Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Neonatology

Serum Calcium, Phosphate and Parathormone Levels in Thalassemic Children with High Ferritin Level

Dr. Pandora Glory[1*], Dr. Md. Al Mamun Hossain[2], Dr. Zannat-ul- Sarmin[3], Dr. Mst. Hasna Hena[4], Dr. Afroza Islam Shuma[5], Dr. Farzana Kabir[6], Dr. Afroza Sultana[7]

[1]Registrar, Department of Neonatology, Dhaka Medical college Hospital, Dhaka, Bangladesh
[2]Assistant professor (Paediatrics), OSD, Department of Neonatology, Dhaka Medical College Hospital, Dhaka Bangladesh
[3]Registrar, Department of Nephrology, Dhaka Medical College Hospital, Dhaka Bangladesh
[4]Junior consultant (Paediatrics), Department of Paediatric Neurology & Development, Dhaka Medical College Hospital, Dhaka, Bangladesh
[5]Assistant Professor, Neonatology, Dhaka Medical College, Dhaka, Bangladesh
[6]Consultant Paediatrics, OSD, BSMMU, Dhaka, Bangladesh
[7]Registrar, Paediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh

DOI: https://doi.org/10.36347/sjams.2024.v12i11.021 | **Received:** 22.09.2024 | **Accepted:** 29.10.2024 | **Published:** 12.11.2024

***Corresponding author:** Dr. Pandora Glory
Registrar, Department of Neonatology, Dhaka Medical college Hospital, Dhaka, Bangladesh

Abstract **Original Research Article**

Background: In thalassemic children with high ferritin level due to iron accumulation in parathyroid gland may developed hypoparathyroidism leading to impaired homeostasis of calcium & phosphate. Parathyroid dysfunctions may not be evident clinically in early state. So the parathyroid status should be evaluated at regular interval. ***Objective:*** To find out the association of serum calcium, phosphate and parathormone levels in thalassemic children with high serum ferritin level. ***Materials and methods:*** The study was a cross-sectional study carried out in Department of Paeditarics, Dhaka Medical College Hospital, Dhaka, Bangladesh during January, 2019 to December, 2019. Total 70 thalassemia patients both male &female were included in this study between the age ranged from 5 to 12 years with serum ferritin level >1000 ng/ml irrespective of chelation therapy. All study subjects were fully evaluated clinically, thoroughly investigated and properly treated as per protocol. ***Results:*** Total 70 patients were included in our study. Male were 39 (55.7%) and female were 31(44.3%). S. Calcium level was decrease in 22(31.4%) patient, S PO4 level increased in 44 (62.9%) patients & parathyroid level was low in 16 (22.9%) patients. ***Conclusion:*** Based on result it could be concluded that thalassemic children age ranged from 5 years to 12 years, presenting with high ferritin level are likely to have low calcium, high phosphate & low parathormone level.

Keyword: Thalassemia, children, high ferritin, calcium, phosphate, parathyroids.

INTRODUCTION

Thalassemia is a group of inherited haemoglobin disorders which is characterized by reduction of synthesis of one or more of the globin chains that leads to imbalanced globin synthesis [1]. The aim of regular blood transfusion in thalassemia is to prevent the anemia with their complications and bone marrow hyperplasia [2]. Frequent blood transfusions lead to iron overload which itself is fatal by the second decade of life. In spite of chelation therapy, iron overload related complications like endocrinopathies are still occurring in thalassemic patients [3]. Hypo parathyroid is characterized by decreased serum calcium and increased serum phosphate levels, accompanied by the decrease the level of parathormones (PTH). This condition may trigger the progression towards neurological problems [4]. It was also observed that thalassemia patients who have high ferritin level more than 1000 ng/ml had more chance of deposition of iron on soft tissue resulting in damage to the endocrine glands like parathyroid gland.

Objectives:

General Objective:

To find out the association of serum calcium, phosphate and parathormone levels in thalassemic children with high serum ferritin level.

Specific Objectives:

- To determine the serum calcium phosphate & parathormone level in the thalassemia children with high serum ferritin level.

- To compare serum calcium, phosphate & parathormone level with serum ferritin in the children with thalassemic children.

MATERIALS & METHODS

This was a cross-sectional study was carried out in children with thalassemia admitted in paediatric department, Dhaka Medical College Hospital, Dhaka, Bangladesh during January, 2019 to December, 2019.

