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Original Research Article

Correlation of Serum Ferritin and Serum Ionized Calcium in Transfusion Dependent Beta Thalassemia Major Patient at Tertiary Care Hospital

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Abstract

Background: Thalassemia is a genetic disorder marked by reduced or absent globin chain synthesis in haemoglobin. Approximately 15 million people globally suffer from thalassemia, with 240 million carriers of β-thalassemia. In India, 30 million are carriers, and 12,000 infants are born annually with severe forms. This study aim to evaluate serum ionized calcium levels in thalassemia major patients and explore the correlation between serum ferritin and calcium levels.

Methods: An observational study (March 2023 - March 2024) at C. U. Shah Hospital, Gujarat, involved 50 children (ages 1-18 years) with transfusion-dependent beta thalassemia. Exclusion criteria included those on calcium, vitamin D supplements, or non-deferasirox iron chelators. Data collection comprised patient's histories, clinical examinations, and blood tests (serum ferritin and ionized calcium). Pearson correlation test was used for statistical analysis.

Results: The majority of patients were in the 5-10 year age group, with a male predominance (64%). Most were from rural backgrounds and the mean age was 8 years. Most children were diagnosed between 6-12 months (52%).A significant negative correlation was found between serum ferritin and serum ionized calcium levels ($r = -0.674$, $p < 0.001$). Treatment with deferasirox significantly reduced serum ferritin levels over time.

Conclusion: This study shows a significant inverse relationship between serum ferritin and ionized calcium levels in transfusion-dependent beta thalassemia major patients. Regular monitoring and effective use of iron chelators are crucial to prevent complications. Future research should explore combined therapies and genetic mechanisms of iron-induced hypoparathyroidism to optimize care.

Keywords: Thalassemia, Iron Overload, Serum Ferritin, Serum Ionized Calcium, Hypoparathyroidism, Iron Chelation Therapy.

Introduction

Thalassemia refers to a spectrum of diseases characterized by the reduction or absence in the synthesis of the globin chains of haemoglobin. Worldwide, approximately 15 million people are estimated to suffer from thalassemic disorders. Reportedly, there are about 240 million carriers of β-thalassemia worldwide, i.e., 1.5% of world population, and in India alone, the number is approximately 30 million with 505 in S.E. Asia [1,2,3]. The burden of haemoglobinopathies in India is high with nearly 12,000 infants being born every year with a severe disorder. These numbers imply that every hour 1 child is born who will suffer with this genetic disorder. The carrier rate for β – thalassemia varies from 1-17 % in India with an average of 3.2% [4, 5]. This means that on an average 1 in every 25 Indians is a carrier of thalassemia. Thalassemia exists in 3 forms:

- Thalassemia trait or the asymptomatic carrier

stage – The carrier does not exhibit anysymptoms and leads an absolutely normal life.

- Thalassemia intermedia – Genotypically the patient is similar to a thalassemia major butdiffers phenotypically in that they do not require regular transfusions.
- Thalassemia major – In β thalassemia major, the production of β-globin chains is severelyimpaired, because both β-globin genes are mutated.

The severe imbalance of globin chain synthesis results in ineffective erythropoiesis and severe microcytic, hypochromic anemia. Clinical presentation of thalassemia major occurs at 6 months of age affected infants fail to thrive and become progressively pale. Feeding problems, diarrhea, irritability, recurrent bouts of fever, and progressive enlargement of the abdomen due to Splenomegaly may occur. Patients are treated by lifelong blood transfusion every 15 to 30 days along with iron chelation therapy.

