INSULIN LIKE GROWTH FACTOR 1 IN CONGENITAL HEART DISEASES

By

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ABSTRACT

Background: *Congenital heart disease (CHD) is the most common cause of major congenital anomalies. Malnutrition is a constant phenomenon among children with congenital heart disease, irrespective of the nature of the cardiac defect and the presence or not of cyanosis. Many factors may influence growth failure in C.H.D. like feeding disorders, inadequate caloric intake and endocrine factors.*

Objectives: *The aim of this work was to evaluate insulin like growth factor 1 in children with congenital heart diseases as possible cause of growth affection.*

Patients and Methods: *After obtaining the approval of the Al-Azhar University Ethical Committee, A cross-sectional study was conducted on sixty children (32 males and 28 females). The study was carried out in Al-Azhar University Hospitals (AL- Hussein &Sayed Galal Hospitals), during the period from January 2017 to May 2019. All patients gave their written informed consents prior to their inclusion in the study. Sixty children divided into 3 groups (control, cyanotic & acyanotic). A blood sample was taken from each participant with the aim of assessment of IGF1. Also Echocardiography, Chest x ray, Electrocardiography had done, Anthropometric measures & Oxygen saturation were measured.*

Results: *we found highly statistical significant (p-value < 0.001) decrease in the level of IGF1 between studied groups. There was no statistical significant difference (p1-value = 0.15) between cyanotic group and acyanotic group. Highly statistical significant difference (p2-value < 0.001) between cyanotic group and control group. Highly statistical significant (p3-value < 0.001) decrease between acyanotic group and control group. Also we found Highly statistical significant difference (p-value < 0.001) between studied groups as regard weight, B.M.I, SD weight for length and height (p-value=0.001).*

Conclusion: *We determined that IGF1 was low in children with congenital heart diseases. It was lower in malnourished more than well nourished, and was also lower in cyanotic more than acyanotic. As when caloric restriction is present, mammals synthesize less IGF-1 and its synthesis in the liver is refractory to GH stimulation*

Key Words: *IGF1, Congenital heart diseases.*

INTRODUCTION

Congenital heart disease (CHD) is the most common cause of major congenital anomalies, representing a major global health problem. Congenital Heart Diseases (CHD) are the most prevalent malformations of neonatal period with an incidence of 0.4%-0.8% in all live births **(Akar et al., 2014)**.

In recent years, progress in the surgery for CHD has undeniably improved the outcome of the disease, which has considerably increased the life expectancy of patients; only a few decades ago, the overall mortality was 4 of every 5 infants, which decreased to less than 2 of every 5 in the last decade **(Azhar et al., 2015)**.

Twenty eight percent of all major congenital anomalies consist of heart defect. Despite remarkable progress in clinical care for affected individuals, CHD remains the leading cause of infant mortality among birth defects. For those that survive infancy, there is a high rate of comorbidities, both cardiac and extra cardiac **(Mita et al., 2017)**.

Poor growth is a common complication in infants with congenital heart disease Children with congenital heart disease are known to exhibit early and progressive falls in their growth trajectory compared to healthy children, with reductions in weight for age (WAZ)score, head circumference and length for age Z score **(Mitting et al., 2015)**.

Within weeks of birth, children with CHD show large, early, statistically significant deficits in weight, length, and HC trajectory compared with matched controls without CHD from the same primary care network. The largest differences in weight occurred at 4 months of age **(Daymont et al., 2013)**.

Failure to observe catch-up growth is presumed to be multi-dimensional and involving multiple patient-related and surgery related factors but so far remains largely uninvestigated **(Li et al., 2019)**.

IGF1 conforms a large protein of 70 amino acids with several structural and functional domains. This pleiotropic hormone possesses endocrine, paracrine, and autocrine effects **(Aguirre et al., 2018)**.

It is known that GH and nutrition are the major factors that regulate hepatic IGF-1 expression, as well as in other organs However, in some other tissues;

IGF-1 expression appears to be regulated by tissue-specific trophic factors. For example, in uterus, oestrogens stimulate IGF-1 expression instead of the GH **(Martín-Estal et al., 2015)**.

Aims of the Study

Assessment of IGF1 in children with congenital heart diseases as possible cause of growth failure.

PATIENTS AND METHODS

This study is acase control study which conducted at the pediatric department of Al_azhar faculty of medicine. The study was carried out on sixty children (32 males and 28 females with mean age 12.12 ± 9.02 months). They were enrolled from Al_azhar faculty of medicine university hospitals (Al-Hussein and Sayed Galal).

Period of study:

From January 2017 to May 2019.They were classified into 3 groups: (**Group I:** the thirty healthy children as acontrol group, **Group II:** 15 case with congenital acyanotic heart diseases, **GroupIII:** 15 cases with congenital cyanotic heart diseases).

