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Original article

25-Hydroxt Vitamin D Serum Level in Children with Congenital Heart Disease

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Abstract

Background & Aim: Identification of 25(OH) Vit D receptors in endothelial cells, smooth muscle cells, and myocytes from the heart has led to the hypothesis that this 25(OH) Vit D is involved in cardiovascular diseases**.** The present study was designed to evaluate 25-hydroxy Vitamin D serum levels in children with congenital heart diseases (CHD's) compared to controls. **Methods**: This case control study included 100 children, divided into 2 groups, Group (A) including 60 children with CHD who were divided into two subgroups (cyanotic and acyanotic) and group (B) including 40 apparently healthy children as a control group. All patients included in the study were subjected to the following: complete history taking, physical examination, echocardiography and serum 25 (OH) vitamin D levels. **Results:** The mean serum 25 (OH) vitamin D level was significantly lower in the CHD group than in the control group. The mean Serum 25 (OH) vitamin D level was significantly lower in the cyanotic group than in the acyanotic patients. There were statistically significant differences between serum 25 (OH) vitamin D levels in various age groups of cyanotic and acyanotic patients. **Conclusion:** Serum level 25(OH) Vit D was lower in CHD children. Among the patients, it was lower in the cyanotic group. So it should be checked in CHD children especially those with cyanotic heart disease.

Keywords: Vitamin D, Congenital Heart Disease; CHD; Children.

Introduction

Congenital heart diseases (CHD's) are major congenital anomalies, which consist of heart defects present since birth. Among all birth defects, CHD's are the main cause of death in infancy. It is the structural abnormality of heart or great vessels, detected either at the time of birth or later in life (1).

Globally, CHD's constitute the major cause of mortality among children, especially in developing countries. It also accounts for more than 20% of infant's death prenatally. The prevalence rate of CHD is estimated to be 8/1000 live births (2).

Vitamin D is one of the fat-soluble vitamins that enhance the intestinal absorption of calcium, phosphate, and zinc. It is essential for bone health, calcium homeostasis, and skeletal mineralization. Vitamin D also has immune-modulatory effects. Serum levels of 25-hydroxy vitamin D [25(OH)D] between 32 and 100 ng/ml are considered adequate, levels between 11 and 32 ng/ml are considered as vitamin D insufficiency, and levels less than 10 ng/ml are considered as severe deficiency (3).

About 90% of vitamin D is produced in the epidermis from 7-dehydrocholesterol (7-DHC) as a reaction to sunlight (solar ultraviolet B radiation; 290–315 nm). Factors that limit the cutaneous production of vitamin D3 include covering of skin, lack of outdoor activities, sunscreen use, old age, female sex, and darker skin pigmentation (4).

Also, new evidence suggests that the relationship between 25(OH) Vit D deficiency and increased risk of other diseases have been raised such as autoimmune diseases namely, diabetes type I, multiple sclerosis, rheumatoid arthritis, hypertension, infectious diseases and malignancies (5).

Identification of Vitamin D receptors in endothelial cells, smooth muscle cells, and myocytes from the heart has led to the hypothesis that this Vitamin D is involved in cardiovascular diseases (6).

The aim of the work was to evaluate 25-hydroxy Vitamin D serum levels in congenital heart disease children compared to controls.

Patients and methods

This study is a case control study which was conducted at Benha University Hospitals, cardiology clinic and general pediatric clinic

during the period from January 2021 to October 2021. The study included 100 children who were divided into 2 groups, Group (A) including 60 children with congenital heart defects who were divided into two subgroups (cyanotic and acyanotic) and group (B) including 40 apparently healthy age and sex matched children who were referred for routine checkup as a control group.

Inclusion criteria:

- Children with congenital heart defects.
- Age from 1 month to 15 years.
- Both sexes (males and females).

Exclusion criteria:

- Using drugs that affect calcium and bone metabolism.
- Chronic liver or kidney disease.
- Endocrine disorder such as hyperparathyroidism.
- Insulin use.
- Using anticonvulsants.

All the patients included in the study were subjected to the following: complete history taking, physical examination: (General examination and Cardiac examination), echocardiography, and serum 25 (OH) vitamin D levels measurement.

Ethical consideration:

This study was approved by the Ethical Committees of Faculty of Medicine, Benha University Hospital. Informed verbal and written consents were obtained from the parents before enrollment in the study.

