Assessment of Serum Leptin Levels in Pediatric Patients of Beta Thalassemia

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ABSTRACT

Background: Beta thalassemia is one of the most common hereditary chronic hematological disorders in our country. Leptin is considered a physiological link between nutritional status and reproductive maturation and function.

Objective: We conducted this study to evaluate serum leptin in pediatric beta thalassemia patients who are transfusion dependent.

Patients and Methods: We selected 32 cases of pediatric patients of beta thalassemia above age of eight years and had delayed growth, and we excluded all individuals suffering from any other problem affecting growth and development. Our patients were being followed up at hematologic outpatient clinics in Zagazig University Hospital and Mansoura Insurance Hospital, in the period from December, 2018 to June, 2020. We compared them by 28 healthy controlled individuals sharing the same age and sex who attended outpatient general clinics.

Results: Coincidence of participants at age and sex but there was significant decrease in height, weight and BMI of cases than control group. Serum leptin was significantly lower in cases of beta thalassemia than control group ($P<0.001$). ROC curve was used for detection the validity and cutoff point of serum leptin in differentiating cases. Area under the ROC curve (0.987) was excellent.

Conclusion: Decreased serum leptin in patients of thalassemia. Cutoff point (982.5) was the best value to detect validity of serum leptin to differentiate cases, with sensitivity of 96.9%, specificity of 89.3%, accuracy of 93.3%, positive predictive value of 91.2% and negative predictive value of 96.2%.

Keywords: Assessment, Beta Thalassemia, Pediatric, Serum leptin.

INTRODUCTION

Beta thalassemia is considered the most common hereditary chronic hemolytic anemia in Egypt as about one thousand per 1.5 million live birth has thalassemia with estimation of 10% as rate of carrier [(1)].

Leptin is an adipokine, which is synthesized and released from adipocytes in response to changes in body fat and binds receptors within the hypothalamus to control appetite. Leptin is considered a physiological link between nutritional status and reproductive maturation and function[(2)]. So sexual development may be triggered by leptin, which can be a metabolic gate of it [(3)].

Brooke and Brown [(4)] reported increased serum gonadotropin hormone levels by the administration of leptin to leptin-deficient patients.

We conducted this study to evaluate serum leptin in pediatric beta thalassemia patients who are transfusion dependent.

PATIENTS AND METHODS

This case control study was carried out on 60 participants, 32 cases of pediatric beta thalassemia patients and 28 healthy children as control. We selected 32 cases of pediatric patients of beta thalassemia above age of eight years and had delayed growth, and we exclude all individuals suffering from any other problem affecting growth and development. Our patients were being followed up at hematologic outpatient clinics in Zagazig University Hospital and Mansoura Insurance Hospital, in the period from December, 2018 to June, 2020. We compared them by 28 healthy controlled individuals sharing the same age and sex who attended outpatient general clinics.

Inclusion criteria:

Any pediatric patient of beta thalassemia above 8 years old up to 15 years old whose diagnosis was confirmed by hemoglobin electrophoresis or high frequency liquid chromatography test, and patients were transfusion dependent beta thalassemia.

Exclusion criteria:

Patients with any other hematologic disorders, patients with any signs of chronic inflammation or chronic infection, patients under growing hormonal or any therapy that affect growth and puberty, any patients with other chronic systemic diseases, syndromatic patients, and patient with metabolic or endocrinal disorders that affect the growth and puberty.

All patients were subjected to:

Complete history and general examination.

Anthropometry: including assessment of growth, weight, length, BMI, Z- Score according to WHO growth charts and puberty assessment of both male and female according to Tanner staging by assessment development of breast in female and testicular size of male in pubertal individuals.

Delayed puberty is defined by absence signs of puberty by age of 13 years in female or 14 years in male [(5)].

Investigation:

Complete blood picture, random blood sugar, serum leptin level by ELIZA kits were measured for all participants. Serum ferritin, thyroid function tests, bone age for cases and sex hormones for pubertal age cases were also measured.