Inclusion criteria:

Childern who has congenital cardiac problems from 2 months to 3 years old.

Exclusion criteria:

Any associated systemic congenital anomalies like (metabolic disorder, Genetic syndrome), Children with chronic infections and Prematurity.

Ethical consideration:

1. Approval from the ethical committees of both pediatric department and Faculty of Medicine Al-Azhar University.
2. Written consent for the study was obtained from the parents of these neonates participating in this study.
3. The data of the patients and the results of the study are confidential and the patients have the right to keep them.
4. The authors received no financial support for the study or the publication.
5. The patients have the right to withdraw from the study at any time.
6. The authors declared that there is no conflict of interest regarding the study and publication.

Methods:

All patient will be subjected to the following:

• Demographic characteristics will be recorded.

• History:

Full history taking with special emphasis on the presence or absence of cyanosis, hospital admission if present, recurrent chest infection, symptoms of heart failure, drug history, feeding habits, caloric intake and presence or absence of complications.

• Examination:

- Thorough physical examination with special emphasis on physical appearance and Stressing on vital data, signs of respiratory distress, clinical evidence of cardiomegaly and audible murmurs and its characters.
- Anthropometric measures (weight, height, BMI,HC).

The study groups were classified to well-nourished and undernourished, if the weight for length Z score was ≥ −3 z score or worse it was classified as severe malnutrition, if the weight for length Z score was −2.0 to -2.99 z score it was classified as moderate malnutrition and if it was −1.0 to −1.99 z score it was considered mild malnutrition.

We classify studied group according to waterlaw to stunted, wasting and combined wasted and stunted.

• Investigation:

- Oxygen saturation by pulse oximeter.
- Electrocardiography: Standard 12-leads electrocardiography will be done for all patients for evaluation of chamber hypertrophy & Axis deviation.
- Chest x ray: Commenting on cardiothoracic ratio and lung vascularity.
- Echocardiography :

Preparation: oral chloral hydrate was used to sedate the children and some cooperative patients did not need sedation.

Position: All patients were examined in the supine position.

Machine: Philips EPIQ7 ultrasound system with X5-1, S8-3, or X7-2 broadband phased-array transducers, depending on the age of the patient.

Views: We examined the heart from different views subcostal, apical, Parasternal and suprasternal and also by different modes (M mode, 2 dimensional, pulsed continues and color flow mapping.

- Lab investigations: C.B.C. and IGF1 which was assessed by ELISA technique.

• Statistical analysis:

All results were expressed as the mean ± stander deviation (SD). Qualitative data were expressed as frequency and percentage.

Statistical analysis was performed using statistical package for the social science for windows (SPSS, Version16, 0, Chicago, IL, USA). The data were analyzed by one-way analysis of variance (ANOVA). To compare the difference among the group; post-hoc testing was performed by the least significant difference (LSD) test. Pearson's correlation test was used for correlating parametric variables. Chi-square test: was used when comparing between non-parametric data. The P-value less than 0.05 were considered statistically significant.

RESULTS

Table (1) General characteristics of studied groups

	Cyanotic group No =15	Acyanotic group No =15	Control No =30	ANOVA X^2	p-value
Age (months): Mean ± SD Range	**10.06 ± 9.6 (2-36)**	**14.0 ± 7.8 (3-30)**	**12.2 ± 9.4 (2-36)**	**F = 0.7**	**P = 0.49**
Sex: Male Female	**8 (53.3%) 7 (46.7%)**	**10 (66.7%) 5 (33.3%)**	**14(46.7%) 16(53.3%)**	**X^2 = 1.6**	**0.447**

p-value < 0.05 is considered significant.
p-value < 0.001 is considered highly significant.

This table shows no statistical significant difference (p-value > 0.05) between studied groups as regard general characters (age and sex).

Table (2) Anthropometric measures of studied groups

Anthropometric measures	Cyanotic group No =15	A cyanotic group No =15	Control No =30	ANOVA	p-value
Weight (Kg) Mean ± SD	5.38±2.19	8.47±2.20	9.65±2.8	F = 14.4	P < 0.001
Height (Cm) Mean ± SD	62.1±8.9	74.67±8.36	73.9±11.07	F = 8.2	P = 0.001
SD(W/L) Mean ± SD	-2.07±1.33	-1.5±1.47	.5±1.27	F = 22.5	P < 0.001
BMI (Kg/m²) Mean ± SD	14.15±3.83	14.83±1.4	17.37±1.63	F = 11.7	P < 0.001
H.C. Mean ± SD	43.67±4.3	43.77±3.09	44.38±3.47	F = 0.27	P = 0.76

The previous table shows: Highly statistical significant difference (p-value < 0.001) between studied groups as regard weight, B.M.I, SD weight for length and height (p-value=0.001).

