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Study of Serum Leptin Level in Children with Cyanotic and Acyanotic Congenital Heart Disease

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ABSTRACT

Background: Leptin balances body weight, but its role in the negative energy imbalance is unclear. Increased energy expenditure reduces newborn with cyanotic congenital heart disease development.

Aim and objectives: The researchers wanted to see how much leptin was in the blood of kid's congenital heart disease (CHD), both cyanotic and acyanotic, as well as to look into its involvement in their growth.

Subjects and methods: In this study, 38 Egyptian patients with congenital heart disease participated (18 with acyanotic CHD and 20 with cyanotic CHD), as well as (20) seemingly normal youngsters of same age, gender, and socioeconomic level as a control group.

Results: A total sample of 58 with mean age 7.7± 4.2, 8.3± 4.1 and 9.1± 3.8 in cyanotic, acyanotic and control groups. Mean of serum leptin among control group was 3.7± 1.3. The mean of serum ghrelin among acyanotic group was 5.3± 1.8. There was positive correlation between age, BMI, O_2 saturation, MAC, and serum leptin. But there was negative correlation between age, BMI, O_2 saturation, mid upper arm circumference (MAC), and serum ghrelin. There was negative moderate statistically significant correlation between serum leptin and serum ghrelin.

Conclusion: Elevated leptin and reduced gherlin levels were found in children with congenital heart diseases, whether cyanotic or acyanotic, suggesting a role for both hormones in regulation of nutrient intake, energy balance and maintenance of body weight in those children.

Keywords: Congenital heart diseases, Serum ghrelin, Serum leptin

INTRODUCTION

Leptin is a newly discovered hormone that affects energy balance and is encoded by the obesity gene. It has both thermogenic and anorexigenic effects in mice, but its role in human energy balance is uncertain [(1)]. Leptin and ghrelin are hormones that have been demonstrated to influence energy balance. Leptin is involved in long-term energy balance maintenance, which reduces appetite and so promotes weight loss. Ghrelin, on the other hand, is a fast-acting hormone that encourages people to consume more food [(2)].

Leptin is a hormone that is mostly produced by adipose tissue, released into blood stream, and it binds to hypothalamic leptin receptors after crossing the blood-brain barrier. It sends and receives data about the triglyceride content of adipocyte, as well as the macronutrient and energy composition of recent food intake [(3)].

Low circulating leptin levels have been found to increase activity of hypothalamic neurons that secret orexigenic peptides and decrease activity of in neurons that secret anorexigenic peptides, thereby increasing appetite and stimulate weight gain [(4)].

The most frequent congenital anomaly in children is congenital heart disease (CHD), which is a major source of morbidity and mortality. CHD prevalence varies greatly amongst research around the world, however it was reported that 1.35 million babies are born with CHD every year [(5)]. Malnutrition is common in children with congenital heart disease, regardless of the kind of abnormality [(6)].

Growth retardation can be caused by inadequate calorie intake due to anorexia, dyspnea, and tachypnea, or increased energy requirements due to increased metabolism, according to studies. However, the actual cause of this low growth is still unknown [(7)].

Congenital cardiac disease causes growth delay for a variety of reasons. Many patients with cyanotic congenital heart illness have a noticeable decrease of fat. Leptin is a hormone produced by adipocytes that is necessary for proper body weight management. Although caloric consumption modulates its circulating levels, leptin regulates adipose tissue mass and corresponds with fat mass. In congenital heart diseases the cyanotic group had lower weight, mid upper arm circumference (MAC), and Triceps Skinfold (TSF) standard deviations than the acyanotic group, although leptin levels were identical [(8)].

The purpose of this research was to see if blood leptin levels in newborns with cyanotic and acyanotic congenital heart disease affected their growth.

SUBJECTS AND METHODS

In this study, 38 Egyptians children with congenital heart disease (18 with acyanotic CHD and 20 with cyanotic CHD) were compared to a control group of 20 seemingly normal children of the same age, gender, and socioeconomic background. Patients were recruited from the University Hospital's Pediatric Cardiology Clinic between February 2020 and January 2021.

Inclusion criteria:

1) patients with acyanotic or cyanotic congenital heart diseases,
2) age from 2 months up to 18 years,
3) parental consent.

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Exclusion criteria:
1) patients with other congenital anomalies,
2) chromosomal abnormalities,
3) any other chronic disease,
4) patients with acquired heart disease.

Control group were selected from general Pediatric Outpatient Clinic in the same period. They were healthy children; non-hospitalized with no pathological findings had recorded in their physical examination.

All patients and control were subjected to the following:

Complete assessment of history including age, sex, nutritional history, family history, admission to hospital, and the reason for admission to the hospital. Anthropometric measurements including length in cm, weight in kg, mid upper arm circumference (MAC) in cm and body mass index (BMI) in kg/m^2.

