

# ASSESSMENT OF FREQUENCY OF ALLOIMMUNIZATION AND ERYTHROCYTE AUTOIMMUNIZATION IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS

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**Abstract-** Life-long red blood transfusion remains the main treatment for severe thalassemia. The development of hemolytic alloantibodies and erythrocyte autoantibodies complicated transfusion therapy in thalassemia patients. The frequency causes and prevention of this phenomenon among 80 transfused thalassemia patients were evaluated in Ali Asghar Children's Hospital during 1998-2004 in a cross-sectional study. In our study the mean age at the initiation of transfusion was 1.7 years (SD = 1.94) and mean interval of transfusion 33.73 day (SD = 20.74). Autoimmunization in 15 patients was positive and 8 patients had hemolytic reaction in transfusion. Our data show that alloimmunization to minor erythrocyte antigens and erythrocyte autoimmunization of significant clinical variables, are frequent findings in transfused thalassemia patients. However data suggest that prevalence of immunization in our patients is less than other Asian countries.

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**Key word:** Transfusion, thalassemia, alloimmunization, autoimmunization, coomb's test, hemolytic reaction

## INTRODUCTION

Life-long red blood cell (RBC) transfusion remains the main treatment for severe thalassemia (1). The use of regular blood transfusion and of chelation therapy with deferoxamine has led to the transfusion of thalassemia major from a fatal disease in early childhood to a chronic illness associated with prolonged survival (2, 3).

The development of anti RBC antibodies (alloantibodies and/or autoantibodies) can significantly complicate transfusion therapy.

Some alloantibodies are hemolytic and may cause hemolytic transfusion reactions and limit the availability of further safe transfusion. Others are clinically insignificant (2).

Erythrocyte autoantibodies appear less frequent but they can result in clinical hemolysis and in difficulty in cross-matching blood. Patients with autoantibodies may have a higher transfusion rate and often require immunosuppressive drugs, splenectomy or alternative treatments (1, 4).

Despite the recognition of autoantibodies are transfusion associated risks, little is known about the extent and causes of these phenomena among thalassemia patients or the appropriate prevention methods (1).

We studied the frequency of alloimmunization and erythrocyte autoimmunization among thalassemia patients who received regular transfusion in Ali Asghar Children's Hospital.

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## MATERIALS AND METHODS

This study was undertaken on 80 patients with thalassemia major who had received regular transfusion in our hospital (Ali Asghar Children's Hospital) during 1994-2004 (cross-sectional). We obtained informed consent from parents of all patients.

Clinical and transfusion records of these patients for a mean age 8.35 years (range 2-15years) were analyzed.

All of patients were examined for the presence of alloimmunization or autoimmunization, these examination include: interval time from start of transfusion, antibody specificity, coomb's test, exposure to nonleukoreduced blood. In cases of a positive DAT (direct anti globin test), detection of IgG, IgM or complement was performed.

Data were analyzed by SPSS software, version 13.

## RESULTS

All of the patients received leukodepleted blood for various time periods. Of the 80 patients there were 37 males (46%) and 43 females (53.8%).

The mean of duration of transfusion was 73.33 days (range 10-108 days). All of the patients received bedside leukofiltered blood. In this study, we identified that 15 patients (18.8%) developed autoantibody, as determined by a persistent or transient positive DAT that ranged between 1+ and 4+ was based on maximum score of 4+. 8 patients (10%) developed immune hemolytic anemia after transfused and all patients required prolonged or recurrent treatment with I.V. Ig and steroids. Of the 15 antibodies 14 were warm IgG antibodies and 1 antibody was cold IgM antibody. Of the 80 total patients 3 developed alloantibody.

The most common clinically significant alloantibody was directed against anti gene in the kell and Rh systems.

Among the 3 alloantibodies detected in our patients ; 1 anti Kell, 1 anti c, 1 anti E, that has been caused hemolytic transfusion reaction or hemolytic

disease. All our patients with alloantibody have more than 10 years of regular blood transfusion (range 2-15 years).

All of the patients had their spleen removed prior to the time of antibody formation.

## DISCUSSION

Management of patients with beta thalassemia is based on adequate and safe blood transfusions and received regular Iron-chelation therapy that improve the quality of life and improve survival of patients with beta thalassemia (5-7).

The development of hemolytic alloantibodies and erythrocyte autoantibodies complicates transfusion therapy in thalassemia patients, have investigated the frequency and causes of that. The factors for alloimmunization are complex and involve 3 main contributing elements. The RBC antigenic difference between blood donor and recipient; the recipient's immune status; and the immuno-dulatory effect of the allogenic blood transfusions on the recipient's immune system (1).

A low rate of alloimmunization may be expected when there is homogeneity of RBC antigens between the blood providers and recipients (8). Previous data on presumed homogenous populations in Greece and Italy showed an overall low rate (5% to 10%) of alloimmunization (1). The majority of patients had a long term exposure to nonleuko poor blood. We postulate a similar activated immune system among our patients who had splenectomy had a higher alloimmunization rate (1). The spleen absence may further enhance the immune response to the infused foreign antigens which are not effectively filtered.

