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## Bone Age and Nutritional Status of Toddlers with Congenital Heart Disease.

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### ABSTRACT

The prevalence of malnutrition and growth failure is higher in children with congenital heart disease (CHD). Different types of cardiac malformations can affect nutrition and growth to various degrees. Bone age (BA) may be delayed in children with (CHD). To assess the adverse effects of (CHD) on growth and to evaluate the additive role of cyanosis and pulmonary hypertension (PH) on (BA) delay. Growth parameters including weight, height and head circumference of 50 cases (27♂ & 23♀) with (CHD) and aged 2-6 years were compared with Egyptian growth curves. Patients were classified into four groups, based on the presence or absence of cyanosis and (PH). A strong positive correlation was found between (PH) and the incidence of (BA) delay. The incidence of (BA) delay in patients with normal pulmonary pressure, mild (PH), moderate (PH) and severe (PH) was 39.2%, 42.8%, 80% and 100% respectively. The decrease in both body weight (in 60% of cases) and body height (in 56% of the patients) was statistically significant, whereas the decrease in head circumference (in 24% of cases) was statistically insignificant. Also, 60% of cyanotic patients had (BA) delay. Cyanosis, that may affect (BA) delay less than (PH), has showed statistical significance difference. Bone age delay and growth retardation are common findings in children with (CHD). Also, cyanosis and/or (PH) may further deteriorate their growth and hence they should be promptly managed, considering the significance of (PH) on (BA) delay and growth retardation.

**Keywords:** congenital heart disease; bone age; nutritional status; toddlers

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## INTRODUCTION

Congenital heart disease (CHD) which is defined as an abnormality in the cardio-circulatory structure or function, is either present at birth or appears much later in life. It represents the most common congenital anomaly and the major leading cause of birth defect (1). It also, represents an important cause of childhood morbidity and mortality worldwide (2).

The prevalence and pattern of (CHD) varies both within and between regions and countries (3), and accounts for nearly one-third of all major congenital anomalies. The worldwide birth prevalence of (CHD) varies over time and a complete overview is missing. The reported total (CHD) birth prevalence, that increased substantially over time, is about 1% of live births and globally occurs in 8/1000 live births (4,5). Furthermore, four of 1000 live births will be affected by severe congenital cardiac malformations, which accounts for 20% of neonatal deaths and up to 50% of infant deaths is attributed to congenital anomalies (6). In the year 2000, the estimated prevalence of (CHD) in the pediatric population was approximately 623,000 (1). The observed significant geographical differences in reported birth prevalence may be attributed to genetic, environmental, socioeconomical, or ethnic origins (5).

Congenital cardiac lesions are classified into two large groups based on the presence or absence of cyanosis. Acyanotic congenital heart diseases were more prevalent than cyanotic heart diseases (7). Acyanotic defects can be divided into two major groups on the basis of their dominant load abnormally imposed on the heart (8,9,10).

Different types of cardiac malformations can affect nutrition and growth to various degrees. Presence of cyanosis and/or Pulmonary Hypertension (PH), which are frequently seen in many patients with (CHD), appear to influence the growth pattern of affected children (11,12,13,14). It has been reported that bone age (BA) may be delayed in children with (CHD) (15). Also, chronic hypoxemia that reduces serum insulin like growth factor I (IGF-I) concentrations, may increase growth failure in patients with cyanotic (CHD) (16). It is suggested that patients with increased pulmonary blood flow and (PH) are more prone to develop malnutrition and growth retardation and cyanotic patients with (PH) are the ones most severely affected (13).

Children with congenital heart disease (CHD) have an increased prevalence of malnutrition and growth failure (17). Malnutrition widely ranges from mild under-nutrition to severe failure to thrive (FTT) (11,18). Failure to thrive is well recognized as a serious problems in children with (CHD). The multifactorial etiology for growth retardation in children with (CHD), can be attributed to decreased energy intake, increased energy requirements and recurrent respiratory infections. Inadequate caloric intake, due to mal-absorption or disorders of carbohydrate metabolism, has been shown to be the most important cause of growth disturbances in children with (CHD) (19, 20,12,13).