Inclusion Criteria:

1. Children of age ranged from 5-12 years with confirmed diagnosis of beta-thalassemia major or E-beta thalassemia.
2. Thalassemic children with serum ferritin level >1000 ng/ml irrespective of chelation therapy.
3. Thalassemic children getting repeated blood transfusion.

Exclusion Criteria:

1. Children diagnosed as thalassemia minor or intermedia.
2. Thalassemic children with serum ferritin levels <1000 ng/ml.
3. Thalassemic children with no history of blood transfusion.
4. Thalassemic children on long term use of drug causing hypocalcemia.
5. Thalassemic children with diagnosed case of chronic renal failure, metabolic disorder, malabsorption, cholestasis, refractory rickets or any other acute disease.

Finally, 70 patients were included in the study according to operational definition.

Operational Definitions

1. Thalassemia: Diagnosed patient of thalassemia, confirmed by Hb-Electrophoresis including the beta thalassemia major & E-beta thalassemia.
2. High ferritin level: Serum ferritin level >1000 ng/ml. (Reference Range: 10-60 ng/ml)
3. Hypoparathyroidism: Serum parathormone level below 18.5 pg/ml. (Reference Range: 18.5-88 pg/ml)
4. Hypocalcemia: Serum calcium level below 8.4 mg/dl. (Reference Range: 8.4-10.2 mg/dl)
5. Hyperphosphatemia: Serum phosphate level more than 5.6 mg/dl. (Reference Range: 3.7-5.6 mg/dl)

Detailed clinical examination was carried out including vitals. Height and Weight of the children were measured. Weight was measured using weight machine (TANITA weight machine, model no: HA650) supplied in hospital with light dress and without footwear. Height of children was measured using stadiometer and standard measuring scale. Measuring tape was attached vertically against the wall and height measured without footwear in standard procedure. Iron status of all thalassemia patient were assessed by using Enzyme Immune Assay for determination of serum ferritin level using Biogen, GmbH model no:6500, made in Germany. Sample was selected by doing purposive sampling after fulfilling the inclusion & exclusion criteria. Informed consent was obtained from their parents. Then with all aseptic precaution 5ml of venous blood was drawn from each and every thalassemia case for parathyroid function tests (PTH Level) using 8K25 ARCHITECT intact PTH Reagent Kit, serum Calcium by automated biochemistry analyzer and serum phosphate done by automated biochemistry analyzer, Atellica, siemens Germany, Beckman coulter-AU680. Data were processed, compiled and analysis was done with Statistical Package for Social Science (SPSS) version 23.0 and comparison was done in study subject. Data were presented in number, percentage, mean and standard deviation. Chi square test was used for categorical variables. Unpaired t-test was used for continuous variables. Data was presented in the form of tables, scatter diagram & pie chart. Significance was assessed at 5% level of significance.

RESULTS

Table-I: Distribution of the thalassemia patients according to demographic variables (n=70)

Variables	Number	Percentage (%)	Mean±SD	Range
Age (years)				
5-8	38	54.3	8.41±1.97	5-12
8-12	32	45.7		
Total	70	100.0		
Sex				
Male	39	55.7		
Female	31	44.3		
Occupation of father				
Banker	11	15.7		
Businessman	18	25.7		
Famer	20	28.6		
Garments worker	8	11.4		
Rickshaw puller	8	11.4		

Variables	Number	Percentage (%)	Mean±SD	Range
Teacher	5	7.1		
Occupation of mother				
Garments worker	3	4.3		
House wife	66	94.3		
Teacher	1	1.4		

Table-I Shows, among 70 thalassemic patient, the mean age was 8.41 ± 1.9 7 years, most of their father's occupation was farmer (28.6%) & mothers' occupation was house wife (94.3%)

Table-II: Distribution of the study patients by history (n=70)

Variables	Number	Percentage (%)
Abdominal distention		
Absent	4	5.7
Present	66	94.3
Family history		
Absent	13	18.6
Present	57	81.4
Consanguinity		
Consanguineous	58	82.9
Non consanguineous	12	17.1
Chelating agent		
Regular	2	2.9
Irregular	67	95.7
Not Getting	1	1.4
History of blood transfusion		
<10 times	5	7.1
>10 times	65	92.9

Table-Il Shows that among the 70 thalassemic patient, 81.4% had same type of family history, 82.9% child were from consanguineous parents, 95.7% got irregular chelating agent and 92.9% has history of blood transfusion more than 10 times.