Table (3) Nutritional status of studied groups

Nutritional status	Cyanotic group No =15	Acyanotic group No =15	Control No =30	X^2	p-value
Malnourished	11(73.3%)	8 (53.3%)	4 (13.3%)	17.13	0.0001
Well nourished	4 (26.7%)	7 (46.7%)	26 (86.7%)		

This table shows highly statistical significant difference (p-value < 0.001) between studied groups as regard nutritional status.

Table (4) types of undernutrition according to waterlow of patients groups

Types	Acyanotic (n=8)		Cyanotic (n=11)		X^2	p-value
Stunted	2	25%	2	18.2%	11.4	0.003 S
Wasting	6	75%	1	9.1%		
Stunted and wasting	0	0%	8	72.7%		

X2: Chi-square test, S: p-value < 0.05 is significant.

This table shows statistically significant difference (p-value < 0.05) between cyanotic group and acyanotic group as regard under-nutrition according to waterlow.

Table (5) level of Insulin like growth factor 1 in the studied groups

	Cyanotic group No =15	Acyanotic group No =15	Control No =30	ANOVA	p-value
IGF1 (ng/ml) Mean ± SD	17.4±4.53	27.2±7.27	70.6±25.01	F = 53.02	P < 0.001
IGF in malnourished	16.91±4.79	22 ± 4.96	45.25 ± 20	F = 23.6	P < 0.001
IGF in well nourished	18.75±4.1	33.14 ± 4.2	74.4± 23.6	F = 62.8	P < 0.001

This table shows highly statistical significant difference (p-value < 0.001) between studied groups as regard IGF and highly statistical significant difference (p-value < 0.001) between studied groups as regard IGF-1 in both malnourished and well-nourished.

Figure (1): comparison between studied groups as regard IGF-1

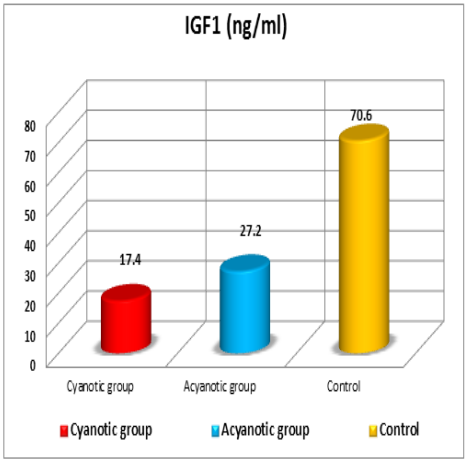

Figure (2): comparison between studied groups as regard nutritional status.

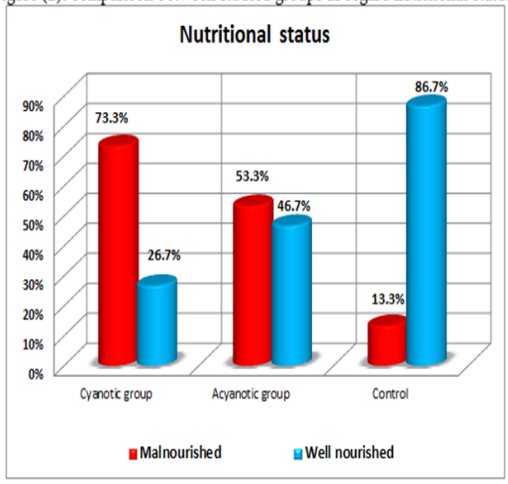

Table (6) SPO2 of studied groups:

	Cyanotic group No =15	Acyanotic group No =15	Control No =30	ANOVA	p-value
SPO2 Mean ± SD	79.2±4.26	94.9±1.49	94.16±1.9	F = 168.4	P < 0.001

This table shows highly statistical significant difference (p-value < 0.001) between studied groups as regard SPO2, No statistical significant difference (p1-value = 0.358) between acyanotic group and control group.

Table (7) ventricular function in studied groups by ECHO

	Cyanotic group No =15	Acyanotic group No =15	Control No =30	ANOVA	p-value
E.F. Mean ± SD	64.2±10.7%	69.17±6.3%	71.06±7.7%	F = 3.4	P = 0.04
F.S. Mean ± SD	38.15±5.47%	40.4±5.92%	42.98±2.78%	F = 5.9	P = 0.004

The previous table shows statistically significant difference (p-value = 0.04) between studied groups as regard Ejection Fraction and Statistically significant difference (p-value = 0.004) between studied groups as regard Functional shortening.