In infants and children with (CHD), the delays in weight gain and growth ranges from relatively mild to failure to thrive; that can result in permanent physical or developmental impairment. Therefore, aggressive feeding strategies must be employed early with these children in order to proven permanent growth disturbances (19).

In western countries, these structural heart diseases are corrected as quickly as are indicted either through catheter procedures or via open heart surgery. In developing countries, however, these interventions are often delayed or not done at all because of non-availability or inadequate facilities (21).

Growth, which begins at conception (22), may be defined as the acquisition of tissue and concomitant increase in body size. Although growth is a multifactorial biological process, influenced by numerous genetic, endocrinal and environmental factors, yet malnutrition marked by various nutrient deficiencies is considered a leading cause of failure to thrive and growth retardation in children (23). Moreover, changes in body composition and anthropometry reflect changes in growth, which provides an indication of nutritional status in pre-adult years (24). Ethnic variations in growth rate are also common. African-American and Asian children tend to mature faster than Caucasian-American children, who are slightly ahead of European children (25).

Due to growth, bones of the skeleton change in size and shape. The "bone age" of a child is the average age at which children reach this stage of bone maturation, while bone aging is a way of describing the degree of maturation of child's bones. Conventionally x-rays of hands and wrists are used for the estimation of skeletal maturity (26). This examination is universally used due to its simplicity, minimal radiation exposure, and the availability of multiple ossification centers for evaluation of maturity (27). Bone age assessment is frequently performed in pediatric patients to evaluate, diagnose and manage growth and endocrine disorders (28-30). The assessed bone age is then compared with the chronological age. A discrepancy between these two values indicates abnormalities in skeletal development.

## PATIENTS AND METHODS

This cross sectional study included fifty toddlers (27♂ & 23♀) with (CHD) and with age range 2-6 years old. They were admitted and attached to Cardiology Unit of Pediatric Department in Tanta University Hospital (during the period between March 2013 and March 2014), for medical management, cardiac catheterization or surgical correction. Patients were classified into four groups according to the presence or absence of cyanosis and pulmonary hypertension "PH": Group I (n=15, 30%): acyanotic without "PH", Group II (n=10, 20%): acyanotic with "PH", Group III (n=13, 26%): cyanotic without "PH" and Group IV (n=12, 24%): cyanotic with "PH". Cases with intra-uterine growth retardation, prematurity, known genetic syndromes, dysmorphic features, chronic systemic disease or protein energy malnutrition were excluded from the study. For every child, a full history was taken and general and local examination were carried out. Also anthropometric assessment was done in comparison with Egyptian growth curves (31). Weight (Kg) was measured using a commercial scale (Seca Scale, Germany); with an accuracy of +10g. The subjects were asked to remove their footwear and wear minimal clothes before weighing them. Standing body height (Cm) was measured to the nearest 0.1 cm, using Holtain Stadiometer with the shoulder in a relaxed position and arms hanging freely and without shoes. Mid upper arm circumference (of the non-dominant arm) was measured to the nearest 0.1 cm with a nonelastic tape measure, midway between the acromial and olecranon processes (32).

Head circumference (cm) was measured with the tape applied firmly over the glabella, just above eyebrows, and occipital protuberance (occipito-frontal circumference) (15). Bone age determination, from the left hand radiograph, was carried out using the digital atlas of skeleton maturation (28).

## RESULTS

Regarding sex distribution of the study groups; group I [n=15: 9 males (60%) and 6 females (40%)], group II [n=10: 5 males (50%) and 5 females (50%)], group III [n=13: 6 males (46.2%) and 7 females (53.8%)] and group IV [n=12: 7 males (58.3%) and 5 females (41.7%)]. All groups showed insignificant sex difference ( $P > 0.05$ ).

Concerning the incidence of delayed bone age, a significant relation was found except in group I (table, 1).

Regarding the relationship between (BA) delay and grades of systolic pulmonary pressure, a significant relationship was observed in patients with moderate and severe (PH) (table, 2).

The results of this study showed a statistical significant decrease in body weight, height and mid upper arm circumference in all groups except group I (table, 3). Whereas, there was no statistical significant relation regarding (HC) in the four studied groups (table, 4).