The association of thalassemia and erythrocyte autoantibodies has not been studied. The true frequency and the clinical spectrum are unknown. Autoantibody formation was mostly IgG, warm antibodies and had significant clinical hemolysis. The antibody development was associated with alloimmunization, exposure to nonleukoreduced blood and absence of spleen (9). The immune response may also be affected by the patient's age at

the start of transfusion and the number blood units a patient receives. The relation between the number of blood units transfused and antibody formation is unknown in thalassemia, but it is an important factor for increased alloimmunization in patients who receive multiple transfusion (9-11). Other patients may have serologic findings of a clinically significant alloantibody without evidence of a hemolytic transfusion reaction (4, 6).

In study of Silvia in 2000 Asian patients 38% of cases had alloantibody and erythrocyte autoantibodies as determined by a positive coomb's test developed in 25% or 16 of the 64 patients, there by causing severe hemolytic anemia in 3 of 16 patients (1). In 2003, Ameen *et al.* reported fifty-seven (30%) patients developed RBC alloantibodies. The most common clinically significant alloantibodies were directed against in the Kell and Rh system. RBC autoantibodies developed in 21 (11%) patients (12).

In 2004, Bhatti reported of 161 patients suffering from beta thalassemia red cell immunization was found to be 6.84%. Red cell alloantibodies were detected in 4.97% patients and direct antiglobulin test was positive in patients (1.87%) with increased hemolysis (13). In our study alloimmunization was observed in 3 cases and belonged mainly to Rh system and rate of red cell autoimmunization was 18.8 % (15 cases). Hyper hemolysis due to acquired red cell autoantibodies was found to be an important complication. We found that there is not any relation between the number of blood units transfused and antibody formation.

### Conflict of interests

The authors declare that they have no competing interests.

## REFERENCES

1. Singer ST, Wu V, Mignacca R, Kuypers FA, Morel P, Vichinsky EP. Alloimmunization and erythrocyte autoimmunization in transfusion-dependent thalassemia patients of predominantly asian descent. *Blood*. 2000 Nov 15;96(10):3369-3373.
2. Thuret I. [Therapeutic management of patients with thalassemia major]. *Bull Soc Pathol Exot*. 2001 May; 94(2):95-97. French.
3. Vichinsky EP, MacKlin EA, Waye JS, Lorey F, Olivieri NF. Changes in the epidemiology of thalassemia in North America: a new minority disease. *Pediatrics*. 2005 Dec; 116(6):e818-825.
4. Argioli F, Diana G, Arnone M, Batzella MG, Piras P, Cao A. High-dose intravenous immunoglobulin in the management of autoimmune hemolytic anemia complicating thalassemia major. *Acta Haematol*. 1990; 83(2):65-68.
5. Wonke B. Clinical management of beta-thalassemia major. *Semin Hematol*. 2001 Oct; 38(4):350-359.
6. Lo L, Singer ST. Thalassemia: current approach to an old disease. *Pediatr Clin North Am*. 2002 Dec; 49(6):1165-1191
7. Olivieri N. Thalassemia: Clinical management. *Baillieres Clin Hematol*. 1998 Mar; 11(1): 147-162.
8. Ho HK, Ha SY, Lam CK, Chan GC, Lee TL, Chiang AK, Lau YL. Alloimmunization in Hong Kong southern Chinese transfusion-dependent thalassemia patients. *Blood*. 2001 Jun 15;97(12):3999-4000.
9. Vichinsky EP, Earles A, Johnson RA, Hoag MS, Williams A, Lubin B. Alloimmunization in sickle cell anemia and transfusion of racially unmatched blood. *N Engl J Med*. 1990 Jun 7;322(23):1617-1621.
10. Fluit CR, Kunst VA, Drenthe-Schonk AM. Incidence of red cell antibodies after multiple blood transfusion. *Transfusion*. 1990 Jul-Aug; 30(6):532-535.
11. Rosse WF, Gallagher D, Kinney TR, Castro O, Dosik H, Moohr J, Wang W, Levy PS. Transfusion and alloimmunization in sickle cell disease. The Cooperative Study of Sickle Cell Disease. *Blood*. 1990 Oct 1;76(7):1431-1437.
12. Ameen R, Al-Shemmari S, Al-Humood S, Chowdhury RI, Al-Eyaadi O, Al-Bashir A. RBC alloimmunization and autoimmunization among transfusion-dependent Arab thalassemia patients. *Transfusion*. 2003 Nov; 43(11):1604-1610.

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13. Bhatti FA, Salamat N, Nadeem A, Shabbir N. Red cell immunization in beta thalassaemia major. J Coll

Physicians Surg Pak. 2004 Nov; 14(11):657-660.

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