

EVALUATION OF VITAMIN D, CALCIUM, LFTS IN BETA THALASSEMIA PATIENTS

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Abstract:

Beta-thalassemia is a severe hereditary blood disorder characterized by ineffective erythropoiesis, chronic anemia, and iron overload due to frequent blood transfusions. This study evaluates liver function tests (LFTs), serum vitamin D, calcium, and ferritin levels in 200 pediatric patients (110 males, 90 females) with beta-thalassemia major. The biochemical analysis revealed that 55.5% of patients had elevated AST levels (>40 U/L), 22% had ALT >56 U/L, and 10% exhibited ALP >129 U/L, indicating potential liver damage due to iron overload. A striking

99% of patients had vitamin D deficiency (<20 ng/mL), highlighting a critical issue in thalassemic children despite adequate sunlight exposure. Serum calcium levels were normal in 71% of patients, while 20% had low levels. Ferritin levels ranged from 1000 to 6000 ng/mL in 61% of patients, with a mean value of 4584.78 ng/mL, substantially over normal limits. A substantial association was found between high ferritin levels and vitamin D insufficiency, indicating a link between iron excess and bone metabolism disruptions. These findings highlight the need for enhanced management techniques, such as vitamin D supplements and iron chelation therapy, to reduce liver dysfunction and bone health deterioration in beta-thalassemia patients.

Key Words: Beta-Thalassemia, LFTS, Ferritin, Vitamin D, Calcium

Introduction:

Cooley originally reported thalassaemia in 1925. Because it is common among Mediterranean people, Whipple and Bradford renamed it in 1932. Thalassaemia is a genetic condition that is characterised by decreased haemoglobin synthesis owing to abnormalities in globin genes [1]. It includes α -, β -, β /HbE-, and $\delta\beta$ -thalassemia, all of which have distinct effects on haemoglobin production [2]. Anaemia and problems such iron overload, bone abnormalities, and organ damage are the results of β -thalassemia, which is brought on by abnormalities in the β -globin gene and causes an imbalance in the α - and β -globin chains [3]. There are three types of the disorder: minor, intermedia, and major. The most severe kind, β -thalassemia major, necessitates iron chelation treatment and transfusions for the rest of one's life [4].

About 1.5% of people worldwide have thalassaemia, and 60,000 babies are born with symptoms each year, mostly in underdeveloped nations [5]. An increased risk of infection as a result of repeated transfusions, bone deformities, iron overload, and endocrine dysfunction are among the complications [6]. For the treatment of iron overload, iron chelation treatments such deferoxamine, deferiprone, and deferasirox are essential; nevertheless, noncompliance can result in serious organ damage [7]. Although bone marrow transplantation is still the sole treatment available, its availability and expense limit its use [8].

In many nations, the prevalence of thalassaemia has decreased as a result of preventive interventions such carrier screening, prenatal diagnosis, and genetic counseling [9]. Iron

overload, osteoporosis, and infection risks continue to be problems despite therapeutic breakthroughs, underscoring the need for better treatments and patient management techniques [10].

Material and Methods:

In this retrospective investigation, 200 child patients with confirm beta-thalassemia major who were less than 20 years old (90 girls and 110 boys) had their biochemical profiles examined. Using sophisticated methods including colorimetry and chemiluminescent immunoassay (CLIA) on Beckman Coulter analyzer, serum was examined for calcium, ferritin, liver enzymes (ALT, AST, and alkaline phosphatase), and vitamin D levels after blood samples were drawn by venipuncture. Data were statistically analyzed for descriptive and comparative metrics, with significance set at $p < 0.05$. Ethical approval and informed consent were obtained, ensuring adherence to ethical guidelines and patient confidentiality.

Results:

The study analyzed biochemical and demographic data from 200 patients with confirmed beta-thalassemia major. All patients are children’s. Out of 200 participants, 110 (55.0%) are male, while 90 (45.0%) are female (Table 1).

Table 1: Demographic and clinical features.

Variables		Numbers	Percentage
Gender	Males	110	55.0
	Females	90	45.0
Age	0-5 Years	107	53.5
	5.5-09 Years	58	29.0
	10-14 Years	26	13.0
	15-20 Years	09	4.5

Figures 1, 2, 3 and 4 show liver function test, vitamin D, serum calcium, and serum ferritin levels in confirmed beta thalassemia patients, with ALT of >56 in 44 patients (22%), AST of >40 in 111 patients (55.5%), ALP of >129 U/L in 20 patients (10%) showing the mean values of Liver

function test parameters in (Figure 1). 99% children's have insufficient level of vitamin D (Figure 2). While 71% with normal serum calcium levels, 20% with low, and only 9% had high calcium levels, (Figure 3). And more than half of the patients (61%) had serum ferritin levels ranging between 1000-6000 ng/ml (Figure 4).

