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Original Article

Predictors of heart failure in children with congenital heart disease

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Abstract

Background Heart failure continues to be a significant contributor to morbidity and mortality in children with congenital heart disease (CHD). Little is known about heart failure in children. Identifying predictors of heart failure in children with CHD can serve to guide preventive strategies to heart failure.

Objective To understand the predictors of heart failure of children with congenital heart disease.

Methods A nested, case-control study was performed using secondary data based on a prospective study previously conducted in Dr. Sardjito Tertiary Hospital in Yogyakarta, Central Java, in years 2011-2013. We included children aged 1 month-18 years who had been diagnosed with CHD by echocardiography. Age, sex, type of CHD, CHD complexity, as well as presence of syndrome, no pulmonary obstruction, pneumonia, and malnutrition were analyzed as potential predictors of heart failure. Results were presented as odds ratios (OR) with 95% confidence intervals (95%CI).

Results A total of 2,646 children were hospitalized in Dr. Sardjito Tertiary Hospital, Yogyakarta, Central Java, during the study period. Congenital heart disease was noted in 216 children (8.16%), 200 (7.5%) of whom met the inclusion criteria. The 100 children with heart failure had median age of 1.5 years and 15% died during hospitalization. Multivariate analysis revealed that acyanotic CHD (OR 2.69; 95%CI 1.45 to 5.00), no pulmonary obstruction (OR 3.05; 95%CI 1.33 to 6.99) and the presence of pneumonia (OR 2.04; 95%CI 1.03 to 4.06) were statistically significant as independent predictors of heart failure in children with CHD. However, sex, age, CHD complexity, as well as presence of a syndrome, and malnutrition were not significantly associated with heart failure in children with CHD.

Conclusion The predictors of heart failure in children with CHD are acyanotic CHD, no pulmonary obstruction, and presence of pneumonia. **[Paediatr Indones. 2022;62:390-5; DOI: https://doi.org/10.14238/pi62.6.2022.390-5**].

Keywords: *congenital heart disease; heart failure; predictor; children*

Congenital heart disease (CHD) accounts for nearly one-third of all major congenital anomalies. The worldwide CHD birth prevalence is increasing.[1] In Indonesia, CHD prevalence was reported to be 8 per 1,000 live births.[2] The increased prevalence may be due to the rapid improvement in prenatal and postnatal early diagnosis by echocardiography, as well as the advances in interventional, surgical, and post-operative treatment.[3,4]

Heart failure (HF) is one of the most common conditions in newborns and children with CHD.[2] It is contributed to 15 million deaths of CHD patients yearly worldwide before the cardiac surgery was enhanced.[5] Heart failure was present in 0.6% of hospitalized CHD patients both in children and young adults with the hospital mortality was 26%,[6] was present in 10-33% of hospitalized CHD patients.[7] The incidence of HF in children predominantly occurred in the 0-1 year old group.[7,8]

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Adult CHD studies suggested that HF may result from the hemodynamic burden of the primary defect, residual lesions after correction or surgery, or the complexity of the defect, sex, arrythmia, pulmonary hypertension, myocardial condition, and/or comorbidities. Mild CHD, such as small atrial septal defect (ASD), typically does not result HF in young children.[9] While the ideal HF management in CHD is cardiac defect correction,[2] a major obstacle is the limited access to cardiac intervention facilities. However, studies have been limited on HF in the pediatric CHD population.[8] Therefore, we aimed to determine the predictors of heart failure in children with CHD.

Methods

We conducted a nested, case-control study to determine the predictors of heart failure in children with CHD using secondary data based on a prospective study previously conducted in Dr. Sardjito Tertiary Hospital in Yogyakarta, Central Java.[10]

Children with CHD (based on echocardiography) aged 1 month-18 years who had been hospitalized (in wards or PICUs) more than 48 hours between years 2011 and 2013 were included. Exclusion criteria were cardiac re-admission, prior CHD surgery or closure catheterization, or incomplete medical records. Nonrandomly sampling technique was chosen during this study. A case was defined as a CHD patient with heart failure. A control was a randomly selected CHD patient who did not develop heart failure. The dependent variable (outcome) was heart failure; the independent variables were age, sex, nutritional status, CHD type, complexity, as well as the presence of pneumonia or syndromes. Heart failure was defined if there was dyspnea on activity or interrupted feeding, poor gain weight, orthopnea, hepatomegaly, increased jugular venous pressure, or edema. A complex CHD was included at least one of the following: transposition of the great aorta (TGA), double outlet right ventricle (DORV), tetralogy of Fallot (ToF), single ventricle, endocardial cushion defect, pulmonal stenosis, pulmonal atresia, double outlet ventricle, tricuspid atresia/stenosis, Ebstein's anomaly, aortic stenosis, mitral insufficiency, and hypoplastic left heart syndrome (HLHS). Defect size (shunt lesion) of atrial septal defect (ASD) was considered as small (>3 mm to <6 mm), moderate (≥6 mm to <12 mm) or large (≥12 mm) defects. Defect size of ventricular septal defect (VSD) was considered as small (<5 mm), moderate (≥5 mm to <10 mm) or large (≥10 mm) defects. Syndrome or chromosomal abnormality diagnosis had not been confirmed by chromosome examination, but was based only on clinical examination and the presence of dysmorphic features.

