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A Cross-sectional study on prevalence and effects of pituitary siderosis on the endocrine status in pediatric patients with transfusion-dependent beta thalassemia

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Abstract

Transfusion-dependent β-thalassemia (TDT) is commonly associated with iron overload and multiple endocrine complications. The aim of the work was to investigate the prevalence and the relationship between pituitary siderosis assessed by magnetic resonance imaging (MRI T2*) and endocrinopathy in pediatric patients with TDT. Forty-two TDT patients, ages 10 to 18, were joined in this cross-sectional study from Mansoura University Children's Hospital in Egypt. Anthropometric evaluation, Tanner staging, laboratory tests and MRI T2* for iron overload assessment were performed. The mean age was 13.7 years and 54.8% were female. Mean height was 148.6 cm: 16.7%. Mean weight was 41.3 kg; Mean BMI was 18.3 kg/m². Hypogonadism (52.4%), short stature (33.3%), and hypothyroidism (26.2%) were the most common endocrine complications. Mean hepcidin/ferritin ratio was 0.13. MRI T2*: Mean was 21.7 ms. The hepcidin/ferritin ratio outperformed ferritin and transferrin saturation in terms of accuracy in distinguishing severity levels. Patients with transfusion-dependent β-thalassemia were more likely to experience hypogonadism, hypothyroidism, and short stature. Hepcidin/Ferritin ratio was highly correlated with MRI T2* severity. The Hepcidin/Ferritin ratio emerged as the most accurate non-invasive marker for assessing disease severity and short stature risk.

Keywords: Endocrinopathy, Hepcidin/ferritin ratio, MRI T2*, Transfusion-dependent β-thalassemia.

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1. Introduction

The genetic mutations that cause beta-thalassemia include nucleotide changes, minor insertions or deletions in the β-globin gene, and in rare instances, large deletions. The globin-chain subunits in the hemoglobin tetramer are impacted by these mutations, which results in an imbalance in the α/β-globin chain ratio and an excess of free α-globin chains, which sets off the disease's most significant pathogenic events: Iron overload, compensatory hemopoietic expansion, chronic anemia/hypoxia, and inefficient erythropoiesis (IE) [1]. An important cause of oxidative stress and membrane damage in red blood cells (RBCs) is the imbalanced synthesis of α-globin. Furthermore, IE is closely associated with disruption of iron metabolism, and the importance of novel participants in this pathway, such as erythroferrone, matriptase-2, and hepcidin, has been revealed [2]. Unbalanced α-globin synthesis causes oxidative stress and membrane damage in RBCs. Furthermore, IE is closely associated to iron metabolism dysregulation, and the relevance of new actors in this route, such as hepcidin, erythroferrone, matriptase-2, among others, has revealed [3].

Overexpression of serum hepcidin levels causes iron-restricted anemia, whereas low serum hepcidin levels are known to improve intestinal iron absorption and decrease iron storage in macrophages, resulting in excess iron. Low serum hepcidin levels in β-thalassemia patients have been linked to increased iron absorption and overload, according to multiple investigations. Hepcidin-mediated iron control is clinically important in thalassemia patients because anemia frequently coexists with iron excess. Hepcidin as a therapeutic target may help regulate iron overload in thalassemia patients [4]. β-thalassemia patients are now classed as either transfusion-dependent (TDT) or non-transfusion-dependent (NTDT) based on their severity of phenotypic. This categorization includes different types of thalassemia syndromes such α-thalassemia, hemoglobin E/β-thalassemia, and combination α- and β-thalassemias [5].

Regular blood transfusions are considered the primary therapy option for TDT patients. Chronic blood transfusion, on the other hand, increases the risk of iron overload and consequent multi-organ damage, as well as acute life-threatening events like allergy, bacterial infections, and acute hemolytic responses [6]. Regular blood transfusions are the primary treatment for β-thalassemia major, which can result in iron overload and organ damage. For example, hypogonadotropic hypogonadism (HH) caused by excessive iron deposition in the anterior pituitary gland causes delayed puberty, and once diagnosed, hypogonadism is usually permanent despite rigorous chelation therapy. Thus, early diagnosis of pituitary iron accumulation before symptoms develop is of critical relevance in high-risk patients [7].

