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Original Article

Failure to Thrive and Bone Growth Retardation in Cyanotic and Acyanotic Congenital Heart Diseases With and Without Pulmonary Hypertension

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ABSTRACT

Background: Growth retardation following malnutrition is prevalent among patients with congenital heart diseases (CHDs). This study was designed to evaluate failure to thrive (FTT) and delay in bone age in children with CHDs who were referred to our hospital and subsequently to determine their relation with cyanosis and the pulmonary artery pressure.

Methods: We enrolled 120 consecutive patients who were referred to Rajaie Cardiovascular, Medical, and Research Center for cardiac catheterization or surgical correction. Growth parameters, comprising height (cm), weight (kg), and head circumference (cm), were measured by an experienced nurse. Bone age was evaluated by taking an anteroposterior wrist X-ray and reported by a radiologist, who was not aware of the exact cardiac diagnosis. The pulmonary artery pressure was measured during cardiac catheterization or surgical correction.

Results: Bone growth retardation, FTT, short stature, and microcephaly were seen in 46.6%, 43.7%, 29.4%, and 5.1% of the patients, correspondingly. There was a significant relationship between the presence of cyanosis and delayed bone age, particularly when O_2 saturation was less than 75% ($P < 0.0001$). The presence of pulmonary hypertension was significantly related to a higher rate of bone growth retardation ($P < 0.0001$). FTT and delayed bone age were significantly different between the cyanotic patients and the children with pulmonary hypertension and the acyanotic patients and those without pulmonary hypertension ($P < 0.05$).

Conclusions: According to our results, delayed bone age and growth retardation are common findings in children with CHDs. The presence of cyanosis and/or pulmonary hypertension may further deteriorate these conditions and should be promptly managed. ***(Iranian Heart Journal 2017; 18(3):35-41)***

Keywords: Congenital heart disease, Cyanosis, Failure to thrive, Pulmonary hypertension, Bone age

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Congenital heart diseases (CHDs) like any other chronic childhood illness have widely heterogeneous effects on patients. Among these effects, growth retardation is one of the most significant. Children afflicted by growth retardation are prone to inadequate nutrition, which may lead to severe malnutrition and even failure to thrive (FTT). Different types of CHDs, especially those associated with cyanosis and/or pulmonary hypertension, may lead to malnutrition and growth retardation. Even some lesions such as left-to-right shunts, vascular rings, and obstructive heart diseases may give rise to growth retardation without the accompanying pulmonary hypertension or cyanosis. Three major causes of growth failure in these children are decreased energy intakes, malabsorption, and increased metabolic demands. In addition, in developing countries like Iran, poor knowledge of parents about nutritional requirement of their children and insufficient financial resources play important roles in this issue. [1, 2, 3] Meanwhile, some of these patients may also suffer from the consequences of different syndromes like Down, Turner, trisomy 18, trisomy 13, and other genetic abnormalities. Consequently, there are different factors contributing to growth impairment in these children.

In general, congenital cardiac anomalies can be classified into 2 major groups: cyanotic and acyanotic. Cyanotic congenital heart defects are classified based on their pathophysiology into lesions with decreased or increased pulmonary blood flows. Acyanotic lesions encompass 2 large groups: defects leading to volume overload (eg, left-to-right shunts, atrioventricular valve regurgitation, and some types of cardiomyopathies) and those resulting in pressure overload often due to ventricular outflow tract obstruction (eg, aortic or pulmonary valve stenosis) or stenosis of the large arteries (eg, coarctation of the aorta). [3]

The aims of the current study were to evaluate FTT and delayed bone age in patients suffering from CHDs and to compare the effects of cyanosis and pulmonary hypertension.

METHODS

Totally, 132 consecutive patients with a diagnosis of CHDs who underwent cardiac catheterization or surgical correction in Rajaie Cardiovascular, Medical, and Research Center from October 2012 to October 2015 were studied. The exclusion criteria were comprised of age less than 6 months, genetic syndromes, and any kind of endocrinopathy and neurologic diseases affecting growth. Eight patients suffering from Down syndrome, 3 patients with hypothyroidism, and 1 patient with Williams syndrome were excluded. CHDs in all the study population were diagnosed by clinical, paraclinical, and laboratory examinations such as chest X-ray, electrocardiography, echocardiography, and catheterization. Additionally, routine blood tests (ie, hemoglobin and hematocrit, Na, K, BUN, and creatinine levels as well as complete blood count, blood group, and Rh), urinalysis, and serologic screening for HBS and HIV were done for all the patients.

Growth parameters, consisting of height (cm), weight (kg), and head circumference (cm), were measured accurately using conventional methods and were plotted on standard growth curves and compared with standard growth charts (www.cdc.gov/nchs). The following definitions were used:

1. Short stature: when the child's height is 2 or more standard deviations (SD) below the mean standard growth curve of normal children with the same age and sex [4]
2. Low birth weight: birth weight less than 2500 g. [5] For these children, specific charts are also available at (http://static1.1.sqspcdn.com/static/f/2

4500/186746/1129059500317/LBW+Premature+Boys.pdf?token).

