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Original Article

Prognostic factors of heart failure in children with left-to-right shunt acyanotic congenital heart disease

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Abstract

Background Anemia is highly prevalent and affects morbidity and mortality in adults with acquired heart disease. However, its role in children with acyanotic congenital heart disease (CHD) is unclear.

Objective To assess anemia and other potential prognostic factors of congestive failure in children with left-to-right shunt acyanotic CHD.

Methods We conducted a case-control study in the Pediatric Cardiology Clinic, Dr. Sardjito Hospital from January to December 2017 in children with left-to-right shunt acyanotic CHD. The case and control groups consisted of subjects with and without heart failure, respectively. Anemia was defined as hemoglobin concentration <11 g/dL. Measured outcome was the prevalence of congestive heart failure, as determined by the Ross criteria. Anemia, defect type, defect size, age at diagnosis, and gender were analyzed by logistic regression analysis as potential predictive factors of heart failure.

Results Of 100 children with left-to-right shunt acyanotic CHD, 50 had heart failure (the case group) and 50 did not (the control group). The prevalence of anemia was 45%. Multivariable logistic regression revealed that defect size was the most significant factor for predicting heart failure, with adjusted OR 7.6 (95%CI 2.5 to 22.8) for moderate shunts and 21.1 (95%CI 6.8 to 65.4) for large shunts. Anemia, type of defect, age of diagnosis, and gender were not statistically significant factors for predicting outcomes.

Conclusion Anemia is not a significant, prognostic factor for heart failure in children with left-to-right shunt acyanotic CHD. However, moderate and large shunts in children with left-to-right shunt acyanotic CHD are predictive of the occurrence of congestive heart failure. **[Paediatr Indones. 2019;59:63-6; doi: http://dx.doi.org/10.14238/pi59.2.2019.63-6]**.

Keywords: *anemia; heart failure; congenital heart disease; prognostic factors*

Anemia is a common nutritional problem that is common in both developed and developing countries. The prevalence of anemia in children in developing countries is around 39%.[1] Anemia increases cardiovascular disease morbidity and mortality caused by compensatory mechanisms of hypoxia, that is by increased heart rate, increased cardiac output, left ventricular hypertrophy and progressive heart enlargement, as well as reduced oxygenation to the heart muscle.[2] Congestive heart failure can occur in patients with congenital heart abnormalities such as atrial septal defect, ventricular septal defect, patent ductus arteriosus, and other structural heart abnormalities that cause increased pulmonary blood circulation volume. Anemia increases the burden on the heart to fulfill tissue oxygen demand, which aggravates heart failure. Anemia increases the burden of heart to fulfill tissue oxygen demand, so that will aggravate heart failure. Previous studies showed that anemia was a strong predictor of death in adult

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patients with acyanotic congenital heart disease (hazard ratio: 3.0; 95%CI 1.46 to 6.13).[2] Anemia increases the hospital length of stay due to heart failure in children with dilated cardiomyopathy [mean 35.1 (SD 40.5) *vs.* 9.97 (SD 9.65) days per year, respectively; P<0.05].[3] Hence, we aimed to assess the role of anemia and other prognostic factors of congestive heart failure in children with left-to-right shunt acyanotic CHD.

Methods

This was a case control study included children aged 1 month to 18 years with left to right shunt acyanotic CHD in the Pediatric Cardiology Clinic, Dr. Sardjito Hospital in 2017. The case group consisted patients with heart failure of class Ross 2 or more,[4] while the control group had patients without heart failure. Patients with chronic renal failure, malignancy, immunodeficiency, autoimmune disease, pulmonary stenosis, or multiple cardiac defects were excluded. The minimum required sample size for case-control study with beta strength 80% and alpha 0.05 significance was calculated to be 50 subjects for each group. Both case and control subjects were randomly selected by a computer program. Patient data obtained from medical records included the following possible prognostic factors of heart failure: anemia, age at diagnosis, gender, size of defect, and type of defect. Anemia was defined as hemoglobin level <11 g/dL. Chi-square test was performed to assess potential prognostic factors of heart failure. Odds ratio was calculated by a 2x2 table with 95% confidence intervals. Multivariable logistic regression analysis was performed on prognostic factors that had a Chi-square result of P<0.25, in order to determine adjusted odds ratios.

The study protocol had been approved by the Ethics Committee of the Universitas Gadjah Mada Medical School.

