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# Assessment of Growth Differentiation Factor-15 in Egyptian Children with Congenital Heart Disease

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## Abstract

*Background:* Congenital heart disease (CHD) is the most common cause of congenital anomalies accounting for 8/1000 live birth. CHD can have a wide range of impacts on a child's health and well-being. Faltering growth is prevalent in up to 66% of children with CHD.

*Aim of Study:* This study aims to measure the serum level of growth differentiation factor-15 (GDF15) in children with congenital heart disease, evaluate the association between elevated serum level of GDF15 in children with CHD and faltering growth.

*Patients and Methods:* This was a cross-sectional study that was conducted at Children Hospital, Pediatric Cardiology unit, Ain Shams University from July 2023 to April 2024. Sixty children were selected 12 to 60 months of age with any congenital heart disease excluding those with syndromic abnormalities, other congenital anomalies, decompensated children with heart failure. All patients' cardiac diagnoses were made based on clinical and laboratory examinations, radiological methods, electrocardiography, and echocardiography. Anthropometric measures including weight, height, weight for age Z score, height for age Z score and body mass index were performed to all patients and serum level of GDF-15 was measured for each child.

*Results:* Our findings revealed that there was a statistically significant increase in GDF-15 level in patients with faltering growth than patients without faltering growth. Our ROC curve analysis shows that the best cutoff point or serum GDF-15 level to differentiate between patients with and without faltering growth was >879 (pg/ml) with sensitivity 94.12%, specificity 92.31%, and area under curve (AUC) of 0.933.

*Conclusion:* We concluded that GDF-15 levels are significantly increase in children with concomitant CHD and faltering growth than in those CHD children with normal body weight.

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***Key Words:*** *Growth Differentiation Factor-15 – Egyptian Children – Congenital Heart Disease.*

## Introduction

**CONGENITAL** heart disease (CHD) is the most common cause of congenital anomalies accounting for 8/1000 live birth. In recent years, progress in the surgery for CHD has improve the outcome of the disease, which has considerably increased the life expectancy of patients **[1]**. Faltering growth is a constant phenomenon among children with CHD irrespective of the nature of the cardiac defect. Many factors may influence growth failure in CHD including feeding difficulties, inadequate caloric intake, increased energy expenditure and endocrine factors. Faltering growth is affecting up to 66% of children with CHD, longer hospital stays, increased perioperative morbidity and mortality, and poor nutritional recovery even after curative cardiac surgery are all related to faltering growth **[2]**.

Plasma growth biomarkers could be used in children with CHD because they are easy to collect and measure regularly and in comparison to other methods like daily weights, which can be inaccurate in patients with congestive heart failure, and total calorie intake, which though it may appear adequate, may not always result in growth, a plasma biomarker related to the underlying physiology created by CHD and associated with faltering growth may provide a better biological measure of the child's current state of growth potential **[3]**.

Growth differentiation factor 15 (GDF-15) is a stress response cytokine which is synthetized and secreted by cardiomyocytes that in turn acts on the liver to inhibit growth hormone (GH) signalling. Children with CHD and faltering growth may have higher levels of growth differentiation factor 15 (GDF-15) than children with CHD alone **[4]**.

This study aims to evaluate the association between elevated serum level of GDF15 in children with CHD and faltering growth so that early nutritional intervention may be started to stop growth retardation and its negative drawbacks **[5]**.

*Aim of the work:*

This study aims to measure the serum level of growth differentiation factor-15 (GDF15) in children with congenital heart disease, evaluate the association between elevated serum level of GDF15 in children with CHD and faltering growth.

## Patients and Methods

This was a cross-sectional study that was conducted at Children Hospital, Pediatric Cardiology unit, Ain Shams University from July 2023 to April 2024.

*Inclusion criteria:*

- Children aged 12 to 60 months of age.
- Both sexes.
- Children with confirmed congenital heart disease of any type.

*Exclusion criteria:*

*Patients with the following were excluded from the study:*

- Patients with syndromic abnormalities and other congenital anomalies.
- Decompensated patients with signs of heart failure.
- Patients with acquired heart disease.
- Parents of children who refused to participate in the study.

*Study procedures:*

All patients' cardiac diagnosis were made on basis of clinical and laboratory examinations, radiological methods, and electrocardiography.

