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MEASUREMENT OF SERUM CALCIUM, PHOSPHATE AND PARATHORMONE LEVELS IN THALASSEMIC CHILDREN

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ABSTRACT

Background: Chronic haemolytic anemia most often results from thalassemia. The symptoms of thalassemia, which include severe anemia needing frequent RCC transfusions, often manifest during the first two years of life. Even while modern transfusion techniques have enhanced thalassemia patients' life expectancy, they have also led to growing iron overload. These patients have endocrine disruption due to iron excess. **Objective:** To measure the level of serum calcium, phosphate and parathormone levels among thalassemic children. **Method:** This cross sectional study was carried out at tertiary hospital from January 2021 to January 2022 where a total of 100 children with thalassemia from 4 years to 14 years that requiring frequent blood transfusion and attending Outpatient and In-Patient Department were included as a sample size. **Results:** During the study, majority belong to 5-10 years age group, 65% and 55% were male. 75% had annual packed cell requirement rate was 120 and 16% had annual cell requirement rate was 240. Majority had higher serum ferritin level, 70% whereas 45% had 8.19mg/dl calcium level followed by 30% had 7.1-8mg/dl calcium level, 15% had >9mg/dl. majority belong to <5mg/dl serum phosphorus level, 45%. Followed by 25% belong to 5-5.9 mg/dl serum phosphorus level, 26% belong to 6-6.9mg/dl. Moreover, according to serum parathormone level in Thalassemia Patient 96% cases belong to 12-65 pg/ml. **Conclusion:** Hypoparathyroidism is more common in those with thalassemia. 10% patients in our research had an inadequate amount of parathormone. There is a considerably higher frequency of hypoparathyroidism in children with thalassemia between the ages of 11 and 14 than in those between the ages of 5 and 10. Therefore, after the age of 10, it is crucial to actively look for hypoparathyroidism so that therapy may begin without delay.

KEYWORDS: Thalassemia, serum ferritin, serum calcium, serum phosphorus.

INTRODUCTION

Blood disorder Its name comes from the Greek words for "sea" (thalassa) and "blood" (haema). Alpha (a) or beta (b) thalassemia is a diverse group of hereditary illnesses characterized by a deficiency in the production of the an or b globin subunits of hemoglobin A.[1,2,3] The current classification of thalassemia is based on whether or not the patient needs frequent blood transfusions to be alive (transfusion-dependent thalassemia, or TDT).[3,4]

According to WHO statistics, around 4% of the population in Bangladesh has the gene for Hb-E and 3% have the gene for beta thalassemia. Five, in Beta thalassemia major and HbEâ thalassemia, the death of red blood cells by oxidative methods is caused by a buildup of excess á-globin chains in erythroid precursors owing to defective production of the â-globin chains. Ineffective erythropoiesis, hemolysis, and anemia are the end consequence of all these alterations, and they are linked to a higher risk of dying in the first few years of life due to congestive heart failure or other chronic anemia-related problems. Once treatment with transfusions and chelation therapy began, however, the situation began to shift.[5-10]

Although chelation treatment may help, receiving many blood transfusions can lead to iron overload, which can increase the body's production of harmful reactive oxygen species. Hypoparathyroidism and hypocalcemia may develop due to the damage done to the parathyroid glands by elevated oxidative stress.[11,12]

Present transfusion regimens protocols have increased the life expectancy with thalassemia, but caused a progressive iron overload. As a result of iron overload those patients develop liver, heart, endocrine abnormalities. Iron deposition in the parathyroid gland, which in turn may cause hypoparathyroidism. Hormones of parathyroid gland especially parathormone and calcitonin hormones regulate normal levels of calcium and phosphorus in blood. Hypoparathyroidism is reported to affect 3% to 7 % of patients and is attributed to iron deposition in the parathyroid.[5-6] Extreme hypocalcaemia is a frequent late event. Early detection requires periodic estimation of calcium homostasis. Serum calcium levels below 7mg/dl, phosphorus above 7mg/dl and low parathormone <12pg/dl is suggestive of hypoparathyroidism.7 Symptoms are usually mild and include paraesthesia, muscle pain and when severe tetany and even convulsions.8 A decrease of parathyroid hormone levels in the absence of symptoms has been reported in over 12% of the patients.