Inspection, palpation, percussion, and auscultation are all part of a cardiac examination. Investigations including oxygen saturation by pulse oximetry, chest X-ray, electrocardiograpy (ECG), and echocardiography using Philips HD 11 machine (Ultrasound Supply, USA) and serum leptin (ng/ml) and ghrelin (ng/dl) levels using enzyme-linked immunosorbent assay (ELISA).

Sampling:

Blood samples of 3 mL were collected by venipuncture from all participants after a fasting period of 3 hours in plain vacutainer tube. Full centrifugation at 3000 rpm for 20 minutes was used to separate the samples. Clear sera were isolated and stored at -20°C until the assay was performed.

The DRG Leptin EL1SA (DRG International, Inc., USA) was used to detect leptin, and the Invitrogen Ghrelin Human ELISA (Thermo Fisher Scientific Inc., USA) was used to assess ghrelin by indirect enzyme linked immunosorbent assay according to the manufacturer's procedure. The amount of leptin in the sample determines the intensity of the colour generated; the absorbance was measured at 450 nm, and their quantities were calculated using a standard curve.

Groups: The studied population was classified into three groups:

Acyanotic group consisted of 18 patients with acyanotic congenital heart disease, they had no central cyanosis and oxygen saturation (SpO_2) was > 98% measured at rest, cyanotic group consisted of 20 unrepaired and people with cyanotic congenital heart disease who were not palliated. They had central cyanosis and oxygen saturation (SpO_2) of 75-85% measured at rest, and control group consisted of 20 healthy children.

All our patients had been fed orally by mouth as other healthy controls. No one of them has nasogastric tube or g-tube.

Ethical considerations:

The study was approved by the Faculty's Ethics Committee of Tanta University. Informed consent was obtained from the guardian of each participant included in the study. The Helsinki Declaration, the World Medical Association's code of ethics for human studies, directed the conduct of this investigation.

Statistical analysis

On an IBM compatible computer, the data were tabulated and analysed using the statistical package for the social sciences software 20 (SPSS Inc., Chicago, Illinois, USA). Means, and standard deviations were used to represent the quantitative data. Significance was defined as a P value of less than 0.05. The Pearson correlation test was used.

RESULTS

Mean age, BMI, MAC, and serum leptin and ghrelin are shown in table 1.

Table 1: Main characteristics and metabolic parameters among groups

Variables	Cyanotic CHD Mean± SD	Acyanotic CHD Mean± SD	Controls Mean± SD
Age (years)	7.7± 4.2	8.3± 4.1	9.1± 3.8
BMI (Kg/m^2)	1.4± 1.1	0.8± 1.6	1.1± 0.9
MAC (cm)	1.9± 1.2	0.6± 0.9	0.8± 1.1
Serum leptin (ng/ml)	2.8± 1.7	2.3± 1.4	3.7± 1.3
Serum ghrelin (ng/dl)	4.9± 1.5	5.3± 1.8	3.4± 1.2

BMI, body mass index; MAC, mid arm circumference

In figure 1 about six participants had ventricular septal defect and five participants had atrial septal defect.

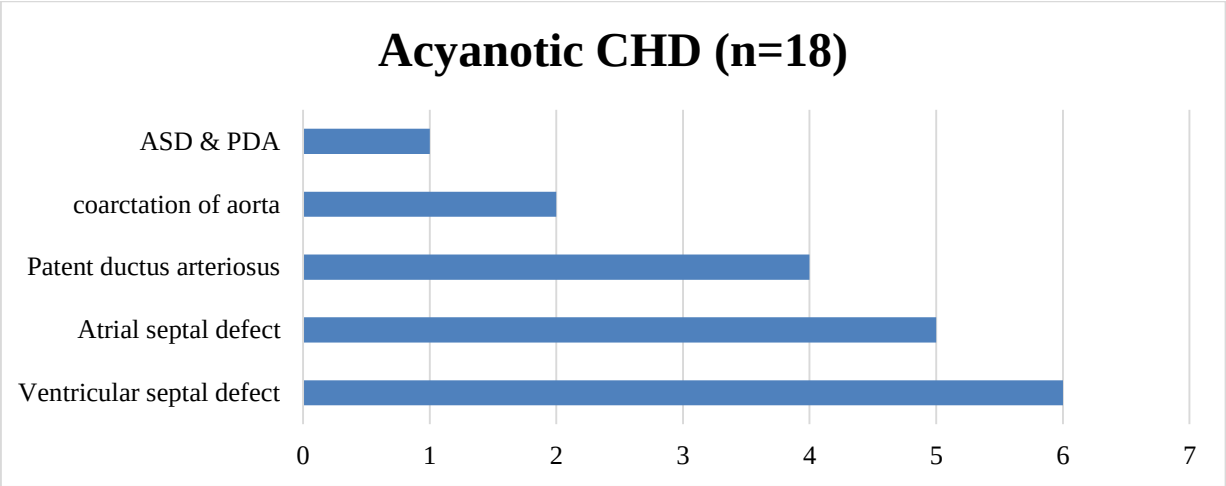

Figure 1: Specific diagnosis among acyanotic group (n= 18)

