



ZINC LEVELS IN PATIENTS WITH BETA THALASSEMIA MAJOR

*¹Noor Fadhil Abbas, ²Besmah M. Ali and ³Bassam Francis Matti

¹Atraanee in Fellowship of Clinical Nutrition, Baghdad Medical City/ Iraq.

²Consultant in Community Medicine, Head of Public Health Unit in Ghazi Al-Hariri Hospital for Surgical Specialties, Baghdad- Iraq.

³Consultant Adult Hematologist, Hematology and Bone Marrow Transplant Center/ Medical City, Baghdad- Iraq.

Article Received date: 19 December 2023

Article Revised date: 09 January 2024

Article Accepted date: 29 January 2024



*Corresponding Author: Noor Fadhil Abbas

Atraanee in Fellowship of Clinical Nutrition, Baghdad Medical City/ Iraq.

ABSTRACT

Background: Beta Thalassemia Major (BTM) is a severe hereditary blood condition that causes anaemia and other consequences by reducing or eliminating haemoglobin beta chain production. These issues have drawn attention to crucial trace elements like zinc. Enzymatic activity, immunological function, and DNA synthesis depend on zinc, a trace element. BTM patients typically have abnormal zinc metabolism, which might affect their health and illness treatment. The aim of study is to evaluate the association between serum zinc and serum ferritin in patients with beta thalassemia major. **Method:** This study involved 90 thalassemia patients from a private lab in Al-Najaf city, analyzing their age, gender, spleen status, blood transfusion frequency, and blood unit usage, along with serum zinc and ferritin levels, using an Italian-made zinc kit from January to October 2023. Exclusions included pregnant women, those on contraceptives, and patients with certain medical conditions. Ethical approval and verbal consent were obtained, ensuring privacy and anonymity. **Results:** In a study of 90 thalassemia patients, 15.5% had a splenectomy, and 63.4% required frequent blood transfusions. The study found no significant differences in serum ferritin and zinc levels across various demographics and conditions within the thalassemia group. However, thalassemia patients had higher mean ferritin levels compared to a control group, with no notable differences in zinc levels between the two groups. **Conclusion:** The study on Beta Thalassemia Major patients shows that serum ferritin and zinc levels are consistent across different demographics and treatments in thalassemia patients, indicating stable zinc metabolism despite varied conditions. Thalassemia patients have higher serum ferritin levels than controls, highlighting iron overload, but their zinc levels are similar to those of the controls. These findings are significant for clinical management and nutritional monitoring of thalassemia.

KEYWORDS: Zinc, beta thalassemia major, serum ferritin.

INTRODUCTION

Beta Thalassemia Major (BTM) is a severe genetic blood disorder characterized by reduced or absent synthesis of the beta chains of hemoglobin, leading to anemia and various complications. Among these complications, the status of essential trace elements like zinc has gained significant attention in recent years. Zinc, a vital trace element, plays a crucial role in numerous biological processes, including enzymatic activity, immune function, and DNA synthesis. Patients with BTM are often found to have altered zinc metabolism, which can have profound implications on their health status and management of the disease.^[1,2] The link between zinc deficiency and BTM is multifaceted. The chronic blood

transfusions that BTM patients undergo can lead to iron overload, which adversely affects zinc absorption and metabolism. Moreover, the chelation therapy used to treat iron overload can also contribute to zinc deficiency. This complex interplay makes the assessment of zinc status in BTM patients both challenging and essential.^[3,4] Research has shown that zinc deficiency in BTM patients can lead to a range of complications. These include growth retardation, delayed sexual maturation, impaired immune function, and increased susceptibility to infections. Zinc plays a pivotal role in growth and development, and its deficiency can exacerbate the already existing growth challenges in BTM patients. Furthermore, the immune system relies heavily on zinc