Statistical Analysis

The data were recorded on an "Investigation report form". These data were tabulated, coded and then analyzed using the computer program SPSS (Statistical Package for Social Science) version 16. Descriptive statistics were calculated for the data in the form of mean, standard deviation (±SD), number and percentage. **Analytical statistics:** In the statistical comparison between the different groups, the significance of difference was tested using one of the following tests. Student's *t*-test was used to compare between the means of two groups of numerical (parametric) data. ANOVA (analysis of variance) was used to compare between more than two groups of numerical (parametric) data. For continuous non- parametric data, Mann-Whitney *U*- test was used for inter-group analysis. Pearson correlation coefficient (r) test was used correlating different parameters. Inter-group comparison of categorical data was

performed by using chi square test (X^2-value). Wilcoxon signed rank test was used for two values within the same group. Some investigated parameters were entered into a logistic regression model to determine which of these factors is considered as a significant risk factor and identify its odds ratio. The sensitivity and specificity were examined at different cutoff points using ROC curve analysis to determine the best cutoff point as well as the diagnostic power of each test. P-value <0.05 was considered statistically significant (S). And a P-value <0.001 was considered highly significant (HS) in all analyses.

Results

There was no statistically significant difference between the patients and control groups regarding age and sex while there was statistically significant difference regarding residence (Table 1).

The mean serum level of 25(OH) vit D was higher in the control group than the CHD group. The difference was statistically significant (Table 2).

The mean serum level of 25(OH) Vit D was higher in the acyanotic group than in the cyanotic patients and the difference was statistically significant (Table 3).

There were statistically significant positive correlations between serum 25 (OH) vit D level and age, weight, height, body surface area (BSA), systolic blood pressure and diastolic blood pressure and there was a statistically significant negative correlation between serum 25 (OH) vit D levels and pulse rate. There were no significant correlations between serum 25 (OH) vit D levels and body temperature, fractional shortening (FS) % and tricuspid annular plane systolic excursion (TAPSE) (Table 4).

There were statistically significant differences between serum 25 (OH) vit D levels of various age groups of cyanotic and acyanotic patients (Table 5).

Table (1): Demographic data of the studied groups.

Characteristics		CHD patients (n=60)	Control group (n=40)	Test of sig.	p-value
Age (months): mean ± SD		27.3 ± 28.1	32.1 ± 42.6	0.7	0.49
Sex: No. (%)	**Female**	28 (46.7%)	19 (47.5%)	0.9	0.9
	Male	32 (53.3%)	21 (52.5%)		
Residence: No. (%)	**Urban**	23 (38.3%)	28 (70%)	9.6	**0.002***
	Rural	37 (61.7%)	12 (30%)		

Table (2): Serum 25(OH) vit D in the studied groups.

Characteristic	CHD patients (n=60)	Control group (n=40)	Test of sig.	p-value
Serum 25(OH) vit D (ng/ml): mean ± SD	5.5±2.6	64.3±36.1	10.3	**<0.001***

Table (3): Serum.25 (OH) vit D in the cyanotic and acyanotic groups.

Characteristic	Cyanotic (n=20)	Acyanotic (n=40)	Test of sig.	p-value
Serum.25(OH) vit D level (ng/ml): (mean ± SD)	2.5±0.97	7.1±1.6	13.5	<0.001*

Table (4): Correlations between serum 25(OH) vit D levels and different variables.

Characteristics	r	p-value
Age / months	0.44	**<0.001***
Weight / kg	0.47	**<0.001***
Height / cm	0.49	**<0.001***
BSA	0.503	**<0.001***
Pulse (b/min)	-0.327	**0.001***
SBP (mmHg)	0.421	**<0.001***
DBP (mmHg)	0.381	**<0.001***
Temperature (^{o}C)	-0.168	0.095
F.S.%	0.112	0.269
TAPSE	0.049	0.630

SBP :systolic blood pressure. BSA body surface area, DBP: diastolic blood pressure. FS: Fractional shortening, TAPSE :Tricuspid annular

Table (5): Serum 25(OH) Vit D in cyanotic versus acyanotic children.