3. Microcephaly: when the head circumference is 2 or more SDs below the mean standard curve of normal children with the same age and sex [6]
4. FTT: weight for age less than the fifth percentile on standard growth charts (Among the different definitions for FTT, we used this definition because it is more practical.) [7]
5. Delayed bone age: skeletal age more than 10% below chronological age

Anteroposterior wrist X-ray was evaluated to determine bone age by an expert radiologist, who was blinded to the patients' age and types of CHDs. In normal subjects, bone age should be roughly within 10% of chronological age (Fig. 1). A greater difference is considered abnormal. [8]

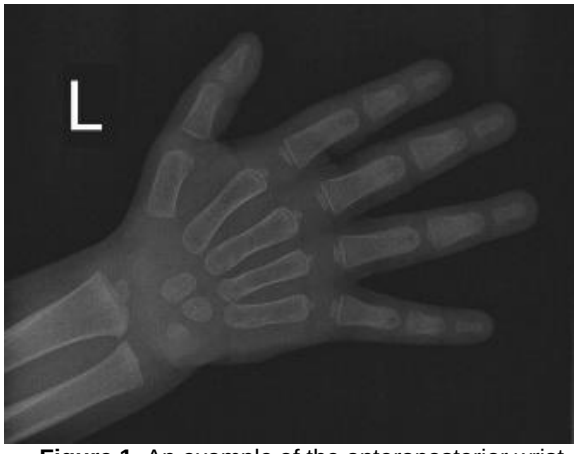

Figure 1. An example of the anteroposterior wrist X-ray of a young baby.

The pulmonary artery pressure, systemic blood pressure, and arterial oxygen saturation were measured. The pulmonary artery pressure was measured during cardiac catheterization or surgical correction. If the mean pulmonary artery pressure was above 25 mm Hg, it was regarded as pulmonary hypertension [9] and if the pulmonary artery pressure (mean and or systolic) was more than 67% of the systemic blood pressure (mean and or systolic), it was considered as severe pulmonary hypertension. [10]

The present study was approved by our local ethics committee and was conducted in accordance with the Helsinki Declaration of the World Medical Association (2000). The parents or guardians of the children enrolled gave written informed consent.

RESULTS

The baseline and angiographic data of the study population are illustrated in Table 1. The minimum age of the patients was 6 months and the maximum age was 180 months. From the 120 patients, 44 (37%) had cyanotic CHDs and 35 (29.4%) pulmonary hypertension. Thirty-five (29.4%) patients had short stature, 21 (18.6%) low weight at birth, and 18 (15.1%) microcephaly. Bone growth retardation and FTT were observed in 56 (47.1%) and 52 (43.7%) patients, correspondingly. During our study, 8 (6.7%) patients underwent pulmonary artery banding, 9 (7.6%) underwent shunt surgery, and 14 (11.8%) had total correction surgery. All the hemodynamic data were gathered during catheterization or surgeries.

O_2 saturation in the cyanotic patients varied between 44% and 88% (mean = 76 ± 6). The mean of the pulmonary artery pressure in the patients with pulmonary hypertension was 47.5 ± 15 mm Hg (range = 30–100 mm Hg).

The relationship between growth status factors and bone growth retardation is demonstrated in Table 2. There were significant differences in all the measured factors, including FTT (P <0.0001), short stature (P = 0.002), head circumference (P = 0. 01), and birth weight (P = 0.04) between the patients with delayed bone age and those with normal bone age; nonetheless, there was no significant difference between them in terms of sex (P = 0.23). The delay in bone age was significantly more frequent in the patients with cyanotic CHDs (P < 0.0001) and those with pulmonary hypertension (P < 0.0001).

Comparisons regarding FTT, short stature, and microcephaly between the patients with cyanotic and acyanotic CHDs can be seen in Table 3. FTT (P = 0.002) and short stature (P = 0.006) were significantly more common among the cyanotic patients, but there was no significant difference between the 2 groups in terms of head circumference (P = 0.31).

Comparisons between the patients with pulmonary hypertension and those without it vis-à-vis FTT, short stature, and microcephaly are presented in Table 4. There were significant differences between the 2 groups in terms of FTT (P = 0.001), short stature (P = 0.004), and microcephaly (P = 0.001).

Table1. Baseline and angiographic data in all the patients

Variables	Mean ± SD / N (%)
Age (mon)	61.54 ±52.01
Sex (male)	56(46.6%)
Height (cm)	102.02±29.49
Weight (kg)	17.7±12.71
Bone age (mon)	51.97±50.12
Birth weight (kg)	3.03±0.56
MPAP (mm Hg)	47.51±15.07
Short stature	35 (29.4%)
FTT	52(43.7%)
Bone growth retardation	56(47.1%)
Microcephaly	18 (15.1%)
Cyanosis	44(37%)
PH	35(29.4%)
Cyanosis with PH	8(18.6%)

MPAP, Mean pulmonary artery pressure; FTT, Failure to thrive; PH, Pulmonary hypertension