Magnetic resonance imaging (MRI) is a valuable method for noninvasively detecting and quantifying tissue iron deposits. Intracellular iron forms with high molecular weights, such as hemosiderin and ferritin, interact with water molecules to cause local magnetic inhomogeneities, which are responsible for the tissue's lower signal intensity. Iron overload is quantified by assessing the loss of signal intensity in the obtained MR images using various approaches [8]. The hepcidin-to-ferritin ratio is an important biomarker for determining the link between iron metabolism and immunological responses in inflammatory disorders. Its capacity to predict illness severity and outcomes, especially in circumstances like septic shock, makes it an important tool in clinical practice [9].

The aim of the work was to investigate the prevalence and the relationship between pituitary siderosis assessed by magnetic resonance imaging (MRI T2*) and endocrinopathy in pediatric patients with TDT.

2. Materials and Methods

2.1. Study design and sampling:

This is a cross-sectional study with 42 transfusion-dependent β-thalassemia patients who were diagnosed based on evidence of hematological investigations.

Inclusion criteria: Age 10-18 years, both sexes and children with TDT.

Exclusion criteria for β-thalassemia: Autoimmune disorders include insulin-dependent diabetes mellitus, autoimmune thyroiditis, Addison's disease, and polyglandular autoimmune endocrinopathy. Children with other chronic systemic diseases that might induce short stature (severe hepatic, renal, or cardiac problems, diabetes mellitus, severe infections). Mild to mild-moderate thalassemia or sickle anemia with infrequent blood transfusions and children receiving hormone therapy for development retardation.

Exclusion criteria for MRI T2*: Presence of pacemakers, coronary and peripheral artery stents, surgical clips or wire sutures and Joint replacement or prosthesis.

2.2. Method

All patients underwent clinical evaluation, laboratory investigations, and imaging studies.

2.2.1. History and clinical examination

A complete history was obtained, including demographics (age, gender), consanguinity, family history of thalassemia, transfusion regimen (ml/kg/year), chelation therapy, age at diagnosis, and age of splenectomy. Clinical examination included general assessment, anthropometric measurements (height, weight, BMI), and pubertal development (Tanner staging). Pallor, characteristic facial features (mongoloid facies), hepatomegaly, and splenomegaly were recorded.

2.2.2. Laboratory Investigations

Pre-transfusion blood samples were obtained for: Complete blood count (CBC), Serum iron and total iron-binding capacity (TIBC); transferrin saturation was calculated as: (Serumiron×100)/TIBC (Serum iron × 100) / TIBC. Serum ferritin (measured within the preceding 3 months). Hepcidin

levels by ELISA (Human Hepcidin 25 Kit, REF: DZE201121020) using a double-antibody sandwich technique. Fasting plasma glucose and HbA1c. Thyroid function (TSH, free T4). Gonadotropins (LH, FSH), estradiol (females), and testosterone (males).

Blood samples (5 ml venous) were collected pre-transfusion: 2 ml in EDTA for CBC and 3 ml in plain tubes for serum separation. Serum was analyzed for iron indices, ferritin, thyroid function, and sex hormones using standard protocols.

2.2.3. MRI T2 Assessment*

All participants underwent pituitary MRI T2* with a 1.5 Tesla system (Ingenia Philips, 16-channel head coil). Morphological assessment excluded mass lesions; pituitary height was measured on midline sagittal images. Pituitary iron deposition was assessed using T2* (STAR) sequences with coronal and sagittal m-FFE_T2 star protocol (TR/TE 198/14 ms, matrix 208 × 127, FOV 230 × 180 mm, slice thickness 3 mm, interleaved gap –0.2 mm, 3 averages). T2* imaging was used as ferritin shortens T1 and T2, while hemosiderin primarily affects T2 relaxation.

2.2.4. Chelation Therapy

Patients received chelation according to ferritin burden: Deferasirox (20–30 mg/kg/day orally before meals), Deferoxamine (20–40 mg/kg/day, 6 days/week) in selected cases. Combined chelation (Deferasirox plus intermittent Deferoxamine infusion 20–40 mg/kg/day for 10 days/month) was used in patients with serum ferritin >3000 ng/ml.