Figure 1: LFTS in Beta thalassemic major patients

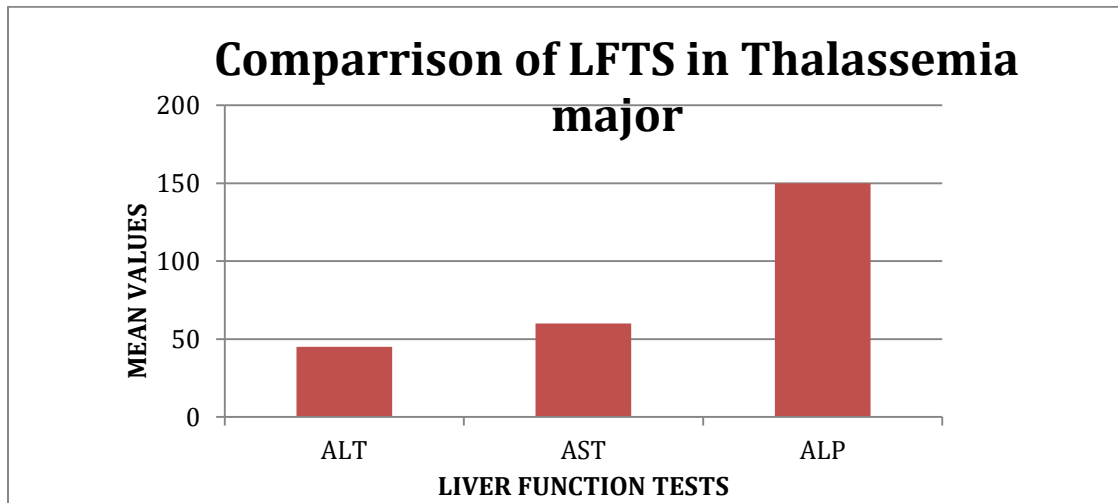


Figure 2: Vitamin D in Beta