The results also showed significant positive correlations between bone age delay and: a- pulmonary pressure ( $r = 0.385$  &  $P < 0.05$ ) (Figure 1), b- patients' weight ( $r = 0.6094$  &  $P < 0.01$ ) (figure 2) and patients' height ( $r = 0.6247$  &  $P < 0.01$ ) (Figure 3).

**Table 1: Comparison of different study groups as regard incidence of delayed bone age**

Study group	Delayed bone age		Total		X <sup>2</sup>	p value
	N	%	N	%		
Group I	4	26.7	15	30	0.635	0.253
Group II	8	80	10	20	5.325	0.001*
Group III	7	53.8	13	26	3.253	0.008*
Group IV	8	66.7	12	60	6.325	0.002*
Total	27	54	50	100	2.362	0.041*

**Table 2: Relation between bone age (BA) delay and grades of systolic pulmonary pressure in the fifty studied patients.**

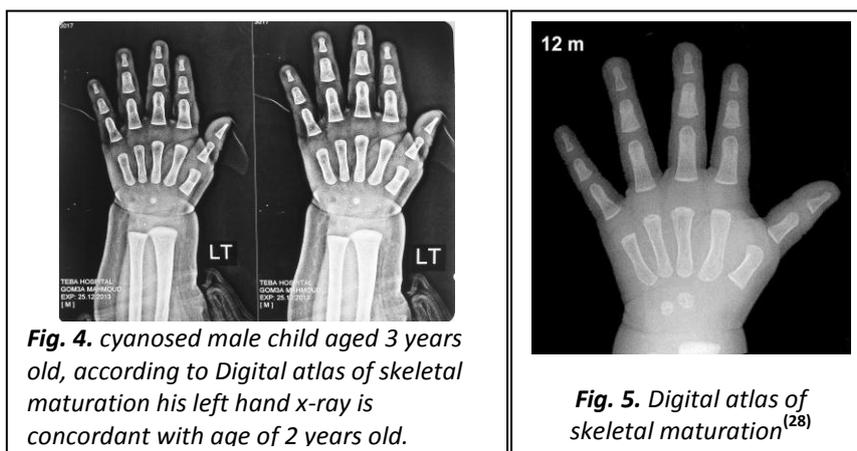
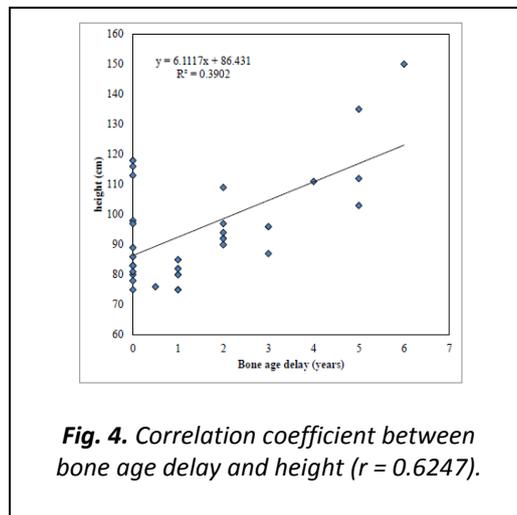
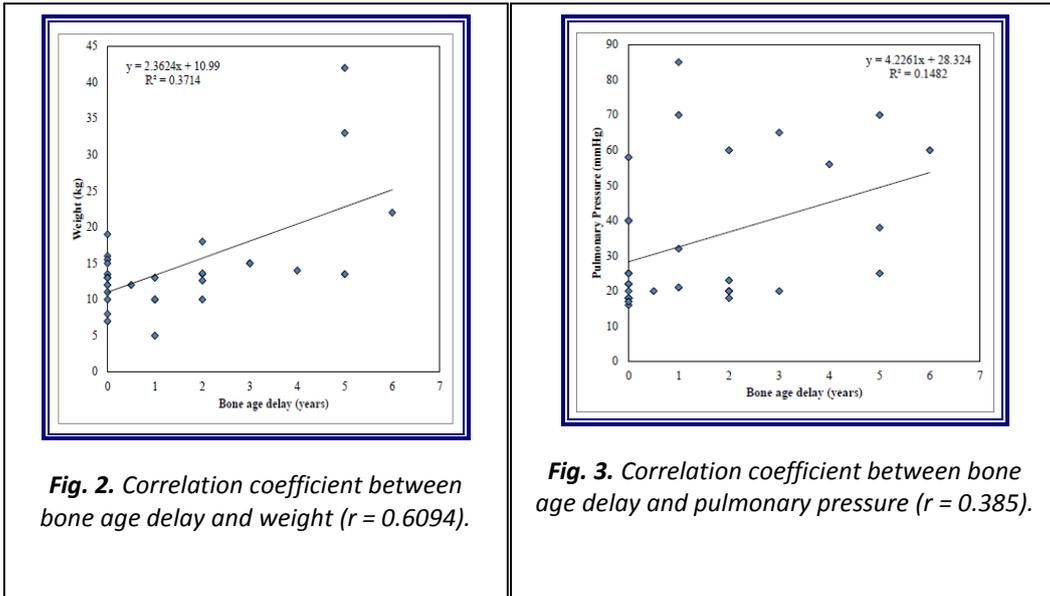
Pulmonary pressure	Normal bone age		Delayed bone age		Total		X <sup>2</sup>	P value
	N	%	N	%	N	%		
Normal: (up to 25 mmHg)	17	60.7	11	39.3	28	100	0.542	0.253
Mild: (25-45 mmHg)	4	57.1	3	42.9	7	100	4.336	0.011*
Moderate: (45-65 mmHg)	2	20	8	80	10	100	4.324	0.024*
Severe: (> 65 mmHg)	0	0	5	100	5	100	8.366	0.001*
Total	23	46	27	54	50	100	1.638	0.041*

