The Impact of Congenital Heart Diseases on Growth Parameters in Children and Their Correlations with Leptin Levels

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Abstract

Children with congenital heart disease (CHD) prone to stunted growth by different parameters including weight, height and head circumference compared to a control groups, to accomplish such aim (110) children aged ranged (20 days – 13 years with CHD) have enrolled in this study, (83) patients with a cyanotic CHD (75.45%) and (27) cyanotic type (24.54%) were compared with (171) healthy controls of similar age and sex groups. This study was done in Al-Hilla teaching hospital during the period November 1, 2017 to October 11, 2018. The results indicate a significant (2.06) retardation in all parameters in patients with CHD related to control and there is a significant retardation in weight (z = 3.06) in children with cyanotic CHD related to a cyanotic type. Also there is a significant retardation (z = 1.01) in height gain in children with cyanotic related to a cyanotic type and finally there is a significant (z = 2.09) decrease in head circumference in children with cyanotic CHD related to a cyanotic type. Serum leptin levels were also lowered in all patients with CHD. The results concluded that children with (CHD) experience early and continues decrement of all growth parameter during their life.

Keywords: (*children, congenital heart diseases, growth parameters, leptin levels*)

Introduction

Congenital heart disease is defined as gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of significant[(1)]. It is considered as third congenital diseases in children and a leading cause of death in infant during first year of life[(2)]. It prevalence is 5 to 8 per 1000 live births that varied in different parts of the world, in a recent study the prevalence has been reported to be ranged 4 to 50 cases per 1000 live Births[(2,14,16)].

Several genetic and environmental risk factors have been introduced for CHD, and most important factors include genetic mutation, alcohol drinking, abusing some drugs (most famous thalidomide and cocaine using during pregnancy)[(4,17)]. The cytokines in many studies were found to have a strong effect on feeding, weight and energy intake in patients with CHD[(5)] . Impaired absorption can also be an important cause of malnutrition in CHD, therefore, children with CHD and delayed growth due to increased work of a cardiopulmonary and consequently, fatigue and loss of appetite, dyspnea, tachypnea and chronic hypoxia were directed to malnutrition [(4,8,15,21).]

Recent studies shows series of serum factors such as leptin, ghrelin and tumor necrosis factor alpha (TNF-) will be changed in these patients. Consequently the rate of absorption of nutrients, growth, weight, energy consumption and storage are changing[(11)]. These children with CHD have normal growth when receiving more calories compared to healthy ones[(9,12)] and malnutrition in these patients effects on the metabolic response to injury and complications and outcomes of cardiac surgery including sepsis, renal dysfunction, necrotizing enterocolitis, hospitalization days[(13,21)].

The CHD is divided into four major groups of cyanotic with and without an increase in pulmonary artery pressure and a cyanotic heart defect with and without an increase in pulmonary artery pressure[(1,20)]. Since it has been shown that the prevalence of growth parameters retardation with CHD were increased in the

last decade in Iraqi population and since leptin hormone has been shown to be involved in long-term regulation of energy balance by suppressing appetite and stimulating weight lost[18] and such correlation has not been studied in Hilla (Babylon province), therefore, this study was undertaken to investigate:

1- The effect of CHD on anthropometries measurements of growth in children involving Weight, height and head circumference between control and cyanotic and a cyanotic CHD.

2- The variation in the effect of cyanotic and a cyanotic CHD on growth parameters.

3- Correlation of serum leptin levels with CHD.

Materials and Method

A study of (110) patients with CHD, (83) with a cyanotic CHD and (27) cyanotic CHD and (171) controls was carriedout between November 1, 2017 to October 11, 2018 in AL Hilla Teaching Hospital. These patients divided into four groups according to their age. The criteria used for including the patients in the study are:

a) Patients with cyanotic and acyanotic CHD.

b) The age of patients ranged from (20 days – 13 years).

c) Parental consent.

