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Novel Transfusion parameters in Blood bank for Thalassemia patients

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Abstract

Introduction: Thalassemia major is most common monogenic disorder in the world. Around 1,00,000 children are born each year with the severe β homozygous state of the disease in India. The objectives of this study was to assess clinical data and novel transfusion parameters of Thalassemia major patients attending tertiary care hospital. This was undertaken as very few studies have been done in this region of the country.

Materials and Method: The study was done at a tertiary care teaching hospital from January 2014 to December 2014. 35 thalassemia major patients who received blood transfusions in the hospital were taken as inclusion. Clinical details, blood transfusion details and novel parameters of transfusion annual blood requirement and its derivatives were collected on proforma for all patients and data interpreted.

Result: Males (80%) outnumbered females (20%) with male to female ratio of 4:1. Nearly half of the study population was aged between 10 to 12 years (51.43). Majority of the patients had one blood transfusion per month (91.43%) and were on chelation therapy (71.43%). Novel transfusion parameters which includes Annual blood requirement, Mean Annual pure red cell requirement, Mean Annual iron load and Mean Daily iron loading were calculated for each patient.

Conclusion: The present study describes the novel transfusion parameters in blood bank for thalassemia major patients attending the tertiary care hospital and emphasizes on maintenance of transfusion record of thalassemia major patients for better management of these patients.

Keywords: Novel parameters, Thalassemia; Transfusion; Chelation; Annual blood requirement

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Introduction

Thalassemia is a group of inherited hemoglobin disorders characterized by reduced synthesis of one or more of the globin chains leading to imbalanced globin synthesis which is the major factor in determining the severity of the disease in the thalassemia syndromes. Beta-thalassemia results from a defect in beta globulin chain production and ranges from clinically silent heterogeneous thalassemia minor to severe transfusion-dependent thalassemia major.[1,2]

Although reliable data are still lacking for many regions of the world, recent data indicate that about 7% of the world's population is a carrier of a hemoglobin disorder, and that 3,00,000-5,00,000 children are born each year with the severe homozygous state of the disease worldwide.[3] Every year approximately 1,00,000 are born with thalassemia in India.[4] The carrier rate for thalassemia gene varies from 1-3% in southern India to 3-15% in Northern India.[5]

These patients with BTM require regular blood transfusions to survive. Regular transfusion with packed red cells is recommended to maintain a pre-transfusion hemoglobin threshold not exceeding 9.5 g/dl, which seems to be associated with adequate marrow inhibition and a relatively low iron burden.[6] Transfusions should generally be given at an interval of three to four weeks. Transfusions should be scheduled in advance and maintained at a fixed schedule. This enables patients and families to establish routines and will improve quality of life. If cardiac insufficiency is present, higher pre-transfusion hemoglobin levels (10 to 12 g/dL) should be maintained with smaller volume transfusions given every one to two weeks. The only curative treatment for this disease at present is bone marrow transplantation or stem cell transplantation. Management of thalassemia is through lifelong blood transfusion and iron chelation therapy. Even this conventional treatment is often unavailable for patients in remote areas.

There is lack of studies in this region of country describing newer and novel transfusion parameters useful in blood bank for thalassemia major patients. Hence, the present study was undertaken.

Materials and Method

The present cross-sectional study was done at a tertiary care hospital from January 2014 to December 2014. 35 β thalassemia major patients who received blood transfusions were selected during the study period using universal sampling method. Prior to the commencement, ethical clearance for the study was obtained from the Institute ethics committee.

The objectives of this study were to assess the clinical data and transfusion record of these patients. All known diagnosed cases of thalassemia major who were 10 years of age and above, and have received

blood transfusions at two to four weeks intervals with or without iron chelation therapy were included. Patients who are known cases of other types of hemoglobinopathies and patients on transfusion dependent anemia other than thalassemia were excluded from the study. Written informed consent was obtained from the selected patients. These patients were interviewed for the demographic details and history of disease. The clinical examination was done for all patients. Blood transfusion data was collected in detail. Proforma consisted of data regarding total number of blood transfusions during lifetime, number of transfusions per month and Chelation therapy. Average hematocrit of packed cells used in our blood bank is 60%. Novel parameters which includes Annual blood requirement and its derivatives Annual pure red cell requirement, Annual iron load and Daily iron loading were calculated for each patient as per the formula.[7]

Annual blood requirement was calculated as per guidelines as below for each patient.