The mainstay of treatment of severe β thalassemia is regular blood transfusion with an attempt to maintain hemoglobin levels greater than 10 g/dl [6]. Repeated blood transfusions results too much iron which in turn can result in damage to the heart, liver and endocrine system, which includes glands that produce hormones that regulate processes throughout the body [7,8,9]. For example, iron deposition in the parathyroid gland, which in turn may cause hypoparathyroidism. As a resultof hypoparathyroidism, low serum calcium levels have been reported in such patients and showingsymptoms of hypocalcemia. Though the life expectancy of patients with thalassemia has greatly improved over the last decade as a result of regular transfusions and increased compliance with iron chelation therapy, however, this improvement is often accompanied by a series of serious complications including osteopenia and osteoporosis [10]. Calcium is an essential mineral for building and maintaining strong bones and teeth. Having strong bones is important for all of us, but it is especially important for people with thalassemia. Limited studies have also shown that supplementation with vitamin D and calcium improves serum calcium status in turn bone health. Hence the study was planned to estimate serum ionized calcium levels in patients with thalassemia major. The main aim of the study was to see the calcium status in thalassemia major patients by estimating serum ionized calcium and estimating of serum ferritin for iron overload thalassemia patients and to determine possible correlation between serum ferritin level and serum ionized calcium level.

Aims and Objectives

- To describe calcium level in transfusion dependent beta thalassemia patient.
- To determine the possible association between serum ferritin and calcium level.
- To observe serum ferritin pattern according to dose and duration of iron chelators.

Material and Methods

This observational study was conducted from March 2023 to March 2024 at C. U. Shah Hospital,Surendranagar, Gujarat, focusing on children aged 1 to 18 years diagnosed with transfusion dependent beta thalassemia. The sample size consisted of 50 children attending the Pediatric OPDor as indoor patients. Inclusion criteria required participants to be within the specified age range and diagnosed with transfusion-dependent beta thalassemia, while those receiving calcium and vitamin D supplementation or taking iron chelators other than deferasirox were excluded. Data collection involved obtaining patient histories from parents, followed by thorough clinical examinations and blood investigations, including serum ferritin and serum ionized calcium levels.

Serum ionized calcium was collected during first day and serum ferritin levels were done every 3 monthly during follow up period. Then all the data was entered in Microsoft Excel 2020 and analyzed using Pearson correlation to examine the relation between serum ferritin and serum ionized calcium level. Statistical package for social science software was used here for analysis of the data. According to time trend of serum ferritin levels, dose adjustment of oral iron chelator (deferasirox) was done and these patients were again re – evaluated after 3 month of starting of deferasirox.

Results:

Table :1 [Patient's Demographics]

Patient's Demographics (n =50)		
Variables	**Frequency (n)**	**Percentage (%)**
Age in groups		
< 5 year	14	28
5-10 year	22	44
10-15 year	08	16
15-18 year	06	12
Gender		
Male	32	64
Female	18	36

Locality		
Rural	36	72
Urban	14	28
Age of Diagnosis		
< 6 Months	11	22
6-12 Months	26	52
1-5 years	12	24
5-10 years	01	02
Family history of thalassemia		
No sibling affected	36	72
One sibling affected	03	06
No sibling	11	22

According to show in Table: 1 among 50 patients, most of the patients were in 5–10-year age group followed by <5-year age groupwith male predominance (64%). Mean age was 8 years. Majority of patients were from rural background (36%). Most of the child was diagnosed as thalassemic at age of 6-12 month (52%) followed by 1-5 year (24%).

A Pearson product-moment correlation was run to determine the relationship between SerumFerritin and Serum ionized calcium level [Table.2]

Table 2: [Pearson Correlation]

Pearson Correlation	Serum Ferritin Level (ng/ml)
Serum ionized calcium (mg/dl)	-0.674**

****. Correlation is significant at the 0.01 level (2-tailed)**

According to shown in **Table :2** Pearson correlation was conducted to examine the relation between Serum Ferritin and serum ionized Calcium level was strongly negatively related to S. Ionized calcium {r= -0.674}, p<0.001}.

