EFFECT OF PULMONARY HYPERTENSION ON GROWTH OF CHILDREN WITH CONGENITAL HEART DISEASE IN FAYOUM GOVERNORATE

By

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ABSTRACT

Background: *The aim of this study is to determine how Congenital Heart Disease as a whole and its related complication named pulmonary hypertension affect children's growth.*

Patients and Methods: *This is an analytical case-control study included 100 healthy controls and 106 children with Congenital Heart Disease (40 cyanotic & 66 Acyanotic). Their ages are ranging from 1 month to 10 years. They were selected from the Fayoum University Children's hospital during the period from May 2020 to November 2021 by simple random method. Echocardiographic evaluation was done. On Egyptian Growth Charts, we measured weight, height for children who were able to stand, or length for infants in a supine position along with their percentiles for age to assess growth. Body Mass Index (BMI) was calculated.*

Results: *The mean±SD weight of cyanotic patients was (8.66±4.1) kg, and Acyanotic patients was (8.63±4.5)kg and the mean±SD heights of both groups were (75.15±14.5) cm,(73.03±76.8) cm, respectively, which were significantly lower than control's mean weight (12.02±11.4) kg , and control's mean height (85.09±16) cm. Acyanotic patients complicated with pulmonary arterial hypertension (29 patients) had statistically significant higher rates of weight retardation and short stature with P-value 0.01 and 0.001 respectively, and by logistic regression analysis they were likely to develop weight retardation and short stature by 6.02 and 3.6 times, respectively, more than children without pulmonary hypertension.*

Conclusion: *The findings of the study confirmed that Congenital Heart Diseases had a detrimental impact on children's growth especially those complicated with pulmonary hypertension.*

Recommendation: *Continuous follow up of pulmonary arterial pressure in Acyanotic Congenital Heart Disease patients. Emphasis on nutritional supplementation with high caloric intake and low volume diet for patients with Congenital Heart Disease is*

considered. Early and rapid intervention for management of pulmonary hypertension to avoid complications is mandatory.

Keywords: *Congenital, Heart, Growth retardation, Pulmonary hypertension.*

INTRODUCTION

For more than a century, preventative child health programs have included growth monitoring in infancy and youth. Short stature or growth retardation is viewed as relatively early indicators of ill health. Except for malnutrition-related growth failure, which is obviously highly reliant on socioeconomic conditions, there are no signs that pathological causes of primary or secondary growth failure have a distinct incidence in various nations. Growth failure occurs everywhere in the globe **(Sahu et al., 2019)**.

A crucial component of pediatric follow-up is evaluating the growth of weight and height. Even when present alone, growth retardation may be the first sign of a chronic illness, thus it must always be looked in. Numerous chronic conditions may be to blame, but in most cases, identifying and treating the condition can lessen its negative effects on growth **(Delagrange and Édouard, 2022)**.

The reason of the child's development delay and the timing of therapy initiation will determine the child's outlook. If their illness is discovered and treated quickly, children could grow to be normal height or close to it. If they wait too late to begin therapy, they run a higher chance of developing low stature and other issues. They will stop growing after the growth plates at the ends of their bones have closed in young adulthood **(Karen and Holly, 2019)**.

Congenital heart diseases (CHD) are a group of heart structural abnormalities that occur during pregnancy and may be diagnosed in utero or after birth **(Gaskin and Kennedy, 2019)**.

Due to effort intolerance and increased caloric needs, the child cannot obtain the nutrients or calories he needs. Heart failure, loss of appetite, improper dietary intake due to effort intolerance brought on by tachypnea and fatigue, increased caloric intake, recurrent respiratory infections like pneumonia with frequent hospital admissions, malabsorption of nutrients from the digestive tract, and deoxygenated blood, known as hypoxia, in cases of cyanotic congenital heart defects are additional factors related to congenital heart disease and may

hinder children's growth **(Julien and Samuel, 2002)**.