Table 2. Relationship between growth status factors and bone age retardation

		Bone Growth Retardation (n=56)	*P*
Sex	male	66(55%)	0.23
	female	54(45%)	
Short stature	+	26(74.3%)	0.002
	-	30(43.4%)	
FTT	+	38(73%)	<0.0001
	-	18(37.3%)	
Microcephaly		14(77.7%)	0.01
Normocephaly		42(47.4%)	
Low birth weight		15(71.4%)	0.04
Appropriate birth weight		41(47.8%)	
Cyanosis	with PH	22(58.3%)	0.007
	without PH	14(29.2%)	
Cyanosis	O_2 sat<75%	9(67%)	<0.0001
	O_2 sat>75%	15(50%)	
Acyanosis	with PH	12(81.5%)	<0.0001
	without PH	17(29.2%)	

FTT, Failure to thrive; PH, Pulmonary hypertension

Table 3. FTT, short stature, and microcephaly in the patients with cyanotic CHDs compared with the patients with acyanotic CHDs

	Cyanotic CHDs (n=44)	Acyanotic CHDs (n=76)	*P*
FTT	27(51.9%)	11(21.1%)	0.002
Short stature	14(40%)	5(14.2%)	0.006
Microcephaly	3(16.6%)	1(5.5%)	0.31

FTT, Failure to thrive; CHDs, Congenital heart diseases

Table 4. FTT, short stature, and microcephaly in the patients with PH compared with the patients without PH

	With PH (n=35)	Without PH (n=85)	*P*
FTT	31(59.6%)	11(21.1%)	0.001
Short stature	16(45.7%)	4(11.4%)	0.004
Microcephaly	6(33.3%)	1(5.5%)	0.001

FTT, Failure to thrive; PH, Pulmonary hypertension

DISCUSSION

Well-being of children is judged by their growth. Any chronic disease, like CHDs, can impair a child's growth. We evaluated the different parameters of growth such as weight, height, head circumference, and bone age in 120 Iranian children suffering from CHDs and found that 43%, 29.4%, and 15.1% of them suffered from FTT, short stature, and microcephaly, respectively. The prevalence of poor weight and height gain seems to be slightly dissimilar in different studies. [11, 12, 13] It has been proven that the etiology of growth failure in patients with CHDs is multifactorial and genetic factors also have an important role in this regard. Thus, the difference can be attributed not only to inadequate energy intake and more energy expenditure but also to different genotypes of heterogeneous groups of children from different parts of the world, which calls for further in-depth investigation. [14] Dalili et al [15] showed that growth retardation was more prevalent among the girls than the boys in their study. In our study, FTT and short stature were more prevalent in the cyanotic patients than in the non-cyanotic ones (P = 0.002 and P = 0.006, respectively). Previous studies have reported the occurrence of acute or chronic malnutrition in about 70% of pediatric patients with cyanotic CHDs and/or congestive heart failure. [16] Studies have shown that retardation in weight and height is more severe in cyanotic CHDs and growth retardation is more significant in cyanotic patients than in acyanotic ones. [17, 18]

The prevalence rate of bone growth retardation among our patients was 47.1%. In our study, delayed bone age was more common in the cyanotic patients whether or not they had pulmonary hypertension. Also, bone age retardation was significantly higher in the patients with cyanotic CHDs without pulmonary hypertension than in the patients with acyanotic CHDs without pulmonary hypertension (P = 0.007). In addition, if O_2 saturation in the cyanotic patients was lower than 75%, the prevalence of bone age retardation was even higher (P = 0.000). These findings also chime in with those reported by other similar studies. [17-19]

Among our acyanotic patients, the prevalence of bone age retardation was significantly higher in those suffering from pulmonary hypertension (P = 0.000). El Batrawy et al [20] also reported the same results. We showed that the prevalence of bone age retardation was higher if the mean pulmonary artery pressure was more than 40 mm Hg (P = 0.000).

Our results also demonstrated a meaningful relation between bone age retardation and the occurrence of FTT, short stature, microcephaly, and low birth weight. Patients with CHDs and cyanosis, pulmonary hypertension, and congestive heart failure appear to have an increased prevalence of growth failure and malnutrition compared to the normal population. [1-3-20] According to the results of the present study, bone-age delay and growth retardation are common findings in children with CHDs. The presence of cyanosis and/or pulmonary hypertension may further deteriorate these conditions and should

be promptly managed. In the present era, most of the congenital heart defects can be corrected if diagnosed early. This study reports a significantly high prevalence of delayed bone age among cyanotic patients with O_2 saturation lower than 75%, pulmonary hypertension patients with a mean pulmonary artery pressure greater than 40 mm Hg, and/or systolic pulmonary artery pressure/systolic aortic pressure greater than 67%. Furthermore, our findings underline the importance of the referral of patients with CHDs and pulmonary hypertension for early corrective surgery. It is vitally important that children with CHDs and increased pulmonary blood flows be placed under precise surveillance in order to minimize the adverse effects of malnutrition and the harmful results of hypoxia and pulmonary hypertension on their growth and bone maturation.

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