Results

Of the 145 patients who met the inclusion criteria, only 50 children were suitable for the case group, and 50 of 95 children were randomly selected for the control group. The proportions of heart defects in our subjects were 28% ASD, 36% VSD, and 36% PDA (**Table 1**). Large defects were seen in 35% of subjects, moderate defects in 33%, and small defects in 32%. Anemia prevalence was 45% of all subjects.

Table 1. Basic characteristics of subjects

Characteristics	(N = 100)
Male, n (%)	39 (39)
Median age (range), months	15.2 (1-204)
Mean heart rate (SD), x/minute	123 (20.3)
Median respiration rate (range), x/minute	32 (20-68)
Median Hb (range), g/dL	11.3 (7.4-20.2)
Defect type, n (%)	
ASD	28 (28)
VSD	36 (36)
PDA	36 (36)
Size of defect, n (%)	
Small	32 (32)
Moderate	32 (32)
Large	36 (36)

Hb=hemoglobin; ASD=atrial septal defect; VSD=ventricular septal defect; PDA=patent ductus arteriosus

Chi-square analysis revealed that anemia, age < 1 year at diagnosis, type of defect, and gender did not significantly differ between those with and without heart failure. Logistic regression analysis showed that subjects with moderate size defect had 7.6 times higher probability of congestive heart failure than small size defect. In addition, subjects with large size defect were 21.1 times more likely to have congestive heart failure than those with small size defects (**Table 2**).

Discussion

The prevalence of anemia was high in children with left-to-right shunt acyanotic congenital heart disease (45%). A previous study in Dr. M Djamil Padang Hospital reported a 34.4% prevalence of anemia in children with acyanotic congenital heart disease.[5] Although anemia was not a significant prognostic factor of congestive heart failure in children with acyanotic congenital heart disease, anemia remains a serious nutritional problem in this population. This prevalence of anemia in acyanotic congenital heart disease was higher compared to the prevalence of anemia in children aged 1-14 years in Indonesia of 27%.[6] Anemia was also associated with the risk of malnutrition (OR 6.5; 95%CI 4 to 8) in children with congenital heart disease.[7]

Table 2. Prognostic factors of congestive heart failure in children with left-to-right shunt acyanotic CHD

	CHF (n = 50)	No CHF (n = 50)	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Anemia, n (%)	23 (46)	22 (44)	1.1 (0.5 to 2.4)	0.84		
Age of diagnosis > 1 year, n (%)	27 (54)	27 (54)	1 (0.5 to 2.1)	1		
Male, n (%)	16 (32)	23 (46)	1.8 (0.8 to 4.1)	0.15	1.8 (0.8 to 4.1)	0.18
Defect type, n (%)						
ASD	12 (24)	16 (32)				
VSD	18 (36)	18 (36)	1.3 (0.5 to 3.6)	0.57		
PDA	20 (40)	16 (32)	1.7 (0.6 to 4.5)	0.31		
Size of defect, n (%)						
Small	5 (10)	27 (54)				
Moderate	18 (36)	14 (28)	6.9 (2.1 to 22.7)	0.001	7.6 (2.5 to22.8)	0.001
Large	27 (54)	9 (18)	16.2 (4.8 to 54.7)	0.001	21.1 (6.8 to65.4)	0.001

Anemia is a predictor of death (OR 3; 95%CI 1.46 to 6.13) in adult CHD patients, and patients with anemia tend to have higher *New York Heart Association* (NYHA) classification of heart failure.[2] In patients with anemia, peripheral perfusion decreases as a result of a decreased vascular resistance. This condition may lead to neurohormonal activation with subsequent reduction in renal blood flow and renal function, resulting in an increase of intravascular volumes due to water and salt retention. The increased intravascular volume and decreased vascular resistance result in increased cardiac work, which may lead to left ventricular hypertrophy and worsening of cardiac function, as well as further decrease in renal function, completing the vicious circle.[8] The difference in the influence of anemia on acyanotic CHD in children and adults may be due to different characteristics of heart failure. Heart failure in CHD is due to impaired ventricular contractions in adults,[9] but related to pulmonary blood vessel congestion due to excessive blood flow through the left-to-right shunt in children.[10] This observation was consistent with our results showing that greater shunt size had higher risk of heart failure.

Regarding the high prevalence of anemia in children with acyanotic CHD, we recommend iron supplementation since the anemia may be caused by iron deficiency. Furthermore, children with moderate to large shunts should be prioritized for immediate defect closure. The limitation of this study was that subjects were only taken from one teaching hospital in Yogyakarta. As such, our results may not be generalized to other children with CHD in Indonesia or to other low-to-middle income settings.

Conflict of Interest

None declared.

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