One of the most dangerous side effects of CHD is pulmonary hypertension. Recent data from healthy subjects has shown that normal mean pulmonary arterial pressure (mPAP) was 14.0±3.3 mmHg. Two standard deviations above this mean value would suggest mPAP >20 mmHg as above the upper limit of normal (above the 97.5th percentile) **(Simonneau et al., 2019)**.

The assessment of child malnutrition, growth, and developmental retardation relies heavily on anthropometric measurements. The percentile correlations of length with age, weight with length, and weight with age are frequently used parameters **(Timothy, 2019)**.

The maximum growth pattern in infancy is represented by weight and length/height, which are two of the parameters that are used the most frequently in our clinical work. Malnutrition was evidently common in children with CHD under the age of five. For these fragile children, it may be necessary to administer nutritional requirements such as low-volume, high-calorie diets **(Tabib et al., 2019)**.

Despite investments in the health system and a significant drop in infant mortality, one in five children in Egypt is affected by stunting, which is a serious public health issue. Wasting has dramatically grown since 2000. Wasting is at 8% and underweight is at 6%, respectively **(UNICEF. Child malnutrition, 2022)**.

AIM OF THE STUDY

The objective of the current study was to determine how much CHD as a whole and its related complication named pulmonary hypertension affect children's growth.

Ethical consideration:

1. The parents or guardians of the study participants gave written approval prior to their enrollment.
2. On March 15, 2020, the Fayoum University Faculty of Medicine's ethical committee approved this study with approval code (R108) at session (70).
3. The patient's carer is able to exit the study whenever they want.
4. The study's findings were kept confidential.
5. The authors of this study did not disclose any funding or conflicts of interest.
6. The study and publications received no funding.

Sample size calculation:

According to Epi Info 2000, the sample size was computed with a precision of (2%), a 95% confidence interval, and a sample size of 106 children with CHD and 100 healthy controls. In order to address issues with non-responses and missing data, the sample size was expanded by 10%. 85% of the study's power was used in the analysis. Convenient samples composed its sample type **(CDC Epi info V7.0.8.3)**.

PATIENTS AND METHODS

Study design:

This analytical case-control study was carried out at the Fayoum University Children's hospital, from May 2020 to November 2021.

Inclusion Criteria:

-Children with unrepaired CHD.

-Patients with CHD who performed minor palliative surgical procedures.

-Patients aged from 1 month to 10 years old.

-Both males and females patients.

Exclusion Criteria:

- Age below 1 month and above 10 years old.
- Patients with CHD who performed major total corrective surgical procedures.
- Patients with chromosomal abnormalities.
- Patients with fetal growth restriction, additional under-nutrition causes and endocrine disorders.

Methodology:

This study included 106 children with Congenital Heart Disease and 100 children apparently healthy cross matched regarding age and sex as a control. They were classified into 3 groups (group I, cyanotic CHD (40 patients), group II, Acyanotic CHD (66 patients), group III, control (100 children) with selected 29 cases complicated with pulmonary hypertension from Acyanotic group of congenital heart disease.

All the studied patients were subjected to:

I. Full history taking was done with stress on cardiac symptoms as effort intolerance, cyanosis, recurrent chest infections, failure to thrive, recurrent chocking.

II. A comprehensive clinical examination, with special attention paid to pallor, cyanosis, respiratory rate, heart rate, hepatomegaly, and other cardiac signs.

III. Each case underwent an ECG, chest x-ray, and

echocardiographic assessment done by a pediatric cardiologist to verify the diagnosis of congenital heart disease and assess the severity of pulmonary hypertension (including both cyanotic and acyanotic heart disease). M-mode, two-dimensional, and Doppler echocardiography were performed using a Vivid 3 phased array scanner in Norway with a 5 MHz transducer. The majority (65%) of patients performed cardiac catheterization.