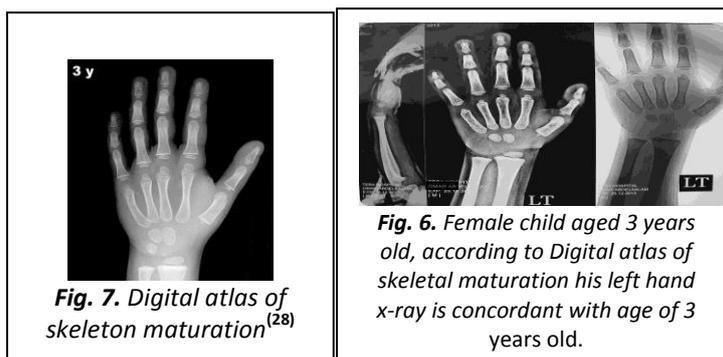
**Table 3: Comparison of different study groups as regard incidence of decreased body weight, height and mid upper arm circumference**

Study group	Total		Decreased weight		p. value	Decreased height		p. value	Decreased MUAC		p. value
	N	%	N	%		N	%		N	%	
Group I	15	30	6	40	0.241	6	40	0.745	4	26.7	0.494
Group II	10	20	8	80	0.001*	7	70	0.001*	5	50	0.033*
Group III	13	26	6	46.2	0.010*	7	53.8	0.015*	6	46.2	0.011*
Group IV	12	60	10	83.3	0.020*	8	66.7	0.039*	6	50	0.009*
Total	50	100	30	60	0.014*	28	56	0.021*	21	42	0.008*

**Table 4: Comparison of different study groups as regard incidence of decreased head circumference (HC)**

Study group	Decreased HC		Total		p. value
	N	%	N	%	
Group I	3	20	15	30	0.241
Group II	2	20	10	20	0.529
Group III	3	23.1	13	26	0.341
Group IV	4	33.3	12	60	0.741
Total	12	100	50	100	0.252





### DISCUSSION

Congenital heart disease (CHD) is the most common cause of major congenital anomalies, representing a major global health problem (5). Children with congenital heart disease (CHD) show significant growth retardation. Bone age calculation is considered, nowadays, an important step in detection and management of growth delay in chronic patients. Moreover, skeletal age assessment is a routine non-invasive procedure which is based on the observation of bone morphology on a radiograph of the non-dominant hand (usually the left hand) of children and young adults. A significant difference between the skeletal age and the actual age of a child is an indication of growth abnormalities (30).