Table (8): Correlation study between IGF-1 and other studied parameters in studied group

Cyanotic group			Acyanotic group			Control group		
	r	p		r	p		**r**	p
Age	0.29	0.29	**age**	**0.52**	**0.046**	**age**	**0.59**	**0.001**
Weight	0.34	0.22	**Weight**	**0.75**	**0.001**	**Weight**	**0.71**	**< 0.001**
Length	0.23	0.41	**Length**	**0.55**	**0.035**	**Length**	**0.58**	**0.001**
BMI	0.45	0.10	**BMI**	**0.82**	**< 0.001**	**BMI**	0.35	0.059
SD	**0.54**	**0.04**	**SD**	**0.90**	**< 0.001**	**SD**	**0.46**	**0.010**
HC	0.30	0.28	**HC**	0.51	0.05	**HC**	**0.53**	**0.003**
EF	- 0.04	0.89	**EF**	0.089	0.751	**EF**	0.036	0.849
FS	0.11	0.69	**FS**	- 0.05	0.85	**FS**	- 0.13	0.487
SPO2	0.04	0.88	**SPO2**	0.061	0.830	**SPO2**	- 0.08	0.68

(r): Pearson correlation coefficient.

In cyanotic group there was: Statistically significant (p-value = 0.04) Positive correlation (r = 0.54) between IGF1 and SD (W/L).

In acyanotic group there were: Statistically significant (p-value < 0.05) Positive correlation between (IGF1 and age), (IGF1 and weight) and (IGF1 and length) and highly statistical significant (p-value < 0.001) Positive correlation between (IGF1 and BMI) and (IGF1 and SD).

In control group there were: Statistically significant (p-value < 0.05) Positive correlation between (IGF1 and age), (IGF1 and length), (IGF1 and SD) and (IGF1 and H.C). And highly statistical significant (p-value < 0.001) Positive correlation between (IGF1 and weight).

DISCUSSION

In this study we measure IGF-1 in congenital heart disease as a possible cause of growth retardation in comparison to control group with no CHD.

As regard to demographic data the result showed that patient and control groups were chosen of the same age and sex with no significant statistical difference.

Comparison between patients with congenital heart diseases and control group regarding growth parameters showed that there was highly significant lower weight, BMI and SD Weight for length (p<0.001), significant lower length (p=.001) and HC were no significant difference in measurements.

This was agreement with Egyptian study **(Hassan et al., 2015)** who reported that all anthropometrics measurement including (weight, height, BMI,) were significantly statistical difference but against our result in HC which they reported it's significantly lower in CHD.

In **(Le Roy et al., 2017)** study at Chile reported A quarter of the studied children had short stature; this number is very higher than the one registered in Chilean children that assist to the public health network (2%), but it is quite similar to international publications of children with CHD.

While in **Chung et al., (2017)** reported that weight and length in children with pulmonary hypertension and tetralogy of fallot were significantly lower than control, and there's significant difference at the weight during 3 to 6 months after corrective surgery of pulmonary hypertension.

In **El-Koofy et al., (2017)** study report that regarding the anthropometric data, nutritional assessment were significantly improved after nutritional interventions by increasing calories and micronutrients.

In our study malnutrition among patients was 63.3% well-nourished was 36.7% and in control group 13.3% malnourished and well-nourished was 86.7, the percent of mal nutrition among cyanotic was 73.3% and well nutrition was 26.7%, and in acyanotic mal nutrition was 53.3% and well nutrition was 46.7%.

This was agreement with **(Hassan, B.A et al., 2015)** prevalence of malnutrition reached 84.0% in cases compared to 20% for the control group. Moreover 71.4% of cases had severe malnutrition.

In contrast to our result, In **(Chowdhury F. et al., 2018)** comparison between cyanotic and acyanotic showed that malnutrition among cyanotic 43.3% and well-nourished 56.7% while in acyanotic malnutrition 76.7% and well-nourished 23.33%.

Several possible studies report improvement of growth velocity after corrective cardiac surgery especially if it became early corrective as reported by **(Martins et al., 2016)** report that Early surgical repair of VSD leads to a significant acceleration of growth within 3 to 6 months after surgery, for both term and preterm, and **(Carmona et al., 2012)** reported that Children submitted to Tetralogy of Fallot repair had pre-operative acute growth restriction and showed post-operative catch-up growth for weight and height.

In our study the pattern of malnutrition according to Waterlow prevalence of wasting among acyanotic congenital heart patients but prevalence of combined wasting and stunting in cyanotic congenital heart patients.

This was agreement with **(Chowdhury et al., 2018)** as they reported that wasting was common in acyanotic while combined stunted and wasting common in cyanotic.