Characteristic	Age Groups (year)	Subgroups (No)	Mean ± SD	Test of sig.	P- value
25 (OH) Vit D (ng/ml)	0-2 (n=44)	Cyanotic (n=14)	2.7± 0.8	9.6	<0.001*
		Acyanotic (n=30)	7.3± 1.7		
	2-5 (n=9)	Cyanotic (n=3)	1.2±0.5	6.5	<0.001*
		Acyanotic (n=6)	6.4±1.3		
	>5 (n=7)	Cyanotic (n=3)	1.8 ± 0.5	4.9	0.004*
		Acyanotic (n=4)	6.9±1.7		

Discussion

The present study revealed that the mean serum 25(OH) vitamin D level was lower in the CHD group than in the control group. The possible causes of vitamin D deficiency in pediatric patients with CHD may be increased metabolism and increased energy, raw materials, vitamins, and minerals consumption in comparison to healthy children. Furthermore, this condition is a result of a disease-related sedentary lifestyle with reduced outdoor activities and longer hospitalization periods leading to limited ultraviolet-induced vitamin D production in the skin.

Our results agree with the majority of the previous studies which analyzed the connection between 25(OH) vitamin D and cardiovascular and different serious illnesses and discussed this relationship with explanations of several mechanisms by which Vitamin D deficiency may be associated with those illnesses. Recent studies (6 & 7) showed that children with CHD had significantly lower levels of 25 (OH) vitamin D compared to healthy subjects. Also, in accordance with our results, another study (8) demonstrated that the mean serum levels of 25(OH) vitamin D was lower in babies with dilated cardiomyopathy than in the ordinary status and that the seriousness of the disease was related to the rate of 25(OH) vitamin D inadequacy. In addition to that, other researchers (9) showed that vitamin D deficiency is commonly seen in patients with heart failure and that vitamin D deficiency exacerbates the condition of the patients.

Another researchers (10) also showed an inverse association between CVD and vitamin D level. They stated that the deficiency of Vitamin D seen in persons with CVD may be because these persons were less healthy and hence less likely to go outdoors to be exposed to sunlight or it may be mediated by a biological mechanism, whereby low Vitamin D causes increased risk of CVD events. Additionally, another study (11) demonstrated that 25(OH) vitamin D insufficiency in infants with left ventricular dysfunction was associated with extreme left ventricular dysfunction and with clear clinical signs. In another study (12) the authors found that vitamin D receptor-deficient mice showed symptoms like cardiac hypertrophy, hypertension, and higher thrombogenicity, suggesting the important role of vitamin D and its receptor in the cardiovascular system.

Furthermore, in a recent study (13) which studied vitamin D status in a group of neonates with CHD, and its relationship with the outcome of heart surgery the researchers found that before the operation, vitamin D levels were not significantly different from that of the control group. With heart surgery, vitamin D levels decreased and the difference between the CHD and control groups became significant.

Our study shows that serum 25(OH) vitamin D level was significantly lower in the cyanotic patients compared to the acyanotic patients. We found that there were a statistically significant differences between serum 25(OH) vitamin D levels in the various age groups of cyanotic and acyanotic patients.

This is in line with previous studies (6,14 &15) which revealed that there was a significant difference between the serum levels of 25(OH) vitamin D in the two groups of their patients (cyanotic and acyanotic). In addition, they found a significant difference between the different age groups of patients.

On the other hand, in recent studies (7 & 13) the authors found no significant difference of vitamin D level in the cyanotic and the acyanotic patients. In another study (9) although the researchers found that lower levels of 25(OH) vitamin D were associated with a higher incidence of CHD, they found that the difference between the mean serum levels of 25(OH) vitamin D in different ages was similar. This finding was not consistent with our findings. This difference may be due to differences in age groups, life style and society.

Before concluding, there are several limitations to our study that should not be neglected when interpreting the findings such as a lack of good corporation by some of the participants, particularly the controls, and the limited sample size, which was limited to patients treated at Benha University Hospitals. As a result, the current findings need to be confirmed by larger sample size studies and multiregional collaboration. Also, future researches should look into other possible causes of 25(OH) vitamin D deficiency in children generally and those with CHD in particular.

Conclusion

From the present study, we concluded that the serum level of 25(OH) Vit D was lower in CHD children, and among the patients, it was lower in the cyanotic group. So it should be checked in CHD children especially those who suffer from cyanotic a heart disease.

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