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Research Article

Association between Alpha- Klotho Protein, Calcium, and Phosphate concentrations in Adult Iraqi Patients with Beta-Thalassemia Major

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Abstract

Background: Beta-thalassemia major is a prevalent global condition characterized by a rapid breakdown of red blood cells. Regular blood transfusions can give rise to problems such as cardiovascular disease, diabetes, osteoporosis, and renal disorders. Alpha-Klotho protein is a protein that has anti-aging properties and is involved in several functions, including reducing oxidative stress, regulating energy metabolism through several routes, and managing calcium and phosphate metabolism.

Objective: This study aimed to assess changes in calcium and phosphate levels, Alpha-Klotho protein concentration, and their associations with cardiac dysfunction in patients with Beta-thalassemia major.

Methods: The study was conducted at Al-Sadr General Hospital and Ibn Albaladi Center of Blood Diseases, Baghdad, and involved 90 participants who were grouped into three groups: Group A: 30 patients with Beta-thalassemia major and heart dysfunction; Group B:30 patients with Beta-thalassemia major without any signs of heart dysfunction; and Group C:30 healthy individuals as a control group. The indicators examined were serum levels of Alpha-klotho protein, calcium, phosphate, and Ferritin. ELISA method was used to assess serum Alpha-klotho protein, whereas serum Ca, serum phosphate, and serum Ferritin were analyzed using the Beckman Coulter AU clinical chemistry analyzers.

Results: The mean values of Serum Alpha-Klotho protein, phosphate, and Ferritin in the patients with beta-thalassemia were greater than those in the control group with P value<0.05. Patients with thalassemia had decreased levels of serum calcium compared to the control group. Additionally, a strong negative association was observed between serum calcium and phosphate levels.

Conclusion: Patients with beta-thalassemia major have significant alterations in calcium and phosphate levels under the control of Klotho protein levels.

Keywords: Calcium; Ferritin, Klotho, Phosphate, Thalassemia.

Introduction:

Thalassemia is a hereditary autosomal recessive blood condition defined by the improper production of hemoglobin (1). Thalassemia is mainly classified into: alpha-thalassemia and beta-thalassemia depending upon the reduced or absent-minded synthesis of the alpha-globin chain or Beta-globin chain of hemoglobin. Beta-thalassemia is categorized into major, moderate, and mild forms according to clinical criteria (2). Beta-thalassemia major is a severe illness recognized as a global issue (3). Ferritin is a widely distributed protein that stores and detoxifies iron. It is crucial in regulating iron balance by keeping it soluble and non-harmful (4). Iron overload occurs in β-TM patients due to numerous blood transfusions, inadequate erythropoiesis, and increased iron absorption via the gastrointestinal tract. The presence of secondary hemosiderosis adversely affects several organs in the body, such as the heart, liver, and endocrine system. Serum ferritin is a frequently employed indicator of Iron levels in individuals with β-TM (5). Calcium and phosphate are crucial elements necessary for maintaining bone strength and stiffness. Furthermore, they play a vital role in muscle activity, the transmissionof nerve impulses, intracellular signaling, and the secretion of different hormones (6). Klotho is a co-receptor for the hormone fibroblast growth factor 23 (FGF23) and has anti-aging properties. Klotho is enzymatically broken and then released into circulation as a substance derived mainly from the kidney. It exerts a wide range of actions in virtually all organs (7). It controls the reabsorption of calcium and phosphate in the kidney and regulates vitamin D metabolism (8). Klotho is mainly produced in the kidney and binds to FGF receptors (FGFRs), enhancing their attraction to FGF-23 and facilitating the excretion of phosphate in urine. The expression of Klotho decreases as renal function declines. Klotho is a substance in the body that has multiple roles and acts as a protective factor for the heart by regulating ion channels. This action is independent of FGF-23 and phosphate (9). High ferritin levels due to iron overload might affect calcium and phosphate metabolism, which may also be linked to Klotho levels. Evaluate the klotho levels in beta-thalassemia patients and correlate them with

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calcium, phosphate, and ferritin levels could provide insights into the complex interactions among klotho, calcium, phosphate, and ferritin, which may lead to better management strategies for beta-thalassemia.
This study aimed to assess changes in calcium and phosphate levels, Alpha-Klotho protein concentration, and their associations with cardiac dysfunction in patients with Beta-thalassemia major.