The patients with other congenital anomalies, with chronic disease or acquired heart diseases were excluded from the study. The control groups were selected from general paediatric and neotal care clinics, and no pathological findings had been shown in their clinical examination. The patients and control were subjected to the following:

- Complete history and physical examination.
- Anthropometric measurement including length in cm, weight in kg and head circumference in cm.
- Investigation including:

1- CXR interpreted by a radiologist

2- E.C.G. standardized at 25 mm/s

3- Echo Philips clearvue 350. USA. Used modes: M-mode, 2D and Doppler both continues and colour.

4- Blood samples were collected by venipuncture from all patients and controls. Samples were centrifuged at 3000 rpm for 20 minutes. Clear sera were separated and kept frozen at -20^{o}C until the time of assay. Leptin was measured using the DRG Elisa (DRG international, Inc., USA) by indirect enzyme linked immunosorbent assay according to the protocol provided by manufacturer. The intensity of the colour developed is proportional to the concentration of leptin in the sample, the absorbance is measured at 450 nm and concentration were determine from standard curve.

Statistical Analysis

The -Z- Statistical test was done to the significance in difference of cyanotic and a cyanotic CHD on growth parameters in comparison with control (Daniel, 2009) [19].

The level of significance taken 95%

$Z_C =$

If $Z_C > 1.96$ mean there is significant differences

Results

The hundred ten children with CHD represented by (83), 75.45% acyanotic group compared with cyanotic CHD (27) 24.54%. The patients were classified into four groups according to their age. (table 1).

Table (1): Classification of children according to age

Age	Control		A cyanotic CHD		Cyanotic CHD	
	Number	%	Number	%	Number	%
<1y	29	16.45%	43	51.80%	17	62.96%
1-2y	35	20.46%	14	16.86%	5	18.51%
2-5y	65	38.01%	14	16.86%	3	11.11%
>5y	42	24.56%	12	14.45%	2	7.4%

Table (2): The effect of CHD on head circumference

Centile	<1y			1-2y			2-5y			>5y		
	Control %	Acyanotic %	Cyanotic %	Control %	Acyanotic %	Cyanotic %	Control %	Acyanotic %	Cyanotic %	Control %	Acyanotic %	Cyanotic %
<3rd	- -	2.32	- -	- -	7.14	- -	- -	- -	- -	- -	- -	- -
3rd	3.44	30.23	17.64	- -	21.42	11.76	- -	7.14	5.88	2.38	25	50
10th	- -	16.27	17.64	2.58	7.14	5.88	1.53	28.57	- -	- -	- -	- -
25th	10.34	2.32	17.64	25.71	- -	- -	7.69	7.14	5.88	9.52	- -	50
50th	31.01	30.23	23.52	28.57	35.71	- -	56.29	21.42	5.88	40.47	58.33	- -
75th	37.97	6.97	17.64	25.71	14.28	11.76	29.23	21.42	- -	16.66	8.33	- -
95th	20.68	9.3	5.88	17.14	14.28	- -	4.61	- -	5.88	- -	8.33	- -
>95th	- -	- -	- -	- -	- -	- -	- -	- -	- -	28.57	- -	- -

Leptin levels were found to be significantly lowered in patients with cyanotic and acyanotic groups compared with controls (P<0.05), Table (3).

Table (3): Serum Leptin Levels in Cyanotic and Acyanotic CHD

	Acyanotic	cyanotic	control groups	P values
Leptin (ng/ml)	1.91.4	1.7 2.1	3.7 2.4	<0.05 P1 = 0.28 P2 = 0.02 P3 = 0.01

Data were expressed as mean standard deviation.

P_1: Acyanotic versus cyanotic groups.

P_2: Acyanotic versus control groups.

P_3: Cyanotic versus control groups.

Discussion

The study shows a statistical significant (z = 2.06) retardation in all growth parameters involving all age groups (below 1year , 1-2years, 2-5years and above 5years) but there is no significant (z = 1.2) differences between cyanotic and a cyanotic CHD in relation to any group. Table (1) shows more details, however, there is early presentation and diagnosis for children with cyanotic CHD possibly due to more aggressive clinical presentation in the infancy which attracts the parents attention to seek early medical help.