Also this agreement with **(Okoromah et al., 2011)** as they reported that wasting was common in acyanotic while stunted was common in cyanotic

While in **(Pandey et al., 2019)** they reported that stunted common in both cyanotic and acyanotic.

Our result antagonist with **(Hassan et al., 2015)**.as they reported that stunted was common in acyanotic and wasting common in cyanotic patients.

Comparing between patients and control group regarding IGF-1 showed that was significant lower in patients groups. When comparing IGF1 as regarding nutritional state it also showed that it was significant lower in patients groups in both malnourished and well nourished.

This was in agreement with **(Chung et al., 2017)** reported that there was notably significant reduction of IGF-1 levels in both pulmonary hypertension and tetrolgy of fallot groups before corrective surgery, normalized 3–6 months after surgical correction of the heart defects.

Also in **(Eren et al., 2013)** study report that Insulin-like growth factor (IGF) 1 and its SDS were significantly lower among patients with CHD (p=0.010) in mean of IGF1and (p=0.047) in its SD comparing to control group.

Also this was in agreement with **(Shiva et al., 2013)** Mean IGF-1 was significantly different between groups (cyanotic, acyanotic and control) (p<0.001). Cyanotic CHD patients had significantly lower IGF-1 levels than acyanotic CHD patients (p=0.003) and healthy subjects (p<0.001).

Our result against **(Surmeli-Onay et al., 2011)** as they reported that serum IGF-1 levels were lower in the acyanotic group than the cyanotic and the control groups (p=0.22; p<0.01).

Also against our result in **(Shiva, S. et al., 2013)** the difference between acyanotic and healthy subjects in IGF-1 levels was not significant (p=0.53).

In our study comparison between studied groups as regard LVEF there was the cyanotic group had mean 64.2±10.7%, the acyanotic group had mean 69.17±6.3% and the control group had mean 71.06± 7.7%. There was statistically significant difference (p-value = 0.04) between studied groups as regard LVEF and no statistical significant difference (p1-value = 0.108) between cyanotic group and acyanotic group.

This was in agreement with **(shiva et al., 2013)** as they reported Mean left ventricle ejection fraction (LVEF) was %58.66±5.40 in cyanotic CHD, %58.86±6.81 in acyanotic CHD and 61.8±3.9 in control group (p=0.04). Control group had significantly higher LVEF than cyanotic (p=0.01) and acyanotic (p=0.04) group, but the difference between cyanotic and acyanotic groups was not significant (p=0.9).

In our study as regard FS statistically significant difference (p-value = 0.004) between studied groups but there was no significant correlation with level of IGF1. It against **(Wnuk et al., 2004)** as they reported a significant positive correlation between SF% and IGF- 1.

In our study there was highly statistical significant difference (p-value < 0.001) between studied groups as regard SPO2, no statistical significant difference (p-value = 0.358) between acyanotic group and control group. There was no significant correlation between SPO2 and level of IGF1.

This was agreement with **(Eren et al., 2013)** as they reported that there was no significant correlation between SPO2 and level of IGF1.

But this antagonist with **(Shiva et al., 2013)** as they reported There was significant positive correlation between IGF-1 and SO2 (r=0.45, p<0.001).

In our study we found significant positive correlation between level of IGF1 and SD weight for length in studied group, and significant positive correlation in acyanotic and control group between level of IGF1 and age, weight and length, also there was significant positive correlation between level of IGF1 and BMI in acyanotic group, lastly there was significant positive correlation between level of IGF1 and HC in control group.

This was agreement with **(Shiva et al., 2013)** as they reported significant positive correlation between IGF-1 and age (r=0.63, p<0.001), IGF-1 and BMI (r=0.40, p<0.001), IGF-1 and height (r=0.37, p<0.001) and IGF-1 and head circumference (r=0.44, p<0.001).

REFERENCES

1. **Aguirre, G.A., De Ita, J.R., De La Garza, R.G. and Castilla-Cortazar, I., (2016):** Insulin-like growth factor-1 deficiency and metabolic syndrome. Journal of translational medicine, 14(1), p.3.
2. **Aguirre, Gabriel A., José Luis González-Guerra, Luis Espinosa, and Inma Castilla-Cortazar. (2018):** "Insulin-like growth factor 1 in the cardiovascular system." In Reviews of Physiology, Biochemistry and Pharmacology, Vol. 175, pp. 1-45. Springer, Cham, 2018.
3. **Akar, Melek, et al. (2014):** "Variety of referral centers and diagnoses of congenital heart diseases that required intervention followed-up in neonatal intensive care unit: Regional Report." Anadulu Kardiyoloji Dergisi: AKD 14.1 (2014): 101.
4. **Azhar, A.S., AlShammasi, Z.H. and Higgi, R.E., (2016):** The impact of congenital heart diseases on the quality of life of patients and their families in Saudi Arabia: biological, psychological, and social dimensions. Saudi medical journal, 37(4), p.392.
5. **Carmona, F., Hatanaka, L.S.,**

Barbieri, M.A., Bettiol, H., Toffano, R.B., Monteiro, J.P., Manso, P.H. and Carlotti, A.P., (2012): Catch-up growth in children after repair of Tetralogy of Fallot. Cardiology in the Young, 22(5), pp.507-513.