Patients, Materials, and Methods
Patients and control:
In the present study, 90 subjects were recruited. Their age ranged from 18 to 30 years. Each participant completed a questionnaire that included the following information: code number, age, sex, date, address, ethnicity, family history of thalassemia, weight, height, and medical history. The study was conducted at Al-Sadr General Hospital and Ibn-AL-Baladi Center of Blood Diseases in Baghdad from 1st, March 2023 to 31st, August 2023. The individuals were categorized into three groups based on clinical and physiological examinations of heart function and the physician's diagnosis using ECG and ECHO tests conducted at Al-Sadr General Hospital and Ibn-AL-Baladi Center of Blood Diseases. Group A consists of 30 patients with β-TM who have heart dysfunction. Group B consists of 30 patients with β-TM who do not exhibit any signs of heart dysfunction. Group C consists of 30 healthy individuals who serve as the control group. This study excluded patients with comorbidities such as Diabetes mellitus, liver disease, brain disease, and kidney disease. Additionally, patients with cancer, obesity, and active infection were also excluded. It is important to note that the medication administered to the patients may have influenced the study's outcomes. All patients and healthy subjects, or their parents, were asked to agree to participate in this study, and their consent was publicly recognized. Blood sampling. Subjects' blood samples were withdrawn during morning hours from 8:00 a.m. to 11:00 a.m. by venesection using a 10 ml disposable syringe. The blood was collected into gel tubes that aid blood clotting and separation of serum. The blood in gel tubes was allowed to clot at 37°C for roughly ten to fifteen minutes. It was then centrifuged at 2000rpm the acceleration due to gravity for ten to fifteen minutes. The resulting serum was separated in sterile Eppendorf tubes and stored at -20°C. For analysis, 0.5 ml of serum was utilized. The following biomarkers were measured in the blood: serum α-Klotho protein, serum calcium, serum phosphate, and serum ferritin. The serum α-Klotho protein is determined using an enzyme-linked immunosorbent assay (ELISA) kit. This kit is a sandwich enzyme immunoassay designed for in vitro quantitative measurement. The ELISA kit is the Klotho-(KL)-SEH757Hu Cloud-Clone Corp (USA). In addition to measuring the Alpha-Klotho protein, the Clinical Automation system by Beckman Coulter is used to measure serum calcium, serum phosphate, and serum ferritin.
Calculation of Body Mass Index
The body mass index (BMI) calculated as weight (Kilograms) divided by the square of height (in meters) was the only anthropometric parameter specified. All subjects were weighted on the same scale, barefoot. Height was measured using a measuring tape.

Statistical Analysis:
The statistical analysis was conducted using the MedCalc software, specifically version 19.6.1. Continuous data were summarized using the median and interquartile ranges and the mean± Standard Deviation (SD). The comparison results were expressed as mean ± SD based on analysis of variance (ANOVA) for each study. A Pearson correlation analysis was performed to see if there was a significant association between the parameters. The alpha level for statistical significance was established at a threshold of $P < 0.05$.

Results:
The demographic characteristics of the participants in the present study are displayed in Table (1). The frequency distribution of people according to sex did not show any significant difference between the beta thalassemia major groups (A and B) and the control group, there were in each group 17 (57.0%) males and 13 (43.0%) females. In Table (1) the Mean±SD for age across the three groups (A, B, and C) are statistically similar, as indicated by the P-value of 0.65 suggesting that age is not a differentiating factor among these groups. There is a difference in BMI across the groups. The group A has a Mean±SD BMI of 20.92± 0.90 Kg/m², group B has 21.12± 0.95 Kg/m², and the group C has 23.72± 1.41 Kg/m². The p-value <0.01 suggests a significant variance, with the control group(C) differing notably from the other two groups (A and B).

Table 1 Descriptive analysis of Age and BMI across the three study groups

Parameter	Group	Mean± SD	Group	P value
Age (Years)	Group A	23.60± 4.75	C	0.753
	Group B	22.67± 4.78	A	0.658
	Group C	22.83± 2.03	B	0.987
BMI Kg/m²	Group A	20.92± 0.90	C	< 0.01
	Group B	21.12± 0.95	A	0.752
	Group C	23.72± 1.41	B	< 0.01

Note: Each parameter's mean and standard deviation (Mean± SD) are provided, along with the P-value indicating the significance of the differences between the groups.

