Correlation between Vitamin D Levels and Heart Failure in Children at Haji Adam Malik Hospital Medan, Indonesia

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Abstract

The objective of this research was to assess the correlation between vitamin D levels and heart failure in children. Vitamin D is a micronutrient affecting the prognosis for heart failure in children. Vitamin D deficiency exacerbate heart failure condition. Moreover, in severe heart failure functional class, vitamin D deficiency is commonly reported. This research was an analytical cross-sectional research carried out in pediatric cardiology polyclinic and inpatient clinic Haji Adam Malik Hospital Medan from September 2020 – January 2021 to assess the correlation between vitamin D levels and heart failure. Vitamin D level assessment was done to 50 pediatric patients with heart failure. Correlation test was done by using Somers' D correlation tests by SPSS 17.0 software. Among 50 research subjects, 40 subjects (80%) suffered from vitamin D deficiency and 14 of them (35%) were classified in class III heart failure. By using Somers' D correlation test, non-significant relationship was observed between vitamin D levels and heart failure conditions (p=0.337; r = -0.079).

Published by IJRP.ORG. Selection and/or peer-review under responsibility of International Journal of Research Publications (IJRP.ORG)

Keywords: vitamin D levels, heart failure, children

1. Introduction

Heart failure is a clinical syndrome when the heart cannot pump enough blood to meet the metabolic needs of the body, restore systemic and pulmonary venous return, or the combination of both activities (Park, 2014). Heart failure in children is a progressive clinical condition caused by cardiovascular or non-cardiovascular abnormalities that cause signs and symptoms such as edema, respiratory distress, growth failure, and activity intolerance accompanied by molecular, circulatory, and neurohormonal disturbances (Hsu and Pearson, 2009). By definition, heart failure in children is the same as heart failure in adults. The differences, however, are in the causes and mechanisms of heart failure (Beggs et al., 2009). In Indonesia, the prevalence and incidence of heart failure in children are hardly recorded.

From the research done in Manado for 3 years, there were 69 new heart failure cases, where 36.2% were rheumatic heart disease (RHD) cases and 23.2% were congenital heart disease (CHD) cases (Park, 2014). CHD was estimated to be found in 8 per 1000 births, with 20% rate of heart failure (Jayaprasad, 2016). With the development of technology intervention in pediatric cardiology and thoracic surgery, either through percutaneous or surgical methods, the incidence of heart failure caused by CHD can be reduced to one to two children per 1000 births (Fahed et al., 2014).

Meanwhile, the prevalence of heart failure caused by RHD in developing countries was reported at 20.1% (Beggs et al., 2009). Other causes of heart failure in children include systemic inflammatory, metabolic, endocrine, and kidney diseases with an undetermined number of cases (Kantor et al., 2013). Children with heart failure and hospitalized have a 20-fold higher risk for death (Hinton and Ware, 2017).

Several epidemiological studies have stated that individuals with low vitamin D levels have increased risks of heart failure, hypertension, and diabetes mellitus. Vitamin D is one of the vitamins that regulates various functions in the human body (Sidarta, 2014). Vitamin D deficiency influences the risk of heart failure through the following mechanisms as follow, vitamin D as an inflammatory modulator, regulates renin-angiotensin-aldosterone system (RAAS) that causes hypertension and clinical heart failure, inhibits the production of parathyroid hormone (PTH) that causes left ventricular hypertrophy, induces hypertrophy in immature cardiac myocytes, and regulate muscular smooth muscle (Savastio et al., 2020). In the study done by Guo et al, there were 16,755 children aged 0 to 6 years old with 25(OH)D serum level between 10.5 – 307.4 mmol/L, and 10.8% and 39.0% prevalence of vitamin D deficiency and insufficiency respectively (Guo et al., 2017). The study done in China in 2019 reported the prevalence of vitamin D deficiency was 59.28% in adults with heart failure, 48.55% in vitamin D insufficient group, and 52.78% in group with normal vitamin D (Wang et al., 2019).

There has not been many research done about vitamin D levels and heart failure in children. In Indonesia, especially in Haji Adam Malik hospital Medan, the research about the correlation between vitamin D levels and heart failure in children has never been done. Therefore, this research aims to assess the correlation between vitamin D levels and heart failure in pediatric patients in Haji Adam Malik hospital.

