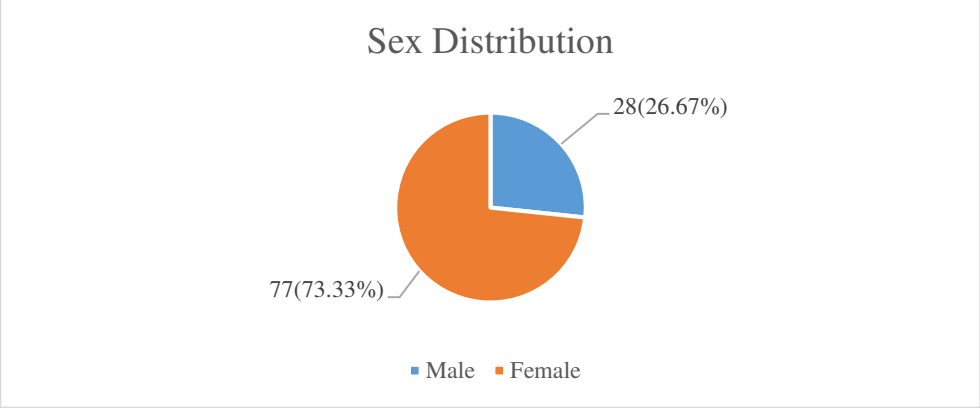


**Figure 1:** Distribution of patients according to sex

Figure 1 shows that sex distribution of the population where, 28(26.67%) were male and 77(73.33%) were Female. Most of the patients belong to female.

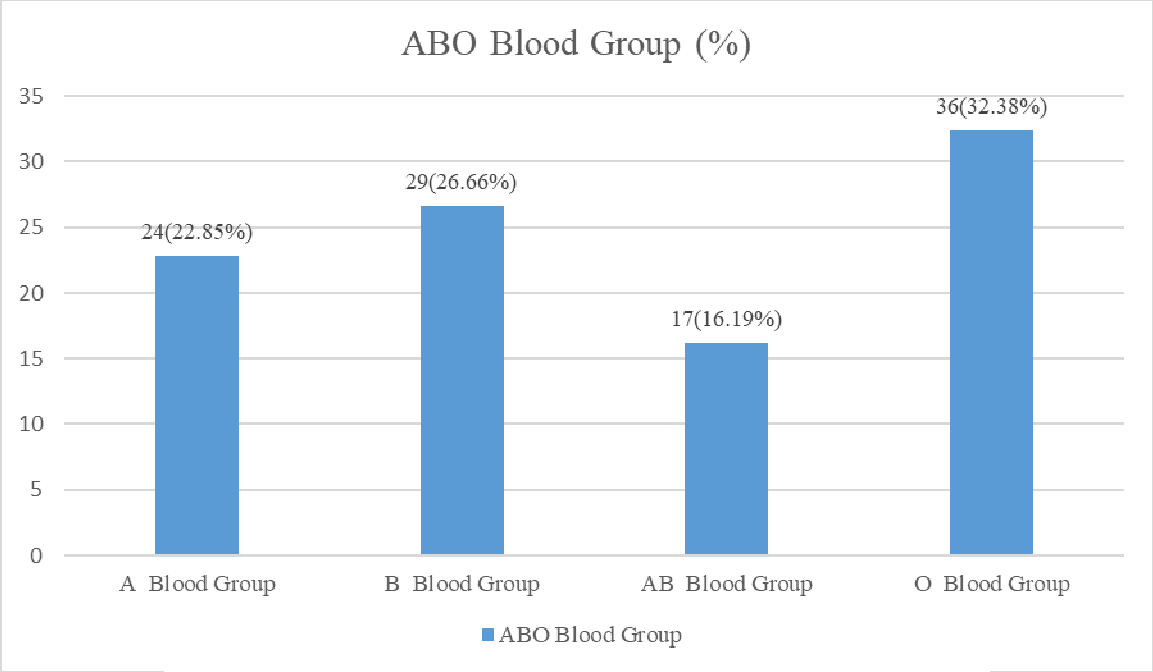


**Figure 2**: Distribution of patients as per their ABO blood group.

Figure 2 shows the distribution of patients as per their ABO blood group, where 24(22.85%) were A blood Group, 29(26.66%) were B blood Group, 17(16.19%) were AB Blood Group and 36(32.38%) were O blood Group. Most of the patients belong to O blood Group.