IV. Cardiac clinical assessment of pulmonary hypertension performed in accordance with the most recent clinical classification of congenital heart disease-related pulmonary arterial hypertension (PAH). According to data from healthy subjects from the 6th WSPH (world symposium on pulmonary hypertension), the average mean pulmonary arterial pressure (mPAP) at rest is roughly 14.0±3.3 mmHg. The threshold for abnormal PAH is indicated by two standard deviations above this mean value which is, mPAP of greater than 20 mmHg (above the 97.5th percentile) **(Galiè et al., 2018)**.

Heart failure was clinically diagnosed in children, using the Ross heart failure classification, which represents the four stages of heart failure. **(Ross, 2012)** Due to changed hemodynamics, nearly three fourths of the subjects had varying degrees of heart failure (76%).

V. Growth assessment was done using Egyptian growth charts for:

a. The child's weight along with their percentiles to the nearest 10 grams while standing using the pediatric electronic scale (Seca model 727) had recorded, while for children who were unable to stand weight was taken into account on the baby weighing scale.

b. Height for children who were able to stand, or length for infants in a supine position, along with their percentiles for age had recorded. Children who were able to stand had their height measured with a stadio-meter to the nearest 0.5 cm; otherwise, an infant measuring board was used to measure length in a supine position.

c. Children's development was evaluated using the Egyptian Growth Charts, which employ percentiles for weight for age and height/length for age. For assessing growth retardation,

we use less than 5th percentile as a cut-off point, which was employed in this study. **(Egyptian Growth Charts, 2002)**.

d. Body Mass Index (BMI) was calculated.

Statistical Analysis:

For data analysis, SPSS software version 22 was used. Descriptive analysis used for qualitative data, in form of percentages and numbers. Arithmetic means and standard deviations used in quantitative data. Independent Student T-Test used to compare two independent groups of quantitative data, use the. Chi-square test was utilized in comparing qualitative data. Logistic regression test used to analyze categorical dependent and independent variables. A P-value of 0.05 was chosen as the cutoff for significance **(IBM SPSS statistics V22.0, 2021, Bland, 2022)**.

RESULTS

Table (1): Anthropometric measurements among studied cases

Variables	Minimum	Maximum	Mean	SD
Age (year)	1 month	10 years	1.92 years	2.04
Weight (kg)	2.5	28	9.68	4.7
Height (cm)	46	134	77.29	16.7
BMI (kg/m^2)	9.47	24.8	15.2	1.9

In cases, the mean±SD of age is 1.92± 2.04 years with a range between 1 month and 10 years. Males represent 51.6 % of cases while females represent 48.4%. The study group had a mean weight of (9.68± 4.7) kg, an average height of (77.29± 16.79) cm, and a mean body mass index (BMI) of (15.2 ±1.9) Kg/m2 as shown in **Table (1)**.

Table (2): Types of congenital heart disease among cases group

Variables	Cases group (n=106)	
	No.	**%**
Cyanotic CHD	**40**	**37.8%**
Tetralogy of Fallot	24	60%
Double outlet right ventricle	3	7.5%
D- transposition of great arteries	9	22.5%
Pulmonary atresia	1	2.5%
Tricuspid atresia	1	2.5%
Double inlet right ventricle	2	5%
Acyanotic CHD	**66**	**62.2%**
VSD	38	57.5%
ASD	6	9.1%
PDA	11	16.7%
ASD&PDA	5	7.6%
ASD&VSD	5	7.6%
VSD&ASD&PDA	1	1.5%

This table shows that the most common type of cyanotic congenital heart diseases was Tetralogy of Fallot (TOF), while isolated peri-membranous outlet ventricular septal defect (VSD) was the most common type of acyanotic congenital heart diseases among study group.