Annual blood requirement (mL/Kg) =

$$\frac{\text{Volume of blood transfused per 4 weeks (mL) x Total number of transfusions in one year}}{\text{Weight of the patient (Kg)}}$$

Later the derivatives were obtained. The data obtained was coded and entered into Microsoft Excel Spreadsheet. The data was analysed using SPSS version 20. Categorical data was expressed in terms of rates, ratios and percentage. Continuous data was expressed as Mean ± standard deviation, median and range.

Results

A total of 35 patients registered under Blood Bank with thalassemia major were included in the study. On physical examination splenomegaly and hepatomegaly were present among 65.71% and 14.29% of the patients respectively. In the present study, the mean age was 13.46 ± 3.67 years and median age was 12 years with younger patients being 10 years and oldest being 23 years as shown in Table 1. Majority (80%) of the patients were males and the male to female ratio was 4:1.The mean duration of disease was 12.29±3.66 years and the mean total number of transfusions was 151.4±45.65 among all the patients as shown in Table 2.

Novel parameters in the present study are Mean Annual Blood Requirement 201 ± 48.66 mL/kg/yr, Mean Annual pure red cell requirement 150.75 ± 36.49 ml/kg*annum, Mean Annual iron load 162.8 ± 39.41 mg, Mean Daily iron loading 0.43 ± 0.11 mg/kg. as shown in Table 1. ABR was <200 ml/kg in 74.29% of patients and >200 ml/kg in 25.71%. Hence as per the guidelines, patients with raised ABR >200 ml/kg were in need of splenectomy. Hence, this signifies the importance of these parameters in clinical decision.

The commonest age group was 10 to 12 years, comprised of 51.43% of the patients followed by 13-15 years age group (25.71%). Most of the patients were aged between 7 to 12 months (45.71%) and 12 to 18 months (42.86%) at the diagnosis of thalassemia major. The history of splenectomy was noted in 17.14% of the patients**.** Majority of the patients received one transfusion per month (91.43%) as shown in Table 3**.** Majority (71.43%) of patients were on chelation therapy**.** Majority of the patients received one transfusion per month (91.43%) and majority of the patients received 100 to 125 blood transfusions during their lifetime (28.57%) followed by 126 to 150 blood transfusions (22.86%) as shown in Table 2. Least number of blood transfusions of more than 250 transfusions was taken by one patient (2.86%) as shown in Table 3.

Table 1: Blood transfusion record including the novel parameters of transfusion for thalassemia patients

Variable			Median	Range	
	Mean	SD		Min	Max
Age (Years)	13.46	3.67	12	10	23
Age at diagnosis (Months)	8.94	6.15	8	3	36
Duration of disease (Years)	12.29	3.66	11.5	6	22
Frequency of transfusion (Month)	1.09	0.28	1	1	2
Total number of blood transfusions	151.40	45.65	139	92	288
Annual Blood requirement (mL/kg/yr)	201	48.66	180	180	360
Mean Annual pure red cell requirement (ml/kg*a)	150.75	36.49	135	135	270
Mean Annual iron load (mg)	162.8	39.41	145.8	145.8	291.6
Mean Daily iron loading (mg/kg)	0.43	0.11	0.39	0.9	0.79

Table 2: Gender distribution compared to other studies

Gender distribution	Chern et al	Amina adil et al	Khalifa et al	Present study
Male	41	68	32	29
Female	48	56	24	6
M: F ratio	0.85	1.21	1.33	4.83
Total	89	124	56	35

Table 3: Data variables of blood transfusion profile in thalassemia patients

Variables	Sub-groups	Total	
		No.	**%**
Age at Diagnosis (Months)	6 or less	3	8.57
	7 to 12	16	45.71
	12 to 18	15	42.86
	> 18	1	2.86
	Total	**35**	**100.00**
Duration of disease (Years)	5 to 10	14	40.00
	11 to 15	14	40.00
	16 to 20	6	17.14
	> 20	1	2.86
	Total	**35**	**100.00**
Frequency of Transfusion	1	32	91.43
	2	3	8.57
	Total	**35**	**100.00**
Number of transfusions	< 100	2	5.71
	100 to 125	10	28.57
	126 to 150	8	22.86
	151 to 175	6	17.14
	176 to 200	3	8.57
	201to 225	3	8.57
	226 to 250	2	5.71
	> 250	1	2.86
	Total	**35**	**100.00**
Chelation Therapy	Yes	25	71.43
	No	10	28.57
	Total	**35**	**100.00**