All patients were subjected to the following: (A) Full history taking including screening tool risk on nutritional status and growth (Strong Kid) questionnaire. (B) General and Local examination including vital signs and oxygen saturation using pulse oximetry, Anthropometric measures including weight in kg, length/height in cm, weight-for-age Z score (WAZ), length/height-for-age Z score (HAZ), length/height-for-weight Z Score (HAZ), body mass index (BMI) and body mass index Z score was performed, plotted and analysed using the World Health Organization growth (WHO) growth charts for children. Body mass index was calculated as the ratio of body weight (kg) and squared height (m.). Faltering growth was defined as WAZ or HAZ < -2, representing the lowest 3% of values within a normal distribution. (C) Echocardiography: Echocardiographic measurements were carried out according to the recommendations of The American Society of Echocardiography using GE Medical system with 7 and 4 s MHz multi-frequency transducers. Doppler, two-dimensional, and M mode were used for the assessment of the type of congenital heart disease. (D) Laboratory investigations: C-reactive protein (CRP) was done using Human CRP ELISA Test Kit as one of each child routine laboratory investigation and was collected from patients' files. CRP >0.5mg/dl is considered elevated and was used as a measure of overall inflammatory status. Also, Hemoglobin (Hb) levels were measured using whole blood Hb quantitative kit method. Anemic status was evaluated according to reference range for children age and sex, Hb level <11.0g/dl was considered anemic child. (E) Serum growth differentiation factor with ELISA, 3ml of blood sample was drawn for each patient by venipuncture while lying in a supine position and stored according to manufacturer's instructions. Serum level of growth differentiation factor-15 was measured for all children using specific enzyme-linked immunosorbent assay ELISA kits (Bioassay Technology Lab., China).

*Statistical analysis:*

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 27. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also, qualitative variables were presented as number and percentages. The *p*-value was considered significant as the following: *p*-value >0.05: Non-significant (NS), *p*-value <0.05: Significant (S), *p*-value <0.01: Highly significant (HS).

## Results

This cross-section study was conducted on 60 patients from the Pediatric Cardiology Unit, Faculty of Medicine, Ain Shams University in a period from July 2023 till April 2024.

Table (1) shows that there was no statistically significant difference between cases with and without faltering growth regarding age and sex distribution with *p*-value of 0.607 and 0.889 respectively.

Table (2) shows that there was statistically significant decrease in weight, height, and BMI of patients with faltering growth than patients without faltering growth. Also, the table shows that there was statistically significant decrease in WAZ score, HAZ score, WHZ score and BMZ Z score in patients with faltering growth than patients without faltering growth.

Table (3) shows that there was no statistically significant difference between patients with and without faltering growth regarding CHD, type of CHD, and saturation levels with *p*-value = 0.203, 0.600 and 0.120; respectively.

Table (1): Comparison between cases with and without faltering growth regarding demographic data and characteristics of the studied cases.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *Age (Months):* | | | | | |
| Median (IQR) | 36.5 (25 – 45) | 31 (19 – 49) | –0.515# | 0.607 | NS |
| Range | 13 – 57 | 12 – 59 | | | |
| *Sex:* | | | | | |
| Female | 11 (42.3%) | 15 (44.1%) | 0.020* | 0.889 | NS |
| Male | 15 (57.7%) | 19 (55.9%) | | | |

*p*-value >0.05: Non-significant. *: Chi-square test.
*p*-value <0.05: Significant. #: Mann-Whitney test.
*p*-value <0.01: Highly significant.

