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Assessment of the vitamin D level and demographic characteristics of children suffering from β-thalassemia in Thi-Qar province

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Abstract

Beta thalassemia is a genetic disorder inherited by autosomal recessive inheritance, is present all over the world . Lifelong transfusions are necessary for people with beta-thalassemia, which can result in an iron buildup in the skin, liver, and kidneys that reduces the production of vitamin D. This study aims to evaluate vitamin D levels, blood groups, and demographic characteristics in beta-thalassemia patients. The current study was conducted at the thalassemia center and hereditary blood disease in Thi-Qar Province with eighty-eight blood samples collected from individuals. It was divided into three groups according to age range, the first group (2-6), the second group (7-11), and the third group (12- 15). In the current study, there was a significant decrease in Vit-D3 levels among thalassemia patients compared to the control group ($p \leq 0.05$) . As for age between the patients group and the control group, the highest proportion of patients in the third age group. As for gender, the results of the study found a non-significant difference at the ($P \leq 0.05$) level between the patients group and the control group. The most common blood group in thalassemia

was O followed by blood groups A, B, and AB. It also shows that the majority of the population was positive Rh.

Keywords: Beta-thalassemia, Vitamin D, ABO groups, Children's suffering

1. Introduction

Genetic disorders known as thalassemia are characterized by decreased hemoglobin production (either beta or alpha chain, or both). Hemoglobin is a protein complex that is responsible for carrying oxygen. Anemia results from the reduction of these proteins, which prevents red blood cells from carrying oxygen. Thalassemia is caused by a mutation or deletion in a gene (Vichinsky *et al*.,2018; Joudah and Hamim, 2023).

Thalassemia is classified into two types: beta and alpha. Deletion of the alpha globin gene or a problem with alpha globin synthesis are causes of alpha thalassemia (Ahmadpanah *et al.*, 2019). Furthermore, beta thalassemia is caused by point mutations in the beta-globin gene. The type of beta gene mutation determines the severity of the mutation, which can be divided into three categories: minor, moderate, and major (Jalil *et al*.,2019).

Before the child turns two, thalassemia's clinical symptoms begin to manifest. Acute anemia requires blood transfusions, along with severe acute anemia, jaundice, recurrent infections, poor appetite, incapacity to thrive, paleness and yellowing of the skin, and organ enlargement (Fibach and Rachmilewitz, 2017). Hemochromatosis and ineffective erythropoiesis are the causes of all these effects (Reading *et al.*, 2014). This disease can result in several complications including growth retardation, hypothyroidism, endocrine dysfunction, progressive liver failure, and abnormal kidney function (Rooks *et al.*, 2012).

Vitamin D is essential for calcium homeostasis and bone mineralization, especially during periods of rapid growth like childhood and puberty. In the liver, vitamin D is converted to 25-OH-vitamin D through hydroxylation. Subsequently, the kidneys carry out additional hydroxylation to produce 1-25-OH-vitamin D3. The most reliable indicator of vitamin D status is serum 25-OH-vitamin D, which is the main circulating metabolite of the vitamin (Agrawal *et al.*, 2016; Jassim and Al-Salih, 2023). The precise cause of the thalassemia-related vitamin D deficiency is unknown. However, according to Singh *et al*. (2012), this is thought to be the resulted of repeated transfusions raising liver iron levels. The hydroxylation of vitamin D is dependent on the liver's 25-hydroxylase enzyme, which is damaged by iron deposition. Patients with thalassemia frequently exhibit hyperpigmentation as well. For people with dark skin, sunlight will not convert vitamin D

(Albayrak and Albayrak, 2013). Children who live in nations with high levels of sun exposure are typically not at risk for vitamin D deficiency (Kashat and Ali, 2021). Still, a study done in Thailand discovered that 90% of patients with thalassemia major and thalassemia intermediate also had deficiencies in vitamin D. This shows that exposure to the sun alone is insufficient for children with thalassemia to produce vitamin D (Singh *et al.*, 2012).

2. Materials and Methods:: Samples Collection

Blood was collected from 88 people, the samples were split into three groups: the first group beta-thalassemia major had (41) samples, the second group beta thalassemia intermedia had (9) samples and the third group the control group had (38) samples. The samples were collected between September 2023 and December 2023 from the thalassemia and genetic blood diseases center in the Thi-Qar province. The age of all groups was from (2-15) years. At the same time, the patient's demographic information included gender, age, place of residence, parental kinship, ABO group, complications, and medical history. ELISA technique was used to determine vitamin D3 titers, according to Norman and Anthony (1998).