thalassemic major patients

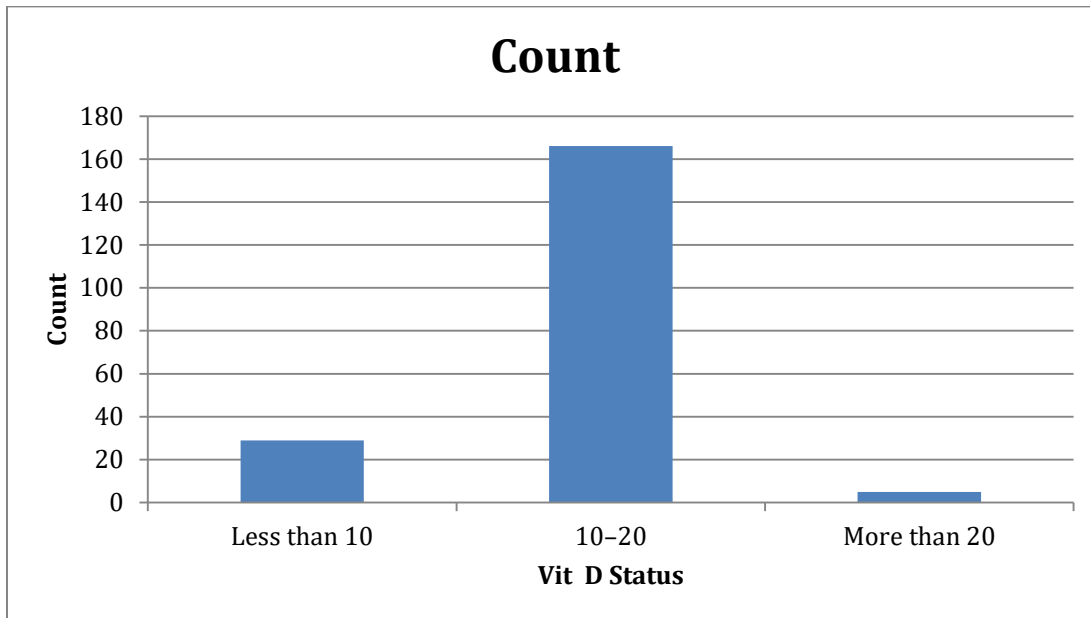


Figure 3: Serum Calcium in Beta thalassemic major patients