Regarding the decreased body weight of the patients, 30/50 (60%) of all patients, had low weight than normal controls, with a statistically significant difference ( $P < 0.05$ ). The incidence of decreased body weight in groups I, II, III and IV was 6/15 (40%), 8/10 (80%), 6/13 (46.2%) and 10/12 (83.3%) respectively. These results revealed a statistically significant difference in groups II, III, and IV, with P value  $< 0.001$ ,  $< 0.05$ , and  $< 0.05$ , respectively.

Concerning the decrease in body height, 28/50 (56%) of the patients had less height than normal, with a statistically significant difference ( $P < 0.05$ ). The incidence of decreased body length in groups I, II, III and IV, was 6/15 (40%), 7/10 (70%), 7/13 (53.8%) and 8/12 (66.7%) respectively. These data revealed a statistically significant difference in groups II, III and IV, with P value  $< 0.001$ ,  $< 0.05$  and  $< 0.05$  respectively.

The results of the present study showed that, in the total sample, 21/50 (42%) had decreased mid upper arm circumference than normal, with a statistically significant difference ( $P < 0.05$ ). The incidence of decreased MUAC in groups I, II III and IV, was 4/15 (26.7%), 5/10 (50%), 6/13 (46.2%) and 6/12 (50%) respectively. These data revealed a statistically significant difference in groups II, III and IV, with P value  $< 0.05$ ,  $< 0.05$  and  $< 0.001$  respectively. Hence, our results agree with that of Jacobs et al. (33) who found that 40% of patients with CHD had subnormal weight and height values, where girls were more impaired in weight and weight-for-height than boys (-1.90 SDS vs -1.52 SDS, and -0.90 SDS vs -0.46 SDS, respectively). However, in the present study the incidence of decreased body weight and height in CHD patients was higher (66.7% and 60% respectively) than that of Jacobs et al. (33) and this may be attributed to the low general health condition and malnutrition factors in our sample.

Our results also agree with that of Varan et al. (34) who studied 89 children with CHD, and found that 65% of the patients were below the 5th percentile for weight and 21.6% were below the 5th percentile for MUAC.

The results of the present study agree with those of Mehrizi and Drash (35) who carried out their study on a large sample (890 children with CHD). They found that 55% of patients had short stature, 52% had poor weight gain and 27% had delayed values of both weight and height for age.

The present study revealed that malnutrition and growth failure were more prevalent in the enrolled patients. Several factors may explain this finding, such as the severity of congenital heart defect, difference in definition and interpretation of growth failure and socioeconomic status of the family. This fact was supported by Samadi et al. (15) who added that the socioeconomic status may be the most significant factor in the

patients. Delay in medical refers and inappropriately postponed surgical interventions seem to be another reason for increased prevalence of growth retardation in this study.

It is worth mention that, reviewing the literature, no earlier studies that evaluated the rate of growth failure using head circumference were found. The present study showed that, in the total sample, only 24% (12/50) had decreased head circumference (HC). The incidence of decreased (HC) in groups I, II, III and IV, was, 3/15 (20%), 2/10 (20%), 3/13 (23.1%) and 4/12 (33.3%) respectively. The differences were statistically insignificant ( $P > 0.05$ ).

Bone age delay in the total sample of the present study was 27/50 (54%), with a statistical significant difference ( $P < 0.05$ ). also, the incidence of bone age delay in groups I, II, III and IV was 4/15 (26.7%), 8/10 (80%), 7/13 (53.8%) and 8/12 (66.7%) respectively, and with statistical significant difference in groups II, III, and IV ( $P < 0.001$ ,  $< 0.05$ , and  $< 0.01$  and respectively).

The results of the present study revealed a higher incidence of bone age delay that was significantly prominent in patients of both groups, with cyanotic and PH (groups II & IV). This finding is supported by Samadi et al. (15) who showed that the delay in bone age was significantly more in both cyanotic patients with PH and cyanotic subjects without PH, compared to those with non of PH and cyanosis.

Samadi et al. (15) also found that patients with PH and without cyanosis had significant disparity in terms of all growth parameters; including weight, height and head circumference as well, bone age delay compared to those with none of PH and cyanosis (group I).