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Principle of leptin assay:

This ELISA kit uses Sandwich-ELISA as the method the microelisa stripplate provided in this kit has been pre-coated with an antibody specific to leptin (LEP).

Ethical consent:

The study was approved by the Ethical Committee of the Faculty of Medicine, Zagazig University.

Informed written consent was obtained from parents of all children participants before recruitment in the study, after explaining the objectives of the work. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 22.0. Qualitative data were described using number and percent. Quantitative data were described using median, range, and interquartile range for non-parametric data and mean and standard deviation for parametric data after testing normality using Kolmogorov-Smirnov test. P value < 0.05 was considered significant.

RESULTS

This table compares between demographic and anthropometric measures of cases and controls and shows coincidence of participants at age and sex but there was significant decrease in height, weight and BMI of cases than control group **(Table 1)**.

Table (1): Demographic and anthropometric measurements among studied groups

	Control N=28	**Cases N=32**	**P**
Age/years Mean±SD	12.29±2.52	12.38±2.62	0.90
Sex Male Female	15 (53.6) 13 (46.4)	19 (59.4) 13 (40.6)	0.65
Weight/kg Mean±SD	46.39±15.24	37.28±10.94	0.009*
Height z score Median (range) (IQR)	-0.5 (-1.2 ,0.7) (-0.78 ,-0.30)	-1.85 (-2.60 , -0.80) (-2.38 ,-1.40)	p<0.001*
BMI z score Median (range) (IQR)	0.70 (-1.0 ,1.3) (0.425 ,0.90)	0.35 (-1.3 ,1.2) (-0.20 , 0.80)	0.01*

*: Statistically significant, SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index

This table shows beta thalassemia cases had significant delayed bone age than control, also cases were significant delayed in puberty than corresponding control according to Tanner staging **(Table 2)**.

Table (2): Comparison of bone age and laboratory findings between studied groups

	Control N=28	**Cases N=32**	**test of Significance**
Bone age			
• Normal	28 (100.0)	11 (34.4)	<0.001*
• Delayed	0 (0.0)	21 (65.6)	
Thyroid function			
• Normal	28 (100.0)	29 (90.6)	0.24
• Clinical hypothyroidism	0 (0.0)	3 (9.4)	
Random blood sugar			
• Normal	28 (100.0)	31(96.9)	1.0
• Diabetic	0 (0.0)	1 (3.1)	
Tanner staging	N=12 (%)	N=16(%)	
• I	0 (0.0)	5 (31.2)	
• II	0 (0.0)	9 (56.2)	0.001*
• III	3 (25.0)	2 (12.5)	
• IV	9 (75.0)	0 (0.0)	

*: Statistically significant

Figure (1) shows that serum leptin was significantly lower in cases of beta thalassemia than control group (P<0.001).