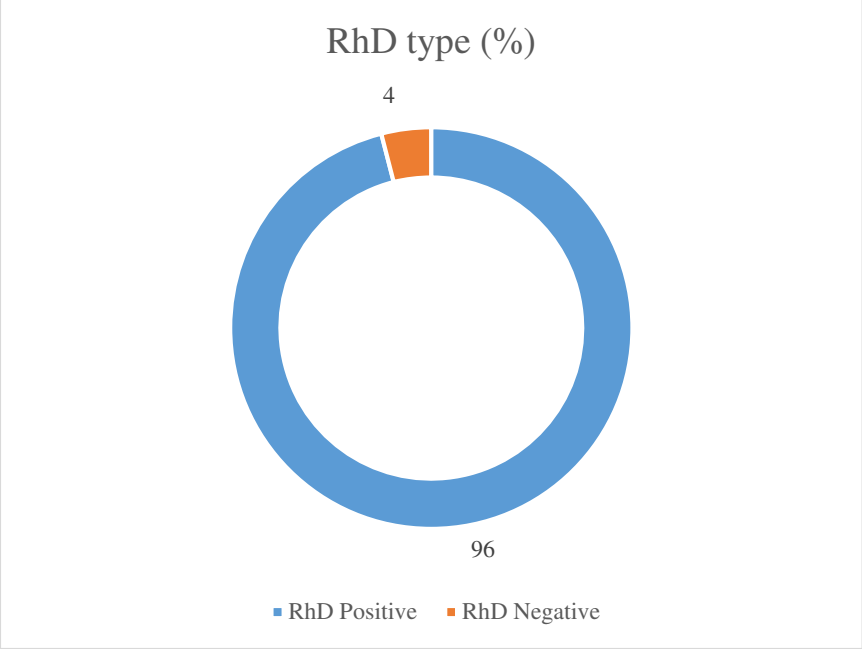


**Figure 3:** Distribution of patients as per their RhD type

Figure 3 shows the distribution of patients as per their RhD type, where 96% were RhD Positive and 4% were RhD Negative.

**Table 2:** Distribution of patients according to number of transfusions they received

| Number of cases | n=105 | % |
|---|---|---|
| **≤50** | 17 | 16.19 |
| **51-100** | 45 | 42.86 |
| **101-150** | 15 | 14.28 |
| **151-200** | 9 | 8.57 |
| **>200** | 19 | 18.09 |

Table 2 shows the cases distribution of patients according to number of transfusions they received, where 17(16.19%) observed in ≤50 cases, 45(42.86%) observed in 51-100 cases, 15(14.28%) observed in 101-150 cases, 9(8.57%) observed in 151-200 cases and 19(18.09%) observed in >200 cases.

**Table 3:** Distribution of patients with respect to age at 1st transfusion.

| Age at 1st transfusion | n=105 | Alloantibody developed |
|---|---|---|
| **<12 months** | 89 | 1 |
| **≥ 12 months** | 16 | 7 |

Table 3 shows that age distribution of patients with respect to age at 1st transfusion. Here, transfusion was 89% and Alloantibody developed 1 when age <12 months. And transfusion was 16% and Alloantibody developed 7 when age ≥ 12 months.

**DISCUSSION**

Alloimmunization complicates transfusion therapy in thalassemia patients with consequent delay in acquiring compatible RBC units. Other major complications are due to the shortened RBC survival and extended deposition of iron in tissue. [15] Several elements may additionally make contributions to the improvement of alloantibodies, including the immune status of recipient, the number of transfusions and the phenotypic heterogeneity that does no longer permit a perfect match between donor and recipient. However, it is not recognized how transfusion elements such as frequency and quantity of RBC transfused contribution to the immunologic reaction. [16]

Some authors have suggested that in chronically transfused patients the improvement of antibodies directed in opposition to these antigens can lead to hemolytic reactions of mild/moderate intensity. [17] Castro and colleagues evaluated the correlation between the number of antigens mismatched in RBC units transfused and the chance of growing alloantibodies in patients with hemoglobinopathies. [18] With the multiplied quantity of required antigens matches, there is a discount in alloantibodies formation up to 70%, however additionally a multiplied concern for the recruitment and typing of matching donors. In particular, it was once tough to assure phenotype-matched RBC units even for MNS antigens, particularly in some durations of the year (i.e., summer) due to the low availability of donors. [19] This study, shows that age distribution of the population, where 49(46.67%) were ≤10 years, 19(18.09%) were 11-19 years, 20(19.04%) were 20-29 years and 17(16.19%) were ≥30years. And sex distribution of the

population where, 28(26.67%) were male and 77(73.33%) were Female.

