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ORIGINAL ARTICLE

Frequency of Hypoparathyroidism in Children Presenting with Beta-Thalassemia Major in Tertiary Care Center

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ABSTRACT

Objective: Aim of our study is to determine the prevalence of hypoparathyroidism in children presenting with beta-thalassemia major in tertiary care center.

Study Design: Cross-sectional study

Place and Duration: The study was conducted at Thalassemia Center Divisional Headquarter Hospital Mirpur Azad Kashmir during the period from February 2021 to July 2021.

Methods: There were eighty eight children with both genders had beta-thalassemia were presented in this study. Age of the patients was between 5-14 years. We have obtained formal permission from the authorities to collect full demographics, including age, sex, body mass index, chelation and transfusion therapy, calcium consumption, the age of beginning of HPT, any symptoms of hypocalcemia. Blood samples were taken for measurement of serum calcium and phosphorus. Prevalence of hypoparathyroidism was calculated among all the cases. SPSS 25.0 version was used to analyze all data.

Results: Majority of the patients were males 48 (60%) and 32 (40%) females in this study. Mean body mass index was 7.12±3.13 kg/m^2. Mean age of the patients was 8.12±6.35 years. 45(56.3%) were on combination therapy and chelation therapy was in 35 (43.7%). Mean serum calcium level was 6.17±3.55 mg/dl and phosphorus level was 4.15±9.97 mg/dl. We found frequency of HPT among 18 (22.5%) cases.5.45±7.17 years was the mean age of beginning HPT. Patients had HPT were mostly on single chelation therapy using deferiprone (DFP).There was high prevalence of hypocalcemia found in 43 (53.8%) cases. Among 43 cases of hypocalcemia, 24 (55.8%) patients were asymptomatic and 20 (44.2%) were symptomatic in which paresthesias & numbness was the most common complication.

Conclusion: We found in this study that the frequency of hypoparathyroidism was a common complication in patients with beta-thalassemia. Frequency of hypocalcemia was high among patients with most prevalent asymptomatic cases. Paresthesias & numbness was the most common complication among symptomatic hypocalcemia.

Keywords: Beta-thalassemia, Hypoparathyroidism, Complications, Hypocalcemia

INTRODUCTION

Approximately 70,000 people in Pakistan are thought to have thalassemia, and 6,000 new instances of thalassemia are diagnosed each year. [1] According to Cornell Medical Center, patients who were monitored from 1960 to 1976 saw a median survival of 17.1 years. [2] Safe blood transfusions have given some people a new lease on life. However, this optimism was accompanied by a slew of side effects, including an iron excess and the need for multiple transfusions. [3]

Hemoglobin diseases with a decreased capacity for binding oxygen are known as -thalassemias, which are recessively passed down. Patients with -thalassemia major (BTM) can now live into their fourth and fifth decades of life because to the introduction of safe transfusions and adjuvant chelation treatment [4,5]. This can lead to iron excess, which can cause endocrine problems ranging from hypogonadism, diabetes mellitus, and hypoparathyroidism (HPT).[6]

A BTM patient's HPT is a major endocrine issue. Iron buildup in the parathyroid gland, which can lead to gland malfunction, and increased hematopoiesis due to chronic anaemia are the most common causes of this problem [7]. Seizures, tetany, laryngeal stridor, and paresthesia in the hands or lips can all be symptoms of HPT, as can other neurological disorders [8]. A major source of illness among the thalassemic population is osteoporosis. Even in individuals with normal gonadal function who are given calcium supplements, dual-energy x-ray absorptiometry [9] shows low bone density, suggesting that there are other variables at play.

Gabriele initially proposed in 1971 that iron excess in thalassemics causes hypoparathyroidism, which then leads to hypocalcemia. In subsequent surveys, many more researchers found it. Delaying chelation therapy may have caused iron to build up in the parathyroid glands, which led to this problem. [10] Damage to the parathyroid gland is caused by a variety of processes, including iron sensitivity, increased collagen deposition, and disrupted microcirculation in the patient. Decreased absorption of calcium by the intestines is a result of hypocalcemia.[11]