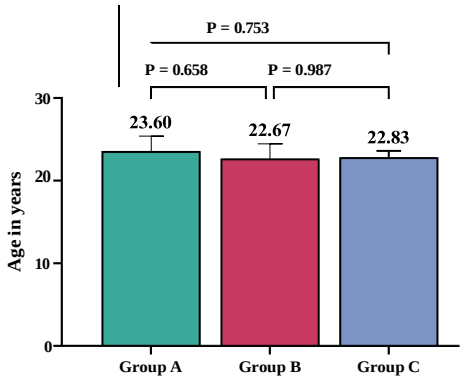

Figure 1 Mean values of age by Groups with 95.00% CI (Confidence intervals) Error Bars.

Table 2 A comparison of serum Klotho, serum Ca, serum phosphate, and Ferritin across the three study groups

Parameter	Group	Mean± SD	Groups	P-value
Serum Klotho (ng/mL),	Group A	4.46± 1.03	C	<0.001
	Group B	5.34± 0.57	A	<0.001
	Group C	1.48± 0.51	B	<0.001
Serum Ca (mmol/L),	Group A	7.94± 1.56	C	<0.001
	Group B	8.71± 0.66	A	0.012
	Group C	8.93± 0.30	B	0.684
Serum PO4 (mmol/L)	Group A	6.57± 1.64	C	<0.001
	Group B	5.89± 1.15	A	0.085
	Group C	3.82± 0.49	B	<0.001
Serum Ferritin (ng/Ml)	Group A	4276.73± 2401.39	C	<0.001
	Group B	4703.17± 3390.18	A	0.777
	Group C	53.20± 17.01	B	<0.001

The results are presented as mean ± standard deviation (SD), and the statistical significance is denoted by the P-value.

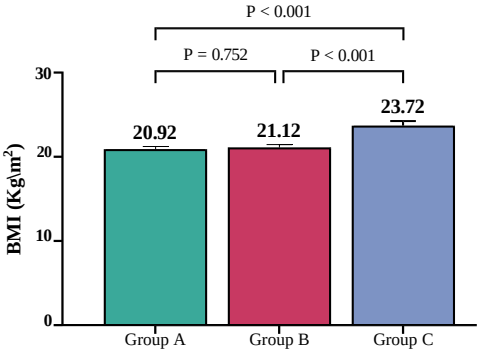

Figure 2 Mean values of BMI by Groups with 95.00% CI Error Bars.

Table 2 compared mean±SD serum levels of Klotho, Ca, phosphate, and Ferritin across groups A, B, and C which were 4.46±1.03 (ng/mL), 5.34±0.57 (ng/mL), and 1.48±0.51 (ng/mL) respectively. group A and B exhibited significantly higher mean values than group C, with a P-value< 0.001, indicating a statistically significant difference, as shown in Table (1). The calcium mean±SD levels in groups A, B, and group C are 7.94 ± 1.56, 8.71 ± 0.66, and 8.93 ± 0.30, respectively. The P-value for this parameter is <0.001, indicating significant statistical differences between the groups. Notably, group A showed a lower mean calcium level than the other two groups, which were statistically similar.

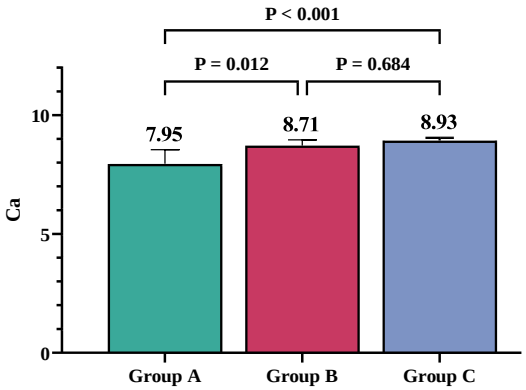

Figure 3 Mean serum levels of Ca by Groups with 95.00% CI Error Bars.

The mean±SD phosphate level for group A was 6.57 ± 1.64 mmol/L, whereas group B had an average level of 5.89 ± 1.15 mmol/L. On the other hand, the group C group has a noticeably lower average level of 3.82 ± 0.49 mmol/L. With a P-value of less than 0.001, this parameter exhibits substantial statistical disparities

across the groups. Group A and Group B had greater phosphate levels than Group C.

