International Journal of Contemporary Pediatrics
Bhalodiya VR et al. Int J Contemp Pediatr. 2023 Mar;10(3):330-333
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20230429

Original Research Article

Correlation of serum ferritin level in transfusion-dependant thalassemia major patients: a study at a medical college affiliated hospital in Gujarat region

Vijay R. Bhalodiya[1], Lalji G. Valiya[2], Niyati A. Mehta[1], Bhavin B. Padhariya[2]*

[1]Department of Pediatrics, [2]Department of Pathology, GMERS Medical College, Junagadh, Gujarat, India

Received: 07 January 2023
Revised: 02 February 2023
Accepted: 04 February 2023

***Correspondence:**
Dr. Bhavin B. Padhariya,
E-mail: dr.bhavin44@gmail.com

ABSTRACT

Background: Beta thalassemia is one of the most common causes of inherited disorder in the world. In India, around 65000-70000 cases of thalassemia are present currently and every years around 9000-10000 new cases are added. Measurement of serum ferritin level gives an idea about when to start iron chelation therapy, which will reduce the concentration of iron in the serum and thereby prevents the multiple organ damages.
Methods: A prospective hospital based study was conducted on 100 children having beta thalassemia major. These children were regularly transfused at our hospital and their serum ferritin level were measured by ELISA based assay. Detailed transfusion history and demographic profile were recorded and compared with serum ferritin level. Results were analyzed with SPSS software and Microsoft Excels.
Results: In present study, mean serum ferritin level in 0-5 year age group was1262 µg/l, in 6-10 years age group was 1963.44µg/l and in 11-18 years age group was 2387.43µg/l. On applying ANOVA test, it was evident that there was a statistically significant correlation between increased serum ferritin level with increasing age of the patient as well as with increasing number of a total blood transfusion.
Conclusions: High serum ferritin level in beta thalassemia is associated with increasing age of children as well as with increasing transfusion dependency. Serum ferritin measurement at regular interval helps in determining the ideal timing to start iron chelation therapy in transfusion dependant thalassemic patients.

Keywords: Ferritin, Thalassemia, Iron chelation

INTRODUCTION

Thalassemia is one of the most common inherited single-gene disorders in the world. Every year approximately 100,000 thalassemia major children are born all over the world, and there are about 65, 000-67,000 beta thalassemia major patients in India at present.[1] Iron overload is a constant and the most important complication in thalassemia.[2] Serum ferritin concentration accurately reflects body iron stores.[3] Apha and beta-thalassemia has spread widely from the Mediterranean region to Southeast Asia and the Middle East.[4,5] Beta-thalassemia major (BTM) patients may suffer from chronic anaemia, owing to hemolysis and erythropoiesis' dysfunction. Therefore, regular red blood corpuscles (RBCs) transfusions is required to maintain the hemoglobin level at 9.5-10.5 g/dl which is crucial for patients' survival.[6] Transfusion induced hemosiderosis becomes the major complication, however hemosiderosis induced morbidity can be prevented by adequate iron chelation therapy.[7]Growth

retardation in thalassemia is because of chronic tissue hypoxia, iron toxicity, nutritional deficiency (zinc, folate) and growth hormone failure.[8] With introduction of iron chelators, survival rates have improved.[9] In India, most thalassemic children are under transfused and do not get appropriate iron-chelation therapy because the cost of treating a thalassemia child is approximately one lack Indian rupees per year. The aim of the present study is to correlate the serum ferritin levels in multi-transfused β-Thalassaemia major patients with other parameters, so that timely corrective measures in the form of iron chelation therapy can be adopted.

METHODS

Study design, location and population

Current study is a prospective and hospital based conducted at GMERS hospital and medical college attached hospital having in-house excellent facility for blood transfusions and iron chelation therapy. We enrolled the children diagnosed with thalassemia major from April 2021 to March 2022 at the paediatric department, GMERS medical college and hospital, Junagadh. A total of 165 thalassemic children had been presented to the centre, out of which, we had enrolled 100 thalassemic children in the study and informed consent were taken from the all enrolled subjects.

Inclusion criteria

Inclusion criteria for current study were; child suffering from β-thalassemia major only as confirmed by Hb-electrophoresis and age of thalassemic child should be between 0-18 years.