2.2.5. Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 27.

The qualitative data was described using numbers and percentages. The Shapiro-Wilk test was employed to ensure that the distribution was normal. The quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The significance of the obtained results was determined at the 0.05 level. Analytical statistics include Pearson's/Spearman's correlation, multivariate linear regression analysis, and Receiver Operating Characteristic (ROC) analysis.

2.2.6. Ethics Considerations

This work was authorized by the Mansoura Faculty of Medicine Institutional Research Board (MFM-IRB) and Mansoura University Faculty of Medicine's local ethics committee. Code number: MD.23.08.798. The participants' personal information was kept anonymous during the study.

3. Results

This study involved 42 transfusion-dependent β-thalassemia patients with mean age 13.7 ± 2.1 years and 54.8% female. Most patients had a history of consanguinity (76.2%), had a positive family history (59.5%), and were early diagnosed. Nearly all required monthly transfusions (95.2%), with an average blood requirement of 115.8 ± 15.2 ml/kg/year. Iron chelation was given as deferasirox alone (59.5%) or in combination with deferoxamine (40.5%).

Clinically, pallor was common (100%), while mongoloid facies (73.8%), splenomegaly (61.9%), and hepatomegaly (33.3%) and splenectomy had been performed in 38.1%. According to the endocrinal disorders, hypogonadism (52.4%) was the most common disorder, followed by short stature (33.3%), hypothyroidism (26.2%), and subclinical hypothyroidism (11.9%) (Table 1).

Table 1.
Demographic data, anthropometric measurements, Tanner staging and clinical data in studied patients.

Characteristics	**Patients = 42**
Male	19 (45.2 %)
Female	23 (54.8 %)
Age (years) Mean ± SD	13.71 ± 2.11
Weight (kg) Mean ±SD	41.29 ± 9.93
Height (cm) Mean ±SD	148.6 ± 10.72
BMI (kg/m2)	18.34 ± 2.51
Consanguinity	32 (76.2%)
Family history	25 (59.5%)
Age of diagnosis of thalassemia (month) Mean ±SD	13.05 ± 12.66
Blood transfusion frequency	
Every month Every 2 months	40 (95.2%) 2 (4.8%)
Amount of blood transfusion (ml/kg/year) Mean ± SD	115.76 ± 15.24
Types of iron chelators	
Deferasirox	25 (59.5%)
Deferoxamine and Deferasirox	17 (40.5%)
Pallor	42 (100%)
Mongoloid facies	31 (73.8%)

Hepatomegaly	14 (33.3%)
Splenomegaly	26 (61.9%)
Splenectomy	16 (38.1%)
Hypogonadism	22 (52.4%)
Short stature	14 (33.3%)
Hypothyroidism	11 (26.2%)
Subclinical hypothyroidism	5 (11.9%)

Note: SD: Standard deviation.

Assessment of pubertal development showed that most participants were in Tanner stages 2–3 across all domains. For pubic hair growth, stage 2 (35.7%) and stage 3 (33.3%) were the most common, with a mean of 2.50 ± 1.04. Among females, breast development was most frequently at stage 3 (47.8%) followed by stage 2 (39.1%) with a mean of 2.78 ± 0.80. In males, external genitalia development was predominantly at stage 2 (47.8%) and stage 3 (31.6%) with a mean of 2.47 ± 0.96 (Table 2).

Table 2.
Distribution of the studied cases according to Tanner staging (n = 42).

Tanner staging	**No. (%)**
Pubic hair growth	
1	7 (16.7%)
2	15 (35.7%)
3	14 (33.3%)
4	4 (9.5%)
5	2 (4.8%)
Min. – Max.	1.0 – 5.0
Mean ± SD.	2.50 ± 1.04
Median (IQR)	2.0 (2.0 – 3.0)
Breast growth for female	
1	0 (0%)
2	9 (39.1%)
3	11 (47.8%)
4	2 (8.7%)
5	1 (4.3%)
Min. – Max.	2.0 – 5.0
Mean ± SD.	2.78 ± 0.80
Median (IQR)	3.0 (2.0 – 3.0)
External genitalia for male	
1	2 (10.5%)
2	9 (47.8%)
3	6 (31.6%)
4	1 (5.3%)
5	1 (5.3%)
Min. – Max.	1.0 – 5.0
Mean ± SD.	2.47 ± 0.96
Median (IQR)	2.0 (2.0 – 3.0)

Note: SD: Standard deviation.