Discussion

Thalassemia major is a homozygous state which causes hemolytic anemia demanding regular blood transfusions. The availability of safe blood transfusions with adjuvant chelation therapy has facilitated and extended the survival rates of these patients and now their life expectancy has escalated to fourth and fifth decades. The patient's weight and pre-transfusion hemoglobin and the volume of transfusion should be recorded at each visit. These values should be periodically reviewed to assess the volume of blood required to maintain the desired pre-transfusion hemoglobin level. Complications of blood transfusion include the risk of mismatched transfusion, allergic reactions, and febrile, non-hemolytic reactions. Annual Blood requirement and its derivatives Annual pure red cell requirement, Annual iron load and Daily iron loading are emerging as better transfusion parameters to assist the clinicians to understand the patients iron overload, need for blood transfusion, chelation and splenectomy for better management of patients. These parameters are significant as quantitative assessment of transfusion requirement and iron over load is possible. If Annual blood requirement (ABR) rise above 200ml/kg, Splenectomy should be considered as a potential strategy to reduce the rate of iron loading.[7]

The mean age observed in the present study was close to that of Chern et al.[6] (14.8 ± 6.9 years) and comparable with the other study from Tehran (15.20 ± 3.1 years) and a study by Khalifa et al[8] (15.9 ± 3.1 years). In a study by Najafipour F et al.[9] in Iran reported mean age was 15.62 ± 4.44 years with youngest patient being 10 years and oldest being 27 years. In another study by Khalifa et al[8] showed age range of patients to be 10-30 years as compared to the present study where the age range is 10-23 years. In the present study majority of the patients (80%) were males with male to female ratio of 4:1. Similarly, study done

by Khalifa et al[8] showed majority of patients were males. The sex distribution pattern observed in the present study was similar to other studies from Kolkata[10] and Rawalpindi.[11] Considering 10 gm% (in accordance with the moderate transfusion regimen) of pretransfusion hemoglobin as the cut off between adequately transfused and under transfused patients, we found that among those receiving transfusions once a month, 100% were under transfused. Similar percentages for those receiving 1 and 2 transfusions per month were 91.42%, and 8.58%, respectively.

In the present study majority of patients (71.43%) were on chelation therapy. Chelation can reduce ABR as shown by study done by Cazzola et al.[12] Keeping pre-transfusion Hb to 9-10 g/dL may be sufficient to provide suppression of erythropoiesis and allow a reduction in blood consumption. This finding was support by a prospective trial during the period of moderate transfusion regimen, where transfusion requirements decreased from 137± 26 to 104 ± 23 mL per kg per year of red cells, the saving in transfusion iron averaging 40 mg/kg/year per patient. The mean serum ferritin also decreased from 2448±1515 ng/mL to 1187±816 ng/mL with half of the patients achieving serum ferritin levels lower than 1000 ng/mL.

The following measures would be optimum for the thalassemia care. Programs that provide acceptable care, including transfusion of safe blood and supportive therapy by chelation, must be established. A careful transfusion record of transfused blood should be maintained for each patient, including all the details of the patient, volume of the administered blood units and haematocrit of the donor units. It is possible to calculate the ABR with this available information which is valuable in early identification of hypersplenism thereby prompting timely splenectomy. Blood transfusion exposes the patient to a variety of risks. Thus, it is vital to continue to improve blood safety and to find ways of reducing transfusion requirements and the number of donor exposures. Adverse events associated with transfusion include: Non-hemolytic febrile transfusion reactions, Allergic reactions, Acute hemolytic reaction, Delayed transfusion reactions, Autoimmune hemolytic anemia, Transfusion-related acute lung injury (TRALI), Transfusion-associated circulatory overload, Transmission of infectious agents including viruses, bacteria and parasites, are a major risk in blood transfusion.[7] A multidisciplinary approach is essential for the optimal management of thalassemia, involving Pediatrician, Hematologist, Transfusion specialist and Transplantation experts. Estimation of Serum ferritin must be done regularly to assess iron overload so as to facilitate chelation therapy if required and prevent complications. There is a need for National guidelines for Thalassemia care in India.

Conclusion

In the present study the clinical, socio-demographic characteristics and newer transfusion parameters useful for blood bank were studied in thalassemia patients. The patients with transfusion dependent thalassemia major need comprehensive care. Transfusion record of all thalassemia major patients needs to be maintained regularly in the hospital blood bank for transfusion requirements of patient and new parameters such as Annual Blood requirement and its derivatives Annual pure red cell requirement, Annual iron load and Daily iron loading are useful to plan the chelation and splenectomy hence, assist the clinician for better clinical outcome.

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