2. Methods

This was an analytical cross-sectional study to assess the correlation between vitamin D levels and heart failure condition in children. The research was conducted in pediatric cardiology polyclinic and inpatient clinic Haji Adam Malik hospital Medan from September 2020 to January 2021. Research samples were children with heart failure who were receiving treatment in pediatric cardiology polyclinic and inpatient clinic Haji Adam Malik hospital Medan during the research period and meeting the inclusion and exclusion criteria. They were selected by consecutive sampling method, with a minimum sample size of 50 subjects based on sample size formula for hypothesis testing in one population with categorical variables. Inclusion criteria were children aged 1 month - 18 years old with heart failure condition and undergoing treatment in pediatric cardiology polyclinic and inpatient clinic Haji Adam Malik hospital Medan. Exclusion criteria were children with heart failure who had received vitamin D supplementation, children suffering from sepsis, liver and renal failure, and children who refused to do laboratory blood test.

Interviews were conducted to obtain demographic data, such as age and gender, as well as clinical data, such as family history of the disease, length of CHD diagnosis, and history of treatment or surgery. Physical examination and anthropometric measurement were done to obtain body weight and height, nutritional status, and heart murmurs data. Echocardiography examination was carried out to assess the left ventricular function based on ejection fraction (EF), fractional shortening (FS), and E/A ratio measurement. All of the research subjects also underwent complete blood test in Clinical Pathology Laboratory Haji Adam Malik hospital Medan to obtain vitamin D levels data.

2.1. Research ethics

Parents of the research subjects were given explanation about the research and they were asked for consent to be involved in the study. This study was approved by Health Research Ethical Committee, Medical Faculty of Sumatera Utara (No. 744/KEP/USU/2020).

2.2. Data analysis

Data collected was analyzed by using Statistical Package for the Social Sciences (SPSS version 17) software system. Univariate analysis was carried out for research subject characteristic data. Categoric data was presented in frequency and percentage. The correlation between vitamin D levels and heart failure in children was assess by using Somers' D correlation test. The significance level and confidence interval used in this study were $p < 0.05$ and 95% respectively.

3. Results

3.1. Research subject data characteristic

This research was followed by 50 pediatric patients, who met the inclusion and exclusion criteria, with heart failure and undergo treatment in both pediatric cardiology polyclinic and inpatient Haji Adam Malik hospital Medan. There were 28 (56%) male and 22 (44%) female patients. The research subjects were aged between 1 month to 18 years old. There were 26 (52%) patients with malnutrition, 9 (18%) patients with poor nutritional status, and 15 (30%) patients with good nutritional status. Based on New York Heart Association (NYHA) functional classification, there were 20 (40%) patients in class III heart failure, 15 (30%) patients in class II, and the remaining 15 (30%) patients were classified as class IV heart failure. The demographic characteristic of research subjects is shown in Table 1.

Table 1. Research subject demographic characteristic

Demographic characteristics	***n* = 50**
Gender, n (%)	
Male	28 (56)
Female	22 (44)
Age, n (%)	
1 month – 11 month old	7 (14)
1 year – 1 year 11 month old	7 (14)
2 year – 4 year 11 month old	7 (14)
5 year – 11 year 11 month old	14 (28)
12 year – 17 year 11 month old	15 (30)
Nutritional status, n (%)	
Malnutrition	26 (52)
Poor nutrition	9 (18)
Good nutrition	15 (30)
Functional class, n (%)	
Class I heart failure	0
Class II heart failure	15 (30)
Class III heart failure	20 (40)
Class IV heart failure	15 (30)

3.2. Echocardiography examination

The average ejection fraction (EF) from 50 research subjects was 76.92% (SD = 6.35%) and the average fractional shortening (FS) was 50.37% (SD = 8.38%). There were 31 (62%) research subjects with reduced EF and FS values. Meanwhile, the average E/A ratio was 3 m/s (SD = 0.81 m/s). There were 38 (76%) patients with reduced E/A ratio. The results of echocardiography examination is presented in Table 2.