Laboratory evaluation showed that the mean hemoglobin was 8.0 ± 0.8 g/dL with microcytosis (MCV 74.8 ± 6.3 fL). Iron overload was obvious, with high serum iron (188.9 ± 61.0 µg/dl), transferrin saturation (90.6 ± 26.2%), ferritin (2680.9 ± 1410.4 ng/ml), and a low hepcidin/ferritin ratio (0.13 ± 0.14). With normal fasting blood sugar (93.4 ± 13.4 mg/dl) but slightly elevated HbA1c (6.0 ± 0.5%).

Hormonal testing revealed low gonadotropins (LH and FSH), as well as decreased testosterone and estradiol levels. Thyroid function tests revealed fluctuating T4 levels and slightly elevated TSH. Among the studied patients, the mean MRI T2* value was 21.72 ± 12.31 ms. According to the severity distribution, 33.3% of patients were within the normal range and about two-thirds of the patients had MRI T2* abnormalities of varied degrees (26.2% had mild affection, 26.2% had moderate affection, and 14.3% had severe affection) (Table 3).

Table 3.
Laboratory investigations in studied patients.

Variables	Mean ±SD
Hb	8.03 ± 0.75
MCV	74.77 ± 6.31
TIBC	216.02 ± 66.46
Serum iron	188.93 ± 61.01
Transferrin saturation (%)	90.64 ± 26.20
Serum ferritin	2680.9 ± 1410.4
Fasting blood sugar	93.43 ± 13.44
HbA1c (%)	6.03 ± 0.54
Hepcidin (ng/dl)	214.28 ± 81.58
Hepcidin/Ferritin Ratio (ng/dl)	0.13 ± 0.14
Estradiol (ng/ml) (n = 23)	21.65 ± 21.31
Testosterone (ng/ml) (n = 19)	1.38 ± 2.71
TSH (uIU/ml)	3.76 ± 1.49
T4 (ng/dl)	1.76 ± 1.60
LH (mIU/ml)	1.42 ± 1.85
FSH (mIU/ml)	2.26 ± 2.11
MRI T2* (ms)	21.72 ± 12.31
Severity Level	
Normal	14 (33.3%)
Mild	11 (26.2%)
Moderate	11 (26.2%)
Severe	6 (14.3%)

Note: SD: Standard deviation.

There was a statistically significant negative association between MRI T2* and transferrin saturation, serum ferritin, and TSH, while there was a statistically significant positive correlation between MRI T2* and estradiol, testosterone, T4, LH, FSH, and the hepcidin/ferritin ratio (Table 4 & Figure 1).

Table 4.
Correlation between MRI T2* and different parameters (n = 42).

		MRI T2* (ms)	
		r_s	p
Age (years)	-0.114	0.473	
Transferrin Saturation (%)	-0.649	<0.001*	
Serum ferritin	-0.755	<0.001*	
Hepcidin (ng/ml)	0.129	0.416	
Estradiol (ng/ml)	0.565	0.005*	
Testosterone (ng/ml)	0.520	0.022*	
TSH (uIU/ml)	-0.505	0.001*	
T4 (ng/dl)	0.607	<0.001*	
LH (mIU/ml)	0.346	0.025*	
FSH (mIU/ml)	0.385	0.012*	
Hepcidin/Ferritin Ratio (ng/dl)	0.862	<0.001*	

Note: rs: Spearman coefficient; *: Statistically significant at $p \leq 0.05$.