Exclusion criteria

Exclusion criteria for current study were; abnormal liver function tests result, presence of active infection at the time of sample collection and hemoglobinopathies other than beta thalassemia major.

All the selected subjects had transfusion-dependent beta-thalassemia who was on chelation therapy with oral iron chelator desferrioxamine for at least 1 year. Study subjects were classified into three age groups: 0-5 years, 6 -10 years and 11-18 years. In these children, serum ferritin level and anthropometric measurement (height, weight, body mass index (BMI), height for age, weight for age) were measured and recorded. Body mass index (BMI) was calculated using the formula of weight (kg) / height (Sq.M). Growth parameters were calculated based on the World Health Organization (WHO) growth charts. Stunting was defined as low height for age (HFA). According to WHO criteria, those children having HFA between -2SD TO -3SD were considered as having moderate stunting and HFA less than -3SD were considered as having severe stunting.

Procedure

From all study subjects, 3 ml bloods were collected by vein puncture into the serum separator vacutainer blood collection tubes. Serum were separated from the tubes and used for serum ferritin level measurement. Serum ferritin level were measured using ELISA based assay kit (Acculite^{R} ferritin kit) by chemiluminescence immunoassay method.

Statistical analysis

Data entry and analysis were done using SPSS (version21) software and Microsoft excels 2013. Analyses of datasets were done using one-way analysis of variance (ANOVA) test. Pearson's correlation was done to assess correlation of various parameters.

RESULTS

Out of a total 100 enrolled patients, 59 patients were males and 41 were females. Mean age of study subjects was 9.75 years with range from 0-18 years. The age-wise distribution of male and female patients is depicted in (Table 1).

Table 1: Age and gender wise distribution of the study subjects.

Age group (years)	Gender		Total
	Male	Female	
0-5	13	7	20
6-10	23	15	38
11-18	23	19	42
Total	59	41	100

Table 2: Age group wise distribution of mean serum ferritin level.

Age group (years)	Serum ferritin (µg/l) Mean±SD	Total patients
0-5	1262.13±962.96	20
6-10	1963.44±957.57	38
11-18	2387.43±965.69	42
ANOVA test: F value=11.2, p=0.000		
Pearson Correlation: r=0.459, r^2= 0.21, p = 0.000		

The median age of first blood transfusion was 8 month in our study. A positive family history of thalassemia major was found in 21% of patients. Parental history of consanguineous marriage was found in 18% of patients. Mean serum ferritin concentration in study subjects was 2037.80µg/l (range 182.8-4235 µg/l). Age group wise distribution of mean ferritin level is shown in (Table 2). It is evident from (Table 2) that on applying ANOVA test, we got F value of 11.2 and p value of 0.00. It indicates that there was a statistically significant increase in serum ferritin level with increasing age of patients. We also performed Pearson correlation and we got r value of 0.459

and r^2 value of 0.21which itself indicates a positive correlation. We divided the patients according to a total number of blood transfusion per year into three groups 6-12, 13-24 and >24 transfusios per year and each group wise mean serum ferritin level were calculated as shown in (Table 3).

Table 3: Serum ferritin level according to a total number of blood transfusions per year.

Total number of blood transfusions per year	Mean serum ferritin (µg/l)	Total patients
6-12	1508.77	28
13-24	2028.32	52
>24	2620.38	20
ANOVA test: F value=9.082, p=0.000		

On applying ANOVA test, we got F value of 9.082 and p value of 0.00. It indicates that there was a statistically significant increase in serum ferritin level with increasing the total number of blood transfusions per year. We had calculated differences in serum ferritin level according to demographic characteristic like male vs. female as well as according to various anthropometric characteristic like BMI, height and weight which are shown in (Table 4). It is evident that there is no statistically significant differences in serum ferritin level when compared for various demographic and anthropometric characteristics as in all these parameters p value for significance were above 0.005 as depicted in (Table 4). We had divided the subjects into three age groups (0-5, 6-10 and 11-18 years) and the requirement of a total number of blood transfusions per year according to these age groups is shown in a graphical form in (Figure 1). It is clearly evident from the graph that as the age of the patients increasing there were also increasing requirement of blood transfusions.