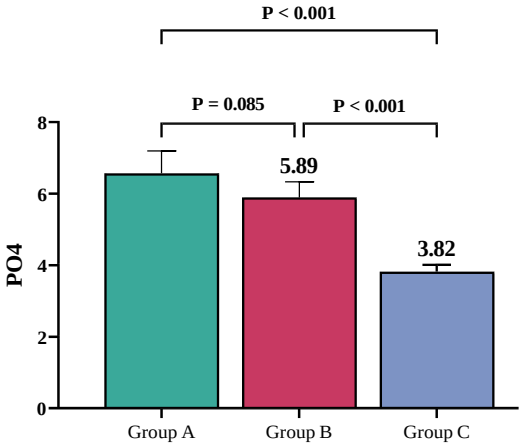

Figure 4 Mean serum levels of PO_4 by Groups with 95.00% CI Error Bars.

Finally, group A had a mean±SD serum Ferritin level of 4276.73 ± 445.93 (ng/mL), which was similar to group B which had a mean±SD serum level of 4703.17 ± 629.54(ng/mL), group C with a significantly lower mean of 53.20 ± 3.16(ng/mL). The *P*-value <0.001 strongly suggested significant differences between the groups, with both group A and group B showing markedly higher Ferritin levels compared to the control group (group C).

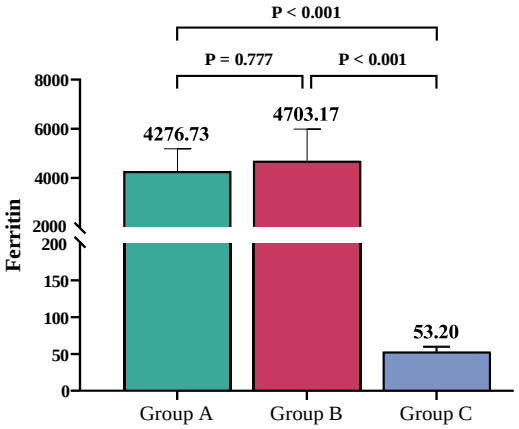

Figure 5: Mean serum levels of Ferritin by Groups with 95.00% CI Error Bars**.**

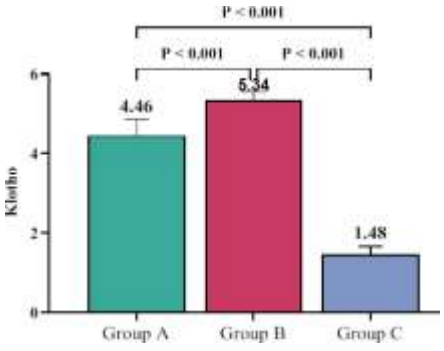

Figure 6: Mean serum levels of Klotho by Groups with 95.00% CI Error Bars.

The matrix for group A shows substantial positive correlations (r=0.41, *P* value<0.05) between phosphate and Ferritin, as well as negative correlations (r= -0.41, *P* value<0.05) between phosphate and Ca.

Table 3 Correlation matrix (Pearson) for group A

Variable	Klotho	Ca	Ferritin	PO4	BMI
Klotho	1	-0.22	-0.18	0.03	-0.22
Ca	-0.22	1	-0.07	-0.41	0.24
Ferritin	-0.18	-0.07	1	0.41	0.10
PO4	0.03	-0.41	0.41	1	-0.25
BMI	-0.22	0.24	0.10	-0.25	1

Values in bold are different from 0 with a significance of level alpha=0.05

In the matrix for group B, there is a significant negative correlation between phosphate and Ca (r= -54, *P* value<0.05). It is important to note that although these relationships are statistically significant, they did not indicate causality. Several causes may alter the connections between these variables, and the varied patterns identified between the two groups may indicate disparities in their demographic or clinical features. These differences emphasize the significance of considering group-specific dynamics when analyzing biomarker correlations in clinical or research environments.