Large amounts of calcium and phosphate, two of the most common minerals in the body, are required for strong bones. Furthermore, they play a crucial part in cellular signaling, intracellular communication, and the release of several glands and hormones. The parathyroid hormone (PTH) is the primary hormone involved in maintaining normal calcium levels in the body. It is the small intestine, bone, parathyroid gland, and kidneys that work together to keep the body's phosphate levels in check. Abnormal phosphate levels may be the result of damage to any of these organs' functions.[15,16]

Serum calcium levels were found to be lower in thalassemia patients compared to controls, whereas phosphate levels were found to be greater. Also, elevated calcium levels were shown to be correlated with elevated serum ferritin concentrations.

Based on the findings of these research, it is possible that the changed calcium and phosphate level in thalassemic patients is caused by iron overload caused by recurrent blood transfusion. Few studies have looked at serum calcium and phosphate levels in transfusion-dependent Thalassemic patients, but the available data isn't enough to draw any firm conclusions.

In this study our main goal is to measure the level of serum calcium, phosphate and parathormone levels among thalassemic children.

OBJECTIVE

To measure the level of serum calcium, phosphate and parathormone levels among thalassemic children.

METHODOLOGY

This cross sectional study was carried out at tertiary hospital from January 2021 to January 2022 where a total of 100 children with thalassemia from 4 years to 14 years that requiring frequent blood transfusion and attending Outpatient and In-Patient Department were included as a sample size. Patient undergo blood investigation for serum calcium, phosphorus and parathormone. A 4ml venous blood was collected in a plain vial aseptically.Serum parathormone was estimated antibody radioimmunoassay.

Inclusion criteria

- Aged from 4-14 years who requiring regular packed red blood cells transfusion.

Exclusion Criteria

- Having some renal disease.
- Malabsorption syndrome.
- On long term anticonvulsant therapy.
- Taking vitamin D and calcium supplementation

RESULTS

Table-1 shows age distribution of the study group where majority belong to 5-10 years age group, 65%. The following table is given below in detail:

Table 1: Age distribution of the study group.

Age group	%
5-10	65%
11-14	35%

In figure-1 shows gender distribution of the study group where 55% were male and 45% were female. The following figure is given below in detail:

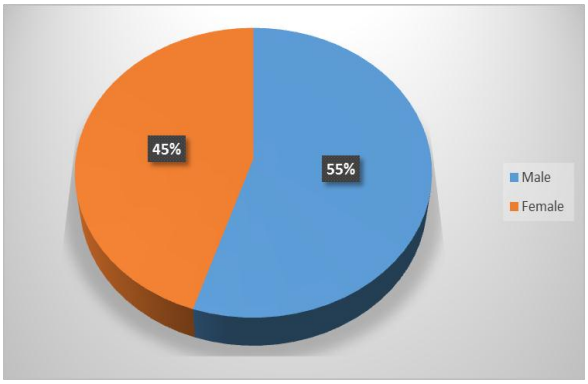

Figure 1: Gender Distribution.

Table-2 shows blood transfusion of the study group where majority required 1unit/month blood transfusion 78%, followed 8% cases need blood transfusion 1.5unit/month, 12% need 2unit/month blood transfusion. The following table is given below in detail:

Table 2: Blood transfusion of the study group.

Frequency	%
1 unit/month	78%
1.5 unit/month	8%
2 unit/month	12%
> 2 unit/month	2%

Table-3 shows Annual Packed Cell Requirement Rate of the study group where 75% had annual packed cell re-

quirement rate was 120 and 16% had annual cell requirement rate was 240. The following table is given below in detail:

Table 3: Annual Packed Cell Requirements.

Annual Packed Cell Requirement Rate	%
120	75%
180	5%
240	16%

Table 4 shows Serum Ferritin Level in Thalassemia where majority had higher serum ferritin level, 70%. The following table is given below in detail:

Table 4: Serum Ferritin Level in Thalassemia.

Serum Ferritin Level in Thalassemia	%
<1000 ng/ml	10%
1000-1500 ng/ml	20%
>1500 ng/m	70%

Table-5 reveals that Serum Calcium Level in Thalassemia Patient where 45% had 8.19mg/dl calcium level followed by 30% had 7.1-8mg/dl calcium level, 15% had >9mg/dl. The following table is given below in detail:

Table 5: Serum Calcium Level in Thalassemia Patient.

Serum Calcium level	%
≤ 6 mg/dl	0%
6.1-7 mg/dl	10%
7.1-8 mg/dl	30%
8.1-9 mg/dl	45%
>9 mg/dl	15%

Table-6 shows serum phosphorus level in Thalassemia Patient where majority belong to <5mg/dl serum phosphorus level, 45%. Followed by 25% belong to 5-5.9 mg/dl serum phosphorus level, 26% belong to 6-6.9mg/dl. The following table is given below in detail:

Table 6: serum phosphorus level in Thalassemia Patient.