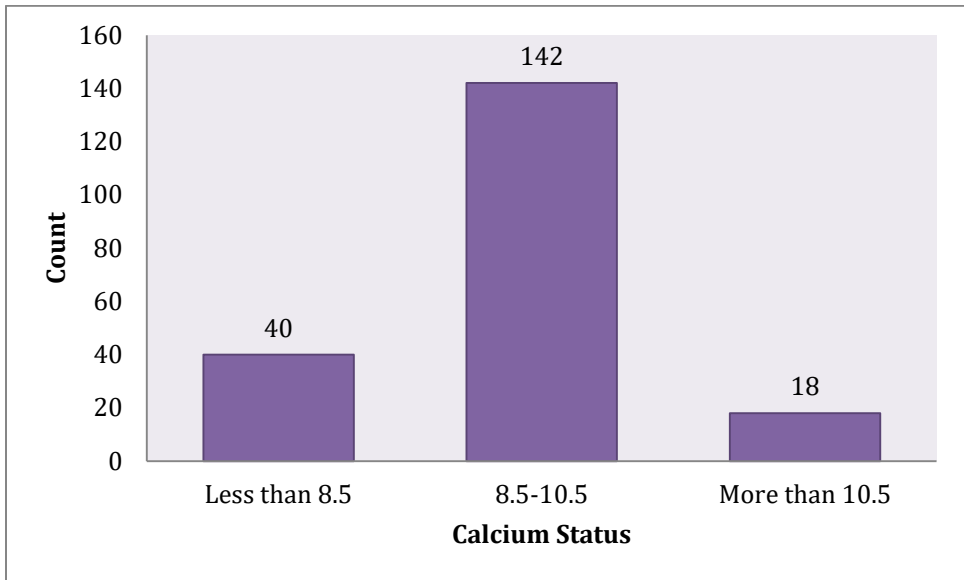
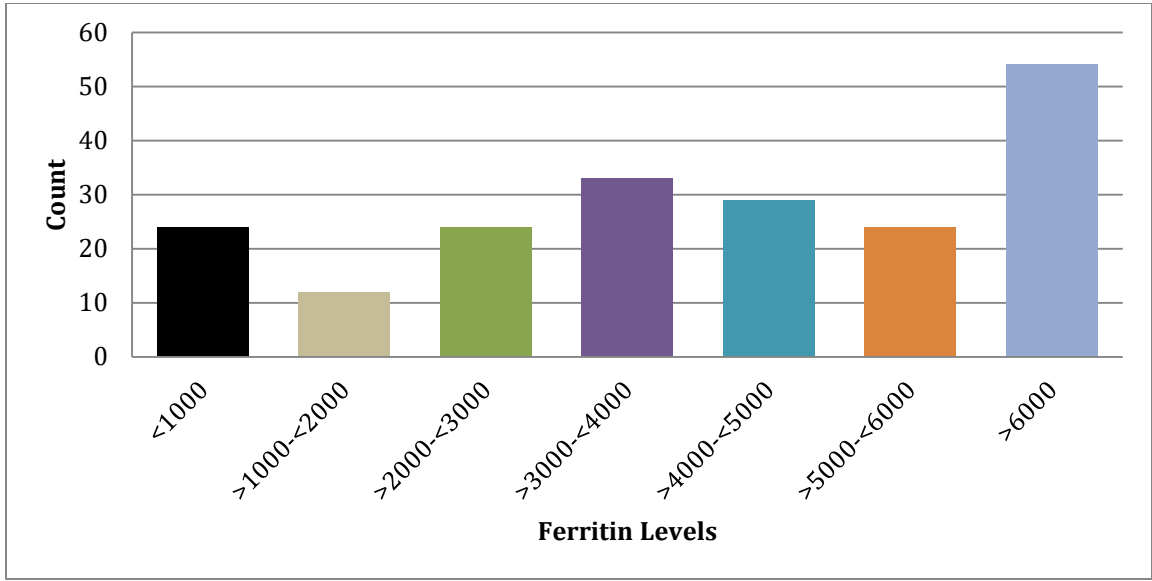
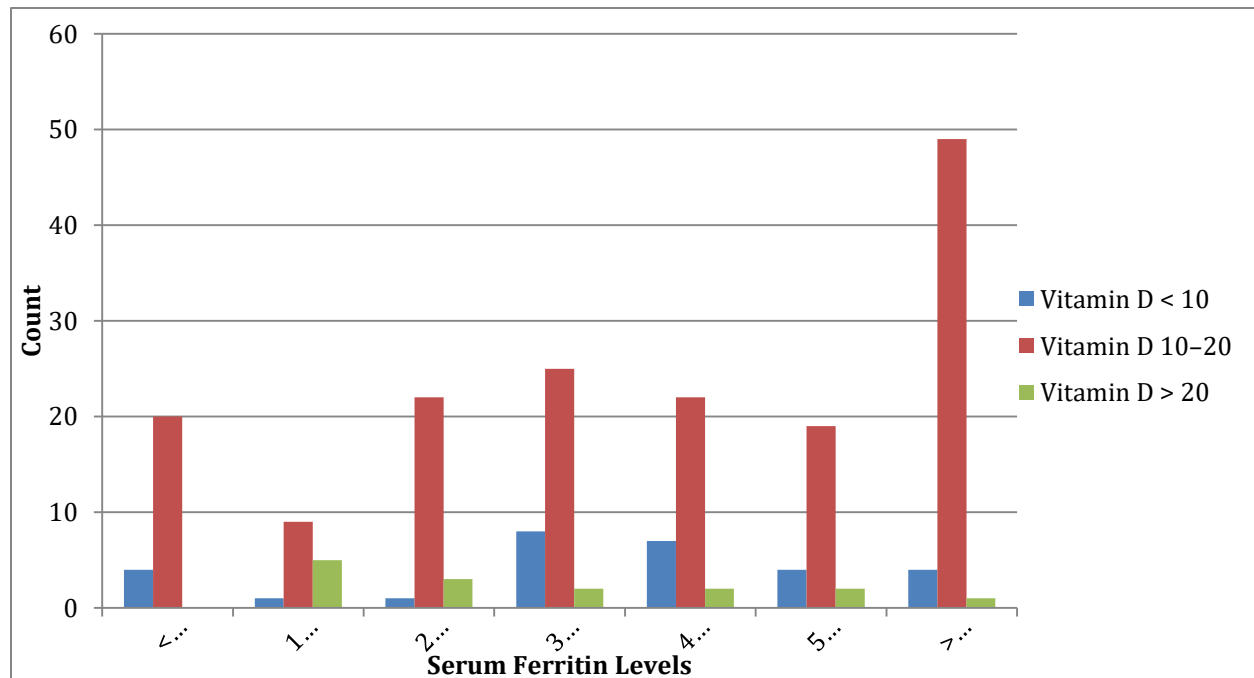