Table 4 Correlation matrix (Pearson) for group B

Variable	Klotho	Ca	Ferritin	PO4	BMI
Klotho	1	-0.20	0.32	-0.12	0.26
Ca	-0.20	1	-0.12	-0.54	-0.08
Ferritin	0.32	-0.12	1	-0.10	0.21
PO4	-0.12	-0.54	-0.10	1	-0.10
BMI	0.26	-0.08	0.21	-0.10	1

Discussion:

This study found no statistically significant sex difference in the distribution of patients and controls between males (57.0%) and females (43.0%). β-Thalassemia major patients' groups showed a significant increase in serum ferritin levels compared to the control group. This finding was consistent with previous Iraqi studies by Talib et.al, Ali EA et.al, and Maki Al-Hindyet.al., which showed a significant increase in serum ferritin levels compared to healthy subjects (10-12). Iron excess often arises from two mechanisms: blood transfusion and insufficient erythropoiesis. In individuals with thalassemia, mutations lead to increased production of GDF15 protein which acts as an inhibitor of the peptide-

hepcidin hormone and transmits a signal to the liver, causing a drop in the amount of Hepcidin and improved iron absorption from the diet. Consequently, erythrocytes that are not functioning correctly are captured in the spleen, causing iron release, ultimately leading to an elevation in ferritin levels (13) There was no significant difference in serum ferritin in β-TM patients group B against group A (*P*-value>0.05) with a slight increase in group B. Which can be explained due to the treatment protocol for heart disease by increased dosage of iron chelators (14) and the influence of cardiovascular medications (15). Thalassemia patients in group A had a significant difference in phosphate levels as compared to groups B and C and A significant reduction in serum calcium levels compared to groups B and C, this result agreed with Sultana MA(6). The elevation in serum phosphate and associated reduction of serum calcium in thalassemia patients with heart dysfunction are attributed to several factors, such as iron accumulation in different tissues, including osteoblasts, frequent blood transfusions, or the use of desferrioxamine as a chelation treatment for iron overload (10). These findings were consistent with prior research showing elevated levels of serum phosphate in individuals with beta-thalassemia major due to chronic hemolysis and transfusions (16), hypoparathyroidism, and reduced kidney function. In this study, patients with renal insufficiency were not included. Therefore, the elevated phosphate levels observed may be attributed to chronic hemolysis or hypoparathyroidism (17). Hyperphosphatemia plays a role in the onset and progression of various cardiovascular diseases and is a significant risk factor for elevated cardiovascular mortality. Previous research has demonstrated that elevated phosphate levels can lead to left ventricular hypertrophy (LVH), myocardial fibrosis, and a higher risk of cardiovascular mortality (18). Iron excess in thalassemia can also impact calcium absorption in the intestines, and there is a mutual relationship between the transportation of iron and calcium in thalassemia (19). Calcium entering cardiac fibers triggers the release of calcium from the sarcoplasmic reticulum, leading to an increase in intracellular calcium concentration. This calcium then binds to troponin C, which controls the interaction between actin and myosin, resulting in muscle contraction (20). Studies have demonstrated that hypocalcemia directly affects heart function, leading to reduced cardiac contractility. A drop is seen in the left ventricular work, stroke, and cardiac indexes. It is a possible factor leading to heart failure (21). The current study demonstrated that the serum Klotho levels in patients with β-TM in groups (A and B) were considerably elevated compared to those in group C. Thalassemia patients experience inflammation and oxidative stress damage due to the direct effects of iron poisoning. Su and Yang determined that α-Klotho may function as an acute phase response, as demonstrated by the elevation of serum α-Klotho protein in response to restraint stress. Crucially, α-Klotho functions as an anti-inflammatory regulator by controlling the synthesis of nuclear factor-κB-associated inflammatory proteins. This leads to a decrease in the production of various pro-inflammatory cytokines and the harmful effects of oxidative stress. α-Klotho provides defense against oxidative stress at both the cellular and organismal levels (22). Thalassemia patients experience impaired calcium absorption, resulting in reduced calcium levels (19). This condition is triggered by certain stimuli that cause the secretion of αKl (23). Soluble Klotho protects against cardiac hypertrophy by suppressing aberrant calcium signaling in the heart, regardless of FGF23 and phosphate levels (24). When comparing the results of thalassemia patients in groups A and B, we observed that the thalassemia group without heart disease has phosphate and calcium concentrations near the expected levels with a higher concentration of klotho than thalassemia patients with heart problems which had low calcium concentration and a significant increase in phosphate levels counteracted by a decrease in klotho concentration. The reduction of Klotho can enhance the action of prooxidative, proinflammatory, and proapoptotic factors, leading to damage of cardiomyocytes in individuals at risk of cardiovascular disease (25).