Serum Phosphorus level	%
< 5 mg/dl	45%
5-5.9 mg/dl	25%
6-6.9 mg/dl	26%
≥ 7mg/dl	4%

Table-7 shows serum parathormone level in Thalassemia Patient where 96% cases belong to 12-65 pg/ml. The following table is given below in detail:

Table 7: Serum parathormone level in Thalassemia Patient.

Serum parathormone level	%
<12 pg/ml	10%
12-65 pg/ml	96%
>65 pg/ml	4%

DISCUSSION

There are many cases of -thalassemia in developing countries, making it the most frequent inherited disease there.[10] About 10% of the world's yearly thalassemic births occur in India.[11] Some Indian ethnic groups, including the Sindhi, Guajarati, Punjabi, and Bengali, have a higher incidence of beta-thalassemia than others. Variability in prevalence between 1% and 17%.[12] Pathological hemoglobinopathies are rather common in India, with an estimated frequency of 1.2 per 1,000 live births.

In one study50 cases mean calcium level is 8.1280±0.86, mean phosphorus level is 5.46±0.875 and mean parathormone level 29.7±19.59 in all 50 cases. Out of 50 cases, 6 (12% cases) had low serum parathormone level which suggest hypoparathyroidism. In these 6 cases, all had low calcium level and 4 had high phosphorus level.[5]

In study done by Cao A, Galanello R, Rosatelli MC, et al. in 1996 suggests that asymptomatic hypoparathyroidism is reported in 3%-7% of patients.5-6 In our study, we found 12% cases had asymptomatic cases. In our study it demonstrates that significantly reduced level of serum calcium, serum parathormone and high phosphorus level in children with thalassemia belong to age group 11-14 years as compared to 4-10 years of age group which suggest that risk of hypothyroidism increasing with age. In our study 75% had annual packed cell requirement rate was 120 and 16% had annual cell requirement rate was 240.

So, in our study it was observed that there is no clear relationship between hypoparathyroidism and APCRR (Annual Packed Cell Requirement Rate) by using Pearson Correlation Test. The cause of hypoparathyroidism in thalassemia is assumed to be iron deposition in parathyroid glands, but the reason why some patients develop hypoparathyroidism and others do not is not exactly known.[15] A number of possible mechanisms have been described to be responsible for glandular damage through iron overload.16 These include free radical formation and lipid peroxidation resulting in mitochondrial, lysosomal and sarcolemmal membrane damage and a number of surface transferrin receptors in the cell and the ability of the cell to protect itself against inorganic iron.

Again, some investigators found no change in serum phosphate level in beta thalassemia patients.

This dissimilarity in findings might be due to variation in nutritional status in study group. Furthermore, the present results suggested greater percentage of Thalassemia patients were affected with hypocalcemia and hyperphosphatemia indicating their impaired of parathyroid function.

Several studies have suggested that parathyroid gland damage occurs in transfusion dependent beta thalassemia may be due to oxidative stress caused by iron overload.

In these patients, excess iron following repeated blood transfusion deposited in various organ including parathyroid gland. These excess iron generate large number of reactive oxygen species (ROS) via Fenton Cs reaction and Haber - Weiss reaction. Reactive oxygen species (ROS) are capable of causing oxidative damage to macromolecules leading to lipid peroxidation, DNA damage and causes damage to parathyroid gland.[2-7]

Again Intracellular iron regulates number of transferrin receptor and serum ferritin levels by interfering the translation of mRNA. When intracellular iron level increase, it stimulates translation of ferritin mRNA and causes degradation of transferrin receptor mRNA. So, there are increase in serum ferritin level and decrease in number of transferrin receptor. As transferrin receptor decrease, excess iron binds with other blood component, leading to formation of plasma non-transferrin bound iron (NTBI). It is potentially toxic and contribute to generation of ROS leading to parathyroid gland damage. As a result decreased serum calcium and increased serum phosphate levels.[8-3]

CONCLUSION

Hypoparathyroidism is more common in those with thalassemia. 10% patients in our research had an inadequate amount of parathormone. There is a considerably higher frequency of hypoparathyroidism in children with thalassemia between the ages of 11 and 14 than in those between the ages of 5 and 10. Therefore, after the age of 10, it is crucial to actively look for hypoparathyroidism so that therapy may begin without delay.

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