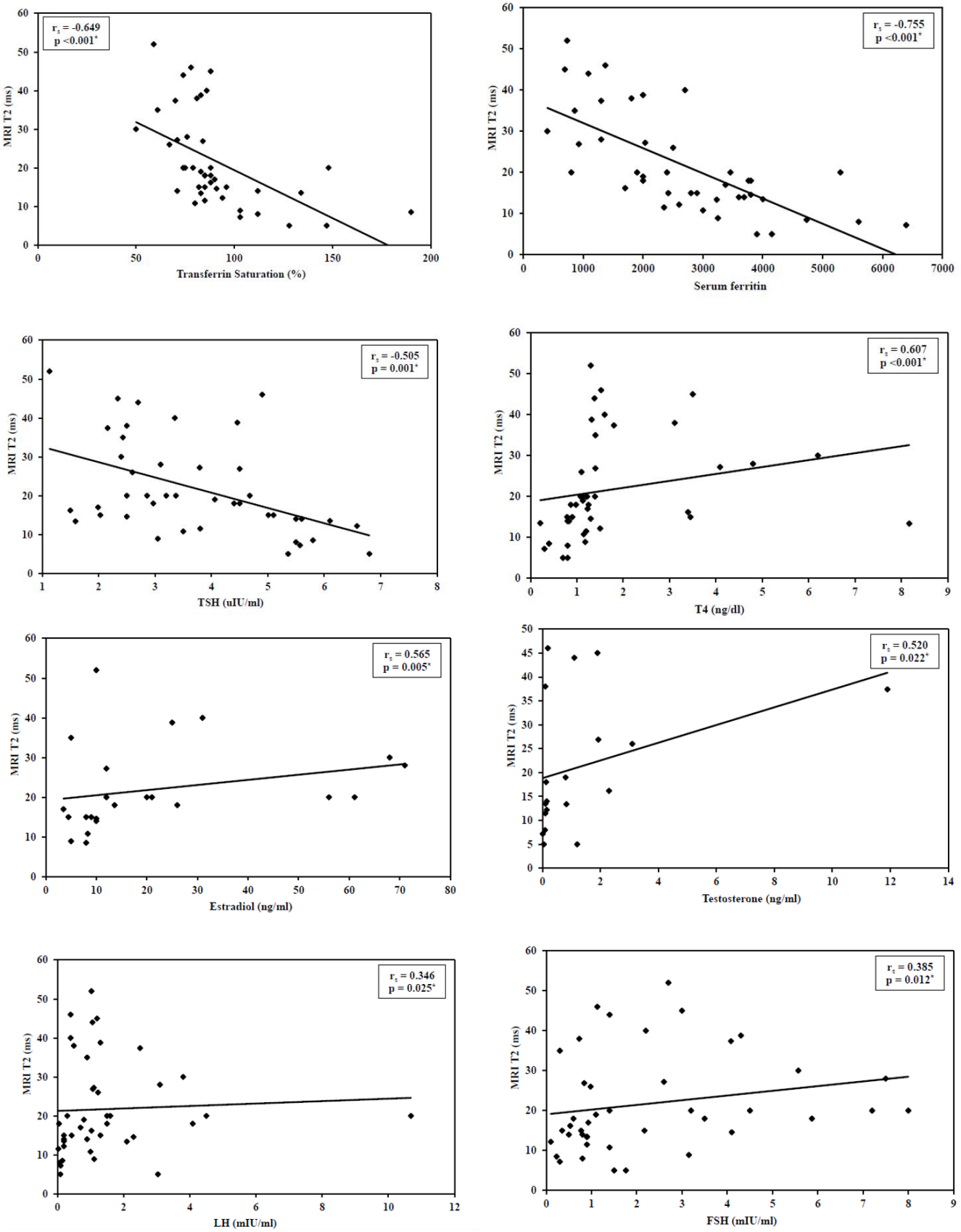

Figure 1.
Correlation between pituitary MRI T2* and different parameters.

The hepcidin/ferritin ratio showed a marked decline with increasing disease severity. Patients within normal group had the highest values with a mean of 0.28 ± 0.15. On the other hand, the ratio was significantly lower in the mild group (mean = 0.08 ± 0.05) and more decreased in the moderate group (mean = 0.04 ± 0.01). The lowest values were detected among

severe cases (mean = 0.02 ± 0.01). Hepcidin/ferritin ratio and disease severity on MRI T2* showed a very statistically significant adverse relationship (Table 5).

Table 5.
Relation between severity level with Hepcidin/Ferritin Ratio (ng/dl) (n= 42).