Table-III: Distribution of the study patients by clinical presentation (n=70)

Variables	Number	Percentage (%)	Mean±SD	Range
Pallor				
Mild	0	0.0		
Moderate	60	85.7		
Severe	10	14.3		
Jaundice				
Absent	65	92.9		
Present	5	7.1		
Fascial dysmorphism				
Absent	4	5.7		
Present	66	94.3		
Liver size (cm)			3.71±1.17	2.0 –6.5
Spleen size (cm)			7.05±2.74	4.0–18.0
Heart rate			102.11±13.73	82–128
Respiratory rate			28.57±5.02	20–38
Temperature			98.79±1.11	97.0–102.0

Table-Ill Shows that among the 70 thalassemic patient most of them had moderate pallor (85.7%), jaundice was present among (7.1%) child, (94.3%) had fascial dysmorphism. The mean palpable liver size was 3.71±1.17 cm, mean palpable spleen size was 7.05±2.74 cm

Table -IV: Association of biochemical parameter with number of blood transfusion & chelation. (N=70)

Variable	Serum Ferritin	Parathormone	Calcium	Phosphate
Blood transfusion				
<10 times (5)	1427.8±1026.9	36.5±5.9	8.89±0.39	5.32±0.99
>10 times (65)	4250.0±2250.4	40.5±21.9	8.23±0.92	5.75±0.98
p-value	0.038	0.690	0.119	0.346
Chelation				
Regular (2)	1475.0±247.0	64.4±42.9	8.71±0.13	4.35±0.49
Irregular (67)	4212.6±2230.2	39.7±20.5	8.26±0.92	5.76±0.97
p-value	0.089	0.106	0.498	0.124

Data were expressed as mean±SD
Unpaired t-test was done to compare between groups

Table-IV shows higher level of ferritin was found in the patient of thalassemia who were getting blood transfusion more than 10 times then patient getting transfusion less than 10 times

Table-V: Association of biochemical parameters with increased ferritin level (n=70)

Variable	Serum Ferritin level (ng/ml)		Total number p-value
	>5000 (n=15) (%)	<5000 (n=55) (%)	
Hypo parathyroid	15(93.75%)	1(6.25%)	16 <0.001*
Hypocalcemia	15(68.18%)	7(31.81%)	22 <0.001*
Hyperphosphatemia	25(73.52%)	9(26.47%)	34 0.006*

