The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90, Page 1444-1447

Serum Leptin Level Assay in Normal and Malnourished Children Aged from One to Five Years

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ABSTRACT

Background: Leptin may be connected to nutrition, malnutrition, and the control of the energy balance.

Objective: This study aimed to assess the relationship between leptin levels and malnutrition status compared to normal nutrition in children aged from 12-60 months.

Subjects and methods: This case-control study was carried out on 66 children in the Nutritional Department and Pediatrics Out-patients Clinic of Zagazig University Children Hospital. They were divided into two groups: Group I included 33 cases as normal nutritional status, and Group II included 33 cases with malnutrition status.

Results: Between the study groups, there was a statistically significant decrease in serum leptin in malnourished group.

Conclusion: The mean value of leptin levels was lower among malnutrition children than normal children.

Keywords: Leptin, Malnutrition, Anthropometric measurements.

INTRODUCTION

An imbalance between nutritional intake and consumption that results in cumulative deficiencies of energy, protein, or micronutrients in children is referred to as pediatric malnutrition and may have a deleterious impact on their growth, development, or other related outcomes [(1)]. Hormonal factors are also necessary for children's normal growth and development. For linear growth, a normal nutritional condition is necessary. The blood level of leptin, a hormone generated by fat cells and a protein of the obese (ob) gene, the body's energy is greatly impacted by this balance by regulating dietary consumption. It is the hormone that regulates development and growth. Total fat mass and leptin concentration are related, with leptin concentrations being greater in obese patients. A symptom of brain deprivation, the drop in leptin following calorie restriction may also have a protective impact [(2)].

Leptin, "thin," or the "satiety hormone", encoded by the obese (ob) gene, which has a mass of around 16 kDa. This hormone, which controls how much body fat is stored, is produced by fat cells. It accomplishes this by modifying both the feeling of hunger and the amount of energy used [(3)]. The level of leptin reflects how much energy is kept in body fat. Circulating leptin levels are directly proportional to body fat percentage and alter abruptly in response to changes in caloric consumption. This is particularly susceptible to a lack of energy [(4)]. Leptin levels are much lower and positively linked with the thickness of the triceps, scapula, and abdominal fat. IGF-I concentrations are considerably lower in severe protein energy malnutrition (PEM) cases compared to normal children, although baseline cortisol and GH concentrations are much higher. Leptin, insulin, and IGF-I are all highly associated with the BMI [(5)]. Energy consumption and nutritional status have an impact on serum leptin levels. Consequently, it can be a sign of excessive energy storage or ongoing malnutrition [(2)].

Children with malnutrition had lower blood leptin levels than healthy children, and researchers hypothesized that this variation caused by a reduction of leptin production due to decreased subcutaneous adipose tissue because of lower calorie intake. Moreover, cytokines (IL, TNF-alpha) g**ldren's parents.**

Statistical Analysis: The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data).

Receiver operating characteristic (ROC) analysis: It is graphical plot of sensitivity against one minus the specificity (false positive rate) for different cutoffs. The optimal cutoff value was determined using **Youden index J** that is the farthest point on ROC curve from the diagonal line of equality [maximum (sensitivity + specificity)-1]. Total area under ROC curve (AUC or AUROC) is a measure of the overall accuracy of a test. The larger the AUC, the better the overall performance of a test to correctly discriminate between diseased and non-diseased subjects. Test characteristics were estimated by ROC curve and included best cutoff value, AUC, its standard error (SE), and *P*-value. In addition, to assess the effectiveness of the test, estimates as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated at the optimal cutoff. P value ≤ 0.05 was considered significant.

RESULTS

Age differences between the examined groups were statistically insignificant. The analyzed groups differed statistically significantly in terms of their parent's income, education level, and gender (the female gender was linked to malnutrition) (illiteracy and low income are associated with malnutrition) (Table 1).