As a result of a variety of factors, hypocalcemia can be rather frequent. Hypoparathyroidism or vitamin D insufficiency, or a resistance to these hormones, is the

most common cause. However, renal illness, end-stage liver disease, or medicines might be to blame. [12,13] Hypocalcemia can manifest as anything from a non-life-threatening condition to a serious medical emergency, depending on the symptoms. Muscle spasms, myalgia, cramps, tetany, seizures, and even dermatitis are all signs of hypocalcemia. Laryngospasm and neuromuscular irritability can potentially be signs of hypocalcemia. Osteoporosis is the most common complication of persistent hypocalcemia. However, severe hypocalcemia can lead to cardiac collapse, hypotension that does not respond to fluids, and dysrhythmias. Acute convulsions, tetany, basal ganglia calcification, parkinsonism, choreoathetosis, and hemiballismus are among the neurological consequences of hypocalcemia. [14]

Iron chelators desferrioxamine (DFO), deferiprone (DFX), and deferasirox (DFX) are the three most often used ones in clinical practise today. The study's goal was to find out how common HPT was in a sample of BTM patients who had had iron chelation treatment.

MATERIAL AND METHODS

In this cross-sectional study was conducted at Thalassemia Center Divisional Headquarter Hospital Mirpur Azad Kashmir during the period from February 2021 to July 2021 and consisted of 80 patients who had beta-thalassemia.We have obtained formal permission from the authorities to collect full demographics, including age, sex, body mass index, chelation and transfusion therapy, calcium consumption, the age of beginning of HPT, any symptoms of hypocalcemia. Patients <5years of age, receiving calcium and vitamin D supplementation, or drugs affecting calcium levels like bisphosphonates, proton pump inhibitors, diuretics, antiepileptics, cisplatin and those did not provide any written consent were not included in this study.

Presented children were aged between 5-14 years. Patients were separated based on whether they had undergone a single iron chelation therapy (DFO, DFP, or DFX) or a combination of therapies. Three millilitres of blood were extracted from individuals through venipuncture in simple tubes with gel. A centrifuge was used to separate the serum from the clotted blood. Afterwards, the sera were frozen and kept at temperatures as low as -20 0 degrees Celsius. The photocolorimetric technique was then used to measure calcium levels in the sera that had been collected. It was decided to use plain test tubes for the experiment and to fill them with the following: 750ml buffer, 250ml CPX solution, and 10ml of the patient's serum. Readings were recorded at 570 nm after 10 minutes of mixing the materials. Hypocalcemics are those whose serum calcium levels are less than 8.6 mg/dl. Prevalence of hypoparathyroidism was calculated among all the cases. SPSS 25.0 version was used to analyze all data.

RESULTS

Majority of the patients were males 48 (60%) and 32 (40%) females in this study. Mean body mass index was 7.12±3.13 kg/m^2. Mean age of the patients was 8.12±6.35 years. 45(56.3%) were on combination therapy and chelation therapy was in 35 (43.7%). Mean serum calcium level was 6.17±3.55 mg/dl and phosphorus level was 4.15±9.97 mg/dl.(table 1)

Table 1: Characteristics of enrolled cases

Variables	Frequency	Percentage
Mean age (years)	7.12±3.13	-
Mean BMI (kg/m^2)	8.12±6.35	-
Sex		
Male	48	60
Female	32	40
Mean Calcium level (mg/dl)	6.17±3.55	-
Mean Phosphorus level (mg/dl)	4.15±9.97	-
Type of therapy		
Single-chelation	35	43.7
combination	45	56.3

We found frequency of HPT among 18 (22.5%) cases.(fig 1)

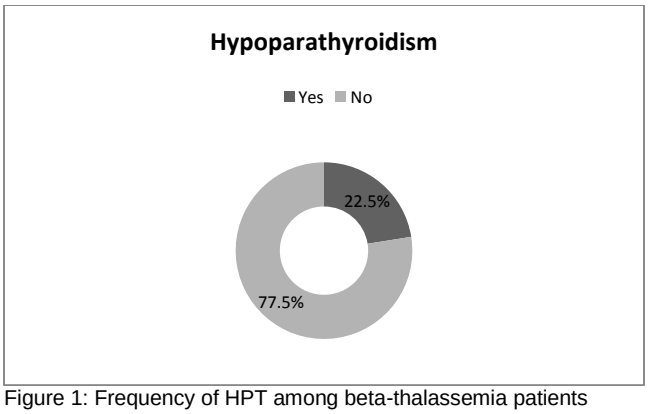

Figure 1: Frequency of HPT among beta-thalassemia patients

5.45±7.17 years were the mean age of beginning HPT. Patients had HPT were mostly on single chelation therapy using deferiprone (DFP).