Chi-square test was done, *significant

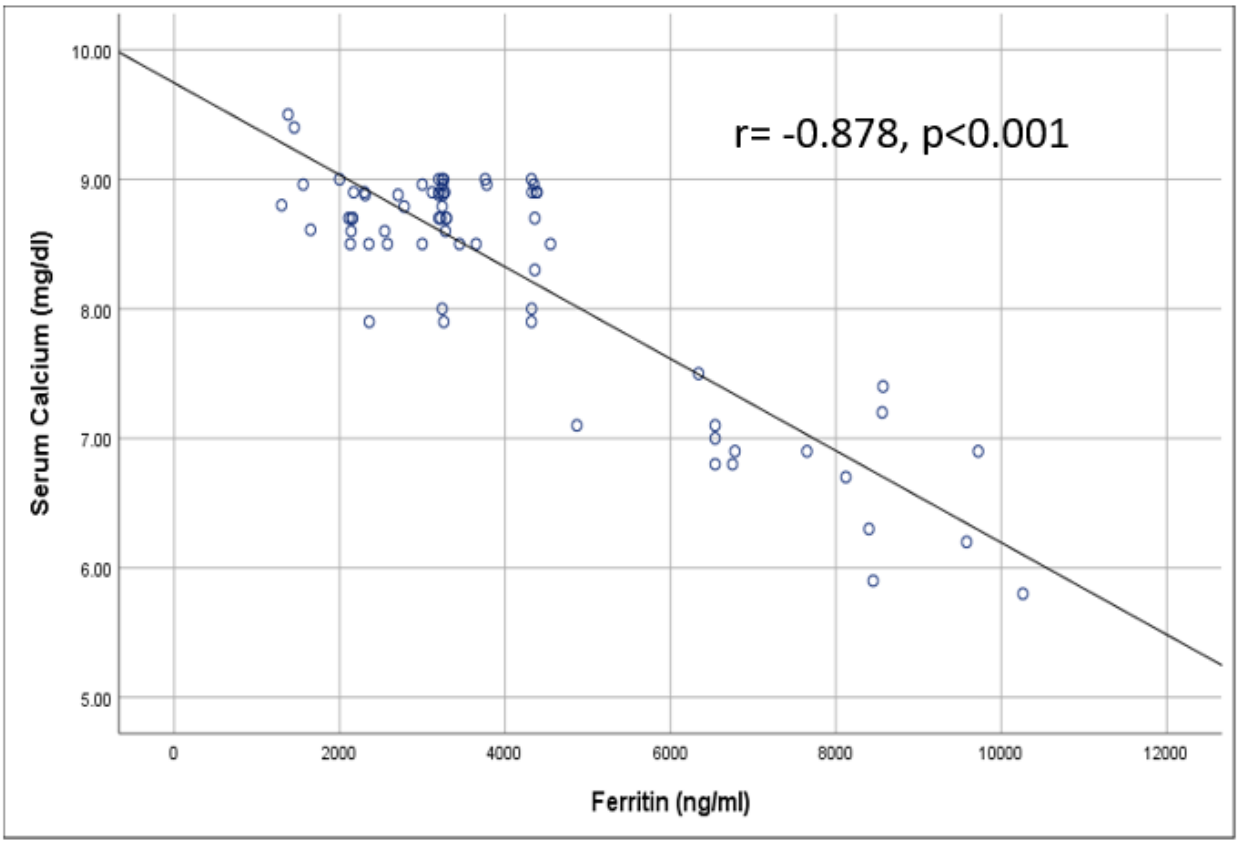

Figure-1: Correlation of S. ferritin with S. calcium

There is negative correlation between S. ferritin and S. calcium which is linear in pattern.

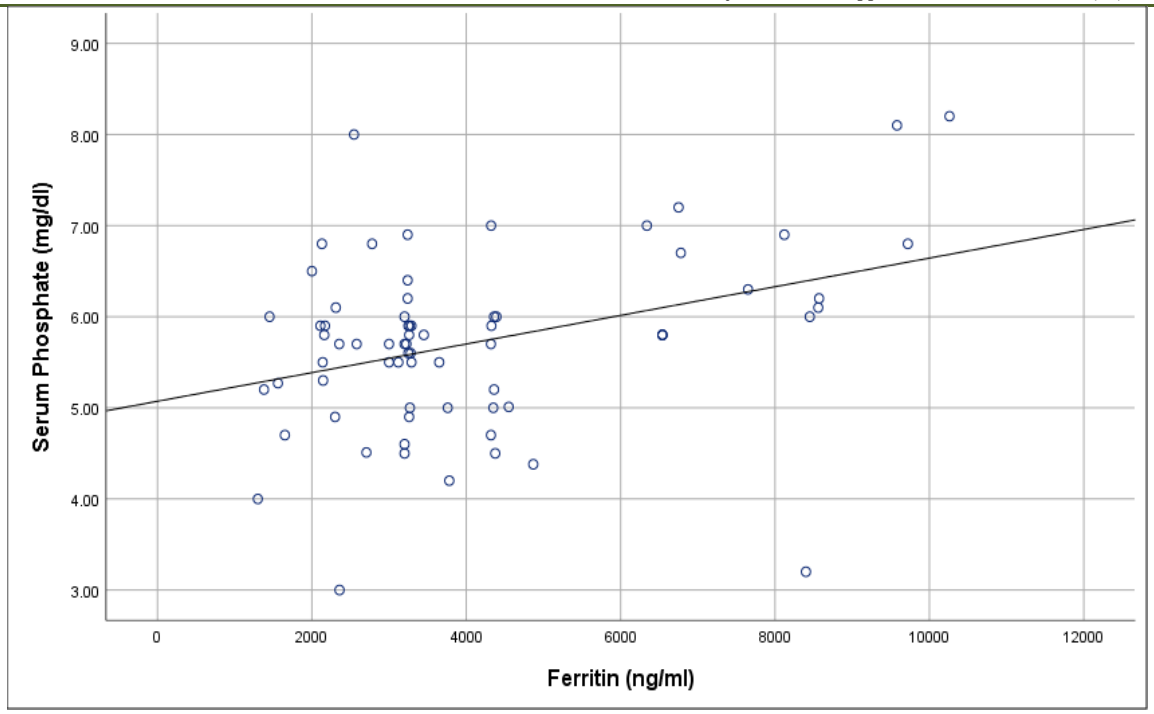

Figure 2: Correlation of S. ferritin with S. Phosphate

There is positive correlation between S. ferritin and S. Phosphate which is linear in pattern.