Analyses were performed using Chi-square or Fisher's exact tests. Multivariate logistic regression was used to identify independent risk factors for heart failure. Variables with P values ≤0.25 in bivariate analysis were introduced into the multivariate test. Statistical significance was set at P≤0.05. This study was approved by the Ethics Committee from Faculty of Medicine of Universitas Gadjah Mada.

Results

Based on data from a previous prospective study during a 27-month study period, 2,646 children were hospitalized. The CHD was noted in 216 children (8.16%), 200 (7.5%) of whom met the inclusion criteria. Of 100 patients were suffering from heart failure (**Table 1**).

Significant predictors of HF in the bivariate analysis were acyanotic CHD, no pulmonary obstruciton, pneumonia, and complex CHD (P<0.05 for all). The independent predictors in the multivariate analysis were acyanotic CHD, no pulmonary obstruction, and the presence of pneumonia. The complex CHD was not independently predictors of CHD (**Table 2**).

Discussion

Heart failure represents an important cause of morbidity and mortality in children with CHD.[11] An estimated 15-25% of pediatric CHD cases develop to HF,[9] with 60% mortality in developing countries.[12] In our study, CHD incidence was 7.5% among hospitalized children. Similarly, a study in Belgium reported an incidence of 6.2% (64/1031),[8] but India reported 1.9%.[13] Our high incidence may have been

Table 1. Baseline characteristics of subjects

Characteristics	(N=200)
Median age at admission (range), years	1.4 (0.1-18)
Died, n (%)	30 (15)
Male, n (%)	102 (51)
Acyanotic CHD, n (%)	
VSD	53 (26)
PDA	44 (21)
ASD	34 (17)
AVSD	7 (3)
PS	3 (1)
Others	1 (0.5)
Cyanotic CHD, n (%)	
TOF	29 (14)
DORV	16 (8)
TGA	9 (4)
Pulmonary atresia	7 (3)
Tricuspidal atresia	3 (1)
Ebstein's anomaly	3 (1)
Others	5 (2.5)
Complex CHD, n (%)	74 (37)
Syndrome/chromosomal abnormality, n (%)	95 (47.5)
Nutritional status, n (%)	
Normal	105 (52.5)
Underweight and stunted	60 (30)
Severe malnutrition	35 (17.5)
Pneumonia, n (%)	50 (25)
CHD with pulmonary obstruction, n (%)	59 (29.5)
Pulmonary hypertension, n (%)	31 (16)
Defect size (shunt lesion), n (%)	
Large	106 (53)
Moderate	32 (16)
Small	42 (21)

CHD=congenital heart disease, VSD=ventricle septal defect, PDA=patent ductus arteriosus, ASD=atrial septal defect, AVSD=atrioventricular septal defect, PS=pulmonary stenosis, TOF=Tetralogy of Fallot, DORV=double outlet right ventricle, TGA=transposition of the great arteries

due to our study being conducted in a tertiary hospital. However, there are no exact data on the prevalence and incidence of CHD in Indonesia.

Acyanotic CHD was the most prevalent type of CHD (65%). The predominant defects in this category were VSD, PDA and ASD, similar to previous global studies.[1,14] The most common cyanotic CHD defects were ToF, followed by DORV and TGA. A previous study in Padang, West Sumatera, Indonesia, reported that the proportion of ToF was 21.8%.[5] Also, a systematic review from 114 countries reported that ToF (5%) and TGA (5%) were prevalent.[1,5]

In our study, we used nonprobability sampling. Of 200 subjects in our study, 15% died during hospitalization, with 12% were death as a result of HF. In contrast, previous studies in the UK and USA reported that incidence of HF in patients with CHD were 10.4% and 1.3%, respectively. On the other hand, a Nigerian study reported that 64.3% of children with CHD had HF.[6,15] Our high rate might have been due to our tertiary hospital setting, in which almost all patients were admitted in unstable hemodynamic conditions. In addition, there were limited cardiac intervention facilities available in year 2011-2013. In developed country with the advanced cardiac disease management, 1 year survival were high up to 97.1% for those with non critical CHDs and 75.2% with critical CHD.[16]

Table 2. Bivariate and multivariate analyses of potential predictors of heart failure in CHD