Several authors suggested that a phenotype match via thinking about exceptional "minors" erythrocyte antigens may also lead to accelerated pre-transfusion Hb levels, diminished extent of RBC transfused and decreased frequency of transfusions in thalassemia patients. However, this research only confirmed the tremendous prevention on the improvement of new alloantibodies after the introduction of a greater stringent phenotype matched transfusion protocol, however clinical preliminary records associated to these RBC transfusions have been absent. [20]

Alloimmunization, a response of the immune system to foreign antigens, is one of the important issues of transfusions, especially in patients who are chronically transfused. [21] In our patients, the pre-transfusion donor vs. recipient matching used to be focused for ABO and RhD antigens. All the patients have been being transfused a non-leukodepleted blood. In Iran, resolution of donors is based totally on clinical and demographic elements and screening tests for blood transfusion transmitted infections function for all blood units. [22] It has been identified that if blood had been matched only for ABO and RhD groups, an excessive rate of alloimmunization would be expected. [23] The most well-known antibodies are towards Kell and subgroups of Rh, which is comparable to different studies. In our study, the distribution of patients as per their ABO blood group, where 24(22.85%) were A blood group, 29(26.66%) were B blood group, 17(16.19%) were AB blood group and 36(32.38%) were O blood group. Most of the patients belong to O blood group. and Patients as per their RhD type, where 96% were RhD Positive and 4% were RhD Negative.

A find out about in Italy amongst patients of thalassemia major via Sirchia et al published a rate of alloimmunization of 5.2% alloantibodies had been located in 74 out of 1432 patients. A whole of 136 alloantibodies had been determined in 74 patients which had been completely restricted to the frequent antigens of Rhesus, Kell, Kidd, Duffy and MNS system. [24] Twenty-one (28%) patients had two alloantibodies and seventeen (23%) had greater than two alloantibodies. Another learns about carried out in Hong Kong amongst patients of Asian descent through HOR - Kung Ho et al 7 confirmed a total ofnine alloantibodies in 68 (7.4%) patients. The alloantibodies determined had been anti-E, anti-M, anti-HLA, anti-BG, anti-BW.

However, many research has additionally pronounced an excessive rate of red cell alloimmunization. A find out about through Singer et al, suggested frequency of alloimmunization of 22% in patients with thalassemia major. [25] He pronounced that 19 red cell alloimmunization have been viewed in 14 out of 64 patients. Three antibodies had been detected in one patient while two antibodies in three patients. Anti-Kell was once most regularly identified. This document additionally interestingly states that patients who receive blood matched for Rhesus and Kell machine from their first transfusion, the rate of alloimmunization is observed to be relatively low. [26] Hence, they inferred that transfusion of blood phenotypically matched for Rh and Kell systems in contrast to blood phenotypically matched for the standard ABO-RhD system should prove to be effective in preventing alloimmunization.

Our present findings show that, that cases distribution of patients according to number of transfusions they received, where 17(16.19%) observed in ≤50 cases, 45(42.86%) observed in 51-100 cases, 15(14.28%) observed in 101-150 cases, 9(8.57%) observed in 151-200 cases and 19(18.09%) observed in >200 cases. And transfusion was 89% when age <12 months and 16% when age ≥ 12 months. In southern Iran, alloantibodies have been discovered only

amongst 5.3% of patients. [27] In other study, Sadeghian et al. indicated that the frequency of alloimmunization in thalassemia patients in northeast Iran is 2.87%. They recognized 12 alloantibodies in 9 patients that all had been in opposition to Rh blood group antigens (D, C and E). The most frequent alloantibodies had been Anti-D (88.88%) and observed by using Anti-C and Anti-E. Higher frequency of alloimmunization observed in female, Rh negative and splenectomies patients. [28] Cheng et al. mentioned that 23% (88 of 382) of Chinese thalassemia primary patients have RBC antibodies. Anti-E (42, 39.3%), anti-Mia/Mur (33, 30.85%), anti-c (14, 13.1%), and anti-Jka (seven, 6.55%) had been the most common antibodies reported. Bhatti et al. [29] showed that 4.97% of 161 patients with thalassemia major have been alloimmunized. RBC alloantibodies belonged commonly to the Rh system even though different antibodies such as anti-K, anti-Jsb, and anti-Jka have been detected. There used to be no exact relation between alloantibodies formation and the age of start blood transfusion, variety of blood transfusions, and patient's race. The most frequent clinically significant alloantibodies had been in opposition to antigens in the Kell and Rh system. These researchers believe that performing a right compatibility evaluation for donor and recipient blood units and using post storage leukodepleted blood are vital elements to decrease alloimmunization in excessive occurrence alloantibodies amongst thalassemia patients.

## LIMITATIONS OF THE STUDY

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

## CONCLUSION

There is relatively excessive rate of alloimmunization in the patients when compared to data. Red cell alloimmunization should not be overlooked in patients with thalassemia foremost receiving regular blood transfusion. It should always be considered if the patient repeatedly suffers from hemolytic transfusion reaction or not being able to preserve hemoglobin at a desired level in spite of regular transfusions. Regular screening for red cell alloantibodies would add towards the better management of these patients.

## RECOMMENDATIONS

A multicenter double blinded study in the divisional/ tertiary hospitals of whole Bangladesh can reveal the real picture. The study period should be long. Multi-disciplinary approach of research work can make a study precise & more authentic in this regard.

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**Conflict of interest:** None declared.

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