CHD: Coronary heart disease, ASD Atrial Septal Defect, PDA: Patent Ductus Arteriosus

According to figure 2 there were nine participants had tetralogy of Fallot and six with transposition of great arteries.

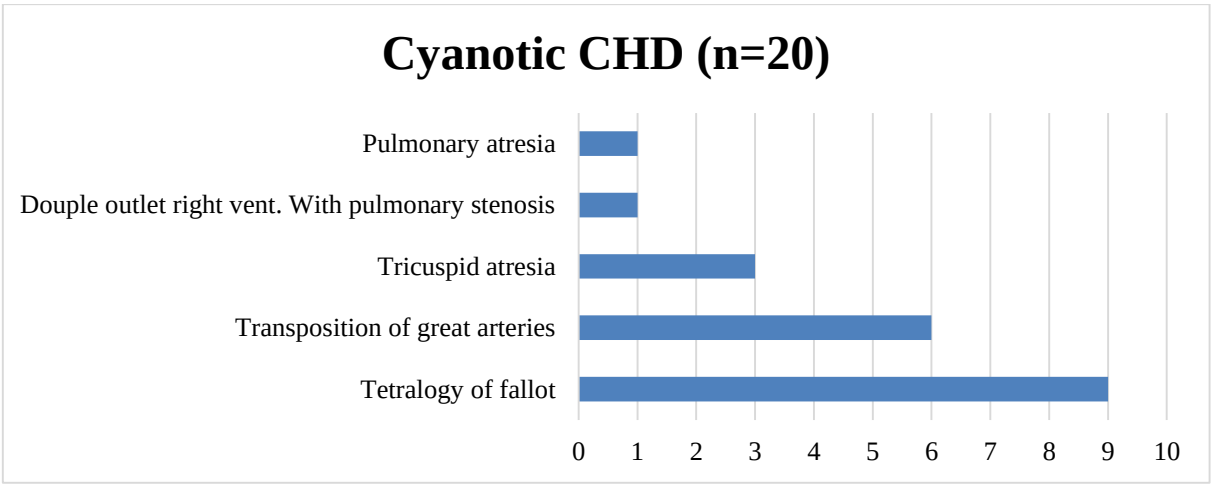

Figure 2: Specific diagnosis among cyanotic group (n=20)

In table 2 there were positive correlation between age, BMI, O_2 saturation, MAC, and serum leptin. But, there were negative correlation between age, BMI, O_2 saturation, MAC, and serum ghrelin. Correlation was applied on the whole sample.

Table 2: Correlation between main characteristics, serum leptin and serum ghrelin

Variables		***Serum leptin***		***Serum ghrelin***	
		r	***p***	***r***	***p***
Age (years)		0.83	**0.004***	-0.67	**0.002***
BMI	**Cyanotic**	0.58	**0.022***	-0.71	**0.005***
	Acyanotic	0.71	**<0.001***	-0.62	**0.001***
	Controls	0.85	**0.031***	-0.81	**<0.001***
O_2 saturation (%)		0.53	**<0.001***	-0.49	**0.002***
MAC (cm)		0.21	**0.041***	-0.33	**0.012***

BMI, body mass index; MAC, mid arm circumference, *: significant

According to table 3 there was negative moderate statistically significant correlation between serum leptin and serum ghrelin. Correlation was applied on the whole sample

Table 3: Correlation between serum leptin and serum ghrelin

Variables	***Serum ghrelin***	
	r	***p***
Serum leptin (ng/ml)	- 0.523	**<0.001***

*: significant

DISCUSSION

This research included 38 Egyptians with congenital cardiac disease. To assess serum leptin levels in children with cyanotic and acyanotic congenital heart disease and investigate its possible role in these children's growth, 18 patients' serum leptin levels in children with cyanotic and acyanotic congenital heart disease, as well as 20 seemingly normal children of similar age, sex, and socioeconomic status, were measured.

For a number of reasons, congenital heart illness causes growth delay [(9)]. Many patients with cyanotic congenital heart illness have a noticeable decrease of lipids. Leptin is a hormone produced by adipocytes that is necessary for proper body weight management. Leptin is a hormone that controls adipose tissue mass and is linked to fat mass; nevertheless, calorie consumption has an impact on circulating levels [(10)].

