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The Association Between Anemia (Hemoglobin Level) and Cardiomegaly Based On Chest

Radiograph and Echocardiography

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ABSTRACT

Background : Anemia is one of the major global problems that continues to this day. According to World Health Organization (WHO) data, anemia is found in 1.62 billion people or equivalent to 24.8% of the world's population while, the prevalence of anemia in children under 6 years of age in Indonesia reached 38.4%. Anemia, if undiagnosed or untreated for a long period of time can lead to multiorgan failure. The cardiovascular system is the most commonly affected system in chronic anemia. Between one-third and two-thirds of patients with severe anemia have cardiomegaly and this will return to normal within a few weeks after the anemia is well managed. This abnormality can be evaluated on chest radiograph or echocardiography.

Objective : This study aims to evaluate the association between anemia and cardiomegaly.

Methods : This was a cross-sectional which was carried out in the pediatric ward and pediatric cardiology outpatient clinic in the year 2022. The research subjects were children diagnosed with anemia, then they would undergo chest radiograph and echocardiography to assess whether there is cardiomegaly or not.

Results : Eighty one children were included in this study. The majority of them were girl, with a total of 43 people (53.1%). The median age of patients in this study was 7.75 years old. In addition, this study also found that the median of patients' body weight and height were 18.3 kg and 116 cm. In this study, the median hemoglobin level was 10.3 g/dL. For the echocardiography parameters in this study, the median of LA/Ao, EF and FS were 1.24, 65% and 35% respectively.

Conclusion : There is no association between anemia and cardiomegaly based on chest radiograph or echocardiography.

Keywords : Anemia, echocardiography, chest radiograph, cardiomegaly, heart enlargement

INTRODUCTION

Anemia is a condition where there is a decrease in the number of erythrocytes or hemoglobin concentration. Hemoglobin is needed to carry oxygen and if the number of erythrocytes or hemoglobin levels are too low or abnormal, there will be a decrease in the blood's capacity to carry oxygen to the body tissues. Anemia is a serious global health problem especially in children and pregnant women.¹ The World Health Organization (WHO) estimates that 42% of children under 5 years of age and 40% of pregnant women worldwide are anemic. According to (WHO) data, anemia is found in 1.62 billion people (95% CI: 1.50-1.74 billion), which is equivalent to 24.8% of the world's population (95% CI: 22.9-26.7%).² In Indonesia, the prevalence of anemia in children under 6 years of age in 2019 reached 38.4%.¹

Despite the relatively high prevalence of anemia, its clinical implications tend to be underestimated in anemic individuals without significant medical problems. Clinical and hemodynamic changes due to short-lasting acute anemia are reversible. However, if undiagnosed or untreated for a long period of time it can lead to multiorgan failure. The cardiovascular system is the most commonly affected system in chronic anemia. Anemia causes hypoxia due to decreased hemoglobin levels, and there are several nonhemodynamic (increased erythropoietin production, decreased hemoglobin affinity for oxygen due to increased 2,3-diphosphoglycerate) and hemodynamic compensatory mechanisms.^{3,4} Anemia increases cardiac output, leading to left ventricular hypertrophy. Increased left ventricular performance results due to increased preload (Frank-Starling mechanism) and increased inotropic state associated with sympathetic activity.³ Chronic anemia leads to progressive cardiac enlargement and left ventricular hypertrophy due to volume overload which can be seen on thoracic x-ray or echocardiography.³⁻⁶

Between one-third and two-thirds of patients with severe anemia have cardiomegaly on chest radiographs. Echocardiography has also shown some hemodynamic changes in anemic patients. Diastolic and systolic left ventricular chamber size will enlarge to increase cardiac output, aiming to improve systemic oxygen delivery.⁴ It should be remembered that anemia has an adverse impact on the cardiovascular system and is associated with a poor cardiovascular prognosis.⁶ To date, published data on the correlation between hemoglobin (Hb) concentration and cardiac enlargement are scarce.