This study shows significant (z = 3.06) retardation in weight between groups of children with CHD and control, also shows significant (z = 2.04) retardation in children with cyanotic CHD, compared with a cyanotic groups, and this is an expected result due to more harmful effect of CHD (cyanotic) on the nutritional

status of children related to shortness of breath which presented as early failure to gain weight that may lead later on to growth retardation with its complications, (Figure 1) shows that weight retardation below the third centile (100%) in children more than 5 years with cyanotic CHD, also more effect of a cyanotic CHD on both groups (<1year and 1–2years, Figure 1) more than other groups (<1year, 53.48%) at the third centile and more details can be shown on (Figure 1), these findings were consistent with other reports[14], mentioned that children with CHD experience early simultaneous decrease in growth trajectory across weight, length and head circumference, this decrement suggests a role for altered growth retardation in child with CHD.

There is a statistically significant (z = 2.28) retardation in height in children with CHD in comparison with controls, but there is a non-significant (z = 1.01) variation between cyanotic and a cyanotic type. These results were also comparable with finding where (52%) below the 16th centile for both length and weight and 27% were below the 3rd centile for weight and lengths, these comparable results probably indicated that the cause of growth retardation in CHD was multifactorial which could be due to inadequate caloric intake and feeding difficulty[11], in our study there was (25.92%) of cyanotic CHD retardation in height and (42.16%) of a cyanotic type with retardation in height, (Figure 2) shows that 50% of children with cyanotic CHD above 5 years at third centile mostly in cyanotic type.

Head circumference was significantly (z = 2.56) reduced in CHD children in comparison with controls, also there was significant (z = 2.09) retardation in cyanotic type related to acyanotic, this may be explained by early affection of children with cyanotic CHD related to sever symptoms associated with sever growth retardation that lead to affection of skull development later on, (Table 2, Figure 3) shows (50%) of cyanotic CHD children aging above 5 years their head circumference on the 3rd centile comparing with acyanotic type (8.33%) reach 95th centile, also (50%) of cyanotic type below 3rd centile while there is less effect of a cyanotic CHD in early infancy, these results were also agreed with Barbara[3] who mentioned that children with CHD had stunted growth and require feeding supplementation in nearly a quarter of them (during infancy) to meet the definition of failure to thrive in first year of life[3].

Leptin is a hormone that is produced mainly by the fatty tissue and released into peripheral circulation and binds to receptors in the hypothalamus to transmit information about triglyceride content of adipocyte, in addition to macronutrient content and energy composition of newly administered food[10]. Low levels of leptin have been found to increase activity of orexigenic peptides and decrease activity of anorexigenic peptides, thereby, increasing appetite and stimulating weight gain[17]. Our study demonstrated that serum leptin levels were significantly lowered compared with controls. These results were consistent with a researcher who found that children with CHD had lowered leptin levels than healthy controls[18], while other researcher found no significant difference in plasma leptin levels between cyanotic and acyanotic patients, however, these studies did not include a healthy control groups to compare with[11,18]. This study also showed that all the anthropometric parameters in all groups were positively correlated with leptin levels. These findings were supported by others[9,11,12].

This study has some limitation since it was a single center study done in Babylon Province and in addition to hemodynamic variability associated with various types of CHD[11]. It was concluded that children with CHD are at increased risk for poor growth parameters and reduced leptin levels in these patients suggesting a role for such hormone in regulating food intake, energy balance and maintenance of body weight. The abnormal hemodynamics and the hypermetabolic state of these patients will compromise nutrition and decreases IGF-1 synthesis with subsequent slowing of linear growth weight gain[20,16].

The incidence of growth disorders in these patients can emphasized that growth retardation in patients with CHD compared with healthy children can be attributed to differences in the factors affecting the growth of CHD children including gender, age, cardiac abnormalities simultaneous multiple valvular lesions and ultimately congestive heart failure that leads to multiple growth problems[3,17].

Conclusions

- There was significant decrease in all growth parameters (z = 2.06) in children with CHD related to control.

- There was a significant retardation in weight (z = 2.09) and head circumference (z = 2.09) between cyanotic and a cyanotic CHD

- There was a non-significant retardation (z = 1.01) in height between cyanotic CHD and a cyanotic CHD.

- Serum leptin level were lowered in both cyanotic and a cyanotic patients with CHD.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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