CHD is a deformity or defect in one or more heart or blood artery structures that arises before birth, during the first few weeks of pregnancy, when the heart is still forming. At birth, such a defect can be found in any area of the heart, and it can cause symptoms at any time during childhood or adulthood. This is one of the most frequent birth malformations, and it is one of the major causes of mortality [(11)]. This defect may be minor enough that the kid may appear healthy at birth and for many years, or it may be significant enough to cause a life-threatening condition in the infant. More than 40%–50% of newborns with CHD are detected within the first week [(12)] whereas 50–60% will be detected during the first month. Ventricular septal defect is the most common CHD after bicuspid aortic valves, atrial septal abnormalities are the second most frequent congenital lesion in adults [(13)].

The level of circulating leptin in humans has been demonstrated to be positively linked with BMI in previous research. Our findings of a positive correlation between serum leptin level with BMI and MAC in cyanotic patients, acyanotic patients, and healthy controls support this view [(10, 13)]. **Rodriguez *et al.*** [(14)] found that there is a positive correlation between serum leptin level and BMI in cyanotic and acyanotic patients. **Fahed *et al.*** [(15)]found that there is a positive correlation between plasma leptin level and MAC in cyanotic and acyanotic patients, which supports our results. **Ozmen *et al.*** [(9)] found that there is a positive correlation between serum leptin level and BMI in obese, overweight, and normal controls and children with CHD. In the study carried out by **Dadarlat-Pop *et al*.** [(16)] plasma leptin levels were correlated positively with BMI only in the acyanotic group, but not in the cyanotic group. Previous research has revealed that the serum level of leptin in patients with cyanotic CHD is much lower than in healthy people, but the levels in this study were not different between the patients and the controls [(17)]. This finding is consistent with the findings of a similar study, which found that serum leptin levels were normal in both CHD patients and controls [(18)]. Previous research has also demonstrated that serum levels of leptin differ among individuals with chronic heart failure (CHF) and cardiovascular disorders, highlighting the debate over the role of leptin as an important element in energy balance and body weight management [(19)]. Various pathophysiological and/or metabolic parameters may have a role in these alterations, which could indicate a significant gap in our understanding of the problem that requires further investigation and discussion [(20)]. Leptin's complicated role in human physiology is only beginning to be understood. As a result, various researches have been conducted on the link between leptin levels and biochemical markers. A positive connection between plasma leptin and insulin levels was found in some of these investigations [(21)].

Malnutrition is a risk for patients with congenital heart disease for a variety of reasons, including decreased energy intake, higher energy demand, or both. Reduced growth in newborns with cyanotic congenital heart disease is due to increased energy expenditure [(22)]. On the other hand, ghrelin “hunger hormone” is secreted mainly by the stomach. Its effects on energy balance are also mediated by the hypothalamus. It increases food intake and obesity by activating hypothalamic orexigenic neuropeptides. Ghrelin also enhances the production and secretion of growth hormone (GH), which in turn stimulates the expression and secretion of hepatic insulin-like growth factor-1 (IGF-1) [(16)]. Ghrelin levels fluctuate throughout a person's life and are largely determined by how much food they consume. Researchers discovered that ghrelin levels in the blood correspond with growth hormone release, and that ghrelin is involved in the regulation of appetite, energy, and body weight, as well as the modulation of cardiovascular functioning [(17)]. This goes with our results that serum ghrelin is negatively correlate with BMI. But according to a study conducted by **Lee *et al.*** [(23)] between the patients and the controls, there was no significant association between ghrelin levels and BMI.

This study contrasts others that have found an increase in ghrelin levels in the blood and/or an inverse relationship between ghrelin levels and BMI in patients [(20)]. When CHD patients were compared to controls, blood leptin levels were considerably lower and serum ghrelin levels were significantly greater. There were no significant variations in leptin or ghrelin levels between the acyanotic and cyanotic groups.

The heterogeneity in anatomy and hemodynamics across different forms of CHD among the analysed groups was the study's weakness.

CONCLUSION

Elevated leptin and reduced ghrelin levels were found in children with congenital heart diseases, whether cyanotic or acyanotic, suggesting a role for both hormones in regulation of nutrient intake, energy balance and maintenance of body weight in those

children. There is positive correlation between age, BMI, O_2 saturation, MAC and serum leptin. Also, there is negative correlation between age, BMI, O_2 saturation, MAC and serum ghrelin. More research is needed to determine the impact of correcting leptin levels and ghrelin changes in children with CHF on growth of those children.

DECLARATIONS

Consent for Publication: I confirm that all authors accept the manuscript for submission

Availability of data and material: Available

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