Table (2): Comparison between cases with and without faltering growth regarding anthropometric measurements of the studied patients.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *Weight (Kg):* | | | | | |
| Mean ± SD | 13.73±2.86 | 9.84±1.96 | 6.245• | 0.001 | HS |
| Range | 8.5 – 20 | 6.5 – 13.5 | | | |
| *Height (Cm):* | | | | | |
| Mean ± SD | 93.12±10.55 | 85.44±9.63 | 2.935• | 0.005 | HS |
| Range | 73 – 114 | 68 – 105 | | | |
| *WAZ Score:* | | | | | |
| Median (IQR) | -0.38 (-0.65 – 0.24) | -2.71 (-2.87 – -2.46) | –6.594# | 0.001 | HS |
| Range | -1.37 – 1.43 | -3.57 – -2.02 | | | |
| *HAZ Score:* | | | | | |
| Median (IQR) | -0.65 (-1.13 – -0.03) | -2.44 (-2.74 – -1.98) | –5.953# | 0.001 | HS |
| Range | -1.97 – 1.47 | -3.47 – -0.31 | | | |
| *WHZ Score:* | | | | | |
| Median (IQR) | 0.05 (-0.15 – 0.43) | -2 (-2.4 – -1.6) | –6.594# | 0.001 | HS |
| Range | -0.84 – 1.84 | -3.23 – -1.06 | | | |
| *BMI:* | | | | | |
| Mean ± SD | 15.9±0.83 | 13.52 ± 0.58 | 13.071• | 0.001 | HS |
| Range | 14.5 – 18.4 | 12.4 – 14.7 | | | |
| *BMI Z Score:* | | | | | |
| Median (IQR) | 0.16 (-0.03 – 0.5) | -1.73 (-2.27 – -1.27) | –6.191# | 0.001 | HS |
| Range | -0.88 – 66 | -2.85 – 1.07 | | | |

*p*-value >0.05: Non-significant. •: Independent *t*-test.
*p*-value <0.05: Significant. #: Mann-Whitney test.
*p*-value <0.01: Highly significant.

Table (3): Comparison between cases with and without faltering growth regarding CHD, type of CHD and Saturation of the studied patients.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *CHD:* | | | | | |
| Acyanotic | 22 (84.6%) | 24 (70.6%) | 1.621* | 0.203 | NS |
| Cyanotic | 4 (15.4%) | 10 (29.4%) | | | |
| *Type of CHD:* | | | | | |
| *Acyanotic:* | | | | | |
| PDA | 3 (11.5%) | 4 (11.8%) | 2.753* | 0.600 | NS |
| VSD | 15 (57.7%) | 13 (38.2%) | | | |
| ASD | 4 (15.4%) | 7 (20.6%) | | | |
| *Cyanotic:* | | | | | |
| TOF | 2 (7.7%) | 6 (17.6%) | | | |
| CCHD | 2 (7.7%) | 4 (11.8%) | | | |

*p*-value >0.05: Non-significant. *: Chi-square test.
*p*-value <0.05: Significant. •: Independent *t*-test.
*p*-value <0.01: Highly significant.

Table (4) show that there was statistically significant increase in the percentage of patients with grade 4 and 5 strong Kids score in patients with faltering growth [29 (85.3%) and 4 (11.8%); respectively] than patients with no faltering growth [0 (0.0%) and 0 (0.0%); respectively] with *p*-value <0.001.

Table (5) shows that there was statistically significant increase in CRP level in patients with faltering growth [6.35 (3.8-10.2)] than patients without faltering growth [4.6 (2.8-6.2)] with *p*-value = 0.027. Also, the table shows that there was statistically significant decrease in hemoglobin level in patients with faltering growth [10.72±0.69] than patients without faltering growth [11.64±0.68] with *p*-value <0.001.

Table (6) shows that there was statistically significant increase in GDF-15 level in patients with faltering growth [1766 (1211-2156)] than patients without faltering growth [689 (598-833)] with *p*-value <0.001.

Table (7) shows that there was statistically significant negative correlation between GDF-15 level and weight [$r$=–0.572, $p$<0.001], height [$r$=–0.317, $p$=0.014], WAZ score [$r$=–0.678, $p$<0.001], HAZ [$r$=–0.579, $p$<0.001] score, BMI [$r$=–0.666, $p$<0.001], BMI z score [$r$=–0.663, $p$<0.001] and hemoglobin level [$r$=–0.486, $p$<0.001]. Also, there was statistically significant positive correlation between GDF-15 level and CRP level [$r$=0.416, $p$=0.001].

Table (8) shows that there was statistically significant increase in GDF-15 level in patients with cyanotic CHD [2069 (1104-2275)] than patients with acyanotic CHD [876.5 (618-1654)] with *p*-value = 0.001. Also, the level of GDF-15 was significantly higher in patients with TOF [2195 (1498.5-2261.5)] and CCHD [1778.5 (1104-2335)] than patients with PDA [552 (490-1822)], VSD [876.5 (709-1518.5)] and ASD [920 (618-1923)] with *p*-value = 0.013.