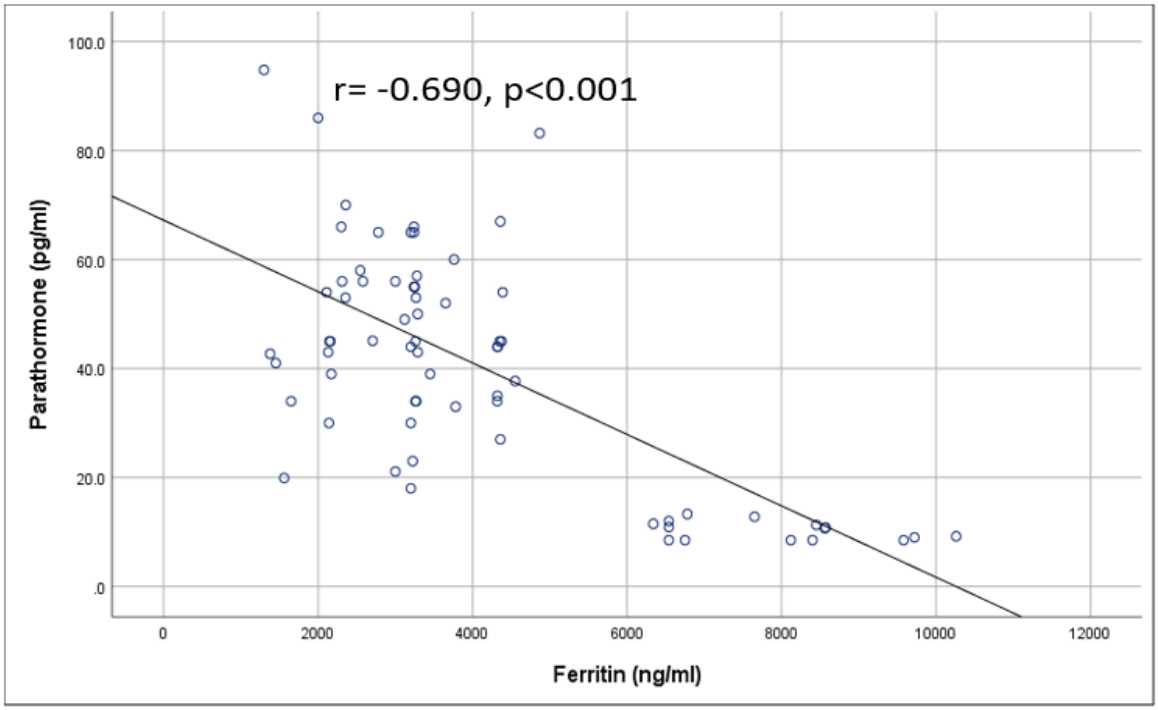

Figure-3: Correlation of S. ferritin with S. Parathormone

There is negative correlation between S. ferritin and S. Parathormone, which is linear in pattern

DISCUSSION

Our study was based on the fact that, despite of the availability of best management of thalassemia patients, some cases of hypoparathyroidism till continue to arise. As most of the patients are asymptomatic, it is very important to keep them under follow up, starting from the early stage of diagnosis.

Within the study population the mean age was 8.41±1.97 years. In similar study conducted in India, the mean age was 11.3 ± 4.05 years [5]. Endocrine

complications are commonly developed after 5 years of age but some studies found age of endocrine complications started from 10 to 12 years of age [1,6].

In our study, majority of the cases (55.7%) were male and male-female ratio was 1.2:1. This difference was not statistically significant. Similar result was found in different studies. Sex did not keep any value in development of hypoparathyroidism in thalassemic patients [1,5].

7.1% of our patient had history of blood transfusion <10 times & their mean S. ferritin level was 1427.8±1026 ng/ml. On the other hand, 92.9% got >10times of blood transfusion & their mean S. ferritin level was 4250.0±2250.4 ng/ml. Among the 70 thalassemic patient, we found 85.7% child with moderate pallor, 94.3% had fascial dysmorphism, 94.3% had abdominal distension. Their mean palpable liver size was 3.71±1.17 cm. and mean palpable spleen was 7.05±2.74 cm.