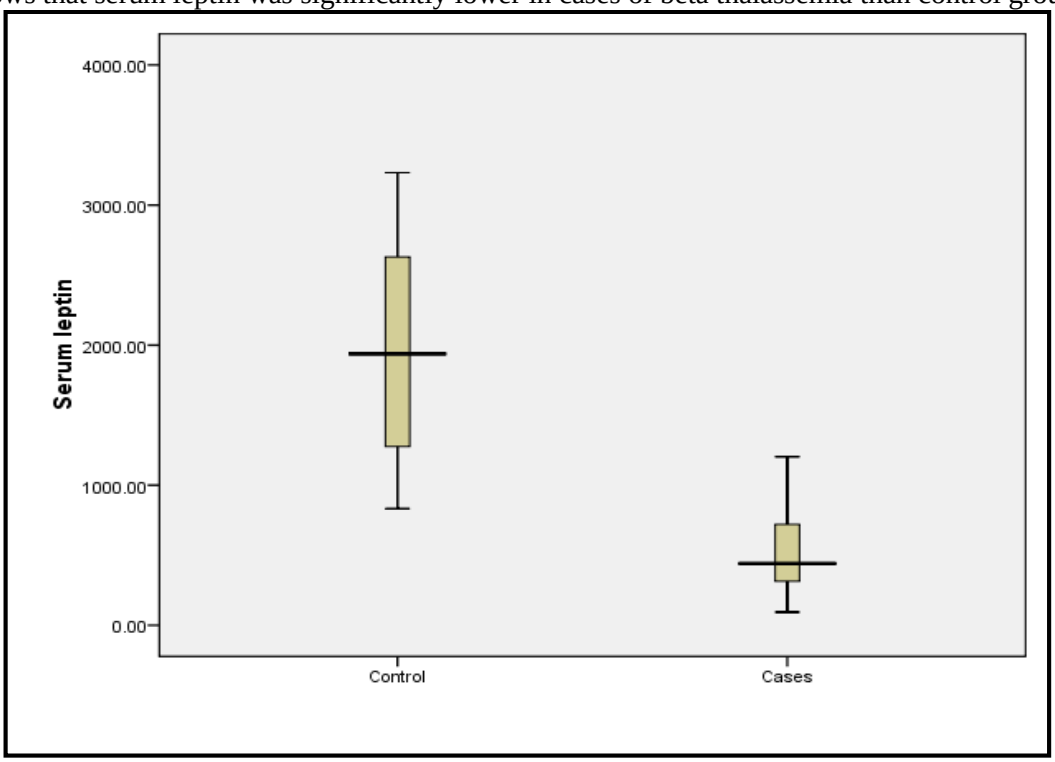

Figure (1): Comparison of serum leptin between cases and control groups

ROC curve for detection the validity and cutoff point of serum leptin in differentiating cases with excellent area under the ROC curve **(0.987)** (**Figure 2).**

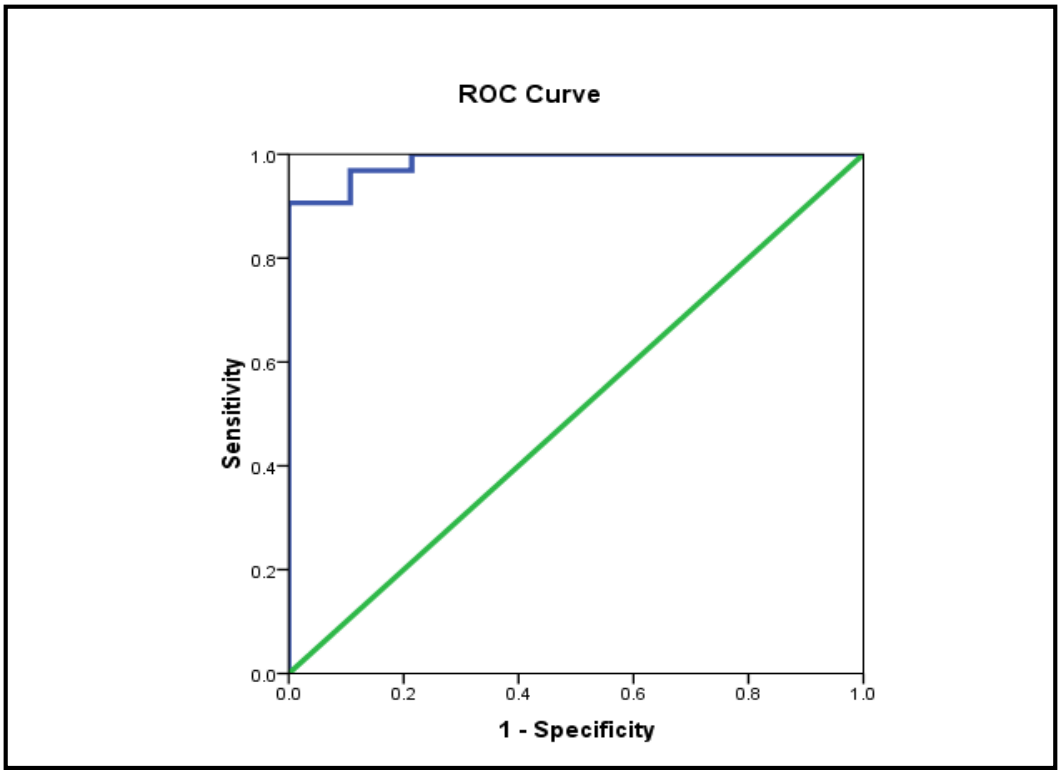

Figure (2): Receiver Operating Characteristics (ROC) curve of serum leptin in differentiating cases