	Severity level				H	P
Hepcidin/Ferritin Ratio (ng/dl)	Normal (n = 14)	Mild (n = 11)	Moderate (n = 11)	Severe (n = 6)		
Mean ± SD.	0.28 ± 0.15	0.08 ± 0.05	0.04 ± 0.01	0.02 ± 0.01	33.078*	<0.001*
Median (Min. – Max.)	0.27 (0.09 – 0.58)	0.07 (0.03 – 0.20)	0.04 (0.03 – 0.06)	0.02 (0.01 – 0.03)		

Note: H: H for Kruskal Wallis test; p: p value for comparison between the studied categories; *Statistically significant at p ≤ 0.05.

Receiver operating characteristic (ROC) curve analysis demonstrated that the hepcidin/ferritin ratio had the highest diagnostic accuracy for predicting disease severity, with an AUC of 0.980 (95% CI: 0.945–1.0; p < 0.001). At a cutoff of ≤0.116, it achieved 96.4% sensitivity, 92.9% specificity, and an overall accuracy of 95.2%. Additionally, serum ferritin performed well, with a cutoff >1805 ng/ml. The performance of transferrin saturation was moderate. Conversely, hepcidin, serum iron, and TIBC showed only moderate diagnostic value. So, we can say that the hepcidin/ferritin ratio emerged as the most powerful discriminator of disease severity, outperforming conventional iron markers (Table 6 & Figure 2).

Table 6.
Diagnostic performance for different parameters to discriminate normal severity from abnormal severity.

	AUC	p	95% CI	Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
Hepcidin/Ferritin Ratio (ng/dl)	0.980	<0.001*	0.945 – 1.0	≤0.116	96.43	92.86	96.4	92.9	95.24
Serum ferritin	0.913	<0.001*	0.828 – 0.98	>1805	92.86	71.43	86.7	83.3	85.72
Hepcidin (ng/dl)	0.626	0.187	0.433 – 0.820	≤224.5	67.86	64.29	79.2	50.0	66.67
Serum iron	0.615	0.230	0.435 – 0.795	>167	64.29	57.14	75.0	44.4	61.91
TIBC	0.662	0.090	0.483 – 0.841	≤214	67.86	50.0	73.1	43.8	61.91
Transferrin Saturation (%)	0.864	<0.001*	0.753 – 0.974	>81	82.14	71.43	85.2	66.7	78.57

Note: AUC: Area Under a Curve ; p value: Probability value; CI: Confidence Intervals; NPV: Negative predictive value; PPV: Positive predictive value; *: Statistically significant at p ≤ 0.05

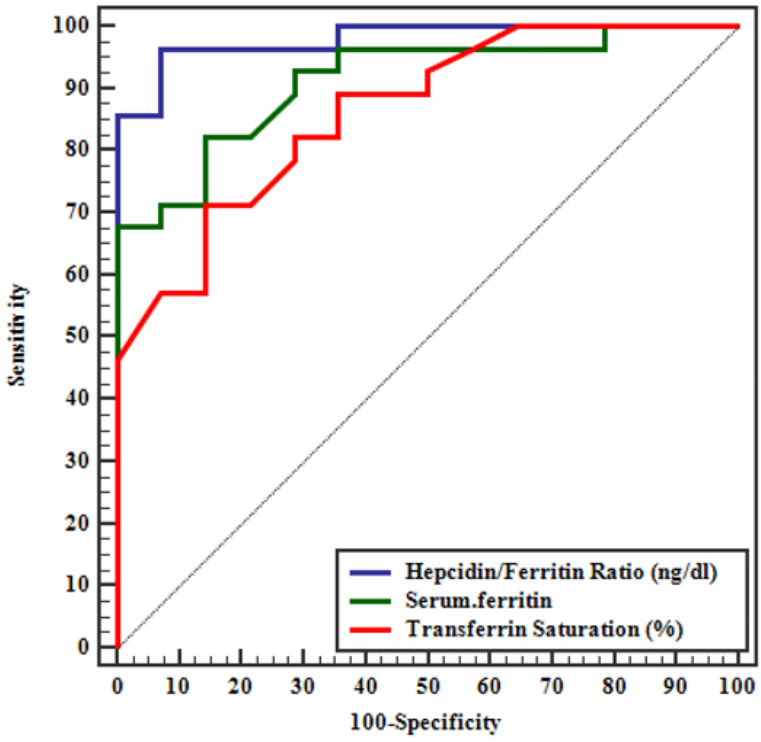

Figure 2.
ROC curve for different parameters to discriminate normal from abnormal severity.