for proper functioning. A deficiency in zinc can impair the immune response, making patients more vulnerable to infections, which are a leading cause of morbidity in BTM.^[5,6] The assessment of zinc status in BTM patients typically involves measuring serum zinc levels, although this method has its limitations. Serum zinc levels can be influenced by various factors, including inflammation and infection, which are common in BTM patients. Therefore, a comprehensive approach, which may include assessing dietary intake, zinc supplementation history, and measuring other biomarkers of zinc status, is often necessary for an accurate evaluation.^[7,8] Zinc supplementation in BTM patients has been a topic of considerable interest. Some studies have suggested that zinc supplementation can improve growth outcomes, enhance immune function, and ameliorate some of the complications associated with the disease. However, the optimal dosage, duration, and long-term effects of zinc supplementation in this population are still under investigation.^[9] Moreover, the relationship between zinc status and the chelation therapy used in BTM is complex. Chelating agents, while essential for managing iron overload, can also chelate zinc, exacerbating its deficiency. This interaction necessitates a careful balance in the management of BTM patients, considering both iron overload and zinc status.^[10] The aim of study is to evaluation the association between serum zinc and serum ferritin in patients with beta thalassemia major.

METHOD

Cross sectional study of 90 patients with thalassemia the data collected from Al-Zahra teaching hospital/Thalassemia department and private laboratory

in Al -Najaf city in period January 2023 to October 2023. All data from patients include: age of patients (years), gender, Spleen status (non-splenectomy, splenectomy), Frequency of blood Transfusion per month (1 time, 2 times, 3 times and more), Blood units per month (1-2, >2), also measured serum zinc using zinc kit (made in Italy) and serum ferritin level. Excluded from the study: Pregnant, Women on oral contraceptive pills, Myocardial infraction, Alcoholic, Liver diseases, Malabsorption diseases, Lung infections and disease, Carcinoma and lymphoma. Before data collection official agreement had been taken from Arabic Council of medical specialty. Verbal consent was obtained from every participant after explaining the aim and objectives of study and ensuring privacy of data and questionnaire filled without names. The statistical analysis was conducted using SPSS 22, with the use of frequency and percentage measures for categorical data. The chi-square test is employed to evaluate the link between categorical variables, whereas the Pearson correlation coefficient measures the correlation between continuous data. The T-test and ANOVA test are utilised to assess the disparities between the mean and median of continuous data. A p-value that is less than or equal to 0.05 is considered statistically significant.

RESULTS

As shown in table 1, 15.5% of patients have splenectomy, 63.4% of patients have 3 times and more blood transfusion. 18.5 ± 12.5 years mean age of patients. 54.4% of thalassemia patients are males and 45.6% of them are females.

Table 1: Distribution of patients with thalassemia according to Spleen status and Frequency of blood transfusion.

	variables	frequency	percentage
Spleen status	non splenectomy	76	84.4
	splenectomy	14	15.6
Frequency of blood Transfusion per month	1 time	7	7.8
	2 times	25	27.8
	3 times and more	57	63.4
Gender	Females	49	54.4
	Males	41	45.6
Blood units per month	1-2	39	43.3
	>2	51	56.7

Table 2 show no significant difference in mean of serum ferritin in all age groups of thalassemia group. Also no

significant difference in mean of serum zinc in all age groups of thalassemia group.

Table 2: Difference mean of Ferritin, Zinc, Age (years) in Thalassemia group.

Variables	Age Groups (years)	N	Mean	Std. Deviation	P-value
Ferritin ng/ml	≥20	68	1689.52	563.28	0.09
	21-40	20	1372.23	809.33	
	>40	2	1214.50	190.21	
Zinc mcg/dl	≥20	68	81.79	41.14	0.6
	21-40	20	75.90	24.75	
	>40	2	100.50	34.64	

P-value ≤0.05 (significant).

Table 3 show no significant difference in mean of serum ferritin in females and males of thalassemia group. Also

no significant difference in mean of serum zinc in females and males of thalassemia group.

Table 3: Difference mean of Ferritin, Zinc, gender in Thalassemia group.

Variables	Groups	N	Mean	Std. Deviation	P-value
erritin ng/ml	Females	49	1493.56	690.53	0.06
	Males	41	1745.77	531.63	
Zinc mcg/dl	Females	49	77.67	40.82	0.4
	Males	41	84.75	34.09	

P-value ≤0.05 (significant).

Table 4 show no significant difference in mean of serum ferritin according to units of blood in thalassemia group.

Also no significant difference in mean of serum zinc according to units of blood in thalassemia group.

Table 4: Difference mean of Ferritin, Zinc according to units of blood in Thalassemia group.

Variables	Groups	N	Mean	Std. Deviation	P-value
Ferritin ng/ml	1-2	39	1690.31	557.02	0.3
	>2	51	1545.86	683.54	
Zinc mcg/dl	1-2	39	82.56	38.48	0.7
	>2	51	79.62	37.71	

P-value ≤0.05 (significant).