Limitation of study:

The study was based on only one Hospital and one center. Hence, the findings don't represent the whole population.

Conclusion:

Klotho protein plays a crucial role in regulating phosphate and calcium metabolism in the body. Patients with thalassemia major have significant alterations in calcium and phosphate under the control of Klotho protein levels. These changes in klotho protein can potentially lead to cardiovascular complications in the future. Estimating klotho protein in beta-thalassemia patients might be helpful for the early detection of calcium and phosphate dysregulation and prevent its complications.

Authors' declaration:

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current research, have been given permission for re-publication attached to the manuscript. Authors sign on ethical consideration's approval-Ethical Clearance: The project was approved by the local ethical committee in (Biochemistry Department) according to the code number (138) on (16/ 5/ 2024).

Conflicts of Interest: None

Funding: None

Author contributions:

Study conception & design: (Ahmed J. Kadhim, Hedef D. El-Yaseen, Ali M. Jawad). Literature search: (Ahmed J. Kadhim, Hedef D. El-Yaseen, Ali M. Jawad). Data acquisition: (Ahmed J. Kadhim,

Hedef D. El-Yaseen, Ali M. Jawad). Data analysis & interpretation: (Ahmed J. Kadhim, Hedef D. El-Yaseen, Ali M. Jawad).Manuscript preparation: (Ahmed J. Kadhim, Hedef D. El-Yaseen, Ali M. Jawad). Manuscript editing & review: (Ahmed J. Kadhim, Hedef D. El-Yaseen, Ali M. Jawad).