Received: 11/08/2022
Accepted: 14/10/2022

Table (1): Comparison between the studied groups regarding demographic data:

Parameter	Malnourished group N=33 (%)	Control group N=33 (%)	χ^2/Z	P
Gender:				
Female	21 (63.6%)	11 (33.3%)	6.066	0.014*
Male	12 (36.4%)	22 (66.7%)		
Education				
Educated	10 (30.3%)	18 (54.6%)	3.97	0.046*
Illiterate	23 (69.7%)	15 (45.4%)		
Age (year):				
Median	2	2.41	-0.908	0.364
IQR	1.37 – 3	2.17 – 4		
Income:				
Poor	22 (66.7%)	10 (30.3%)	8.735	0.003*
Good	11 (33.3%)	23 (69.7%)		

*p ≤ 0.05 is statistically significant.

Serum leptin correlated positively with either the entire range of height, weight, or mid-arm circumference, which is statistically significant (Table 2).

Table (2): Correlation between serum leptin and both anthropometric data of studied malnourished patients

Z score	Serum leptin	
	r	P
Height	0.534	<0.001**
Weight	0.559	<0.001**
MAC	0.564	<0.001**

r Spearman rank correlation coefficient.

Regarding serum leptin, a statistically significant difference existed between the tested groups. Those who were undernourished had much lower leptin levels (Table 3).

Table (3): Comparison between the studied groups regarding serum leptin:

Parameter	Malnourished group Mean ± SD	Control group Mean ± SD	t	P
Serum leptin (ng/ml)	3.07 ± 0.72	6.42 ± 1.15	-8.635	<0.001**

**p≤0.001 is statistically highly significant.

Table (4) showed that the best serum leptin cutoff for predicting malnutrition was 5.3655, with an area under curve of 0.928, sensitivity of 87.9%, specificity of 84.8%, positive predictive value (PPV) of 85.3%, negative predictive value (NPV) of 87.5%, and overall accuracy of 86.4%.

Table (4): Performance of serum leptin in prediction of malnutrition:

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
≤5.3655	0.928	87.9%	84.8%	85.3%	87.5%	86.4%	<0.001**

**p≤0.001 is statistically highly significant AUC area under curve

Among factors significantly associated with malnutrition, serum leptin significantly increased risk by 40.6 folds (Table 5).

Table (5); Binary logistic regression analysis of factors significantly associated with malnutrition.

	β	p	AOR	95% C.I.	
				Lower	Upper
Leptin (≤5.3655)	3.704	<0.001**	40.600	9.876	166.899

**p≤0.001 is statistically highly significant AOR adjusted odds ratio CI confidence interval

The relationship between serum leptin and the quantity or intensity of blood, mucus and undigested food in the stool, or the presence of protozoa was statistically insignificant (Table 6).

Table (6): Correlation between serum leptin and result of stool analysis of studied malnourished patients

	Serum leptin	
	r	P
Blood	0.156	0.387
Mucus	0.143	0.428
State of digestion	0.12	0.507
Presence of protozoa	0.047	0.794

r Spearman rank correlation coefficient

The relationship between serum leptin and the kind of feeding, the rejection of food, or the discomfort during feeding was statistically insignificant (Table 7).

Table (7): Relation between serum leptin and feeding parameters among malnourished patients:

	Mean ± SD	t	P
Mode:			
Artificial	3.24 ± 0.76		
Mixed	2.75 ± 0.63	0.327	0.724
Breast	3.34 ± 0.81		
Refusal:			
No	3.84 ± 0.91	1.459	0.155
Yes	2.77 ± 0.67		
Pain:			
No	2.99 ± 0.62	-0.35	0.729
Yes	3.24 ± 0.81		

Independent sample t test.

DISCUSSION

The current study's findings showed that there was no statistically significant difference in the ages of the analyzed groups.

Akib *et al.* [2] conducted their study and reported that the switch from nursing to breast milk substitute occurs at two years old, which makes this age the most susceptible to nutritional deficiencies, according to their study.

In this study, Serum leptin positively correlated with either the Z score for height, weight, or mid-arm circumference, which was statistically significant.

Body mass index (BMI) and the quantity of body fat were strongly correlated with serum leptin concentrations; obese people had greater amounts than normal people do, while severely underweight people have much lower levels [7]. In a comparable research, **Büyükgebiz *et al.*** [8] discovered a significant (p 0.05) positive connection between mean blood leptin concentrations and the proportion of patients' weights that were standard for their height.