Table 2: Age at the time of HPT and use of iron chelation therapy

Variables	Frequency	Percentage
Mean age at start of HPT (years)	5.145±7.17	
HPT Cases on Therapy		
Deferiprone (DFP)	9	50
Desferrioxamine (DFO)	4	22.2
Deferasirox (DFX)+Deferiprone (DFP)	5	27.8

Table 3: Frequency of hypocalcemia and complications associated with it

Variables	Frequency	Percentage
Hypocalcemia		
Yes	43	53.8
No	37	46.2
Types of Hypocalcemia		
Symptomatic	20	44.2
Asymptomatic	24	55.8
Complication of Symptomatic Hypocalcemia		
Paresthesias & numbness	9	45
Hyperpigmentation	5	25
Myalgias	3	15
Carpopedal spasm	3	15

There was high prevalence of hypocalcemia found in 43 (53.8%) cases. Among 43 cases of hypocalcemia, 24 (55.8%) patients were asymptomatic and 20 (44.2%) were symptomatic. In these symptomatic hypocalcemia cases paresthesias& numbness was the most common complication.(table 3)

DISCUSSION

In children and adolescents, beta thalassemia major is the most frequent hemolytic anaemia, especially in locations where consanguinity is common. Endocrine problems owing to iron overload continue to emerge in these individuals despite the use of frequent transfusions with chelation [16]. Hypoparathyroidism leading to low calcium and high phosphorus levels is one of these complications typically occurring in second decade of life. As a well-known consequence of BTM, HPT is very infrequent and decreasing in frequency due to advances in chelation treatment. Iron excess can cause glandular damage in a variety of ways, according to several studies. Free radical generation and lipid peroxidation, which results in mitochondrial, lysosomal, and sarcolemmal membrane damage, as well as a number of surface transferrin receptors in the cell, have been linked to HPT, although the reason why some individuals develop HPT and others do not is not understood. [17]

In this study 80 children of both genders had beta-thalassemia were included. 5-14 years were the patients age with mean age 8.12±6.35 and body mass index was 7.12±3.13 kg/m^2.Results of our findings were related to the previous studies.[18] 45(56.3%) were on combination therapy and chelation therapy was in 35 (43.7%). Mean serum calcium level was 6.17±3.55 mg/dl and phosphorus level was 4.15±9.97 mg/dl. Same findings were presented in a study conducted by El-Din LB et al.[19]Serum calcium levels are regulated by a delicate balance of PTH, vitamin D, and calcitonin, all of which play a role in the diagnosis of HPT. [20]We found frequency of HPT among 18 (22.5%) cases. This prevalence was comparable to the previous studies.[19,21]In patients with BTM, growth retardation is common and becomes more apparent around puberty due to the lack of a growth spurt. These include chronic anaemia, a lack of vitamin B12, iron toxicity, and endocrine abnormalities. [22] 5.45±7.17 years were the mean age of beginning HPT. Patients had HPT were mostly on single chelation therapy using deferiprone (DFP).[19-[21]

There was high prevalence of hypocalcemia found in 43 (53.8%) cases. Among 43 cases of hypocalcemia, 24 (55.8%) patients were asymptomatic and 20 (44.2%) were symptomatic. In these symptomatic hypocalcemia cases paresthesias& numbness was the most common complication. According to Aleem A and his colleagues, the vast majority of hypocalcemics with thalassemia were not symptomatic and only 2/8 (25 percent) had hand paresthesias.[23] According to De Sanctis et al just 12.5 percent of hypocalcemics were experiencing symptoms. Symptomatic hypocalcemia was more common in our sample with ß-thalassemia major than in this research. [24]In most cases, additional endocrine and/or cardiac problems occurred before to or shortly after the beginning of HPT. If serum ferritin levels can be kept below 2500 ng/l, the prognosis for life is optimal for thalassemia patients, however some individuals who get optimum care in terms of current standards do acquire major endocrine damage [24].

Regular monitoring of individuals at risk for these endocrinopathies is suggested due to the possibility of reversing these illnesses utilising extensive iron chelation treatment at an early stage. A patient's age, serum ferritin, and haemoglobin levels all have a role in the pace of growth failure. Preventing hypoclacemia and hypocalcemictetany in children with beta thalassemia major in their second decade of life calls for the use of calcium and vitamin D supplements. According to the findings of previous study, it's critical to keep haemoglobin levels within normal ranges, assess parathyroid hormone on a regular basis, keep track of growth parameters, and use iron chelation therapy to treat iron overload.[21]

CONCLUSION

We found in this study that the frequency of hypoparathyroidism was a common complication in patients with beta-thalassemia. Frequency of hypocalcemia was high among patients with most prevalent asymptomatic cases. Paresthesias& numbness was the most common complication among symptomatic hypocalcemia.

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