Table 5 show no significant difference in mean of serum ferritin in splenectomies and non-splenectomies of thalassemia group. Also no significant difference in

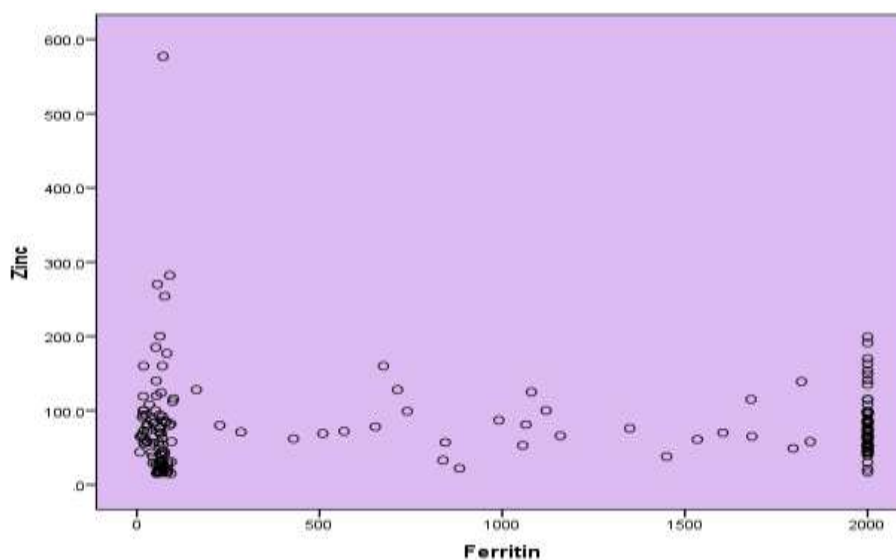
mean of serum zinc in splenectomies and non-splenectomies of thalassemia group.

Table 5: Difference mean of Ferritin, Zinc splenectomy in Thalassemia group.

Variables	Groups	N	Mean	Std. Deviation	P-value
Ferritin ng/ml	non splenectomies	76	1642.27	592.25	0.2
	splenectomies	14	1424.89	820.30	
Zinc mcg/dl	non splenectomies	76	81.02	38.00	0.9
	splenectomies	14	80.21	38.47	

P-value ≤0.05 (significant).

As shown in fig 1; there is no significant correlation between Ferritin and zinc in Thalassemia group.



P-value = 0.8 (not significant).

As shown in table 6 there is significant difference mean of Ferritin, according to thalassemia and Control groups. Mean of ferritin in thalassemia patients is Haigh than control patients, but there is no significant difference

mean of zinc to according to thalassemia and Control groups.

Table 6: Difference mean of Ferritin, Zinc according to Thalassemia and Control groups.

Variables	Groups	N	Mean	Std. Deviation	P-value
Ferritin ng/ml	Thalassemia	90	1608.46	632.57	0.0001
	Control	90	59.28	28.83	
Zinc mcg/dl	Thalassemia	90	80.90	37.86	0.5
	Control	90	74.88	70.18	

P-value ≤ 0.05 (significant).

DISCUSSION

Beta Thalassemia Major presents significant challenges in terms of management and monitoring, particularly concerning iron overload and trace element imbalances. The demographic data indicating that 15.5% of patients have undergone splenectomy and 63.4% require frequent blood transfusions underscores the clinical severity of BTM.^[11] The mean age of patients being 18.5 ± 12.5 years with a slight male predominance (54.4%) is consistent with previous studies.^[12,13] Remarkably, our results indicate no significant differences in serum ferritin and zinc levels across various demographic and clinical subgroups within the thalassemia population. This includes age groups, gender, frequency of blood transfusions, and splenectomy status. This finding is particularly interesting considering that ferritin is a standard biomarker for iron overload, a common complication in BTM due to regular blood transfusions.^[14] The lack of variation in ferritin levels could imply effective iron chelation therapy across the subgroups.^[15] Similarly, the stable levels of serum zinc across these subgroups suggest that, contrary to some assumptions, BTM does not inherently disrupt zinc metabolism.^[16] This challenges the notion that BTM patients are universally at risk of zinc deficiency, a hypothesis that has been suggested due to the potential impact of regular blood transfusions and chelation therapy on micronutrient absorption.^[17] Furthermore, the absence of a significant correlation between serum ferritin and zinc levels in our study indicates that the regulatory mechanisms of iron and zinc may be independent in BTM patients. This finding contrasts with the hypothesis that iron overload in thalassemia could influence other trace elements, including zinc.^[18] Comparing thalassemia patients with a control group, we observed a significant difference in mean serum ferritin levels, with thalassemia patients showing higher levels. This is expected, given the iron overload associated with chronic transfusions in BTM.^[19] However, the absence of a significant difference in serum zinc levels between thalassemia and control groups further supports the notion that zinc metabolism might be relatively unaffected in BTM. Our findings contribute to a more nuanced understanding of iron and zinc metabolism in Beta Thalassemia Major. The lack of significant