Also, the table shows that there was statistically significant increase in the level of GDF-15 with the increase in Strong Kids score. The level of GDF-15 was significantly higher in patients with Strong Kids Q score 4 and 5 [1752 (1156-1982) and 2241 (2019.5-2352.5); respectively] than patients with Strong Kids Q score 2 and 3 [619 (594-726) and 845 (778.5-1059.5); respectively] with *p*-value <0.001.

The previous ROC curve shows that the best cut off point for GDF-15 level to differentiate between patients with and without faltering growth was >879 (pg/ml) with sensitivity 94.12%, specificity 92.31% and area under curve (AUC) of 0.933.

Table (4): Comparison between cases with and without faltering growth regarding Strong Kids Score of the studied cases.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *Strong Kids Score:* | | | | | |
| 2 | 19 (73.1%) | 0 (0.0%) | 56.437* | 0.001 | HS |
| 3 | 7 (26.9%) | 1 (2.9%) | | | |
| 4 | 0 (0.0%) | 29 (85.3%) | | | |
| 5 | 0 (0.0%) | 4 (11.8%) | | | |

*p*-value >0.05: Non-significant. *p*-value <0.01: Highly significant.
*p*-value <0.05: Significant. *: Chi-square test.

Table (5): Comparison between cases with and without faltering growth regarding CRP and hemoglobin level of the studied patients.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *CRP:* | | | | | |
| Median (IQR) | 4.6 (2.8 – 6.2) | 6.35 (3.8 – 10.2) | -2.205# | 0.027 | S |
| Range | 1.4 – 18 | 1.8 – 24 | | | |
| Elevated | 7 (26.9%) | 21 (61.8%) | 7.186* | 0.007 | HS |
| Normal | 19 (73.1%) | 13 (38.2%) | | | |
| *Hb:* | | | | | |
| Mean ± SD | 11.64 ± 0.68 | 10.72 ± 0.69 | 5.159• | 0.001 | HS |
| Range | 10.7 – 13.1 | 9 – 12 | | | |
| Anemic | 3 (11.5%) | 22 (64.7%) | 17.135* | <0.001 | HS |
| Normal | 23 (88.5%) | 12 (35.3%) | | | |

*p*-value >0.05: Non-significant. •: Independent *t*-test.
*p*-value <0.05: Significant. #: Mann-Whitney test.
*p*-value <0.01: Highly significant.

Table (6): Comparison between patients with and without faltering growth regarding GDF-15 of the studied cases.

| | No Faltering Growth No. = 26 | Faltering Growth No. = 34 | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| *GDF -15 (pg./ml):* | | | | | |
| Median (IQR) | 689 (598 – 833) | 1766 (1211 – 2156) | -5.714# | 0.001 | HS |
| Range | 490 – 1104 | 475 – 2457 | | | |

Table (7): Correlation of GDF-15 with other studied parameters among the studied patients.

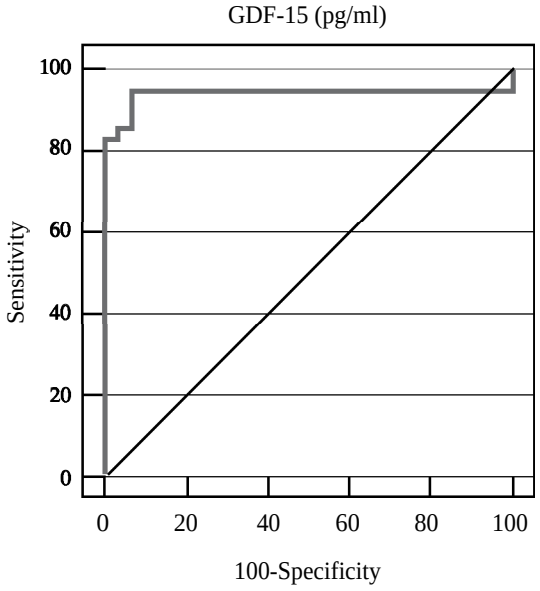
| | GDF -15 (pg/ml) | |
|---|---|---|
| | *r* | *p*-value |
| Age (Months) | -0.155 | 0.237 |
| Weight (Kg) | -0.572** | 0.001 |
| Height (Cm) | -0.317* | 0.014 |
| WAZ Score | -0.678** | 0.001 |
| HAZ Score | -0.579** | 0.001 |
| WHZ Score | -0.701** | 0.001 |
| BMI | -0.666** | 0.001 |
| BMI Z-Score | -0.663** | 0.001 |
| CRP | 0.416** | 0.001 |
| Hb | -0.486** | 0.001 |