2.1: Statistical Analysis

All of the data of the current study were statistically evaluated by utilizing Microsoft Windows Excel (version 2019) and SPSS version 26 (Statistical Package of Social Science), based on one-way ANOVA and the least significant difference at P values of ≤ 0.05 or ≤ 0.01.

4 . Results

4.1. Comparing the demographic characteristics between the patient groups and control group

The current results recorded a significant increase at $p \leq 0.05$ according to age between the patient group and the control group, was noted the highest proportion of patients in the third age group was 40%.

As for gender, the results of the study found a non-significant difference at the $p \leq 0.05$ level between the patient group and the control group. Also, The current results showed a significant difference at the level of probability $p \leq 0.05$ according to place of residence, as it showed that the highest percentage was for the patients group who lived in the countryside, 78.0%, as in Table (1).

Table 1: Comparing the demographic characteristics between the patient groups and control group

Demographic characteristic		Patients		Control		Total		p. value
		No.	%	No.	%	No.	%	
Age in years	2 – 6	15	30.0	14	36.84	29	32.95	0.013
	7 – 11	15	30.0	16	42.11	31	35.23	
	12 – 15	20	40.0	8	21.05	28	31.82	
Total		50	56.82	38	43.18	43.18	100	
Sex	Male	25	50.0	19	50.0	44	50.0	1.00
	Female	25	50.0	19	50.0	44	50.0	
Total		50	56.82	38	43.18	88	100	
Residency	City	11	22.0	37	97.37	48	45.45	< 0.001
	Countryside	39	78.0	1	2.63	40	54.55	
otal		50	56.82	38	43.18	88	100	
Age-CalX^2= 8.64 Sex-CalX^2= 0.00 Residency-CalX^2= 116.7								

4.2. Prevalence of thalassemia according to ABO groups

The prevalence of O, B, A, and AB is shown in Table (2) , Figure (1), and the most common blood group in thalassemia was group O (36.8%) followed by blood groups A , B and AB (28% , 20% and 6%), respectively. It also shows that the majority of the population was positive Rh and a few were negative Rh.

Table 2: Prevalence of thalassemia according to ABO groups

	Patients		**Control**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
A-	1	2.0	0	0.0	1	1.14
A+	14	28.0	8	21.1	22	25.00
B-	2	4.0	0	0.0	2	2.27
B+	10	20.0	14	36.8	24	27.27
AB-	0	0.0	0	0.0	0	0.00

AB+	3	6.0	3	7.9	6	6.82
O-	2	4.0	0	0.0	2	2.27
O+	18	36.0	13	34.2	31	35.23
Total	50	56.82	38	43.18	88	100
CalX²=16.4 TabX²= 12.59 DF=6 p. value 0.012						