6. **Chowdhury, F., Hoque, M., Ali, M.M. and Hossain, M.A., (2018):** Comparison of growth in children with cyanotic and acyanotic congenital heart disease in a tertiary care hospital. Journal of Bangladesh College of Physicians and Surgeons, 36(2), pp.64-69.

7. **Chung, H.T., Chang, Y.S., Liao, S.L. and Lai, S.H., (2017):** The effects of corrective surgery on endothelial biomarkers and anthropometric data in children with congenital heart disease. Journal of International Medical Research, 45(2), pp.493-503.

8. **Daymont, C., Neal, A., Prosnitz, A. and Cohen, M.S., (2013):** Growth in children with congenital heart disease. Pediatrics, 131(1), pp.e236-e242.

9. **El-Koofy, N., Mahmoud, A. M., & Fattouh, A. M. (2017):** Nutritional rehabilitation for children with congenital heart disease with left to right shunt. Turkish Journal of Pediatrics, 59(4).

10. **Eren, E., Cakir, E. D. P., Bostan, O., Saglam, H., & Tarim, O. (2013):** Evaluation of the endocrine functions in pediatric patients with cyanotic congenital heart disease. Biomedical Research, 24(2), 211-215.

11. **Hassan, B.A., Albanna, E.A., Morsy, S.M., Siam, A.G., Al Shafie, M.M., Elsaadany, H.F., Sherbiny, H.S., Shehab, M. and Grollmuss, O., (2015):** Nutritional status in children with un-operated congenital heart disease: an Egyptian center experience. Frontiers in pediatrics, 3, p.53.

12. **Le Roy, C., Larios, G., Springmüller, D. and Clavería, C., (2017):** Nutritional assessment in infants with congenital heart disease: comparison of two anthropometric classifications. Rev Chil Pediatr, 88(6), pp.744-750.

13. **Li, L., Kuanrong, L. I., An, C., Fan, J., Guo, C., Liang, S. ... & Hu, C. (2019):** Identification of risk factors affecting catch-up growth after infant congenital heart disease surgery: rationale and design of a multicentre prospective cohort study in China. BMJ Open, 9(8), e030084.

14. **Martín-Estal, I., de la Garza, R.G. and Castilla-Cortázar, I., (2016):** Intrauterine growth retardation (IUGR) as a novel condition of insulin-like growth factor-1 (IGF-1) deficiency. In Reviews of Physiology, Biochemistry and Pharmacology Vol. 170 (pp. 1-35). Springer, Cham.

15. **Martins, L.C., Lourenço, R., Cordeiro, S., Carvalho, N., Mendes, I., Loureiro, M., Patrício, M. and Anjos, R., (2016):** Catch-up growth in term and preterm infants after surgical closure of ventricular septal defect in the first year of life. European journal of pediatrics, 175(4), pp.573-579.

16. **Mita, S.A., Salim, M., Haque, M.A., Shahriar, A., Zakia, M.N.U., Salam, A.A., Rahman, A.R. and Jafar, A.H.M., (2017):** Comorbidities with Congenital Heart Disease among Hospitalized Children in a Specialized Cardiac Hospital in Bangladesh. Cardiovascular Journal, 9(2), pp.83-89.

17. **Mitting, R., Marino, L., Macrae, D., Shastri, N., Meyer, R. and Pathan, N., (2015):** Nutritional status and clinical outcome in postterm neonates undergoing surgery for congenital heart disease. Pediatric Critical Care Medicine, 16(5), pp.448-452.

18. **Okoromah, C.A., Ekure, E.N., Lesi, F.E., Okunowo, W.O., Tijani, B.O. and Okeiyi, J.C., (2011):** Prevalence, profile and predictors of malnutrition in children with congenital heart defects: a

case–control observational study. Archives of disease in childhood, 96(4), pp.354-360.

19. **Pandey, N. and Pooniya, V., (2019):** Clinico-epidemiologic profile of children with congenital heart disease in a tertiary care hospital in North India. Journal of Advanced Medical and Dental Sciences Research, 7(8), pp.92-95.

