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Endocrinopathies' Prevalence in Beta-Thalassemia Major Patients

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Abstract. Chronic anemia is a hallmark of thalassaemia major, a hereditary hemoglobinopathy. Iron deposits in a variety of tissues, including endocrine glands, as a result of excessive iron overload and inadequate chelation. Calculate the number of patients with thalassemia major who have endocrinopathies. The research design used in this study is an observational retrospective cohort. All BTM patients older than two who visited the Dubai Thalassemia Center between December 2023 and June 2024 had their electronic medical records searched for retrospective data. This evaluation comprised fasting glucose, morning cortisol, bone profile (including parathyroid hormone), pituitary and gonadal function, and thyroid function. In order to rule out diabetes mellitus, hypogonadism, hypothyroidism, hypoparathyroidism, and hypoadrenalism, these profiles were examined. Forty individuals with transfusion-dependent thalassemia had an average age of 17.43 ± 2.76 years. Of them, 53.3% were women. Approximately 76.92% had an endocrine problem of some kind. The most frequent endocrine presentation, occurring in 50% of individuals under the age of 20, was hypogonadotropic. Hypoparathyroidism (10.0%), hypothyroidism (3.3%), and glucose intolerance (26.7%) were present in one-third. Among adult Iraqi patients with beta-thalassemia, endocrine problems are highly prevalent. This highlights the significance of monitoring for early detection and replacement therapy, as well as awareness for their development. There was no correlation seen between serum ferritin and the onset of endocrinopathy.

Highlights:

1. Endocrinopathies were highly prevalent (76.9%) among beta-thalassemia major patients, with hypogonadism being the most common (50%).
2. Additional endocrine disorders included glucose intolerance (26.7%), hypoparathyroidism (10%), and hypothyroidism (3.3%).
3. Findings underscore the need for routine endocrine monitoring and early intervention to improve quality of life in thalassemia patients.

Keywords: Beta-thalassaemia; Endocrinopathy, prevenance

Introduction

One of the biggest challenges to thalassemia major (TM) patients' quality of life is endocrinopathies. Iron accumulation in several endocrine organs and persistent anemia are endocrine consequences for this common transfusion-dependent form of

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thalassemia. Because iron storage has advanced, endocrine problems are typically discovered in the second decade of life [1]. Determining the prevalence of endocrinopathy in TM is made more difficult by changes in hemoglobin levels as well as the kind, length, and degree of chelation [2]. The most prevalent endocrine conditions among 3817 TM patients were hypogonadism (40.8%), growth retardation (30.8%), glycemic abnormalities (9.9%), hypoparathyroidism (6.9%), and hypothyroidism (3.2%), according to the Thalassemia International Federation (TIF) study group on growth and endocrine complications [3]. According to a research, even with proper chelation, 9.7% of people were at risk of developing an endocrine issue after five years [4].

Cooley and Lee were the first to describe beta-thalassaemia major, an inherited monogenic illness [5]. It is brought on by a mutation at the ß-globin gene locus, which causes the α-globin chain to persist in bone marrow erythroid precursors linked to severe dyserythropoietic anemia [6]. Patients with thalassaemia major now have a longer life expectancy thanks to advancements in supportive care, better monitoring of comorbidities, and early diagnosis [7]. Lifelong blood transfusions combined with frequent iron chelation therapy are the cornerstone of management in order to reduce the harmful effects of chronic iron deposition and buildup in tissues [6]. Nevertheless, these patients are at risk for chronic organ failure, specifically in the skeletal, endocrine, cardiovascular, and hepato-biliary systems [8].

The endocrine system seems to have a particularly strong influence on iron deposition. Numerous hypothalamic-pituitary endocrine issues can result from significant pituitary iron deposition, which has been shown to begin as early as the first ten years of life [9]. The endocrine glands—the thyroid, parathyroid, pancreas, and gonads—are also directly harmed. First, the thyroid gland is susceptible to cell death as a result of the influence of free unbound iron particles, in addition to the effects of hypoxia from chronic anemia [10]. Second, like any other gland, the parathyroid gland seems to be affected by toxic iron. In addition to less commonly occurring overt or symptomatic hypoparathyroidism with hypocalcemia symptoms such seizures and tetany, this can cause subclinical hypoparathyroidism [11]. Third, there is evidence that iron's detrimental effects are not specific to the pancreas. Teens who receive repeated blood transfusions have been shown to exhibit insulin resistance and elevated insulin secretion prior to developing diabetes, compared to controls who do not have thalassemia [12]. Furthermore, children and adolescents getting insufficient or no chelation therapy showed more indicators of insulin resistance than their peers receiving iron chelation therapy [13]. Growth failure and hypogonadism are thought to be among the most common endocrinopathies in surviving thalassemia patients, primarily due to hemosiderosis [14].

There is little information available on the prevalence of endocrinopathies in thalassemia in our nation. The quality of life for people with thalassemia may be enhanced by recommendations for endocrinological follow-up, early identification, and treatment of endocrine problems. Thus, our goal is to record and assess every

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characteristic as well as biochemical and hormonal factors linked to endocrine problems in thalassemia patients. Thus, the purpose of this study was to examine the endocrinopathies associated with thalassemia in Iraq.