Table (3): Incidence of pulmonary hypertension among studied cases of Acyanotic group of CHD

Classification of Acyanotic group according to presence of pulmonary arterial hypertension (PAH) n=66		
Acyanotic CHD with PAH	29	43.9%
- Left to right correctable shunts	26	39.3%
- Eisenmenger syndrome	3	4.5%
Acyanotic CHD without PAH	37	56.1%

Selected 29 cases complicated with pulmonary hypertension from acyanotic group of congenital heart disease (3 cases of them having Eisenmenger syndrome, and 26 cases with left to right correctable shunts) is shown in **Table (3)**.

Table (4): Weight and height correlations in different study groups

Study group (n=206)	Weight (kg)		Height (cm)	
	Mean±SD	p-value	Mean±SD	p-value
Cyanotic CHD(n=40)	8.66 ± 4.1	**<0.001***	75.15±14.5	**<0.001***
Acyanotic CHD(n=66)	8.63± 4.5		73.03± 16.8	
Controls (n=100)	12.02±4.7		85.09±16	

This table shows statistical significant difference between cyanotic, acyantic and control groups regarding weight and height.

Table (5): Comparison between cases with pulmonary arterial hypertension (PAH) and cases without PAH regarding weight and height

Growth parameters	Weight			Height		
	Normal	underweight	p-value	Normal	Short stature	p-value
Acyanotic CHD						
Without PAH	30 (81.1%)	7 (18.9%)	**0.01***	31 (83.8%)	6 (16.2%)	**0.001***
With PAH	15 (51.7%)	**14 (48.3%)**		13 (44.8%)	**16 (55.2%)**	

This table shows significant increased incidence of underweight children and short stature in cases with PAH than in cases without PAH.

Table (6): The risk factors for growth retardation in patients with congenital heart disease using logistic regression analysis

Variables	B	SE	Sig.	OR	95%Confidence interval (CI)
Weight retardation					
Age	-	0.14	0.2	0.8	0.6-1.08
Pulmonary Hypertension	**1.3**	**0.6**	**0.02***	**3.6**	**1.18-10.9**
Short Stature					
Age	-	0.1	0.5	0.9	0.7-1.2
Pulmonary Hypertension	**1.8**	**0.6**	**0.002***	**6.02**	**1.9-19**

By using a multivariate logistic regression model to examine the explanatory power of various risk factors for growth retardation, study demonstrates that PAH has an OR = 3.6 for weight retardation and a p-value of 0.002 and an OR = 6.02 for short stature, both of which are statistically significant predictive effects for the incidence of growth retardation. This showed that individuals with PAH increased the incidence of weight retardation and short stature in children by 3.6 and 6.02 times, respectively as shown in **Table (6)**.

DISCUSSION

CHD clearly has a detrimental impact on children's growth. In fact, the current study is searching how pulmonary hypertension brought on by CHD affects children's growth. According to results of the current study, Acyanotic patients with PAH secondary to congenital heart disease showed higher rates of weight retardation and short stature.

Similarly, study showed that the prevalence of malnutrition in children with CHD aged under 5 years was noticeably high at a center in Iran. The administration of nutritional requirements such as low-volume and high-calorie diets should be considered for these vulnerable children. **(Tabib et al., 2019)** The goal of rehabilitation

for children with PAH must be to encourage weight gain and growth. This can be done by increasing oral intake, encouraging breastfeeding through health education of mothers, attempting to reduce feeding-related effort intolerance, meeting caloric needs, ensuring adequate oxygen supply while feeding, and increasing appetite, which may be suppressed by some medications **(Alvisi et al., 2015)**.

Numerous studies have examined the potential role of high-calorie formulas to meet the nutritional requirements necessary for healthy growth because infants with CHD have high energy expenditure and require fluid intake restriction as part of their management to prevent adverse clinical outcomes, including necrotizing enterocolitis and mortality. In comparison to standard formula (1.4 g/100 mL, 67 kcal/100 mL), the use of an energy-enriched formula or a protein-dense formula led to a quicker achievement of the nutritional objective with a higher rate of weight growth and higher levels of serum albumin and amino acids **(Argent et al., 2017)**.