The results of the present study revealed a higher incidence of bone age delay in group II and IV, with very highly significant difference ( $P < 0.001$ ). In this respect, the study clues that PH alone (in group II and IV) was responsible for bone age delay, regardless other factors.

In the present study, patients were classified into four subgroups, regarding the mean arterial pulmonary pressure, according to Samadi et al. (15) to clarify the role of (PH) on bone age delay: normal (up to 25 mmHg), mild PH (up to 45 mmHg), moderate PH (up to 65 mmHg), and sever PH ( $> 65$  mmHg). Then bone age delay was evaluated in each subgroup. The incidence of bone age delay was 39.3%, 42.9%, 80% and 100%, respectively. This means that, the higher the PH, the more bone age delay observed (i.e. the incidence of bone age delay was 100% in patients with severe PH). This finding confirms that hypothesis that PH is the main factor responsible for bone age delay. Hence, our results agree with those concluded by Samadi et al. (15).

It has been reported that, patients with CHD and cyanosis, pulmonary hypertension and congestive heart failure appear to have an increased prevalence of growth failure and malnutrition compared to normal population.(14) It is well known that malnutrition accompanies and contributes to morbidity in CHD. Optimizing nutritional status improves surgical outcome and is associated with reduced morbidity (34,20,36,37).

Comparing the incidence bone age delay in cyanotic (15/25, 60%) and acyanotic patients (12/25, 48%) revealed a slightly higher significant difference ( $P < 0.05$ ). Therefore, it is suggested that growth retardation is more relevant to pulmonary hypertension than cyanosis except for bone age. Samadi et al. (15) have attributed this to the role of hypoxemia in reducing serum levels of IGF-I, which consequently delays the appearance of bony centers.

There are various results about the pathophysiology and the effect of cyanosis in children with (CHD)(38,39,14). Tambic-Bukovac and Malcic (40) who carried out their on 223 children with CHD, have shown that growth failure was significantly more prevalent in cyanotic cases compared to acyanotic ones. Also, Cameron et al. (41) and Leite et al. (42) have concluded that cyanotic congenital heart diseases in children results in more pronounced growth retardation compared to acyanotic ones. On the contrary, it has been concluded that, in children with CHD, no significant correlation exists between physical growth parameters and the presence of cyanosis (43,44). Moreover, some authors have reported that the prevalence of growth failure in acyanotic patients is higher than cyanotic ones (33,28).

To explain such disparate findings, it is important to consider the role of factors other than cyanosis. Therefore, in some reviews, the effect of pulmonary hypertension on the status of growth parameters and skeletal maturation is evaluated. Varan et al. (34) suggested that, in patients with CHD, pulmonary hypertension was the most prominent factor associated with failure to thrive.

In the review done by Vaidyanathan et al. (14) congestive heart failure and pulmonary hypertension were significant predictors of growth disturbance consistent with the findings of present study.

In the present study, both cyanosis and pulmonary hypertension were associated with a significantly higher prevalence of bone age retardation. Unfortunately the only study relating bone age with CHD, is that done by Samadi et al. (15).

Pelargonio et al. (44) showed the adverse effects of congenital heart diseases on the appearance and development of ossification centers in roentgenograms. Whereas, Dinleyici et al. (16) have put cyanosis forward to be a risk factor for delay in bone age. They found that 37/94 (39.4%) of CHD patients and 16/54 (29.6%) controls had malnutrition and the difference between cyanotic and acyanotic patients, with respect to malnutrition, was statistically significant (57.9% and 34.6%,  $p < 0.05$ ) (16). Thus the findings of these two studies are consistent with those of the present study.

In conclusion, bone age delay and growth retardation are common findings in children with (CHD). In addition, cyanosis and/or "PH" may further deteriorate (CHD) child's growth and hence, they should be promptly managed, considering the significance of "PH" on "BA" delay and growth retardation. Also, because the etiology of growth failure in children with CHD is multifactorial, then further studies are recommended to assess the role of different factors in such case. Also, considering the lack of recent studies assessing the role of CHD and the separate effects of cyanosis and pulmonary hypertension on the appearance and growth of bony centers, further reviews should be designed.

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