This table shows cutoff point (982.5) was the best value to detect validity of serum leptin to differentiate cases **(Table 3)**.

Table (3): Validity of serum leptin in differentiating cases

	AUC (95% CI)	Cut off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Serum leptin	0.987 (0.97-1.0)	982.5	96.9	89.3	91.2	96.2	93.3

AUC: Area Under curve, PPV: Positive predictive value, NPV: Negative predictive value

DISCUSSION

Logically, there was no significant difference regarding age and sex between case and control groups.

All anthropometric parameters including height, weight and BMI were significantly lower in case group than control group. This findings are concomitant with **Fahim *et al.*** [6] study that revealed 49% of thalassemia patients were short stature, 47% were underweight and 3% low BMI in Upper Egypt**. Dhouib *et al.*** [7] also reported 26% short stature in thalassemia patients in his study**.** Lower percentage of short stature at thalassemia patients 20% only had been reported by **Sharma *et al.*** [8]**. Al-Naama *et al*.** [5] also reported that height, weight, BMI and BMI Z-score were all significantly lower in patient of beta thalassemia major group than healthy group. On the other hand, **Salih *et al.*** [9] reported in their study that only 60% of thalassemia patients were underweight but the rest were normal or overweight. Additional study was carried by **Muhammad *et al.*** [10] on pediatric thalassemia patients with age range from 2 to16 year and found about 58% of cases were malnourished, 35% healthy and 5.5% were overweight or obese. This difference from our results may be due to the difference in age group, size of to their study, management and control of thalassemia.

In our study we also assessed pubertal development for individuals at both groups who were around the age of puberty by using Tanner staging, we found that there were significant delayed puberty among beta thalassemia pubertal patients than pubertal control participants. Delayed puberty at patients of beta thalassemia group was also confirmed by results of assessment of pubertal hormones. These results are agreed by **Eshaqh-hosseini *et al*.** [11] who reported 70%:80% of cases of delayed puberty had hypo gonadotrophic hypogonadism in their study, also **De Sanctis *et al.*** [12] revealed that the most prevalent endocrinal problems in transfusion dependent beta thalassemia patients was hypogonadism. Another study made by **Yaman *et al.*** [13] detected that 9% of beta thalassemia patients between ages of 14 and 17.5 years had delayed puberty**.**

In our study we detected a delayed bone age at about 65% of patient group mainly with aging depending on plain X-ray on the left hand. **Hattab** [14] also found lesser bone age in thalassemia patient compared with normal children. Assessment of skeletal age was found to be sub optimal with chronological age in children and adolescent thalassemia patients in other study, which explained this defect by low bone mass density [15]**.** Many studies reported that about 40-50% of beta thalassemia major patients suffer from osteoporosis or osteopenia [13, 15, 16].

According to our results serum leptin level was significantly lower in our beta thalassemia cases than control. This result is in agreement with **Shahramian *et al.*** [17] who reported that serum leptin levels was lower in thalassemia patients than control. Another study made by **Elsayh *et al.*** [18] found similar results with lower serum leptin level in thalassemia major patients in compared with control ($p<0.001$)**,** also **Karami *et al.*** [19] investigated serum leptin level at beta thalassemia patients and found that it was significantly lower than control.

CONCLUSION

Validity of serum leptin to differentiate cases yielded sensitivity of 96.9%, specificity of 89.3%, accuracy of 93.3%, positive predictive value of 91.2% and negative predictive value of 96.2%

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