Variables, n (%)	HF (n=100)	No HF (n=100)	Bivariate		Multivariate	
			OR (95%CI)	P value	OR (95%CI)	P value
Male	54 (54)	48 (48)	1.27 (0.73 to 2.22)	0.39		
Age < 1 year	49 (49)	41 (41)	1.38 (0.79 to 2.42)	0.26		
Acyanotic CHD	77 (77)	53 (53)	2.97 (1.61 to-5.46)	<0.001	2.69 (1.45 to 5.00)	0.002
Complex CHD	27 (27)	47 (47)	0.42 (0.23 to 0.75)	0.003	1.25 (0.36 to 4.37)	0.73
Presence of syndrome	51 (51)	44 (44)	1.33 (0.76 to 2.31)	0.32		
Pneumonia	33 (33)	17 (17)	2.41 (1.23 to 4.69)	0.009	2.04 (1.03 to 4.06)	0.04
Undernutrition	51 (51)	44 (44)	1.33 (0.76 to 2.31)	0.32		
No pulmonary obstruction	84 (84)	57 (57)	3.96 (2.04 to 7.7)	<0.001	3.05 (1.33 to 6.99)	0.009
Nutritional status						
Normal	49 (49)	56 (56)				
Underweight and stunted	29 (29)	31 (31)	1.07 (0.57 to 2.1)	0.84		
Severe malnutrition	22 (22)	13 (13)	1.93 (0.9 to 4.2)	0.1		

CHD=congenital heart disease

Pneumonia was an independent predictor of HF in children with CHD. In our study, pneumonia was found in 25% of cases, of whom 66% developed HF. The VSD, ASD, PDA, and DORV were the most common CHD types with comorbid pneumonia at 50%, 24%, 11%, and 5%, respectively. It is similar to reports in Nigeria reported that CHD pediatric patients with pneumonia were three times more likely to have HF compared to those without pneumonia (OR=3.02).[17,18]

The causes and clinical presentations of HF in children differ greatly from those in adults. In children, HF is most often caused by CHD and cardiomyopathy with excessive of preload (diastolic filling volume and maximal stretch length), excessive of afterload (resistance of the peripheral vasculature) mechanism, or arrhythmia leading to increased pulmonary blood flow. In adults, coronary artery disease and hypertension are prevalent etiologies of HF, leading to heart contractility disturbances.[19-21]

In children, the common cause of heart failure is CHD without pulmonary obstruction, leading to increased pulmonary blood flow (PBF). Our study demonstrates that patients without pulmonary obstructive lesions were 3 times more likely to have HF. Increased PBF disrupts the normal physiological mechanism of the alveolar fluid layer at the interface between air and the lung tissue, including opsonin and macrophage activity, both of which increase the risk of lung infection and inhibit the process of infection clearance. Pulmonary edema caused by an increase in pulmonary capillary pressure causes fluid shifts, sending protein and erythrocytes into the alveoli.[22] Age at onset and symptom severity depend on defect size. Children with large VSDs and PDAs tend to have HF manifestation in early life, usually accompanied by severe comorbidities such as pneumonia.[17,18,23]

Acyanotic CHD is another HF independent predictor in children with CHD. Children with acyanotic type CHD was almost three times more likely to have HF than those with cyanotic type CHD. The acyanotic CHD with HF were predominantly having the moderate-to-large shunt lesion types (42%). Similarly, previous study in Nigeria and India reported that VSD was the most commonly having HF (50% and 46%, respectively).[17,24]

Male gender, under 1 year of age, CHD complexity, presence of syndromes, and undernutrition were also not significant predictors of HF in our study. Previous studies reported that male gender was inconclusive as a predictor of HF in children.[24-27] In addition, another study reported that age grouping of 1-10 years was associated with HF and mortality in CHD.[28] Our subjects may have suffered HF for a long time before admission or had already taken anti-congestive drugs. Hence, we may not have been able to detect differences in gender or age. Single ventricle lesions were significantly associated with an increased likelihood of HF (OR 2.14), controlling for development of comorbid pulmonary hypertension.[29] However, the common defects of complex CHD in our study were conotruncal/non-single ventricle complex

lesions, such as ToF, DORV, pulmonary atresia, Ebstein's anomaly, and total anomalous pulmonary venous drainage (TAPVD). Syndrome diagnoses were found in 47.5% of children with CHD, 53% of whom had HF. In our study, the syndrome or chromosomal abnormality diagnosis had not been confirmed by chromosome examination, but was based only on clinical examination and the presence of dysmorphic features. Undernutrition was also not a predictor of HF in our study. Undernutrition was found in 47.5% of cases, with 35 of patients (37%) were suffering from severe malnutrition and 60 of patients (63%) were suffering from underweight-stunted. Undernutrition in CHD is usually caused by inadequate intake, malabsorption, tachycardia, tachypnea, anorexia, as well as energy imbalance and increased resting energy consumption.[30] Our CHD subjects may have had predominantly normal or decreased PBF.

The limitation of our study was conducting it at only a single referral tertiary hospital, such that our results cannot be generalized to other hospitals in Indonesia. In conclusion, the predictors of heart failure in children with CHD are acyanotic CHD, no pulmonary obstruction, and the presence of pneumonia. Understanding the predictors of HF in CHD is crucial to choosing appropriate strategies to prevent HF.

Conflict of interest

None declared.

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