4. Discussion

Frequent blood transfusions are necessary for the conventional treatment of β-thalassaemia major. Excess iron builds up as a result, first in the reticuloendothelial system and then in all parenchymal organs, primarily the heart, pituitary, and pancreas, causing major and occasionally lethal clinical problems [10].

Iron deposition may begin in the anterior pituitary gland in the first decade of life, but clinical symptoms are usually not apparent before puberty. Only reduced gonadotropin reserve was observed at the earlier stage, with intact gonadotropin pulse. Until hypogonadism occurs an asymptomatic process of pituitary siderosis may occur [11]. Due to its non-invasive, contrast-free ability to evaluate iron overload in multiple organs, MRI is an essential tool in the current treatment of thalassemia patients [12].

The female predominance in this study came in consistence with Yılmaz, et al. [13]. and Çelik, et al. [14] who reported that females represented 58.6% and 65.7 %, respectively. However, higher male prevalence (60%) was demonstrated by Hagag, et al. [15]. The differences in gender distribution across studies may reflect variations in inclusion criteria and age groups.

In the current study, the mean body height was 148.6 ± 10.72 cm with 16.7% falling below 3rd percentile. The mean body weight was 41.29 ± 9.93 kg with only one case below 3rd percentile. The mean BMI was 18.34 ± 2.51 kg/m^2 with 11.9% below 3rd percentile. This came in agreement with El-Hawy and Saleh [16] who reported a mean BMI of 17.91±17.39 kg/m^2 in thalassemic patients. Growth retardation in thalassemic children may be linked to chronic anemia produced by inadequate transfusion, hypoxia, and other endocrine abnormalities owing to iron excess, impairing puberty development and growth [17].

In this study, the manifestations included pallor in 100%, mongoloid facies in 73.8%, hepatomegaly in 33.3%, splenomegaly in 61.9% and 38.1% had splenectomy. This agreed with Morad, et al. [18] who reported that pallor and jaundice were the most common features in thalassemic patients, while hepatomegaly and splenectomy were the most common signs. This can be explained by that splenomegaly in thalassemia results from chronic hemolysis and ineffective erythropoiesis, often progressing to hypersplenism and splenectomy. Hepatomegaly is mainly linked to extramedullary hematopoiesis and transfusion-related iron overload, while mongoloid facies reflect skeletal deformities caused by marrow hyperplasia in inadequately transfused patients [19].

In the present study, endocrine complications were relatively common, hypogonadism in more than half of the cases (52.4%) with short stature in 33.3%, hypothyroidism reported in 26.2% of patients and subclinical hypothyroidism in 11.9%. Hypogonadism was the most common detected abnormality in the current study in 52.4%. This was similar to a large study from 2017 on 613 transfusion-dependent BTH patients. They showed that 46.8% had hypogonadism, 8.3% for hypothyroidism [20]. Another cohort identified the hypogonadism to be 44.5% [21].

Regarding hypothyroidism, our findings are comparable to those of [13] who reported hypothyroidism in 34.6% of their cohort, 37% had short stature, and 50% had pubertal delay. Similarly, in a large multicenter study involving 3817 patients with thalassemia major, pubertal delay identified as the most frequent endocrinological complication, while growth hormone deficiency and hypothyroidism were less common, occurring in approximately 8% and 3.2% of patients, respectively [22]. In contrast, the most prevalent condition was pubertal delay or arrest (46.8%), followed by short stature (33.8%) and hypothyroidism (15.9%) [23]. This was lower as compared to a study from Central India which included 50 children that found delayed puberty in 71.7% [24]. Compared to the gonadal and GH axis, the thyroid pituitary axis appears to be less vulnerable to iron deposition damage. Since the prevalence of thyroid disorders is less than hypogonadism and short stature [18]. Taken together, these results emphasize that endocrine dysfunctions particularly pubertal delay, hypogonadism, and growth impairment are consistently reported across different cohorts, although prevalence rates vary depending on patient age, sample size, and transfusion/chelation protocols.