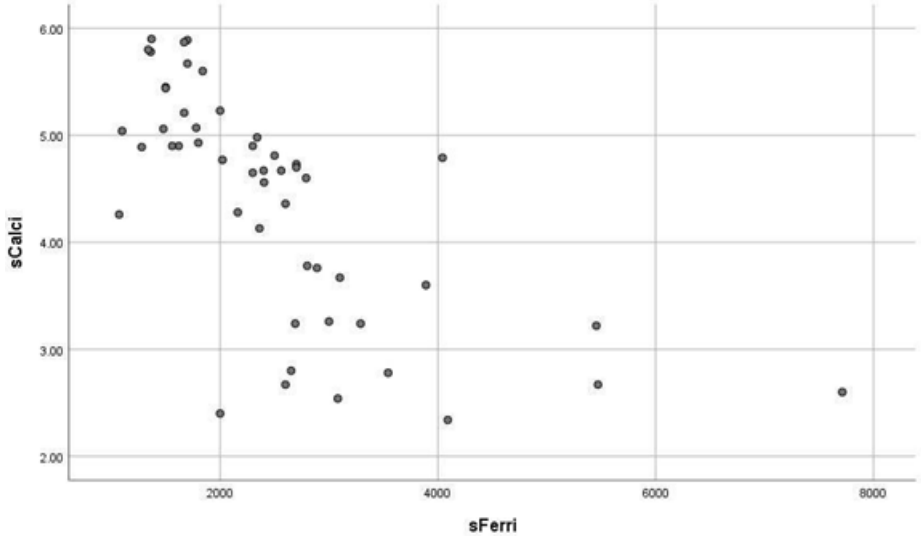

Figure 1: Dot Scatter plot for Serum Ferritin Level and Serum ionized calcium

X axis: Serum Ferritin level (ng/ml)
Y axis: Serum ionized calcium level (mg/dl)
(Normal range of Serum ionized calcium level 4.83 – 5.52 mg/dl, which was measured by NULYTE electrolyte Analyzer machine)

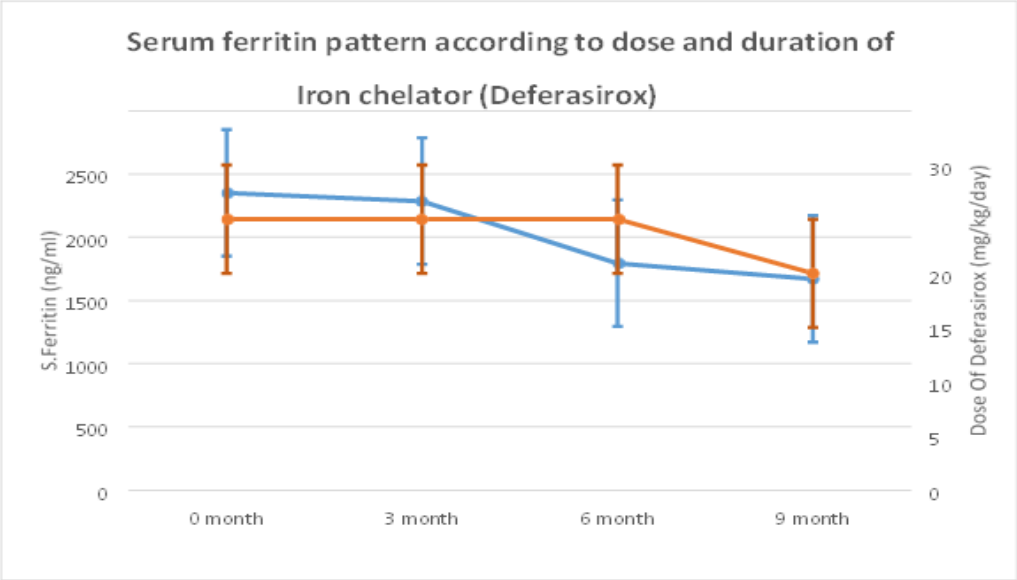

Figure 2:

This graph [Figure : 2] showing time trend of Serum ferritin level and according to dose adjustment of deferasirox (oral iron chelators).This shows that during each subsequent follow up,

"Treatment with deferasirox produced significant reduction in median serum ferritin levels in patients".