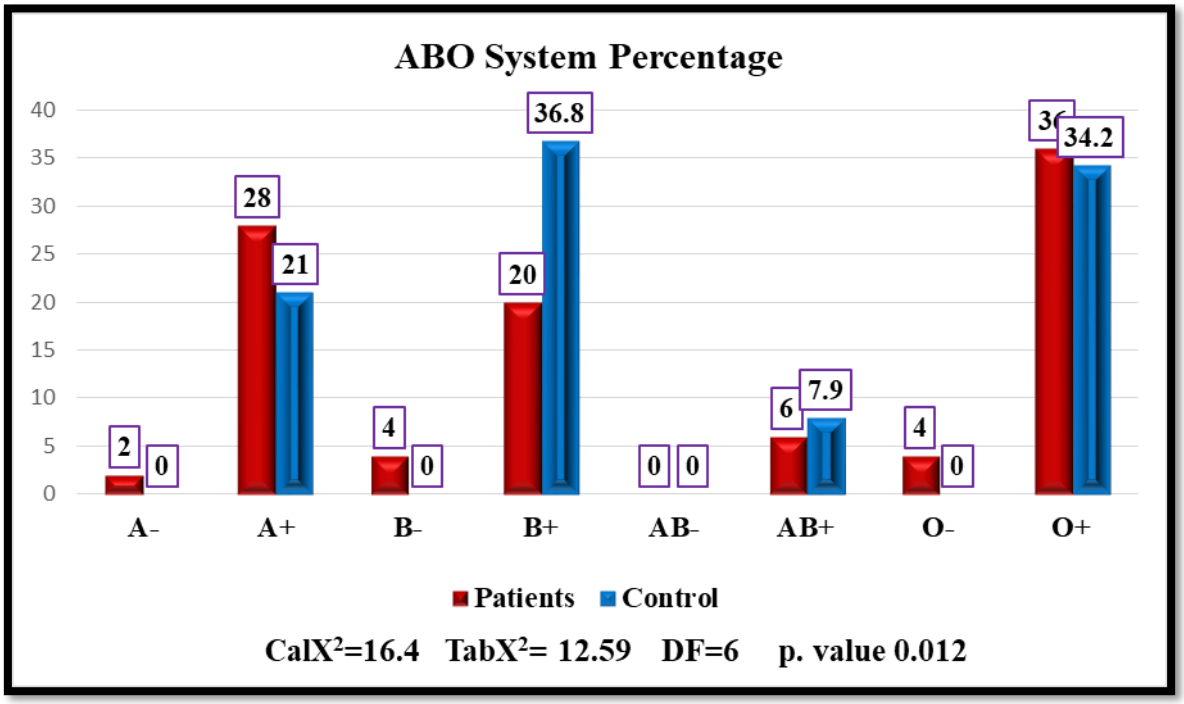

Figure 1: Prevalence of thalassemia according to ABO groups

4.3.Comparing descriptive characteristics and complications of thalassemia Patient with the control group

According to the type of thalassemia disease, the current results showed a significant difference at p. ≤ 0.05; the highest proportion of patients had thalassemia major at 82% and the lowest, with thalassemia intermediate 18%. The study found that 42% of patients had splenomegaly, 34% had hepatosplenomegaly, 10% had hepatomegaly and only 14% had no disease complication—a significant difference at p. value ≤ 0.05—according to disease complication. The study found that, in terms of parent consanguinity, 16% of patients had parent strangers, whereas 30% of patients had parents from the first and second degree and 24% of patients had parents from the third degree. This difference was not statistically significant at p < 0.05. In terms of illness

history, the current study revealed that 72% of patients developed the disease when they were younger than a year old and 2% of patients developed it when they were older than five years. These differences were statistically significant at p. value < 0.05, as indicated in Table (3).

Table 3 : Compare descriptive Characteristics and Complications of Thalassemia Patients with control group

Patients Characteristics	Thalassemia Type		p. value
	No.	%	
Major	41	82.0	< 0.001 CalX2=20.4
Intermediate	9	18.0	
Total	50	100	
	Complications		
Hepatomegaly	5	10.0	0.003 CalX2=14.3
Hepatosplenomegaly	17	34.0	
Splenomegaly	21	42.0	
Non	7	14.0	
Total	50	100	
	Parent consanguinity		
First degree	15	30.0	0.451 CalX2=2.64
Second degree	15	30.0	
Third degree	12	24.0	
Stranges	8	16.0	
Total	50	100	
	History of the disease		
Less than year	36	72.0	< 0.001 CalX2=60.5
2 – 3 years	6	12.0	
4 – 5 years	7	14.0	
More than	1	2.0	

Total	50	100	

4.4.Evaluation of Ferritin and Vit-D3 in Thalassemia Patients and Control Group

The present results showed that the level of Vit-D3 decreased significantly in thalassemia patients groups compared with control group, while, the level of ferritin were increased significantly in thalassemia patients than in the control group at $p \leq 0.05$ as in Table (4).

Table 4: Evaluation of Vit-D_3 in thalassemia patients and control group

Parameters	Patients No. 50	Control No. 38	p. value
	Mean ± S. D		
Vit-D_3	21.79 ± 4.29	30.50 ± 9.02	0.013
Ferritin	2160.0 ± 659.5	38.56 ± 11.38	< 0.001

4.5.Evaluation of Ferritin and Vit-D3 in Thalassemia Patients According to Disease Type

The present results indicated that the level of ferritin was increased significantly in patients with thalassemia major than in patients with thalassemia intermediate, while, the level of Vit-D3 was not scored significantly according to thalassemia type at p. value ≤ 0.05 as in Table (5).

Table 5: Evaluation of ferritin and Vit-D_3 in thalassemia patients according to disease type

Parameters	**Intermediate No. 9**	**Major No. 41**	**p. value**
	Mean ± S. D		
Ferritin	1580.8 ± 554.4	2287.2 ± 615.9	0.003
Vit-D_3	24.21 ± 3.40	19.37 ± 3.89	0.070

5. Discussion

In our current study, the age distribution of thalassemia syndrome showed a significant rise ($p \leq 0.05$) in thalassemia. Patients aged 12 years or older can suffer several complications, the most significant of which is an elevation in ferritin that affects the health of the heart, kidneys, and

endocrine system in addition to viral infections that result in a high death rate (Haghpanah *et al.,* 2018). The findings of (Al-attar and Shekha, 2006 and Tawfeeq, 2017) are consistent with this outcome.