In the current study, overall, the study population clustered around Tanner stages 2–3, with only a small proportion having reached advanced pubertal stages (4–5). This supported by previous studies that revealed that most patients with beta thalassemia showed signs of delayed puberty [25, 26].

The included cases in this study had mean MRI T2* of 21.72 ± 12.31 ms. Previous investigations varied greatly; in one, 84 thalassemia patients ranging in age from 4 to 34 years had a mean MR T2* level < 14.9 ms [27]. In another study, 180 patients with thalassemia major, ages 12 to 48, had a mean MR T2* level of less than 5.9 ms [28]. Additionally, Yılmaz, et al. [13] found a mean MR T2* level was 12.8±4.34 ms. The discrepancy between the results of the available studies can be explained by the differences between the population size and age range of the participants.

In our study, there was a statistically significant negative correlation between MRI T2* with transferrin saturation and serum ferritin. This correlation allows a quantification of the pituitary T2 time and therefore offers an index of pituitary siderosis. This agreed with Karadag, et al. [29] and Morad, et al. [18] who showed that there was a statistically significant negative correlation between pituitary T2* with serum ferritin. In contrast, positive correlation was reported between pituitary T2* values and serum ferritin [30].

Our investigation found a significant positive correlation between MRI T2* values and several hormonal markers (estradiol, testosterone, T4, LH and FSH). This is consistent with recent findings from Morad, et al. [18] who found comparable correlations between pituitary T2* and ferritin, FSH, LH, and growth hormone. Likewise, previous study emphasized that with pituitary iron overload can begin as early as four years of age and with the pubertal delay becoming evident about a decade later, often when changes are irreversible. In addition, iron toxicity and chronic hypoxia, multiple factors such as genetic background, nutritional status, chelation adherence, endocrinopathies and chronic liver disease also contribute to impaired growth and the pubertal development in thalassemia patients [31].

Our patients' hepcidin levels were normal in our trial, which was consistent with recent research that found posttransfusion hepcidin levels were closer to normal, possibly as a result of decreased erythropoietic drive. Hepcidin levels in thalassemia patients receiving continuous transfusions are similar to those in non-thalassemia patients, which may indicate that dietary iron absorption is generally normal, particularly after transfusion. They proposed that a follow-up study to improve the care of patients with chronic transfusion-associated β-thalassemia could involve measuring their serum hepcidin levels [3].

On MRI T2*, our investigation revealed a highly statistically significant inverse relationship between the hepcidin/ferritin ratio and disease severity, with the ratio clearly declining as disease severity increased.

Because serum hepcidin levels are incorrect, it may not be sufficient to identify and distinguish between various levels of iron overload in patients with β-thalassemia. Since serum ferritin cannot predict changes in total body iron in individuals with transfusion iron overload, it may not be a good diagnostic biomarker on its own. With an accuracy of 99.2%, the median hepcidin-to-ferritin ratio of the cases was found to be significantly decreased when compared to the controls. This suggests that it could be a useful indicator for diagnosing iron overload in patients with β-thalassemia [32]. Furthermore, it was discovered that both before and after the transfusion, the hepcidin-ferritin ratio was much lower. Clinical assessment of hepcidin (together with the hepcidin-ferritin ratio) may prove to be a valuable biomarker of erythropoiesis and iron kinetics in complex patients since hepcidin seems to integrate erythropoietin and iron-loading signals [3].

This study is limited by its single-center design and small sample size, which may limit generalization. Furthermore, the absence of a healthy control group restricts direct comparison of findings.

5. Conclusion

Patients with transfusion-dependent β-thalassemia were more likely to experience hypogonadism, hypothyroidism and short stature. Serum ferritin and the Hepcidin/Ferritin ratio were highly correlated with MRI T2* severity, indicating an obvious iron overload. The Hepcidin/Ferritin ratio emerged as the most accurate non-invasive marker for assessing disease severity and short stature risk.

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