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Assessment Of Serum Insulin Like Growth Factor 1 (IL-GF1) In Children With Congenital Heart Diseases.

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ABSTRACT

Congenital heart diseases (CHDs) refer to any abnormality in cardio circulatory structure or function that is present at birth regardless of whether it is found later. Children with congenital heart disease have been accounted to demonstrate significant growth retardation both prenatally and postnatally. Insulin like growth factor 1(IGF-1) is a well-known biochemical marker in the growth of mammals. And it works as heart tissue survival factor. We aim to assess the serum level of insulin like growth factor -1 hormone in infants and children with cyanotic and acyanotic congenital heart disease and to look for a possible relationship between IGF-1 concentration as growth parameter with degree of cyanosis of these children. This study was conducted on 60infants and children(38 males &22 females) 30 with congenital heart disease attending the pediatric cardiology unit and the pediatric cardiology outpatient clinic, Zagazig University hospitals. Their ages ranged from 2 months to 2 years, 30 healthy children of sex and age matched to the patients were taken as control group. Patients then divided into two groups ,group I with CHD which subdivided into two group :group Ia (acyanotic group) and Ib (cyanotic group),group II control group .and then IL-GF1 measurement and other lab values were assessed in groups. The current study reports a very high prevalence of malnutrition in our CHD patients, in particular, severe forms of wasting and stunting. also showed that serum level of IGF-1 was statistically significantly lower in the group of CHD patients compared to serum IGF-1 level of the controls ($P<0.001$), cyanotic group had less serum IGF-1 concentration than acyanotic group. the cutoff pointof IL-GF1 of less than or equal to 2087 can be used as a predictor for delayed growth with sensitvity of 86.7%, specificity of 90%, PVP of 100% and PVN of 91.7%. we determined that the most important factor on serum IGF-1 levels is cyanosis for this reason we believe that chronic hypoxia plays a significant role in the pathogenesis of growth failure.

Keywords: congenital heart disease-insulin like growth factor(IL-GF1)-cyanosis.

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INTRODUCTION

Congenital heart diseases (CHDs) defined as any abnormality in cardio circulatory structure or function that is present at childbirth regardless of whether it is found later [1].

After birth, a newborn normally loses around 5% to 10% of their birth weight. By about age 2 weeks, a newborn should begin to put on weight and develop rapidly. By age 4 to 6 months, an infant's weight ought to be double their birth weight. During the second half of the primary year of life, development is not as rapid [2].

Children with inborn heart disease have been accounted to demonstrate significant growth retardation both prenatally and postnatally [3]. Diverse types of cardiac malformations can affect nourishment and development to different grades[4].

Recent surgical advances have took into consideration early correction or palliation in most cases, numerous types of inborn heart diseases are complicated and not promptly responsive to repair in early infancy. In these conditions, surgical repair is usually delayed until the point that the infant achieves a particular weight, yet the unfavorable impacts of chronic hypoxemia on development make this a troublesome objective to accomplish. [3].

Insulin like growth factor 1(IGF-1) is an outstanding biochemical marker in the development of vertebrates, it is secreted in response to growth hormone to induce tissue development, it additionally also works as a survival factor in heart tissue , IGF- has appeared to be engaged with myocardial development, remodeling and suppression of apoptosis [5].so we want to study the serum levels of IGF-1 in children with cyanotic heart diseases and their growth parameters.

Aim of the study : the study aimed to assess the serum level of insulin like growth factor -1 hormone in infants and children with cyanotic and acyanotic congenital heart disease and to look for a possible relationship between IGF-1 concentration as growth parameter with degree of cyanosis of these children.

SUBJECTS AND METHODS

Study design: The current study is a case-control study that was performed in Pediatric Cardiology Unit at Zagazig University Children Hospitals during the period from February 2017 till May 2018. The study protocol was approved by Ethics Committee, Faculty of Medicine and Zagazig University. An informed verbal consent from parents was provided after explanation of the nature and the purpose of the investigations to the parents prior to participation in the study.