References

1. Zeiny SM. The correlation between HLA class II and β-thalassemia major in Al-Karama Teaching Hospital. J Fac Med Baghdad. 2016;58(4):366–70.;58(4):366–70. https://doi.org/10.32007/jfacmedbagdad.584287.
2. Faraj SA. Hemostatic parameters in Thalassemia patients; a single institute experience. J Fac Med Baghdad. 2016 ;58(2):132–5. https://doi.org/10.32007/jfacmedbagdad.582223.
3. Mohammad RL, Sadiq F, Hashem A. Information and practice of self-administration about the injection of Deferoxamine among adolescent thalassemia patients in the al-Najef city. Ann Rom Soc Cell Biol. 2021 May 20 ;25(6):2413–7. https://annalsofrscb.ro/index.php/journal/article/view/5856.
4. Liu Y, Yang R, Liu J, Meng D, Zhou Z, Zhang Y, et al. Fabrication, structure, and function evaluation of the ferritin-based nano-carrier for food bioactive compounds. Food Chem. 2019 Nov 30;299:125097. https://doi.org/10.1016/j.foodchem.2019.125097.
5. Soliman A, Yassin M, Alyafei F, Alaaraj N, Hamed N, Osman S, et al. Nutritional studies in patients with β-thalassemia major: A short review. Acta Biomed. 2023;94(3):1–14. https://doi.org/10.23750%2Fabm.v94i3.14732.
6. Sultana MA, Akhter QS. Serum calcium and serum phosphate levels in transfusion-dependent beta-thalassemia. J Bangladesh Soc Physiol. 2018 Dec 26;13(2):54–8. http://dx.doi.org/10.3329/jbsp.v13i2.39478.
7. Neyra JA, Hu MC, Moe OW. Klotho in Clinical Nephrology: Diagnostic and Therapeutic Implications. Clin J Am Soc Nephrol. 2021 Jan 1 ;16(1):162. https://doi.org/10.2215/cjn.02840320.
8. Portales-Castillo I, Simic P. PTH, FGF-23, Klotho and Vitamin D as regulators of calcium and phosphorus: Genetics, epigenetics and beyond. Front Endocrinol (Lausanne). 2022 Sep 29;13:992666. https://doi.org/10.3389%2Ffendo.2022.992666.
9. Navarro-Garcia JA, Rueda A, Romero-Garcia T, Accedes-Ripoll J, Rodríguez-Sánchez E, González-LA Fuente L, et al. Enhanced Klotho availability protects against cardiac dysfunction induced by uremic cardiomyopathy by regulating Ca2+ handling. Br J Pharmacol. 2020;177(20):4701–19.
10. Talib NH, Al-Yaseen HD, Jawad AM. Serum Preptin Level in Iraqi Beta Major Thalassemia Patients. Indian J Forensic Med Toxically. 2022;16(1):913–9. https://doi.org/10.37506/ijfmt.v16i1.17614.
11. Ali EA, Agbayani AA, Alabaman SA, Altham KA. Serum hepcidin and ferritin level changes in Iraqi adult patients with non-transfusion dependent beta-thalassemia major and intermedia. Int J Pharm Res. 2020;13(1):1373–8. https://doi.org/10.31838/ijpr/2021.13.01.301.
12. Maki Al-Hindy HAA, Mousa MJ, Shaker AK. No significant relationship of ferritin levels to the levels of platelet-derived growth factor (PDGF) in the peripheral blood of transfusion-dependent β-thalassemia major patients with growth retardation. Int J Pharm Res. 2020;12(3):568–75. http://dx.doi.org/10.31838/ijpr/2020.12.03.0.
13. Youssry I, Samy RM, AbdelMohsen M, Salama NM. The association between growth differentiation factor-15, erythroferrone, and iron status in thalassemic patients. Pediatr Res 2023. 2023 Jul 18 ;1–6. https://doi.org/10.1038/s41390-023-02729-5.
14. Shah FT, Porter JB, Sadasivam N, Kaya B, Moon JC, Velangi M, et al. Guidelines for the monitoring and management of iron overload in patients with haemoglobinopathies and rare anaemias. Br J Haematol. 2022 Jan 1;196(2):336–50. https://doi.org/10.1111/bjh.17839.
15. Sirbu O, Sorodoc V, Jaba IM, Floria M, Stoica A, Profire L, et al. The influence of cardiovascular medications on iron metabolism in patients with heart failure. Med. 2019;55(7):1–11. https://doi.org/10.3390/medicina55070329
16. Urmi SFH, Begum S, Munira FT, Das KC. Serum Calcium, Phosphate and Ferritin Level in Adult Male Patients with Transfusion Dependent Thalassemia. Bangabandhu Sheikh Mujib Med Coll J. 2023 Nov 20;2(2):97–100. http://dx.doi.org/10.3329/bsmmcj.v2i2.69841.
17. Saki F, Omrani GR. Evaluation of serum Fibroblast growth factor-23 in patients with betathalassemia major compared to healthy population. Iran J Pediatr Hematol Oncol. 2022;12(3):182–9. http://dx.doi.org/10.18502/ijpho.v12i3.10061.
18. Zhou C, Shi Z, Ouyang N, Ruan X. Hyperphosphatemia and Cardiovascular Disease. Front Cell Dev Biol. 2021 Mar 4;9. https://doi.org/10.3389%2Ffcell.2021.644363.
19. Yu U, Chen L, Wang X, Zhang X, Li Y, Wen F, et al. Evaluation of the vitamin D and biomedical statuses of young children with β-thalassemia major at a single center in southern China. BMC Pediatr . 2019 Oct 23;19(1):1–8. https://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-019-1744-8.
20. Aguiar P, Cruz D, Rodrigues RF, Peixoto L, Araújo F, Ducla Soares JL. Hypocalcemic cardiomyopathy. Rev Port Cardiol (English Ed. 2013 Apr 1;32(4):331–5. http://www.revportcardiol.org/en-hypocalcemic-cardiomyopathy-articulo-S2174204913000597.
21. Baqi DH, Ahmed SF, Baba HO, Fattah FH, Salih AM, Ali RM, et al. Hypocalcemia as a cause of reversible heart failure: A case report and review of the literature. Ann Med Surg . 2022 May 1;77:103572. https://pmc/articles/PMC9142408/.

22. Maes M, Moustafa SR, Al-Hakeim HK, Alhillawi ZH. In Transfusion-dependent Thalassemia, Increased Iron Overload is Associated with Lower Serum Alpha-klotho, Which is Strongly Associated with Lower Total and Ionized Calcium Concentrations. 2020;(July):1–31. https://doi.org/10.20944/preprints202007.0347.v1.