differences in serum ferritin and zinc levels across different subgroups within the thalassemia population, and between thalassemia and control groups, suggests that individual characteristics like age, gender, transfusion frequency, and splenectomy status do not significantly influence these parameters. This highlights the importance of personalized monitoring and management strategies in BTM. Further research is warranted to explore the underlying mechanisms governing iron and zinc homeostasis in thalassemia and to determine the clinical implications of these findings.

CONCLUSION

The study on Beta Thalassemia Major patients reveals several crucial insights: Serum ferritin and zinc levels do not significantly differ across various demographics and treatment modalities within the thalassemia group, indicating a consistent metabolic handling of these elements regardless of age, gender, blood transfusion frequency, or splenectomy status. Notably, while thalassemia patients exhibit significantly higher serum ferritin levels compared to controls, reflecting the iron overload characteristic of the condition, zinc levels remain comparable between thalassemia patients and controls. This suggests that despite the challenges of managing iron overload in thalassemia, zinc metabolism remains relatively stable. These findings are important for the clinical management and nutritional monitoring of thalassemia patients.

REFERENCES

- Karunaratna AMDS, Ranasingha JGS, Mudiyanse RM. Zinc Status in Beta Thalassemia Major Patients. *Biol Trace Elem Res*, 2018 Jul; 184(1): 1-6. doi: 10.1007/s12011-017-1158-0. Epub 2017 Sep 23. PMID: 28940159.
- Choudhry VP. Quality of Life in Thalassemia Major. *Indian J Pediatr*, 2018 Nov; 85(11): 957-958. doi: 10.1007/s12098-018-2792-z. Epub 2018 Sep 21. PMID: 30242607.
- Zardkhoni SZ, Moghaddam AG, Rad F, Ghatee MA, Omidifar N, Ghaedi M, Etemadfar P. Serum Zinc Level in β -Thalassemia Major: A Retrospective Study in Southwest Iran. *Hemoglobin*, 2021 Mar;