METHODS

This is an observational study with cross-sectional design which was done in the pediatric ward and pediatric cardiology outpatient clinic in the year 2022. The sampling technique used was consecutive sampling, with minimum sample of 56 subjects. The population in this study were all children diagnosed with anemia. Inclusion criteria were anemic patients aging maximal 18 years old and had undergone chest x-ray and echocardiography. These two tests were done in order to evaluate whether the patient develop cardiomegaly or not. Exclusion criteria were patients who had undergone definitive surgery, patients who had took iron supplementation in the last 3 months, as well as those who had other anemic conditions such as chronic kidney disease or hemolytic anemia.

This research was conducted after obtaining informed consent from patients regarding the study and data that were going to be collected. The data collected were patient's identity (name, age, body weight and height), patient's hemoglobin level, patient's cardiomegaly status (based on chest x-ray and echocardiography) and patient's echocardiography parameters (LA/Ao, EF, and FS). The diagnosis of anemia is based on the hemoglobin range by WHO.⁷

Data were then tabulated into master table using SPSS software. Categorical data were presented in proportion and frequency, while numerical data were presented in either mean±standard deviation or median depends on the results of the normality test. The correlation between mean perfusion pressure and renal resistive index will be analyzed using Spearman correlation test.

RESULTS

Characteristics of Study Subjects

There were a total of 81 subjects in this study. The characteristics of the subjects of this study are shown in table 1.

Table 1. Characteristics of Study Subjects

| Characteristics | Median (Min-Max) |
|-------------------|---------------------|
| Gender, n(%) | |
| • Boy | 38 (46.9%) |
| • Girl | 43 (53.1%) |
| Age (years) | 7.75 (0.3 – 17.75) |
| Body Weight (kg) | 18.3 (3.8 – 71.4) |
| Body Height (cm) | 116 (50 – 167.5) |
| Hemoglobin (g/dL) | 10.3 (3.8 – 15.4) |
| LA/Ao | 1.24 (1.10 – 1.46) |
| EF (%) | 65 (45 – 89) |
| FS (%) | 35 (21 – 58) |

Based on table 1, it was found that the majority of subjects were girl, with a total of 43 people (53.1%). The median age of patients in this study was 7.75 years old. In addition, this study also found that the median of patients' body weight and height were 18.3 kg and 116 cm. In this study, the median hemoglobin level was 10.3 g/dL. For the echocardiography parameters in this study, the median of LA/Ao, EF and FS were 1.24, 65% and 35% respectively.

Association Between Anemia and Cardiomegaly Based on Chest Radiograph

Table 2. Association between anemia and cardiomegaly based on chest radiograph

| Anemia | Chest Radiograph | | Total | p value |
|--------|------------------|--------------|------------|---------|
| | Normal | Cardiomegaly | | |
| Normal | 35 (43.2%) | 1 (1.2%) | 36 (44.4%) | 0,093* |
| Anemia | 39 (48.1%) | 6 (7.4%) | 45 (55.6%) | |
| Total | 74 (91.4%) | 7 (8.6%) | 81 (100%) | |

*Chi Square test

Based on the Chi Square test in table 2, there is no significant association between anemia and cardiomegaly based on chest radiograph where the p value is > 0.05 .

DISCUSSION

In this study, there was no association between anemia and cardiomegaly based on either chest radiograph or echocardiography. The association between anemia and cardiomegaly in children is still being considered. From several studies, there are also no studies that specifically discuss the association between cardiomegaly and anemia. Some studies have only linked cardiomegaly as one of the clinical manifestations of pediatric cardiac disorders (such as heart failure, cardiomyopathy, or myocarditis) with anemia. For example, studies conducted by Puri et al and Isezuo et al. Puri et al stated that anemia can increase the risk of heart failure in children and worsen heart damage due to cardiomyopathy in pediatric patients with heart failure, while Isezuo et al supported the results of the study from Puri et al by stating that anemia can be the most common cause of heart failure in children, including other causes such as congenital heart disease, bronchopneumonia, rheumatic heart disease, and dilated cardiomyopathy.^{8,9}