Serum leptin content was connected positively with arm circumference (r = 0.27; p 0.05) and BMI in undernourished children, while age and leptin levels did not correspond. The levels of serum leptin and body weight were found to be positively correlated by **Al Biltagi *et al.*** [9] and **Czaja-Bulsa *et al.*** [10].

Clinically and statistically, the control group's body weight was substantially greater (10.61± 1.03 kg vs. 5.71± 0.38 kg; p 0.001) than that of the PEM group (group B) [10]. According to **Hafez *et al.*** [11], who sought to learn more about the connection between children's BMI and serum leptin? Serum leptin levels were shown to significantly positively correlate with overweight females, according to their findings. In other words, as BMI rises, serum leptin rises as well. Their study's results go counter to the belief of many scientists who think leptin holds the key to managing obesity. Leptin levels and H/A, MUAC/A levels are positively correlated, according to other investigations [12].

The current investigation revealed that there was a statistically significant difference in blood leptin levels between the analysed groups (significantly lower in malnourished group). This is in agreement with **Akib *et al.*** [2] observation based on the findings using the Mann-Whitney test where they discovered that kids with good nutritional status and those with malnutrition had differing leptin levels. The median value for malnourished children, according to this study, was lower by 9.23 (6.02-197.2) ng/mL than it was for healthy children, which was 30.95 (6.02-89.36) ng/mL. This is because adipose tissue loss brought on by decreased food intake causes leptin production to decline in malnourished children and blood leptin levels, which indicate this adipose tissue loss, correlate with the severity of malnutrition in children. This is also supported by **Soliman *et al.*** [13], who found lower blood leptin levels in malnourished kids than in healthy kids and hypothesised that this rise was brought on by a reduction of leptin secretion caused by low hypodermic adipose tissue as a result of lower calorie intake. This is in agreement with the study of **Mehmet *et al.*** [14], who sought to establish the link between leptin concentrations, body weight, and effects of leptin on children that are severely undernourished. Malnourished children had lower blood leptin levels than the control group, according to their research (P 0.001). Additionally, No distinction could be made between children with marasmus and those with kwashiorkor (KWO) in terms of blood leptin levels (P > 0.05).

According to **Haspolat *et al.*** [15], marasmic children's blood leptin levels were significantly lower than those of healthy control participants. Previous investigations have shown that children with PEM have lower serum leptin levels than normal kids. This is in line with the conclusions of **Al Biltagi *et al.*** [9] who showed that PEM children had considerably lower blood leptin levels than control children. Additionally, their research revealed that marasmic patients had considerably lower serum leptin levels than KWO patients (p 0.05). The anorexic hormone leptin, therefore may help to explain why KWO children have greater anorexia than children with marasmus.

In a similar study, children with mild-to-moderate PEM as well as severe PEM had decreased leptin concentrations [16]. Additionally, serum leptin levels in investigations on malnourished children were shown to be lower than those in the control group [17]. A number of researchers discovered drops in blood leptin levels in proportion to the severity of malnutrition in children with malnutrition and noted that this was a reflection of adipose tissue loss [18].

The evidence suggests that leptin synthesis may be reduced in prolonged and severe malnutrition, which may lead to increased calorie intake and an energy distribution that favors fat [19]. Additionally, after weight gain in malnourished children, low blood leptin levels rise [20].

However, patients with PEM had low blood leptin levels and no association between leptin and body fat. Similar findings were obtained by **Büyükgebiz *et al.* [8],** who found no connection between blood leptin levels and total body fat.

The best cutoff of serum leptin in prediction of malnutrition was ≤ 5.3655, with an AUC of 0.928, a sensitivity of 87.9%, a specificity of 84.8%, a PPV of 85.3%, an NPV of 87.5%, and an overall accuracy of 86.4% (p 0.001).

CONCLUSION

It was concluded from this study that the mean value of leptin levels was lower among malnutrition children than normal children. Leptin levels showed significant correlation with anthropometric indicators.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

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