*p*-value >0.05: Non-significant.
*p*-value <0.05: Significant.
*p*-value <0.01: Highly significant.
Spearman correlation coefficient

Table (8): Relation of GDF-15 with other studied parameters among the studied patients.

| | GDF -15 (pg/ml) | | Test value | *p*-value | Sig. |
|---|---|---|---|---|---|
| | Median (IQR) | Range | | | |
| *Sex:* | | | | | |
| Female | 991.5 (635 – 1764) | 475 – 2367 | -0.604• | 0.546 | NS |
| Male | 1157.5 (724 – 1822) | 523 – 2457 | | | |
| *CHD:* | | | | | |
| Acyanotic | 876.5 (618 – 1654) | 475 – 2367 | -3.417• | 0.001 | HS |
| Cyanotic | 2069 (1104 – 2275) | 619 – 2457 | | | |
| Type of CHD: | | | | | |
| *Acyanotic:* | | | | | |
| PDA | 552 (490 – 1822) | 489 – 1923 | 12.627# | 0.013 | S |
| VSD | 876.5 (709 – 1518.5) | 524 – 2090 | | | |
| ASD | 920 (618 – 1923) | 475 – 2367 | | | |
| *Cyanotic:* | | | | | |
| TOF | 2195 (1498.5 – 2261.5) | 726 – 2296 | | | |
| CCHD | 1778.5 (1104 – 2335) | 619 – 2457 | | | |
| *Strong Kids Q:* | | | | | |
| 2 | 619 (594 – 726) | 490 – 879 | 35.344# | 0.001 | HS |
| 3 | 845 (778.5 – 1059.5) | 583 – 1456 | | | |
| 4 | 1752 (1156 – 1982) | 475 – 2367 | | | |
| 5 | 2241 (2019.5 – 2352.5) | 1805 – 2457 | | | |

*p*-value >0.05: Non-significant.
*p*-value <0.05: Significant.
*p*-value <0.01: Highly significant.




| Cut off point | AUC | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|
| >879 | 0.933 | 94.12 | 92.31 | 94.1 | 92.3 |

AUC: Area under curve.
PPV : Positive predictive value.
NPV: Negative predictive value.

Fig. (1): Receiver operating characteristics (ROC) curve to assess GDF-15 to differentiate between cases with and without faltering growth.

## Discussion

Congenital heart disease (CHD) is the most common congenital defect worldwide. Incidence of significant CHD is 8 per 1000 live births, this does not include minor defects, which often present later in childhood or adult life. CHD have a wide range of impacts on a child's health and well-being. Approximately 25% of CHD children require cardiac care in the first year of life **[6]**.

Children with congenital heart disease (CHD) are more likely to experience faltering growth, which is defined as WAZ or HAZ < –2, representing the lowest 3% of values within a normal distribution **[7]**. Up to 66% of children with CHD may be affected by faltering growth which is associated with longer hospital stays, higher perioperative morbidity and mortality, and poor nutritional recovery even following successful heart surgery **[8]**.

Due to heterogeneity for growth faltering among children with the same anomalies and physiology, early identification of CHD children who are more prone to have faltering growth is crucial to begin early nutritional intervention and potentially reverse the hazardous effects of faltering growth **[9]**.

A plasma biomarker related to the underlying physiology created by CHD and associated with faltering growth may offer a more biological measure of the child's current state of growth potential **[8]**.

Kato et al., have shown that children with CHD and Faltering growth have greater levels of growth differentiation factor 15 (GDF-15) than do children with CHD alone. GDF-15, a cytokine involved in the stress response, has been connected to several forms of cellular stress, such as hypoxia, mitochondrial dysfunction, liver disease, heart failure, and renal failure *[10]*.