Discussion:

Among 50 patients, most of the patients were in 5-10 year age group followed by <5 year age group with male predominance (64%). Male preponderance was also reported by other studies [11]. Mean age was 8 years. Majority of patients were from rural background (36%). Most of the child was diagnosed as Thalassemic at age of 6-12 month (52%) followed by 1-5 year (24%).

This observational study reveals a significant negative correlation between serum ferritin and serum ionized calcium levels ($r = -0.674$, $p < 0.001$). This strong inverse relationship underscores the complex pathophysiological mechanisms at play in thalassemia patients who undergo regular blood transfusions to manage severe anemia.

Iron overload is a well-documented consequence of repeated blood transfusions in thalassemia patients. Excess iron is deposited in various organs, including the liver, heart, and endocrine glands, notably the parathyroid glands. Iron deposition in the parathyroid glands can impair their function, leading to hypoparathyroidism and consequently hypocalcaemia [12,13]. The results of this study corroborate these findings, showing that increased serum ferritin levels, indicative of iron overload, are associated with decreased serum ionized calcium levels. Similar studies have reported that hypoparathyroidism in thalassemia patients leads to low serum calcium levels, manifesting as symptoms of hypocalcemia such as tetany, seizures, and cardiac issues [14].

The findings of this study align with previous research highlighting the adverse effects of iron overload on calcium metabolism. For instance, a study by De Sanctis et al. reported a prevalence of hypocalcemia in thalassemia patients due to iron-induced hypoparathyroidism, emphasizing the need for regular monitoring of calcium levels in these patients [15]. Furthermore, a study by Wonke et al. indicated that iron chelation therapy, particularly with deferasirox, significantly reduces serum ferritin levels and mitigates iron overload, thereby potentially improving calcium homeostasis [16]. This study's findings support this observation, demonstrating that treatment with deferasirox led to a significant reduction in median serum ferritin levels over time [Figure : 2]

The strong negative correlation between serum ferritin and serum ionized calcium highlights the necessity for comprehensive management strategies in thalassemia patients. Regular monitoring of both iron and calcium levels should be an integral part of the management protocol. The effective use of iron chelators, such as deferasirox, not only helps in controlling iron overload but may also prevent the secondary complications of hypocalcemia by reducing iron deposition in the parathyroid glands.

Limitations of the Study:

The importance of early intervention and consistent follow-up in managing thalassemia major. Incorporating calcium and vitamin D supplementation into the treatment regimen may help improve serum calcium levels and support bone health, reducing the risk of osteopenia and osteoporosis in these patients. Studies have shown that calcium and vitamin D supplementation can

significantly enhance bone mineral density and overall calcium status in thalassemia patients, providing a holistic approach to their care.

While this study provides valuable insights, further research is necessary to explore the long-term benefits of combined therapeutic strategies, including the potential role of newer iron chelators and more effective supplementation regimens. Longitudinal studies could help establish a clearer understanding of the optimal management strategies for maintaining calcium homeostasis and preventing bone-related complications in thalassemia patients.

Moreover, investigating the genetic and molecular mechanisms underlying iron-induced hypoparathyroidism could open new avenues for targeted therapies. Understanding the variability in response to iron chelation therapy among different patient populations may also help in personalizing treatment plans to achieve better outcomes.

Conclusion

In conclusion, this study elucidates the significant inverse relationship between serum ferritin and serum ionized calcium levels in transfusion-dependent beta thalassemia major patients. These findings underscore the need for a balanced approach in managing iron overload and calcium homeostasis to prevent the cascade of complications arising from chronic blood transfusions. By adopting a comprehensive monitoring and management strategy we can improve the overall prognosis and quality of life for patients with beta thalassemia major. Future research should continue to explore the interplay between iron and calcium metabolism and investigate innovative therapeutic approaches to optimize patient care in this complex genetic disorder.

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