23. Cui W, Leng B, Wang G. Klotho protein inhibits H2O2-induced oxidative injury in endothelial cells via regulation of PI3K/AKT/Nrf2/HO-1 pathways. 2018 ;97(5):370–6. https://cdnsciencepub.com/doi/10.1139/cjpp-2018-0277

24. Xie J, Yoon J, An SW, Kuro-o M, Huang CL. Soluble Klotho Protects against Uremic Cardiomyopathy Independently of Fibroblast Growth Factor 23 and Phosphate. J Am Soc Nephrol . 2015 May1;26(5):1150–60. https://pubmed.ncbi.nlm.nih.gov/25475745/

25. Olejnik A, Franczak A, Krzywonos-Zawadzka A, Kałużna-Oleksy M, Bil-Lula I. The Biological Role of Klotho Protein in the Development of Cardiovascular Diseases. Biomed Res Int. 2018;2018. https://doi.org/10.1155/2018/5171945.

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العلاقة بين بروتين ألفا كلوثو وتركيزات الكالسيوم والفوسفات لدى مرضى بيتا ثلاسيميا الكبرى البالغين العراقيين

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الخلاصة:

خلفية البحث: بيتا ثلاسيميا الكبرى (β-TM) هي حالة عالمية منتشرة تتميز بالانهيار السريع لخلايا الدم الحمراء. يمكن أن تؤدي عمليات نقل الدم المنتظمة إلى مشاكل مثل أمراض القلب والأوعية الدموية والسكري وهشاشة العظام واضطرابات الكلى. بروتين كلوثو هو بروتين له خصائص مضادة للشيخوخة ويشارك في عدة وظائف، بما في ذلك تقليل الإجهاد التأكسدي، وتنظيم استقلاب الطاقة من خلال عدة طرق، وإدارة استقلاب الكالسيوم والفوسفات.

الاهداف: تشير فرضيتنا إلى أن التغيرات في مستويات بروتين كلوثو لدى الأفراد الذين يعانون من بيتا ثلاسيميا الكبرى قد تؤدي إلى تغييرات في استقلاب الكالسيوم والفوسفات. هدفت هذه الدراسة إلى تقييم التغيرات في مستويات الكالسيوم والفوسفات، وكذلك تركيز بروتين كلوثو، وارتباطها بخلل وظائف القلب لدى مرضى بيتا ثلاسيميا الكبرى.

المرضى وطرق العمل :المواد وطرق العمل: أجريت الدراسة في مستشفى ابن البلدي/بغداد وتكونت من 90 مشاركا تم تقسيمهم إلى ثلاث مجموعات: المجموعة (أ): 30 مريضا يعانون من مرض بيتا ثلاسيميا الكبرى وخلل في القلب. المجموعة ب: 30 مريضا مصابين بـ بيتا ثلاسيميا الكبرى دون أي علامات لخلل في القلب. والمجموعة ج: 30 فردا أصحاء كمجموعة ضابطة. وكانت المؤشرات التي تم فحصها هي بروتين الفا كلوثو والكالسيوم والفوسفات والفيريتين في مصل الدم. تم استخدام طريقة ELISA لتقييم الفا كلوثوبروتين في مصل الدم، في حين تم قياس تركيز الكالسيوم والفوسفات والفيريتين في مصل الدم باستخدام جهاز التحليل الذاتي للكيمياء السريرية بيكمان كولتر.

النتائج: كانت القيم المتوسطة مصل الدم كلوثو والفوسفات والفيريتين في المرضى الذين يعانون من مجموعات بيتا ثلاسيميا أكبر من تلك الموجودة في المجموعة الضابطة. كان لدى مرضى الثلاسيميا انخفاض في مستويات الكالسيوم في مصل الدم مقارنة بالمجموعة الضابطة. بالإضافة إلى ذلك، لوحظ وجود ارتباط سلبي قوي بين مستويات الكالسيوم والفوسفات.

الاستنتاج: كانت مستويات الكلوثو والفوسفات والفيريتين في مصل الدم أكبرفي مجموعات بيتا ثلاسيميا مقارنة بالمجموعة الضابطة. بالإضافة إلى ذلك، لوحظ وجود علاقة سلبية قوية بين الكالسيوم والفوسفات.

الكلمات المفتاحية: الثلاسيميا، كلوثو، الفوسفات، الكالسيوم، الفريتين.