20. **Shiva, S., Samadi, M., Shateri, M.M. and Habibzadeh, A., (2013):** Growth parameters and insulin like growth factor-1: Comparison between cyanotic and acyanotic congenital heart disease and normal children. Life Sci J, 10, pp.577-80.

21. **Surmeli-Onay, O., Cindik, N., Kinik, S.T., Ozkan, S., Bayraktar, N. and Tokel, K., (2011):** The effect of corrective surgery on serum IGF-1, IGFBP-3 levels and growth in children with congenital heart disease. Journal of Pediatric Endocrinology and Metabolism, 24(1-2), pp.483-487.

22. **Wnuk, W., Hnatyszyn, G., Konefał, H., Dawid, G., Czeszyńska, M.B., Pankiewicz, E. and Horodnicka-Józwa, A., (2004):** Cord blood leptin, insulin, C-peptide, IGF-1 and IGF-2 levels in relation to echocardiographic measurements in infants of diabetic mothers: preliminary report. Medical Science Monitor, 10(2), pp.28-32.

مؤثر النمو 1 الشبيه بالانسولين فى امراض القلب الخلقية

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قسم طب الأطفال وحديثى الولادة, قسم الباثولوجيا الإكلينيكية, كلية الطب, جامعة الأزهر

تعد أمراض القلب الخلقية هي السبب الأكثر شيوعا للتشوهات الخلقية والتي تمثل مشكلة صحية عالمية كبرى. لذلك فأن أمراض القلب الخلقية هي التشوهات الأكثر شيوعًا في المواليد بنسبة 0.4 ٪ -0.8 ٪ في جميع المواليد الأحياء و لا تزال أمراض القلب الخلقية هي السبب الرئيسي لوفيات الرضع بين العيوب الخلقية. بالنسبة لأولئك الذين بقوا على قيد الحياة في سن الطفولة ، هناك نسبة عالية من الأمراض المصاحبة ، سواء في القلب أو خارجه.

يعد ضعف النمو هو أحد المضاعفات الشائعة عند هؤلاء الأطفال فهم يعانون من التأخر المبكر والتدريجي في مسار النمو مقارنة مع الأطفال الأصحاء ، مع انخفاض في الوزن ل العمر وكذلك الطول.

هذا الضعف فى النمو وكذلك الإخفاق فى رجوع معدلات النمو بسبب عديد من العوامل ولا تزال حتى الآن تحتاج إلى المزيد من البحث.

هرمون النمو ووسيطه ، عامل النمو الشبيه بالانسولين1 مهم بشكل أساسي للنمو في الأطفال سواء كان لديهم مرض القلب الخلقي أم لا وتشير الدلائل الناشئة إلى أن مسار هرمون النمو/ معامل النمو الشبيه بالأنسولين 1 قد يكون غير طبيعي في الأطفال الذين يعانون من أمراض القلب الخلقية.

الهدف من الدراسة:

تقييم عامل النمو الشبيه بالانسولين1 في الأطفال الذين يعانون من أمراض القلب الخلقية كسبب محتمل لفشل النمو.

خطوات الدراسة:

هذه الدراسة هي دراسة أجريت في قسم طب الأطفال بكلية الطب بنين القاهرة جامعة الازهر, وقد أجريت الدراسة على ستين طفلاً (32 ذكور) و 28 أنثى مع متوسط عمر (12.12 ± 9.02 شهر). تم تسجيلهم من كلا من مستشفى الحسين الجامعي وسيد جلال الجامعى وقد كانت فترة الدراسة من يناير 2017 إلى مايو 2019, وتم تصنيفهم إلى 3 مجموعات (الأولى ثلاثون طفلاً يتمتعون بصحة جيدة كمجموعة مراقبة, والثانية 15 حالة أمراض قلب خلقية غير مصاحبة بزرقة ، وأما الثالثة فتتكون من 15 حالة لديهم أمراض قلب خلقية مصحوبة بزرقة.

معايير الاشتمال: الأطفال الذين يعانون من مشاكل قلبية خلقية من شهرين إلى 3 سنوات.

معـــايير الاســـتبعاد: إذا وجـــد أي تشـــوهات خلقيـــة أخـــري مثـــل خلـــل بالتمثيل الغذائي أو متلازمة وراثية أوالخداج.

وقـــد تـــم أخـــذ موافقـــة مـــن اللجـــان الأخلاقيـــة لكـــل مـــن قســـم الأطفال وكلية الطب جامعة الأزهر.