Methodology

The research design used in this study is an observational retrospective cohort. All BTM patients older than two who visited the Dubai Thalassemia Center between December 2023 and June 2024 had their electronic medical records searched for retrospective data.

Data pertaining to the sociodemographic and clinical features of the patients were taken from the medical records for this retrospective analysis. Two distinct data collection sheets were used to retrieve data from the medical records of male and female patients. For both sexes, sociodemographic and physiological information was collected, including the patient's height, weight, nationality, gender, and birthdate. Vitamins, prescription compliance, and daily dairy product consumption were also collected. The secondary sex characteristics of both males and females were recorded. Clinical information that was retrieved included liver function tests, bone health, thyroid profiles, and full blood counts. Hemoglobin electrophoresis and DNA analysis were used to confirm the initial diagnosis of BTM, which was based on the clinical presentation.

Result

Table 1. Physical and demographic traits of beta thalassemia patients

	n	**%**
Age (years) ; Mean (sd)	17.43 (2.76)	
Gender		
Male	18	**47.0**
Female	**22**	**53.0**

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Table 2. Endocrinopathies' prevalence in 40 beta-thalassemia patients

Parameter	Hypogonadism		Hypoparathyroidism	Hypo Thyroidism	Diabetes Mellitus	No Endocrinopathy
	Hypo Gonadotrophic	Normo Gonadotrophic				
No. (M/F)	20 (12/8)	8 (2/6)	4 (1/3)	1 (0/1)	10 (7/3)	9 (7/2)
Prevalence	50%	23.3%	10.0%	3.3%	26.7%	26.7%
Ferritin level	5667±3413	7983±2620	5632±2038	4950	**6452±3979**	5981±3663

Table 3. Endocrinopathy prevalence in 40 homozygous beta-thalassaemic patients based on the number of disorders

Parameter		Number of Endocrinopathy			
		0	1	2	3
No. (M/F)		10 (7/3)	15 (6/9)	10 (5/5)	5(2/3)
Prevalence		26.7%	40%	26.7%	6.7%
Age at Study (years)	Mean ± SD	18.0±2.6	20.6±3.0	22.4±4.4	26.0±4.2
	Median	19.0	21.0	21.5	24.0
	Range	17-24	17-28	18-32	21-27
Ferritin (µg/L)					
Mean ± SD		5755±3644	6324±2936	6878±3342	4874±323
Range		865-11809	3248-12473	568-12540	3933-5348

Discussion

Patients with beta-thalassaemia major frequently have metabolic issues, such as endocrine dysfunction, which can affect one or more endocrine glands. Although the

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exact mechanism is unclear, iron overload and its burden are the most likely cause, along with lipid peroxidation, oxidative stress, and the production of free radicals [15].

In line with the findings of other authors, a high prevalence of endocrine disorders was noted in beta-thalassaemic individuals in the current study [16-18], The most common endocrine condition was hypogonadism, which affected 73.3% of patients (50% hypogonadotrophic and 23.3% normogonadotrophic). According to reports, the pituitary-gonadal axis is extremely vulnerable to iron deposition, which causes these glands to hypofunction, especially in the form of secondary hypogonadism. Even with iron chelation therapy, this condition is rarely curable [19].

Thalassaemia major is also known to cause disruption of calcium homeostasis, which may be brought on by chronic liver involvement, vitamin D shortage, bone marrow enlargement, or hypoparathyroidism. In our series, three thalassaemic patients (10.0%) had primary hypoparathyroidism, two of whom also had two other endocrinopathies, and one of whom had a third endocrinopathy. The reported prevalence of hypoparathyroidism ranged from 3.6% to 13.5% when compared to others [20,21] In a related study conducted in Saudi Arabia, Aleem et al. found that 20% of the 40 thalassaemic patients they examined had hypoparathyroidism. Najafipour et al. also found a high frequency of 41% for hypocalcemia.23 Despite reports that hypoparathyroidism is more prevalent in men with a 4:1 male to female ratio [22,20].

Ten individuals (26.7%) developed diabetes mellitus; insulin was administered to seven of these patients (5 males and 2 females) who had severe hyperglycemia. Iron overload in the pancreatic beta-cells, which leads to pancreatic dysfunction, is the most plausible mechanism for diabetes mellitus [23]. Other contributing variables include genetic predisposition, liver illness, insulin resistance, or a family history of diabetes [24]. Studies have shown that up to 24% of people with beta-thalassemia also have diabetes mellitus [25]. Diabetes appears to be rare among beta-thalassaemics younger than sixteen [26].

Conclusion

In conclusion, the current study showed that endocrine issues were more common in individuals with β-thalassemia and that there was a substantial association between genotype and the degree of clinical illness. Significant correlations between serum ferritin levels and the presence of endocrine disorders were also discovered, underscoring the crucial part iron excess plays in the emergence of these conditions.

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