Figure 4: Serum Ferritin in Beta thalassemic major patients



Most patients complaining of vitamin D deficiency had high serum ferritin levels and nearly all patients with ferritin levels exceeding 2001 ng/ml complained of vitamin D deficiency or insufficiency as shown in (Figure 5).

Figure 5: Vitamin D status among different serum ferritin levels



The frequency distribution of participants' ages reveals a diverse range of values, with the most common ages being 2.00 years (12.5%), 5.00 years (11.0%), and 6.00 years (10.0%). Ages of 1.00 years and 4.00 years also appear frequently, with proportions of 8.5% and 10.5%, respectively. Other age groups, such as 3.00 years (8.0%), 8.00 years (8.0%), and 7.00 years (6.5%), contribute smaller percentages. Less frequent ages, including 9.00 years (3.5%), 11.00 years (2.0%), and 13.00 years (3.0%), highlight the variability among participants.

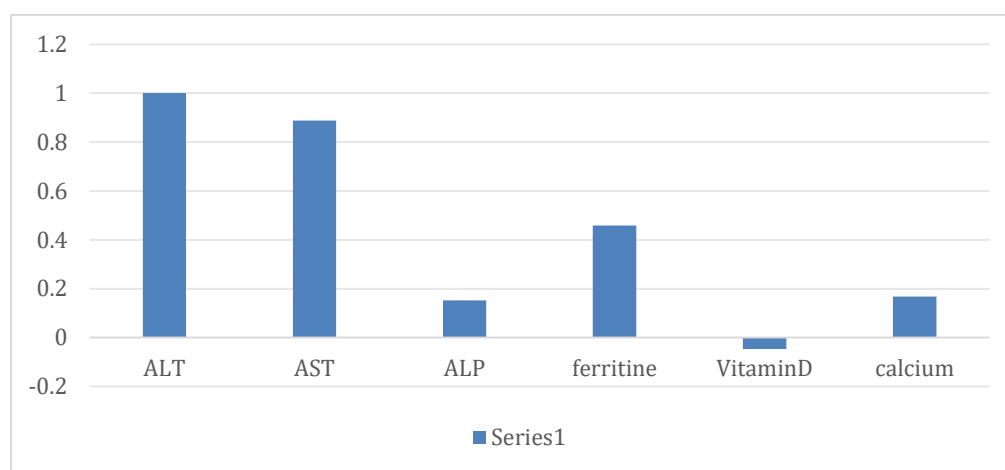
Rarely represented ages, such as 1.50 years, 3.50 years, 4.50 years, and 20.00 years (each accounting for 0.5%), emphasize the wide age distribution in the sample. The cumulative percentage indicates that 64.5% of the participants are aged 6.50 years or younger, reflecting a younger skew in the dataset. This comprehensive frequency distribution showcases a well-dispersed age range among the 200 participants (Table 2) (Figure 5).

Table 2: Correlation between ALT, AST, ALP, Ferritin, Vitamin D and Calcium

Variables	1	2	3	4	5	6
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ALT	1	.888**	.152*	.459**	-.046	.168*
AST		1	.171*	.498**	-.004	.161*
ALP			1	.033	.005	.286**
Ferritin				1	-.098	.180*
Vitamin D					1	.068
Calcium						1

Figure 5: Correlation between ALT, AST, ALP, Ferritin, Vitamin D and Calcium



These results highlight gender-based differences in iron overload, liver function, and vitamin D deficiency, emphasizing the need for tailored management strategies in beta-thalassemia major patients.

Discussion:

Depending on the mutation, hemolytic anemia can be seen in thalassemia, a hereditary blood illness. Labile plasma iron levels rise as a result of frequent blood transfusions and the rapid destruction of the red blood cells. Iron in plasma binds to transferrin; if transferrin's binding capacity is exceeded, the extra iron is deposited in different organs, such as the liver, where it is stored as ferritin. Our study is conducted to evaluate the function of liver after have iron overload and the evaluation of vitamin D and serum Calcium in body. All of the children in this study had β thalassemia major. Males made up more than half of them (55%).

The laboratory results of B-thalassemia patients in this investigation indicated ALT of >56 in 44 patients (22%), AST of >40 in 111 patients (55.5%), ALP of >129 U/L in 20 patients (10%), and

ferritin levels of >1000 ng/mL in 148 patients (74%). Of the 198 children tested, 99% had a vitamin D level of <20 ng/ml. The laboratory results and diagnostic features of the diagnosis of B-thalassemia patients were more or less comparable to the laboratory profile of our investigated individuals. [11].

Organ harm is likely to result from this buildup in tissues [12]. Our research aimed to evaluate the harmful consequences of high iron accumulation on liver cells. We found significantly higher levels of AST, ALT, and ALP in patients with ferritin levels more than 4000 ng/mL. Our findings were consistent with those of another study that found higher LFTs in persons with transfusion-dependent thalassemia and confirmed iron deposition as the underlying cause [13]. This study revealed a significant prevalence (99%) of Vitamin D deficiency and insufficiency in multi-transfused thalassemia patients. The mean Vitamin-D levels of our study patients were 13.5ng/mL. Vitamin D deficiency and insufficiency are reported to be high in thalassemic patients in many countries despite the presence of good sunshine and routine prescriptions. This agrees with; Merchant et al. who found vitamin D deficiency in 62% of Indian thalassemia major children [14].

The results revealed in this study about Calcium was 71% which means majority of major thalassemia children's have normal calcium levels, and only 20.0% had low serum calcium levels, this result goes with a survey conducted in Doha, Qatar revealed that 5% of thalassemia patients had low serum calcium levels [15].

The mean serum ferritin level was 4584.78ng/ml, which is significantly higher than the standard suggested values for healthy persons. Normal blood ferritin levels for males and women are 12–300 ng/mL and 12–150 ng/mL, each [16]. This goes with Rashid Merchant et al., who found that all children had high serum ferritin levels [17].