Subjects: This study was conducted on 60 infants and children (38 males & 22 females) 30 with congenital heart disease attending the pediatric cardiology unit and the pediatric cardiology outpatient clinic in Zagazig University hospitals, their ages ranged from 2 months to 2 years. Thirty healthy children of sex & age matched to the patients were taken as control group.

Inclusion criteria:

- Age group ranged from 2 months to 2 years.
- Patients with CHD: All patients' cardiac diagnoses were made on the basis of clinical examinations and investigations including electrocardiography, and echocardiography. These were confirmed by cardiac catheterization and angiography when needed.
- Healthy children were randomly chosen among patients with no heart disease and of normal growth visiting children general clinic of zagazig university hospital.
- Control children were free from other malformations or signs of other disease.

Exclusion criteria:

- Patients with history of prematurity, intrauterine growth retardation, known genetic malformations, dysmorphic features and neurologic disability.
- Patients with acquired cardiac lesions as rheumatic heart disease and cardiomyopathy.

The studied children were divided into the following groups:

- **Group I (CHD group):** 30 patients having congenital heart diseases (8 males and 7 females) their mean age was (15.9+3.49) months.

Group **I** was furtherly subdivided according to the type of congenital heart diseases whether cyanotic or acyanotic into the following 2 groups:

- **Group Ia (Acyanotic group):** 15 patients with acyanotic congenital heart disease (8 males and 7 females) their mean age was (15.9+3.49) months.
- **Group Ib (Cyanotic group):** 15 patients with cyanotic congenital heart disease (8 males and 7 females) their mean age was (15.9+3.49) months.
- **Group II (control group):** 30 children (14 males and 16 Females) their mean age was (16.3+4.95) months.

Methods:

All the studied groups were subjected to the following:

❖ **Complete history taking with special emphasis on:**

- Age of onset of the complaint
- The presence of cyanosis and cyanotic spills
- The prenatal and natal history
- Presence of complications as cyanotic spells or symptoms and signs of congestive heart failure, recurrent chest infection and failure to thrive.
- Nutrition history
- Development and motor milestones.
- Family history of similar condition in the family and consanguinity.

❖ **Thorough physical examination with special emphasis on :**

- Physical appearance.
- The arterial blood pressure and other vital signs.
- Complete cardiac examination
- Abdominal examination

❖ **Anthropometric measures**

❖ **Malnutrition**

❖ **Developmental assessment**

Investigations:

Chest x- ray –Echocardiography- CBC- C Reactive Protein (CRP)- Liver Function Tests (LFT)- Kidney Function Tests (KFT)- Serum electrolytes- Arterial blood gases- Serum insulin like growth factor 1 (S.IGF1) by ELISA technique.

Statistical Methods:

We use SPSS program version 15 for data analysis and interpretation .according to categorical data we use Chi square (χ^2) test .for comparison of the quantitative variables between the groups, we use kruskal wallis analysis (ANOVA) with Mann Whitney U test .according to (p value) we consider P value more than 0.05 statistically insignificant while P value less than 0.05 is statistically significant.

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RESULTS

Studying the demographic data as shown in **table1,** it is demonstrated that is there was non-significant difference between the studied groups as regarding age of babies and sex, with mean age of control group of 16.3 ± 4.95, while the mean age of the CHD group is 15.9 ± 3.49 .

Table 1: Studying of demographic data in between the studied groups:

Variable	Control group (n=30)		CHD group (n=30)		t-test	P value
Age: (months):						
Mean ± SD Range	16.3 ± 4.95 5 – 24		15.9 ± 3.49 4 - 24		0.362	0.719 (NS)
	No.	**%**	**No.**	**%**	**χ^2**	**P value**
Sex:						
Female Male	16 14	53.4 46.7	14 16	46.7 53.3	0.266	0.605 (NS)

Table 2: Studying of nutritional history of the studied groups:

Variable	Control group (n=30)		CHD group (n=30)		t-test	P value
Age of weaning:						
Mean ± SD Range	5 ± 0.92 4 - 6		5.23 ± 0.97 4 - 7		-0.794	0.432 (NS)
	No.	**%**	**No.**	**%**	**χ^2**	**P value**
Feeding:						
Artificial: Breast: Mixed:	4 20 6	13.3 66.7 20	13 11 6	43.3 36.7 20	7.613	0.055 (NS)

According to the dietary history of the examined group, the **table2** demonstrates the characteristics of the nutrition. As indicated by control group the mean age of weaning is 5±0, 92 with about 20 of 30 children had breast feeding while 4 children had artificial feeding.in CHD group the mean age of weaning is 5.23±0.97 with about 13 of 30 had artificial feeding and about 11 had breast feeding. The table shows that there was non-significant difference between the studied groups as regarding age of weaning and feeding pattern.

Table 3: Nutritional status of the studied groups:

Variable	Acyanotic group (n=15)		Cyanotic group (n=15)		χ^2	p-value
	No.	**%**	**No.**	**%**		
Nutritional status:						
Normal: Malnutrition:	4 11	26.7 73.3	1 14	6.7 93.3	2.16	0.141 (NS)
Pattern of malnutrition:						
Under nutrition: Wasting: Stunting:	2 1 8	18.2 9.1 72.7	2 5 7	14.3 35.7 50	2.408	0.300 (NS)
Degree:						
Moderate: Severe:	8 3	72.7 27.3	3 11	21.4 78.6	6.57	0.01 (S)

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Table3 demonstrates that there was no statistical significant difference between the studied groups as regarding nutritional status. Malnutrition was observed to be non-significantly higher in Cyanotic group when compared to the acyanotic group (93.3% versus 73.3% respectively).Also, the difference was non-significant between them as regarding pattern of malnutrition. Severe malnutrition was found to be significantly higher in Cyanotic group than in acyanotic group (78.6% versus 27.3% respectively).

Table 4: Studying of IL-GF 1 of the studied groups:

Variable	Control group (n=30)	Acyanotic CHD (n=15)	Cyanotic CHD (n=15)	F	p	LSD
IL-GF1:(pg/ml)						
Mean ± SD Range	2806.7±690 2000 – 4000	1633.3± 675.1 600 – 2800	965± 336.5 250 –1400	48.91	<0.001 (HS)	<0.05 [1] <0.05 [2] <0.05 [3]

IL-GF1 is measured in all the studied groups to detect the relation between its levels and growth abnormalities and physical differences in studied groups .**table 4** This table shows that growth factor was significantly lower in cyanotic group than in control and acyanotic groups (965, 2806.7 and 1633.3 respectively).**table 5** shows that cutoff pointof IL-GF1 of less than or equal to 2087 can be used as a predictor for delayed growth with sensitvity of 86.7%, specificity of 90%, PVP of 100% and PVN of 91.7%.(**figure1**)

Table 5: Performance of IL-GF1 level as a predictor of delayed growth among the studied groups:

Cutoff point	AUC	Sens.	Spec.	PVP	PVN	accuracy	P value
≤ 2087	0.936	86.7%	90%	100%	81.8%	91.7%	<0.001