In instances of severe beta-thalassemia, the issue might not show up until the second part of the infant's first year of life. The condition may remain hidden until then due to the interaction between fetal hemoglobin and the production of γ globin chains. Many homozygous patients may go years without experiencing any significant symptoms, including anemia. According to (Traivaree *et al* ., 2018), milder forms are frequently discovered by accident and at different ages. There are no obvious differences between the sexes when it comes to thalassemia because it is a genetic disorder that is equally transmitted from parents to children. According to this outcome is consistent with (Al-attar and Shekha, 2006).

The results showed a significant increase in the induced thalassemia syndrome in rural areas. This is because many rural residents follow tribal customs that involve mating and not being receptive to other families. This outcome agrees with Tawfeeq (2017) . Al-Attar and Shekha, 2006, the models' random selection or their inclusion of participants of all ages without discrimination may have contributed to the compatibility of the two studies.

Blood groups state that the high frequency of blood group O individuals in the world is beneficial because it suggests that there will be adequate blood available in an emergency (Mohssin *et al.*,2015). In descending order, the blood group arrangement percentages in the current study were O,A,B and AB. This result was consistent with researches conducted by (Mahmood *et al.,* 2014; Haider and Al-Maliki, 2015; Hashim *et al.,* 2020) that looked into the distribution of ABO blood groups in thalassemia patients in Iraq.

Regarding the contribution of family history to the prevalence of thalassemia, several studies carried out locally, regionally, and worldwide agreed with the findings of the current study (Asadi-Pooya and Doroudchi, 2004; Abid *et al.*,2019; Akinci *et al.*,2021). harmful gene variations are prevalent in people related to consanguineous marriages. Sadly, Iraq is not an exception when it comes to the serious health problems brought on by thalassemia. Since the first reports on thalassemia in Iraq were published in 1960, these inherited diseases have come to be recognized as significant health problems in this region. One of the main causes of this increase is inbreeding, or closed marriage, which directly affects the concentration and inheritance of faulty genes from parents to children (Odah *et al.*, 2022).

According to study, beta thalassemia patients had lower levels of vitamin D compared to people without this condition, thus agreeing with the study of Agrawal and colleagues (2016) that the average vitamin D level in the beta thalassemia group was significantly lower (8.85 ng/ml)

compared to the control group. Those who do not suffer from thalassemia (16 ng/ml). It is unknown what specifically causes vitamin D deficiency in people with thalassemia. According to Singh *et al.* (2012), this is thought to be the result of repeated transfusions increasing the concentration of iron in the liver. Iron accumulation in the liver interferes with the function of the liver's 25-hydroxylase enzyme, which is required to convert vitamin D into 25-hydroxy-vitamin D. Patients with thalassemia frequently exhibit hyperpigmentation as well. For those with dark skin, sunlight cannot convert vitamin D (Albayrak and Albayrak, 2013).

Vitamin D status can also be affected by nutrient intake in particular, energy, protein, and fat intake have an impact on vitamin D levels. Increased energy and protein consumption are the outcome of ineffective erythropoiesis in thalassemia patients. Protein is needed for the synthesis of the enzymes that contain 95–99% of the total 25(OH)vitamin D as well as vitamin D binding proteins and receptors. Additionally, eating of fat is known to increase vitamin D levels, especially in terms of aiding in the absorption of vitamin D (Herawati *et al.*, 2020). When exposed to ultraviolet B radiation, the body primarily uses the cholesterol in the skin to synthesize vitamin D. When adults with fair skin pigmentation fully expose their bodies for 10 to 15 minutes, they can produce 10,000–20,000 IU of vitamin D3 in 24 hours; individuals with darker skin pigmentation need to expose themselves for 5 to 10 times longer to produce the same amount of vitamin D. The amount of UV radiation available for the production of vitamin D is influenced by a multitude of factors other than the amount of time spent outdoors. According to Wagner and Greer (2008), these variables include skin pigmentation level, body mass, season, place of residence, exposed skin area, and level of UV protection .

5. Conclusion

A metabolic abnormality that lowers serum vitamin D levels is experienced by children with beta-thalassemia. Vitamin D insufficiency is caused by iron accumulation in the skin and hyperpigmentation, and when iron accumulation in the liver increases, vitamin D deficiency results.

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