Table 2. Echocardiography examination result

Echocardiography	*n* (%)	Average (SD)
EF, %		76.92 (6.35)
Normal	19 (38)	
Reduced	31 (62)	
FS, %		50.37 (8.38)
Normal	4 (8)	
Reduced	31 (62)	
E/A ratio, m/s		3 (0.81)
Normal	12 (24)	
Reduced	38 (76)	

3.3. Vitamin D level examination

The average vitamin D level from all research subjects was 16.38 ng/mL, with the lowest and highest levels being 0.9 ng/mL and 44.6 ng/mL respectively. There were 2 (4%) patients suffering from severe vitamin D deficient, 40 (80%) patients suffering from vitamin D deficient, and 3 (6%) patients with insufficiency of vitamin D. The result of vitamin D level examination was presented in Table 3.

Table 3 also shows vitamin D levels based on the NYHA functional classification, where the average vitamin D level in class II heart failure was 16.77 ng/mL (SD = 7.81 ng/mL), while the average vitamin D level in class III and IV heart failure was 17.54 ng/mL (SD = 10.13 ng/mL) and 25.53 ng/mL (SD = 14.45 ng/mL) respectively. There were 20 (40%) patients with class III heart failure, while 15 (30%) patients each in class II and IV heart failure. The analysis by using Kruskal Wallis test showed no significant differences in vitamin D levels and functional classification of heart failure (p = 0.867).

Table 3. Vitamin D level examination

Parameter	Value	p
Vitamin D level, average (SD), ng/mL		
Class II heart failure	16.77 (7.81)	
Class III heart failure	17.54 (10.13)	0.867
Class IV heart failure	25.53 (14.45)	
Vitamin D level, n = 50		
Average (SD), ng/mL	16.38 (8.32)	
Vitamin D status, n = 50		
Severe deficient, n (%)	2 (4)	
Deficient, n (%)	40 (80)	
Insufficient, n (%)	3 (6)	
Normal, n (%)	5 (10)	

3.4. Correlation between Vitamin D level and heart failure

In class II heart failure, there were 2 (40%) patients with normal vitamin D levels, while 13 (32.5%) patients were vitamin D deficient. Meanwhile, in class III heart failure, there were 2 (40%) patients with normal vitamin D level, 3 (100%) patients had insufficient vitamin D level, while 14 (35%) patients were deficient and 1 (50%) patient was severely deficient of vitamin D. In class IV heart failure classification, there was 1 (20%) patient with normal vitamin D level, 13 (32.5%) patients with vitamin D deficiency, and 1 (50%) patient with severe vitamin D deficiency. By using Somers' D correlation test, non-significant relationship were observed between vitamin D level and heart failure ($p = 0.337$, $r = -0.0790$). The relationship between vitamin D and heart failure is presented in Table 4.

Table 4. Correlation between vitamin D levels and heart failure

Vitamin D status	Heart failure classification			*r*	*p*
	Class II	Class III	Class IV		
Normal	2 (40)	2 (40)	1 (20)	-0.0790	0.337
Insufficient	0	3 (100)	0		
Deficient	13 (32.5)	14 (35)	13 (32.5)		
Severe deficient	0	1 (50)	1 (50)		

4. Discussion

There were more male research subjects, such as 28 (56%) patients, than female patients in this research with the highest number of research subjects, 15 (30%) children, were between 12 years to 17 years and 11 months old. The study done in Taiwan by Tseng reported inpatient heart failure incidence rate at 7.4 per 100,000 patients aged 0 – 14 years old. However, there were more female patients than male (8.8 vs 6 per 100,000 cases) and most research subjects were in 0 – 4 years old age group (21.7 per 100,000 population) (Tseng, 2010). In this research, however, no assessment of the correlation of gender and age to heart failure incidence.

Rahman et al in their study in Surabaya have reported 42.5% cases of heart failure with malnutrition, 25% cases with poor nutrition, whereas only 1.5% research subjects with heart failure who were obese (Rahman et al., 2020). Similarly, Ratanachu and Pongdara observed 53% of their research subjects with heart failure suffered from malnutrition, 3% were obese, 28% suffered from poor nutrition, and 16% of them were stunted (Ratanachu and Pongdara, 2011). In this research, over half (52%) of the research subjects with heart failure suffered from malnutrition.

There were many factors that cause nutritional disorders in children with heart failure, such as hemodynamic factors or low growth potential, such as low birth weight. Other causes of malnutrition may be inadequate nutrition intake, inefficient energy absorption and utilization, and/or increase in energy requirement (Rodica, 2013). Differences in growth and development between healthy children and children with heart failure could be related to different factors, such as gender, age, heart defects, simultaneous multiple congenital heart diseases, and congestive heart failure (Noori et al., 2017). The study in Iran by Noori et al found that cytokines have strong effects on appetite, growth, body weight, and energy intake in patients with heart failure (Noori et al., 2016).