Conclusion:

This study highlights the significant biochemical disturbances in pediatric beta-thalassemia major patients, emphasizing the detrimental effects of iron overload on liver function and vitamin D metabolism. Most patients exhibited elevated liver enzymes, indicating potential hepatocellular injury. Furthermore, nearly all patients had vitamin D deficiency, underscoring the need for routine monitoring and supplementation to prevent bone-related complications. While

most patients maintained normal calcium levels, a subset exhibited deficiencies that could contribute to long-term skeletal issues. The high serum ferritin levels reinforce the importance of strict iron chelation therapy to minimize organ damage. These findings stress the necessity for comprehensive, individualized management strategies to improve the overall health outcomes of beta-thalassemia major patients.

References:

1. Ali AH. Normal reference values of some hematological parameters among adult sudanese people in elmatama locality (Doctoral dissertation, Salwa Ahmed Alsayed).
2. Windiastuti E, Nancy YM, Mulatsih S, Sudarmanto B, Ugrasena ID. Buku Ajar Hematologi Onkologi Anak. Jakarta: Badan Penerbit Ikatan Dokter Anak Indonesia. 2018.
3. Thiagarajan NR, Delhi Kumar CG, Sahoo J, Krishnamurthy S. Effect of vitamin D and calcium supplementation on bone mineral content in children with thalassemia. *Indian Pediatrics*. 2019 Apr;56:307-10.
4. Hay D, Weatherall DJ. Thalassaemias. *eLS*. 2017:1-6.
5. Vichinsky ep. Changing patterns of thalassemia worldwide. *Annals of the new york academy of sciences*. 2005 nov;1054(1):18-24.
6. Alciato F, Sainaghi PP, Castello L, Bergamasco L, Carnieletto S, Avanzi GC. Development and validation of an ELISA method for detection of growth arrest specific 6 (GAS6) protein in human plasma. *Journal of Immunoassay and Immunochemistry*. 2008 mar 18;29(2):167-80.
7. Telfer P, Coen PG, Christou S, Hadjigavriel M, Kolnakou A, Pangalou E, Pavlides N, Psiloinis M, Simamonian K, Skordos G, Sitarou M. Survival of medically treated thalassemia patients in Cyprus. Trends and risk factors over the period 1980-2004. *Haematologica*. 2006 Jan 1;91(9):1187-92.
8. Majolino i, othman d, rovelli a, hassan d, rasool l, vacca m, abdalrahman n, abduallah c, ahmed z, ali d, ali k. The start-up of the first hematopoietic stem cell transplantation center in the iraqikurdistan: a capacity-building cooperative project by the hiwa cancer hospital, sulaymaniyah, and the italian agency for development cooperation: an innovative approach. *Mediterranean journal of hematology and infectious diseases*. 2017;9(1).

9. Origa r, comitini f. Pregnancy in thalassemia. *Mediterranean journal of hematology and infectious diseases*. 2019;11(1).
10. Terpos e, voskaridou e. Treatment options for thalassemia patients with osteoporosis. *Annals of the new york academy of sciences*. 2010 aug;1202(1):237-43.
11. Chernecky cc, berger bj. *Laboratory tests and diagnostic procedures*. Elsevier health sciences; 2012 dec 1.
12. Hamid n, shafique mf, niaz h. Frequency and significance of electrocardiographic changes in beta thalassemia major patients. *Pakistan armed forces medical journal*. 2022 feb 28;72(1):136-40.
13. Fianza pi, rahmawati a, widihastha sh, afifah s, ghozali m, indrajaya a, pratama dm, prasetya d, sihite ta, syamsunarno mr, setiabudi d. Iron overload in transfusion-dependent indonesian thalassemic patients. *Anemia*. 2021;2021(1):5581831.
14. Merchant r, udani a, puri v, d'cruz v, patkar d, karkera a. Evaluation of osteopathy in thalassemia by bone mineral densitometry and biochemical indices. *The indian journal of pediatrics*. 2010 sep;77:987-91.
15. Soliman a, adel a, wagdy m, al ali m, elmulla n. Calcium homeostasis in 40 adolescents with beta-thalassemia major: a case-control study of the effects of intramuscular injection of a megadose of cholecalciferol. *Pediatric endocrinology reviews: per*. 2008 oct 1;6:149-54.
16. Berdoukas V, Farmaki K, Carson S, Wood J, Coates T. Treating thalassemia major-related iron overload: the role of deferiprone. *Journal of blood medicine*. 2012 Oct 19:119-29.
17. Merchant R, Udani A, Puri V, D'cruz V, Patkar D, Karkera A. Evaluation of osteopathy in thalassemia by bone mineral densitometry and biochemical indices. *The Indian Journal of Pediatrics*. 2010 Sep;77:987-91.