Our cross-sectional study was conducted on 60 children with congenital heart disease at the Pediatric Cardiology Unit, Faculty of Medicine, Ain Shams University from July 2023 to April 2024. Our study aimed to measure the serum level of growth differentiation factor-15 (GDF-15) in children with congenital heart disease and to evaluate the association between elevated serum level of GDF-15 in children with CHD and faltering growth.

Our findings revealed that there was a statistically significant increase in GDF-15 level in patients with faltering growth than patients without faltering growth. Our ROC curve analysis shows that the best cut off point for GDF-15 level to differentiate between patients with and without faltering growth was >879 (pg/ml) with sensitivity 94.12%, specificity 92.31% and area under curve (AUC) of 0.933.

Similarly, Paneitz et al. discovered that, with an AUC of 0.75 (0.68-0.82) for GDF-15, ROC analysis could significantly differentiate faltering growth. According to their findings, GDF-15 performs well in the classification of faltering growth based on its AUC, which suggests that GDF-15 may be a promising growth biomarker for children with CHD *[4]*.

Moreover, Zhou et al., reported that the sensitivity, specificity and AUC of GDF-15 on CHD were 91.25%, 74.00% and 0.821 respectively *[11]*.

There are two potential processes that connect between GDF-15 and faltering growth in CHD patients. First, prior research on animals has shown that, even at moderate levels, GDF-15 can reduce appetite without the help of other hormones associated with fullness or hunger, such as leptin, glucagon-like peptide 1 (GLP-1), or the melanocortin 4 receptor *[12]*.

Second, an important study by Wang et al. demonstrated that growth hormone (GH) is inhibited at the liver by cardiac-derived GDF-15, which lowers the release of insulin-like growth factor 1 (IGF1) *[13]*.

Our findings revealed that there was statistically significant negative correlation between GDF-15 level and weight, height, WAZ score, HAZ score, BMI and hemoglobin level.

In accordance with our results, Johnen, Tsai et al., found a statistically significant negative correlation between GDF-15 level and weight and BMI. This is because GDF15 has been demonstrated to mediate body weight loss by acting on the hypothalamus to regulate food intake by decreasing Neuropeptide Y (NPY) and increasing Proopiomelanocortin (Pomc) expression *[12,14]*.

Also, our study found that there was statistically significant positive correlation between GDF-15 level and CRP level.

Quintana et al., explained these findings by the hypothesis that although numerous CHD-related comorbidities have been linked to chronic inflammation, which is frequent in children with CHD, its function as a contributor to or mediator of faltering growth has not been previously investigated. GDF-15 demonstrated a strong correlation with CRP, which is consistent with research in individuals with various cardiac conditions such as myocardial infarction and chronic heart failure *[15]*.

Moreover, we found that there was a statistically significant increase in GDF-15 level in patients with cyanotic CHD than patients with acyanotic CHD.

Zhou, Kagiyama, Norozi, Li, Saraf, et al.'s several earlier studies of CHD patients showed that the GDF-15 level was statistically significantly higher in these individuals. Additionally, they have linked higher GDF-15 levels to more severe heart failure as well as a higher risk of clinical events and death *[11,16-19]*.

Additionally, Wang et al., found that Compared to healthy controls, children with CHD had higher levels of GDF-15. This difference was even greater in children with congenital heart disease who also had heart failure and faltering growth *[13]*.

The results of Paneitz et al., support these findings because our sample exhibited high proportions of faltering growth and high GDF-15 levels for diseases known to be related with heart failure, such as TOF with pulmonary atresia, AVSD, and VSD *[4]*.

Finally, Barton, Dinleyici, Onay, Peng et al., shown that GDF15 may be the cause of clinical growth faltering linked to paediatric cardiac disease, which frequently has lower circulating IGF1 and IGFBP3 levels. This supports the clinical relevance of our findings beyond animal models *[20-23]*.

The plasma GDF15 concentrations of children with heart disease who had either normal body weight or faltering growth were determined by Baggen, Wang, Wollert et al., Compared to age- and gender-matched healthy control children, both groups of children with heart disease had significantly higher plasma GDF15 levels, which is consistent with earlier research showing elevated plasma GDF15 in adult heart disease *[13,24,25]*.

Significantly, children with concurrent heart illness and faltering growth have plasma GDF15

levels that are 80% greater than those of children with heart disease but normal body weight, indicating that elevated GDF15 represents an underlying mechanism that links congenital heart disease and faltering growth ***[13]***.