The sole known adverse reaction was acute diarrhea, which was most likely brought on by the enriched formula's greater osmolarity. Consideration must be given to recommendations regarding calorie intake based on age and the recommended dietary allowance (RDA) tables **(Scheeffer et al., 2020)**.

In agreement to our study, a study was done in 2016 showed that particularly in those who have PAH linked to CHD, PAH was linked to stunted growth. Height for age could be used as an additional, globally accessible clinical measure to track patients' clinical conditions **(Ploegstra et al., 2016)**.

In the present study the percentage of males and females with congenital heart disease was nearly equal. The majority of studied group were unrepaired CHD patients who did not perform any total surgical corrections in spite of their wide range of age. This can be explained as only 10 (0.94%) patients older than 4 years, (three Eisenmenger syndrome cases, and seven patients had palliative surgical procedures while awaiting total surgical correction). The children under the age of 4 years old had mild or moderate CHD, making them either not candidates for surgical correction or added to the waiting list.

Contrarily, a 2015 Indian study that included CHDs in patients of all ages, from

newborns to adults, found that males were more likely than girls to be impacted by congenital heart disease **(Bhardwaj et al., 2015)**.

The current study found that Acyanotic CHDs were the most frequent than cyanotic group, and the most common type of cyanotic congenital heart diseases was Tetralogy of Fallot (TOF), while isolated peri-membranous outlet ventricular septal defect (VSD) was the most common type of acyanotic congenital heart diseases among study group.

In agreement, a study by Bhardwaj found that Acyanotic CHDs were more common than cyanotic CHDs. The most frequent isolated CHD was a ventricular septal defect (33%) followed by an atrial septal defect (19%). The most common CHD in cyanotic patients was TOF (16.8%) **(Bhardwaj et al., 2015)**.

LIMITATIONS

It is crucial to consider several limitations on our investigation. With a bigger sample size and multiple growth assessment methods, we could more precisely assess growth retardation.

CONCLUSIONS

The findings of the study confirmed that Congenital Heart Diseases had a detrimental impact on children's growth especially those complicated with pulmonary hypertension.

RECOMMENDATIONS

Continuous follow up of pulmonary arterial pressure in Acyanotic Congenital Heart Disease patients. Emphasis on nutritional supplementation with high caloric intake and low volume diet for patients with Congenital Heart Disease is considered. Early and rapid intervention for management of pulmonary hypertension to avoid complications is mandatory.

Author's Contributions:

H.H.S.: Create the idea, conceived the study, design; and shared in drafting, editing and revision of the manuscript.

A.Y.E.: Statistical analysis; and shared in drafting, editing and revision of the manuscript.

REFERENCES

1. **Alvisi P., Brusa S., Alboresi S., Amarri S., Bottau P., Cavagni G., et al. (2015):** Recommendations on complementary feeding for healthy, full-term infants.Ital J Pediatr.; 41: 36. http://doi.org/10.1186/s13052-015-0143-5.
2. **Argent AC., Balachandran R., Vaidyanathan B, Khan A. and Kumar R. K. (2017):** Management of undernutrition and failure to thrive in children with congenital heart disease in low-and middle-income countries. Cardiology in the Young.; 27(S6):S22-S30.

https://doi.org/10.1017/S104795111700258X.

3. **Bhardwaj R, Rai SK, Yadav AK, Lakhotia S, Agrawal D, Kumar A, et al. (2015):** Epidemiology of Congenital Heart Disease in I ndia. Congenital heart disease. 2015; 10(5):437-46.

4. **Bland M. (2022):** 4th ed. Oxford: Oxford University Press; 2015. An Introduction to Medical Statistics. [Google Scholar] https://doi.org/10.4103%2Fijcm.IJCM_255_17. Last access.

5. **CDC EPI INFO VERSION 7.0.8.3 READ ME FILE:** CDC Retrieved 2011-11-17. . https://www.cdc.gov/epiinfo/index.html.