The present study was undertaken to assess serum calcium, phosphate and parathormone levels in transfusion dependent thalassemia. We found that among the 70 patients, the mean S. ferritin was 4119.87 ng/ml, mean Calcium was 8.28 mg/dl, mean S. Phosphate was 5.72 mg/dl & mean S. Parathormone was 40.22 pg/ml.

31.4% patient found hypocalcemic (<8.4mg/dl) & 62.9% patient found hyperphosphatemia (>5.6mg/dl). Hypocalcemia & hyperphosphatemia was associated with serum ferritin levels in most of the studies [1,7]. However, some researchers found no significant change in serum calcium level in beta thalassemia patients with high ferritin level. This dissimilarity might be due to variation in nutritional status [8].

We found 16 (22.9%) patients had low parathormone level <18.8pg/ml within this 70-thalassemia patient who had serum ferritin level more than 1000 ng/ml. Similar result was found in different studies. 22% of the thalassemia patients had hypoparathyroidism, with a serum ferritin level above 2,000 µg/L [5]. 18% thalassemic child found hypoparathyroidism & their serum ferritin level was more than 2,500 µg/L [4]. On the other hand, in another study done in department of endocrinology, acıbadem hospital, turkey on 90 thalassemia children, found parathormone level were higher than normal range in 23 (25.6%) patients. They explained that 25-OHD deficiency and a raised PTH usually indicates secondary hyperparathyroidism unless there is concomitant primary hyperparathyroidism. Hypocalcemia increases as the patient grows older because the need for transfusions also rises as a consequence of increasing growth, expansion of bone marrow, which causes hemosiderosis and organ dysfunction.

Phosphate level was found significantly increased, serum calcium level was significantly decreased & low parathyroid level found with high ferritin level in comparison to the children having ferritin <1000ng/ml. So, we can say that S. calcium, S. phosphate & S. parathormone is associated with high S. ferritin level.

Limitations:

This was a single centre study & the sample size was minimum. Age >12 years were not included. The study does not represent the whole thalassemia population

CONCLUSION

The findings of this study showed that there is an association between high ferritin level with low calcium, high phosphate & low parathormone level.

REFERENCES

1. Karim, M. F., Ismail, M., Hasan, A. M., & Shekhar, H. U. (2016). Hematological and biochemical status of Beta-thalassemia major patients in Bangladesh: A comparative analysis. *International journal of hematology-oncology and stem cell research*, *10*(1), 7.
2. El-Nashar, M., Mortagy, A. K., El-Beblawy, N. M., El-Gohary, E., Kamel, I. M., Rashad, M., & Mouharam, W. A. (2017). Parathyroid hormone in pediatric patients with β-thalassemia major and its relation to bone mineral density; a case control study. *Egyptian Journal of Medical Human Genetics*, *18*(1), 75-78.
3. Shah, S. (2015). Assessment of serum calcium and phosphorus levels among transfusion-dependent beta thalassemia major patients on chelation therapy. *Journal of Postgraduate Medical Institute*, *29*(3).
4. Bazi, A., Harati, H., Khosravi-Bonjar, A., Rakhshani, E., & Delaramnasab, M. (2018). Hypothyroidism and hypoparathyroidism in thalassemia major patients: a study in Sistan and Baluchestan Province, Iran. *International Journal of Endocrinology and Metabolism*, *16*(2).
5. Shetty, B., & Shenoy, U. V. (2014). Prevalence of hypoparathyroidism (HPT) in beta thalassemia major. *Journal of clinical and diagnostic research: JCDR*, *8*(2), 24.
6. Sultana, M. A., & Akhter, Q. S. (2018). Serum calcium and serum phosphate levels in transfusion dependent beta thalassemia. *Journal of Bangladesh Society of Physiologist*, *13*(2), 54-58.
7. Mohey, Z.M., El-Deen, Ismail, A.M. (2019). Some endocrine changes in children with beta

thalassaemia major. *The Egyptian society of haematology*. *39*(3), 103-108.

8. Pirinççioğlu, A.G., Gökalp, D. & Söker, M. (2017). Parathyroid Functions in Thalassemia Major Patients', Annals of Clinical Endocrinology and Metabolism. *Heighten scientist publication. 5*(1), 25-31.