Table 4: Serum ferritin level according to demographic and anthropometric characteristics.

Characteristics		Age (years)	BMI (kg/m^2)	Height (Cm)	Weight (kg)	Serum ferritin (µg/l)
Total	**Mean±SD**	9.82 4.79	15.27 2.33	121.61 19.34	23.25 8.70	2001.3 963.5
	Minimum	1	11	74	9	182.8
	Maximum	22	23.55	163	53	4235
Gender	**Male**	9.66	15.08	122.27	23.17	1969.3
	Female	10.05	15.53	120.66	23.37	2047.2
P value		0.693	0.348	0.684	0.912	0.693

Table 5: Comparison of mean serum ferritin level in present study with various national and international studies.

Study performed by	Region where study performed	Year in which study conducted	Mean serum ferritin level (µg/l)
Choudhry et al.[13]	India	2004	6723
Shah et al.[14]	Western India	2010	3456
Rehman et al.[15]	Pakistan	2004	2861
Cunningham et al.[16]	North America	2004	1696
Present study	Western India	2022	2001

DISCUSSION

Thalassemia is the single most common monogenetic haemolytic anaemia in India. Repeated blood transfusion is required for survival of thalassemic individuals. Due to repeated blood transfusion excessive iron get accumulated in the body leading to a condition known as hemosiderosis. Hemosiderosis is the major cause of late morbidity and mortality in patients with thalassemia major. Serum ferritin measurement is an easy and cost effective test which helps in deciding the ideal timing for starting of iron-chelation theray. Iron chelation therapy prevents iron induced tissue injury and thus prolongs life expectancy. In present study, 59% patients were males and 41% were females. Gender differences in the present study correlates well with studies performed by Torres et al, Najafipour et al, Ikran et al which had 60%, 64% and 64% males respectively and 40%, 36% and 36% females respectively.[10-16] In present study, all the enrolled subjects had elevated serum ferritin level and their mean serum ferritin level was 2001µg/l. Present study's this result of mean serum ferritin level correlates well with the various national and international studies shown in the (Table 5). In present study, there were no statistically significant differences in mean serum ferritin level when compared for various anthropometric characteristics like BMI, height and weight. Similar results were found in study performed by Pemde.[17] It was evident from our study that as the thalassemic children grow older, they were required more number of blood transfusion annually. Those patients who were requiring more blood units per year also had more increased serum ferritin level in their blood. Thus, in thalassemia major as the children grow older, their blood

show proportionately increased level of ferritin irrespective of gender, height and weight of the children.

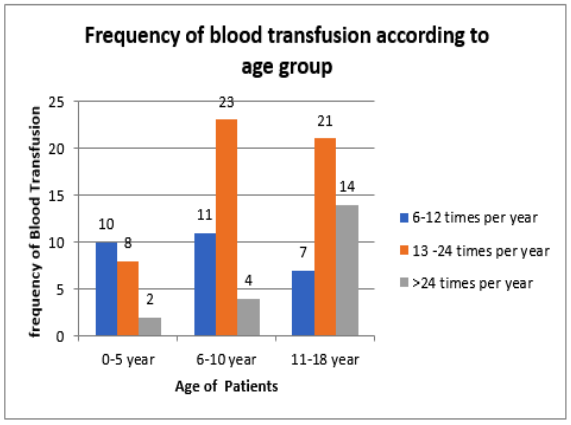

Figure 1: Total number of blood transfusion per year according to age groups.

Limitations

The limitation of the study was small sample size.

CONCLUSION

It was concluded from current study that by considering the serum ferritin level as suitable, rapid, cost effective and accurate measures for indicating iron overload in the body and thus it helps in deciding ideal timing to start iron chelation therapy in thalassemia major patients.

ACKNOWLEDGEMENTS

Authors acknowledge paediatrics department and central laboratory services of GMERS medical college and hospital, Junagadh for their cooperation throughout the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhalodiya VR, Valiya LG, Mehta NA, Padhariya BB. Correlation of serum ferritin level in transfusion-dependant thalassemia major patients: a study at a medical college affiliated hospital in Gujarat region. Int J Contemp Pediatr 2023;10:330-3.