6. **Delagrange, M., Édouard, T. (2022):** Le retard de croissance staturo-pondérale [Delayed growth in height and weight]. Soins. Pediatrie, puericulture. 43(327), 10–15. https://doi.org/10.1016/j.spp.2022.06.003.

7. **Egyptian Growth Charts. (2002):** Cairo University, Faculty of Medicine, Diabetic Endocrine and Metabolic Pediatric Unit and the National Research Center- Cairo, Egypt, in collaboration with Wright State University, school of Medicine, Department of Community Health Life span, Health Research Center.

8. **Galiè N, McLaughlin V, Rubin L, Simonneau G. (2018):** An overview of the 6th World Symposium on Pulmonary Hypertension. Euro Resp J; DOI: 10.1183/13993003.02148-. DOI: 10.1183/13993003.02148-2018.

9. **Gaskin, Kerry and Kennedy, F. (2019):** Care of Infants, Children and Adults with Congenital Heart Disease. Nursing Standard. 34 (8). pp. 37-42. ISSN 0029-6570 https://doi.org/10.7748/ns.2019.e11405.

10. **IBM SPSS statistics V22.0 (2021):** https://www.ibm.com/support/pages/spss-statistics-220-available-download. Last access May 2022.

11. **Julien I.E Hoffman, Samuel Kaplan. (2002):** The Incidence of Congenital Heart Disease. J Am Coll Cardio; 39(12): 1890-900. https://doi.org/10.1016/s0735-1097(02)01886-7.

12. **Karen Gill, Holly Mc Gurgan. (2019):** Updated on Understanding Delayed Growth and How It's Treated. Health line, January 10,. https://www.healthline.com/health/delayed-growth-symptom.

13. **Ploegstra MJ, Ivy DD, Wheeler JG, et al. (2016):** Growth in children with pulmonary arterial hypertension: a longitudinal retrospective multiregistry study. Lancet Respir Med. 4(4):281-90.https://doi.org/10.1016/S2213-2600(16)00069-2.

14. **Ross RD. (2012):** The Ross classification for heart failure in children after 25 years: a review and an age-stratified revision. Pediatric cardiology.; 33(8):1295-300.

15. **Sahu, S. K., Rajaa, S., Vijayageetha, M., Selvaraj, K., Sambath, P. M., & Roy, G. (2019):** Strengthening growth monitoring among under-5-year children to fight childhood undernutrition in India. Journal of family medicine and primary care. 8(1), 231–238.

https://doi.org/10.4103/jfmpc.jfmpc_225_18.

16. **Scheeffer, V.A., Ricachinevsky, C.P., Rodrigues, N., Tha, A., Salamon, F., Feij, F., et al. (2020):** Tolerability and Effects of the Use of Energy-Enriched Infant Formula After Congenital Heart Surgery: A Randomized Controlled Trial. JPEN J. Parenter Enter. Nutr. 44, 348–354.https://doi.org/10.1002/jpen.1530.

17. **Simonneau G, Montani D, Celermajer DS, Denton CP., Gatzoulis MA. , Krowka M, et al. (2019):** Haemodynamic definitions and updated clinical classification of pulmonary hypertension. European Respiratory Journal. ; 53(1). https://doi.org/10.1183/13993003.01913-2018.

18. **Tabib A, Aryafar M, Ghadrdoost B. (2019):** Prevalence of Malnutrition in Children with Congenital Heart Disease. J ComprPed.; 10(4):e84274. https://dx.doi.org/10.5812/compreped.84274.

19. **Timothy Sentongo. (2019):** A New Approach to Comprehensive Growth and Nutrition Assessment in Children.PediatrAnn. ;48(11):e425–e433 https://doi.org/10.3928/19382359-20191017-01.

20. **UNICEF. (2018):** Child malnutrition: unfolding the situation in Egypt .UNICEF Egypt data snapshot- issue 1. https://www.unicef.org/egypt/media/2686/file. Last access January 2022.