Wollert et al., explained that the heart uses both GDF15 and ANP/BNP as hormones to modify the body in ways that lessen cardiac burden: ANP/BNP lowers blood pressure, while GDF15 limits body growth. These parallels point to a common endocrine system that the heart uses to synchronize cardiac and systemic functions ***[25]***.

The normal heart produces undetectable levels of GDF-15; hence the basal level of circulating GDF-15 most likely originates from non-cardiac sources, according to Kato et al.'s explanation of these findings. Their cardiac-specific GDF-15 knockdown investigations imply that all the higher circulating GDF-15 above basal level in the heart disease condition was caused by cardiac-derived GDF-15 ***[10]***.

It is evident that the extra GDF-15 in circulation from the heart has a major physiologic effect on liver GH signaling. One explanation for this could be that GDF-15's signaling is significantly altered by a concentration rise of four to five times ***[13]***.

An alternative hypothesis is that basal circulation GDF-15 from non-cardiac sources differs biochemically from heart-derived GDF-15 and may have more biological activity ***[26]***.

In the same line with us, the distribution of the new biomarker GDF-15 in a sizable population of patients with stable congestive heart failure was reported by Eindhoven et al., Although GDF-15 levels in this cohort vary widely, patients with CHD accompanied by higher pulmonary pressures tended to have the highest levels of GDF-15. These findings imply that GDF-15 may prove to be a valuable diagnostic aid for CHD patients ***[27]***.

*Conclusion:*

We came to the conclusion that GDF-15 levels are significantly increase in children with concomitant CHD and faltering growth than in those CHD children with normal body weight.

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# تقييم عامل تمايز النمو الخامس عشر لدى الأطفال المصريين المصابين بأمراض القلب الخلقية

المقدمة: تعد أمراض القلب الخلقية من أكثر التشوهات الخلقية شيوعًا حيث تبلغ نسبة حدوثها ١٠٠٠/٨ مولود حى. النمو المتعثر هو مصطلح وصفى يستخدم عندما يكون النمو غير كاف مقارنة بالمعايير المتوقعة.

الهدف من الدراسة: هدفت دراستنا إلى قياس مستوى عامل تمايز النمو الخامس عشر بالدم لدى الأطفال المصابين بأمراض القلب الخلقية وتقييم الارتباط بين ارتفاع مستوى عامل تمايز النمو الخامس عشر بالدم لدى الأطفال المصابين بأمراض القلب الخلقية وتعثر النمو.

المرضى وطرق العلاج: أجريت دراستنا المقطعية على ستين طفلاً مصابين بأمراض القلب الخلقية فى القلب فى قسم الأطفال، كلية الطب، جامعة عين شمس فى الفترة من يوليو ٢٠٢٣ إلى ابريل ٢٠٢٤. وقد تمت الحصول على الموافقة للدراسة من مجلس قسم طب الأطفال.

النتائج: أظهرت نتائجنا وجود زيادة ذات دلالة إحصائية فى مستوى عامل تمايز النمو الخامس عشر لدى المرضى الذين يعانون من تعثر النمو مقارنة بالمرضى الذين لا يعانون من تعثر النمو. كما وجدنا أن هناك زيادة ذات دلالة إحصائية فى مستوى عامل تمايز النمو الخامس عشر فى المرضى الذين يعانون من أمراض القلب الخلقية المقرونة بزرقه مقارنة بالمرضى الذين يعانون من أمراض القلب الخلقية غير المقرونة بزرقه.

الخلاصة: وخلصنا إلى أن التشخيص الدقيق المبكر للأطفال المصابين بأمراض القلب الخلقية يجب أن يكون الهدف الرئيسى لطبيب الأطفال فى مواجهة هذه الحالات منذ الثانية الأولى لتجنب العواقب الخطيرة المحتملة لأن هؤلاء الأطفال معرضون بشكل كبير لخطر تعثر النمو. لقد خلصنا أيضًا إلى أن مستوى المصل لعامل تمايز النمو الخامس عشر يمكن أن يمثل مؤشرًا حيويًا جديدًا للنمو للمساعدة فى اتخاذ القرار السريرى لدى الأطفال المصابين بأمراض القلب الخلقية مع تعثر النمو.