The study done by Witte et al in the UK analyzed echocardiography parameter from the research population, such as heart failure patients with vitamin D deficiency. They found that 75%

from the research subjects suffered from diastolic heart failure. Patients with vitamin D deficiency had significantly longer EDD and ESD (Witte et al., 2016). In this research, there were 31 (62%) patients with reduced EF value, another 31 (62%) patients with reduced FS value, and 38 (76%) patients with reduced E/A ratio. As for vitamin D diagnosis, there were 3 classifications in children as follow, normal level when 25-hydroxyvitamin-D [25(OH)-D] level in blood was between 30 – 100 ng/mL, insufficient when 25-hydroxyvitamin-D [25(OH)-D] level in blood was between 21 – 29 ng/mL, and deficient when 25-hydroxyvitamin-D [25(OH)-D] level in blood was <20 ng/mL (Beggs et al., 2009).

The study done by Wang et al in China showed 59.28% and 48.55% prevalence of vitamin D deficiency and insufficiency respectively in adult groups with heart failure, while 52.78% prevalence of normal vitamin D level in the group (Wang et al., 2019). In the research done by Gotsman et al in Israel, the prevalence of vitamin D deficiency ([25(OH)D] level <25 nmol/L) was higher in patients with heart failure than in control group (28% vs 22%, p value = 0.00001). There were only 8.8% heart failure patients and 10.1% patients from other research group with optimum vitamin D level ([25(OH)D] level ≥75nmol/L) (Gotsman et al., 2012). In this research, the majority of heart failure patients (80%) suffered from vitamin D deficiency. Moreover, there were 2 (4%) patients with severe deficiency and 3 (6%) patients had insufficient vitamin D level.

Kusunose et al in their study in Japan reported the effects of vitamin D deficiency to death in the hospital was higher in NYHA III – IV patients than NYHA I – II (NYHA III-IV: OR: 0.63, p <0.001 and NYHA I-II: OR: 0.72, p = 0.014) (Kusunone et al., 2021). Similarly in this research, 14 (35%) patients with class III heart failure had the average vitamin D level of 17.54 ng/mL, with p value 0.337 and r = -0.790. The negative value indicated that the lower the vitamin D level, the higher the functional classification of heart failure.

Low vitamin D level increases the functional class in heart failure patients as the result of disease-associated sedentary lifestyle that reduced outdoor activities and subsequently limiting UVB-induced vitamin D production in the skin. This is related to the fact that reduced physical activity is also a consequence of heart failure and closely related to NYHA classification. The mechanism that may link vitamin D deficiency ad heart failure is the regulation of 1,25(OH)2D on myocardial gene expression. Several genes upregulated in myocardial hypertrophy were found to be suppressed by 1,25(OH)2D treatment. Vitamin D has also been proven to reduce the activation of RAAS in the systemic and cardiac functions that contributed to cardiac hypertension and hypertrophy. Furthermore, cardioprotective effect of 1,25(OH)2D with its anti-inflammatory effect was confirmed in an interventional trial of 1,25(OH)2D in heart failure patients. Myocardial calcium hemostasis, which is important for cardiac contractility and electrophysiology, is also partially regulated by 1,25(OH)2D and mediated by its effect on ion channel and enzymatic reactions. The exact mechanism needs to be further clarified, but it appears that sufficient vitamin D status is important to prevent myocardial hypercontractility and maintain diastolic function (Pilz et al., 2008).

This research is the first research in North Sumatra to assess the correlation between vitamin D levels and heart failure condition in children, despite the insignificant correlation. The result of this research, however, can become a reference for further research to find other methods to determine vitamin D levels in children with heart failure to serve as the guideline for vitamin D supplementation. Furthermore, allowing more attention to vitamin D levels and changes in physical activity in heart failure patients.

5. Conclusion

There was no significant relationship observed between vitamin D levels and heart failure in children (p=0.337; r=-0.079) in this research.

Acknowledgements

The author would like to thank all the staff in the Faculty of Medicine, Universitas Sumatera Utara for the extensive support during the study.

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