- 45(2): 103-106. doi: 10.1080/03630269.2021.1918149. Epub 2021 Apr 26. PMID: 33896336.
4. Erdoğan E, Canatan D, Ormeci AR, Vural H, Aylak F. The effects of chelators on zinc levels in patients with thalassemia major. *J Trace Elem Med Biol.*, 2013 Apr; 27(2): 109-11. doi: 10.1016/j.jtemb.2012.10.002. Epub 2012 Nov 16. PMID: 23164519.
 5. Jumaan RM. Serum Copper, Zinc and Copper/Zinc Ratio and their Relationship to Age and Growth Status in Yemeni Adolescent Girls. *Sultan Qaboos Univ Med J.*, 2008 Nov; 8(3): 291-9. PMID: 21748074; PMCID: PMC3074839.
 6. Gonoodi K, Moslem A, Darroudi S, Ahmadnezhad M, Mazloun Z, Tayefi M, Zadeh SAT, Eslami S, Shafiee M, Khashayarmanesh Z, Haghighi HM, Ferns GA, Ghayour-Mobarhan M. Serum and dietary zinc and copper in Iranian girls. *Clin Biochem*, 2018 Apr; 54: 25-31. doi: 10.1016/j.clinbiochem.2018.02.006. Epub 2018 Feb 10. PMID: 29438682.
 7. Wieringa FT, Dijkhuizen MA, Fiorentino M, Laillou A, Berger J. Determination of zinc status in humans: which indicator should we use? *Nutrients*, 2015 May 6; 7(5): 3252-63. doi: 10.3390/nu7053252. PMID: 25954900; PMCID: PMC4446750.
 8. Motadi SA, Mbhenyane XG, Mbhatsani HV, Mabapa NS, Mamabolo RL. Prevalence of iron and zinc deficiencies among preschool children ages 3 to 5 y in Vhembe district, Limpopo province, South Africa. *Nutrition*, 2015 Mar; 31(3): 452-8. doi: 10.1016/j.nut.2014.09.016. Epub 2014 Oct 22. PMID: 25701334.
 9. Abdollahi M, Ajami M, Abdollahi Z, Kalantari N, Houshiarrad A, Fozouni F, Fallahrokni A, Mazandarani FS. Zinc supplementation is an effective and feasible strategy to prevent growth retardation in 6 to 24 month children: A pragmatic double blind, randomized trial. *Heliyon*, 2019 Nov 1; 5(11): e02581. doi: 10.1016/j.heliyon.2019.e02581. PMID: 31720482; PMCID: PMC6839004.
 10. Suwanphoerung W, Klinmalai C, Rattanasiri S, Pakakasama S, Anurathapan U, Hongeng S, Chongviriyaphan N, Apiwattanakul N. Association of zinc deficiency with infectious complications in pediatric hematopoietic stem cell transplantation patients. *PLoS One*, 2022 Dec 27; 17(12): e0279439. doi: 10.1371/journal.pone.0279439. PMID: 36574381; PMCID: PMC9794056.
 11. Farmakis D, Porter J, Taher A, Domenica Cappellini M, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. *Hemasphere*, 2022 Jul 29; 6(8): e732. doi: 10.1097/HS9.0000000000000732. PMID: 35928543; PMCID: PMC9345633.
 12. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. *Bull World Health Organ*, 2008 Jun; 86(6): 480-7. doi: 10.2471/blt.06.036673. PMID: 18568278; PMCID: PMC2647473.
 13. Borgna-Pignatti C, Rugolotto S, De Stefano P, Zhao H, Cappellini MD, Del Vecchio GC, Romeo MA, Forni GL, Gamberini MR, Ghilardi R, Piga A, Cnaan A. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *Haematologica*, 2004 Oct; 89(10): 1187-93. PMID: 15477202.
 14. Origa R, Galanello R, Ganz T, Giagu N, Maccioni L, Faa G, Nemeth E. Liver iron concentrations and urinary hepcidin in beta-thalassemia. *Haematologica*, 2007 May; 92(5): 583-8. doi: 10.3324/haematol.10842. PMID: 17488680.
 15. Fung EB, Xu Y, Kwiatkowski JL, Vogiatzi MG, Neufeld E, Olivieri N, Vichinsky EP, Giardina PJ; Thalassemia Clinical Research Network. Relationship between chronic transfusion therapy and body composition in subjects with thalassemia. *J Pediatr*, 2010 Oct; 157(4): 641-7, 647.e1-2. doi: 10.1016/j.jpeds.2010.04.064. Epub 2010 Jun 12. PMID: 20547400; PMCID: PMC2936667.
 16. Coates TD, Carson S, Wood JC, Berdoukas V. Management of iron overload in hemoglobinopathies: what is the appropriate target iron level? *Ann N Y Acad Sci.*, 2016 Mar; 1368(1): 95-106. doi: 10.1111/nyas.13060. PMID: 27186942.
 17. Fung EB, Kwiatkowski JL, Huang JN, Gildengorin G, King JC, Vichinsky EP. Zinc supplementation improves bone density in patients with thalassemia: a double-blind, randomized, placebo-controlled trial. *Am J Clin Nutr*, 2013 Oct; 98(4): 960-71. doi: 10.3945/ajcn.112.049221. Epub 2013 Aug 14. PMID: 23945720; PMCID: PMC3778866.
 18. Berdoukas V, Coates TD, Cabantchik ZI. Iron and oxidative stress in cardiomyopathy in thalassemia. *Free Radic Biol Med*, 2015 Nov; 88(Pt A): 3-9. doi: 10.1016/j.freeradbiomed.2015.07.019. Epub 2015 Jul 26. PMID: 26216855.
 19. Rasel M, Mahboobi SK. Transfusion Iron Overload. [Updated 2023 Apr 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK562146/>.