Anemia itself consists of various types, with iron deficiency anemia being the most common anemia in children. According to Wittekind et al, iron deficiency anemia can cause secondary cardiomyopathy which can lead to cardiomegaly, but the pathogenesis of cardiomyopathy is still unclear. This statement is in accordance with research conducted by Shalby et al, who stated that the cardiovascular system can be affected by the occurrence of anemia as a non-hematological manifestation in pediatric patients with iron deficiency anemia. Cardiomegaly, arrhythmia, left ventricular hypertrophy, and heart failure can occur when the state of iron deficiency anemia continues. Odeyemi et al also agree with this statement, stating that anemia can worsen the damage that has occurred to the heart, especially the myocardium, if iron deficiency anemia is not treated immediately.^{10,11}

Shalby et al in their study explained that iron deficiency anemia and cardiomegaly are interrelated. According to Shalby et al, the cardiovascular system can occur as a non-hematological clinical manifestation in patients with iron deficiency anemia due to increased cardiac output. Cardiac output that occurs is a compensation for meeting the oxygen needs of the tissues. Compensation occurs in the form of increased blood volume, pulse frequency, and stroke

volume. If these three things left untreated, it could cause cardiomegaly, arrhythmia, left ventricular hypertrophy, and heart failure.¹²

Wittekind et al also further discussed the relationship between iron deficiency anemia and cardiac dysfunction in their case report. In the case report, the cardiac dysfunction found was left ventricular and atrial enlargement. Wittekind et al said that left ventricular enlargement is caused by iron deficiency cardiomyopathy, while left atrial enlargement occurs due to increased pressure during chronic blood filling of the left ventricle. Wittekind et al did not elaborate on the pathophysiology of cardiomegaly in the patient and only stated that iron deficiency anemia and dilated cardiomyopathy occurred simultaneously.¹⁰

In addition to iron deficiency anemia, thiamin response megaloblastic anemia (TRMA) can also cause cardiomegaly. Zaferanloo et al have published a case report of a 2-year-old girl with Thiamin Response Megaloblastic Anemia (TRMA). The report showed that the patient's Hb was 8.9 g/dL and there was enlargement of the ventricle and right atrium. On echocardiogram examination, the patient was found to have cardiomegaly. The pathophysiology of cardiomegaly or other cardiovascular complaints has not been explained in the report, but Zaferanloo et al stated that 27% of patients with TRMA also experienced other cardiovascular complaints such as sudden death, stroke, heart failure, proximal atrial tachycardia, atrial fibrillation, and congenital heart disease (ventricular or atrial fibrillation).¹³

Lipshultz et al assessed the association of cardiomegaly due to cardiomyopathy with different types of anemia than some of the studies listed above. Lipshultz et al discussed the association of cardiomegaly secondary to cardiomyopathy with iron overload in pediatric patients with hereditary anemia (sickle cell disease, thalassemia α and β), leukemia, sideroblastic anemia, or renal failure. Iron overload in these cases can occur either due to multiple blood transfusions or due to increased absorption in the gut when the body's erythropoiesis is impaired. Lipshultz et al stated that cardiomyopathy occurs due to free radicals that cause lipid membrane peroxidation and oxidative damage to nucleic acids in cardiomyocytes. The free radicals themselves are formed due to excessive amounts of iron in the blood circulation because the amount of iron is not proportional to the transferrin iron binding capacity.¹⁴

Lipshultz et al also explained how thiamin deficiency can cause cardiomegaly due to cardiomyopathy. According to Lipshultz et al, thiamin deficiency causes vasodilation of blood vessels. This vasodilation can cause right heart failure and pulmonary hypertension resulting in an increase in cardiac output. If not treated immediately, depression of myocardial function will occur and cause cardiomyopathy with one of the symptoms being cardiomegaly.¹⁴

CONCLUSION

There is no association between anemia and cardiomegaly based on either chest radiograph or echocardiography.

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