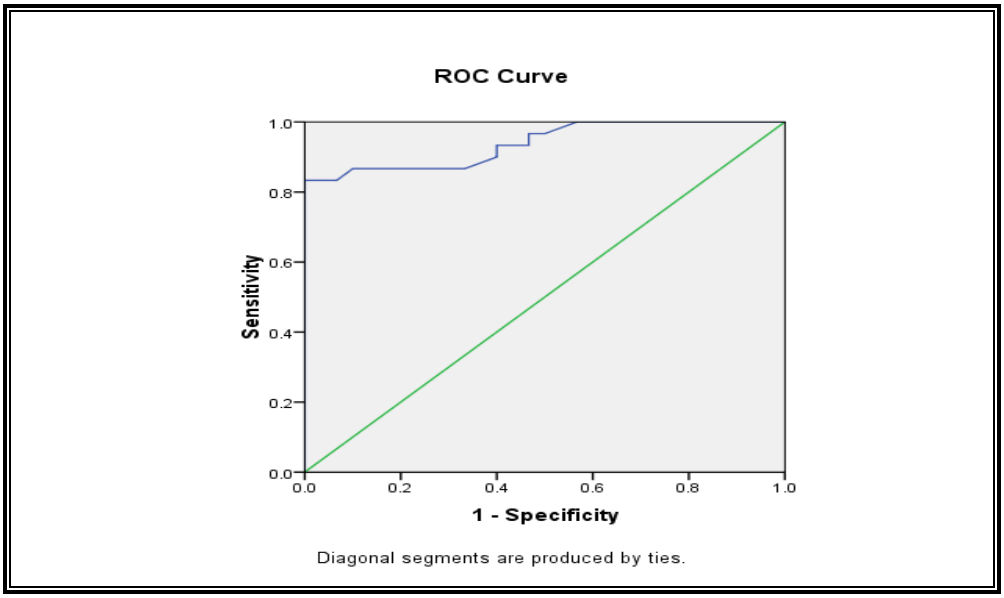

Fig 1: Performance of IL-GF1 level as a predictor of delayed growth among the studied groups

DISCUSION

Our study was directed on 30 patients with congenital heart disease Group (I) diagnosed at the pediatric cardiology unit in zagazig University hospital, their age ranged from 2 months to 2 years old. Thirty sex and age matched healthy infants and children constituted as control group Group (II). Group I was furtherly subdivided into Group (Ia) 15 Acyanotic patients (8 males and 7 females) and Group (Ib) 15 Cyanotic

patients (7 males and 8 females). In the present study, the outcomes revealed statistically non-significant difference between the mean age of controls (16.3±4.95 months) and that of the congenital heart disease, patients indicating good matching between the studied groups denoting that this group of children is appropiate for being control to our patient group for comparative purpose. Considering the gender, the difference between groups I, group II and was statistically non-significant (P**>** 0.05). [6] and [7]in agreement with our study reported that there is no significant statistical difference regarding the sex in their group of children with CHD.

Comparing the weight affection to height in congenital heart disease patients, both cyanotic and acyanotic groups were stunted and under weight as compared to controls but height was more affected in cyanotic group. This is in concurrence with (**Hallioglu et al., 2003)**[8] who found a statistically significant difference in weight between cyanotic, acyanotic and control groups. Also we agree with (**Jacobs et al., 2000)** [9]who expressed that acyanotic infants were markedly underweight with less affection of the linear growth while cyanotic infants showed equally impaired length and weight.

The present study reports a very highpredominance of malnutrition in our CHD patients, in particular, severe forms of wasting and stunting. Overall, the prevalence of CHD-related malnutrition was 83.3%, with 68% of cases having severe malnutrition and 32% had moderate undernutrition. Among cases, the relative proportions of wasting, stunting and underweight were 24%, 60% and 16%, respectively. Contrary to the usual distribution of growth deficiency in the general pediatric population according to WHO reports, stunting was the most prevalent type of malnutrition in our study, rather than underweight and wasting (**de Onis etal., 1997)**[10] (**WHO Multicentre Growth Reference Study Group, 2006)**[11]**.**

Our present work showed that serum level of IGF-1 was statistically significantly lower in the group of CHD patients compared to serum IGF-1 level of the controls (P<0.001), cyanotic group had less serum IGF-1 concentration than acyanotic group. Our results are in accordance with (**Barton et al., 1996)**[7] who similarly found that infants with CHD had lower IGF-1 levels than controls and (**Bernstein et al., 1992)** who demonstrated that serum IGF-1 level was decreased by almost half in experimental models with chronic hypoxemia secondary to CHD, also (**Tsung- Po Tsai., 2010)**[12] revealed that serum IGF-1 concentration was reduced in infants with isolated VSD versus normal age – matched control infants.

CONCLUSION

We determined that the most important factor on serum IGF-1 levels is cyanosis for this reason we believe that chronic hypoxia plays a significant role in the pathogenesis of growth failure.

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