وقد أجري لكل مشارك الأتى:

تســـــجيل الخصـــــائص الديموغرافيـــــة مـــــن ناحيـــــة النـــــوع والعمـــر , أخـــذ التـــاريخ المرضـــي خاصـــة حـــدوث زرقـــة مـــن عدمـــه , الفحـــص البـــدنى الشـــامل والتأكيـــد علـــى البيانـــات الحيويـــة وعلامـــات الضـــائقة التنفســـية , وســـماع اصـــوات القلـــب ووجـــود لغـــط ام لا بالســـماعة الطبيـــة , وتـــم كـــذلك أخـــذ القياســـات البشـــرية (الـــوزن ، الطـــول ، مؤشـــر كتلـــة الجســـم , ومحـــيط الـــرأس) وتـــم تحديـــد اذا مـــا كـــان المشـــارك يعـــانى مـــن ســـؤ التغذيـــة أم لا , واذا كـــان لديـــه ســـؤ تغذيـــة تـــم تحديـــد درجتهـــا (شـــديدة , متوســـطة أم بســـيطة) وكـــذلك تـــم تقســـيمهم طبقـــا لقاعـــدة –واترلـــو- إلـــى يعـــانى مـــن هـــزال ام تقـــزم ام كلاهما.

كـــذلك تـــم قيـــاس نســـبة تشـــبع الأكســـجين بالـــدم عـــن طريـــق الجلد و تم عمل رسم قلب و أشعة سينية للصدر.

كـــذلك قـــد تـــم فحـــص القلـــب عـــن طريـــق الموجـــات فـــوق الصـــوتية باســـتخدام جهـــاز EPIQ7 مـــن Philips مـــع نطـــاق موجة عرضية X5-1 أو S8-3 أوX7-2.

المشـــاهدات: درســنا القلــب مــن أمــاكن مختلفــة مثــل منطقــة التقــاء الاضــلع الصــدرية الســفلية و فــوق القــص ، القمــي ، و المجــاور للقــص وأيضــا مــن خــلال أوضــاع مختلفــة (وضــع أم ، ثنــائي الأبعاد وغيره).

وتــم ســحب عينــات مــن الــدم لإجــراء تحاليــل مختبريــة مثــل صــورة الــدم الكاملــة وقيــاس نســبة معامــل النمــو 1 الشــبيه بالإنسولين.

وقــد بينــت هــذه الدراســة : أن نســبة ســؤ التغذيــة كانــت هــى الأعلــى فــى مجموعــة أمــراض القلــب الخلقيــة المصــاحبة بزرقــة حيــث بلغــت 73.3% , وتلتهــا مجموعــة أمــراض القلــب الخلقيــة الغيــر مصــحوبة بزرقــة بنســبة 53.3% , أمــا مجموعــة الــتحكم فقــد كانــت نســبة ســؤ التغذيــة قليلــة حيــث كانــت مــن الدرجــة البســيطة و بنسبة 13.3%.

أمــا عــن نســبة معامــل النمــو 1 الشــبيه بالإنســولين فقــد بينــت الدراســة أنــه أقــل فــى مجموعــات المرضــي بالنســبة لمجموعــة الــتحكم بفــرق ذو دلالــة إحصــائية كبيــرة , كمــا قــد بينــت أنــه أقــل فــى مجموعــة المرضــي المصــاحبين بزرقــة أقــل مــن المــرض ولكــن بفــرق لــيس ذو دلالــة إحصــائية , كــذلك قــد بينــت الدراســة أنــه أقــل فــى المرضــي المصــابون بســؤ تغذيــة عــن المرضــي غيــر المصــابين بســؤ تغذيــة , وقــد بينــت الدراســة انــه لا توجــد علاقــة ذات دلالــة إحصــائية بــين نســبة معامــل النمــو 1 الشــبيه بالإنســولين ونسبة تشبع الأكسجين بالدم.

الإستنتاج:

من هذه الدراسة يمكن استنتاج أن معامل النمو 1 الشبيه بالإنسولين نسبته منخفضة عند الأطفال المصابين بأمراض القلب الخلقية , هذا الإنخفاض موجود سواء كان هناك سؤ تغذية أم لا لكنه يكون أكثر إنخفاضا إذا كان هناك سؤ تغذية, كذلك يكون أكثر إنخفاضا في الأطفال المصابين بأمراض القلب الخلقية المصاحبة بزرقة.

التوصيات:

من هذه الدراسة يمكن أن نتوصل إلي بعض التوصيات أهمها هى قياس وتقييم معامل النمو 1 الشبيه بالإنسولين حيث أن انخفاضه يمكن أن يكون سببا محتملا لتأخر النمو فى الأطفال الذين يعانون من أمراض القلب الخلقية, احتمالية إجراء أبحاث مستقبلية عن تأثير إعطاء معامل النمو 1 الشبيه بالإنسولين لأطفال أمراض القلب الخلقية ويعانون من تأخر في النمو بهدف معالجة هذا التأخر.