Research Article

Profile and Risk Factors of Children with Isolated Ventricular Septal Defect in dr. Cipto Mangunkusumo Hospital

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Abstract

Ventricular septal defect (VSD) is the most prevalent congenital heart disease (CHD). While various risk factors for isolated VSD exist, the specific risk factors and patient profiles for isolated VSD cases at dr. Cipto Mangunkusumo Hospital (CMH) remains undisclosed. Thus, this study aims to investigate this information. Data were obtained from medical records and or patients' parent interviews. The data were then analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for Windows. The chi-square and Fisher's exact tests were used to investigate the association of the variables. This case-control study investigated 40 isolated VSD patients and 40 control patients, aged 1 month to 18 years, at CMH in 2020. For the risk factors, the presence of a genetic syndrome such as Down syndrome [OR 2.143 (CI 95% 1.682–2.729), p=0.02] was confirmed from 40 VSD patients as the only risk factor of isolated VSD in this population. However, several other parameters including socio-economic status (p=0.491), maternal age when pregnant (p=0.745), paternal smoking (p=0.370), maternal gestational diabetes (p=0.494), maternal smoking history during pregnancy (p=1), and maternal alcohol intake history during pregnancy (p=1) did not associate with isolated VSD in this population. Children with Down syndrome are at risk of isolated VSD, compared to children without a genetic syndrome.
Keywords*: ventricular septal defect, congenital heart disease, children, profile, risk factors*.

Profil dan Faktor Risiko Anak dengan Defek Septum Ventrikel Terisolasi di Rumah Sakit dr. Cipto Mangunkusumo

Abstrak

Defek septum ventrikel (VSD) adalah penyakit jantung bawaan (PJB) yang paling sering ditemukan. Meskipun terdapat berbagai faktor risiko untuk VSD terisolasi, profil pasien dan faktor risiko spesifik pada kasus VSD terisolasi di RSUPN dr. Cipto Mangunkusumo (RSCM) belum diketahui. Oleh karena itu, penelitian ini bertujuan untuk meneliti hal tersebut. Data diperoleh dari rekam medis dan atau wawancara dengan orang tua pasien. Data dianalisis menggunakan Statistical Package for Social Sciences (SPSS) versi 20 untuk Windows. Uji chi-square dan Fisher's exact tests digunakan untuk menganalisis hubungan antar variabel. Studi kasus kontrol ini meneliti 40 pasien VSD terisolasi dan 40 pasien kontrol berusia 1 bulan hingga 18 tahun di RSCM pada tahun 2020. Untuk faktor risiko, keberadaan sindrom genetik seperti sindrom Down [OR 2,143 (CI 95% 1,682–2,729), p=0,02] merupakan satu-satunya faktor risiko VSD terisolasi dalam populasi ini. Parameter lain seperti status sosial ekonomi (p=0,491), usia ibu saat hamil (p=0,745), kebiasaan merokok ayah (p=0,370), diabetes gestasional ibu (p=0,494), riwayat merokok ibu selama kehamilan (p=1), dan riwayat konsumsi alkohol selama kehamilan (p=1) tidak menunjukkan hubungan dengan kejadian VSD terisolasi dalam populasi ini. Anak dengan sindrom Down memiliki risiko lebih tinggi mengalami VSD terisolasi dibandingkan anak tanpa sindrom genetik.
Kata kunci: *defek septum ventrikel, penyakit jantung bawaan, anak, profil, faktor risiko*.

Introduction

Congenital heart disease (CHD) is the most common congenital disease, affecting 6–10 infants per 1,000 live births, with isolated ventricular septal defect (VSD) being the most prevalent, constituting 37% of all CHD cases.[1,2] The incidence of VSD ranges from 0.4 to 3.3 per 1,000 live births, often leading to hemodynamic failure due to improper left-to-right ventricular shunting. While many VSDs close spontaneously, larger defects may require intervention to prevent complications, such as ventricular dysfunction, pulmonary hypertension, and arrhythmias.[1] Premature birth and low birth weight are potential risk factors, with 41% of VSD cases linked to low birth weight, though a conclusive link with preterm infants is unestablished.[3] CHD affects 40% of Down syndrome (DS) patients, with VSD and atrioventricular septal defect (AVSD) being the most common, having prevalence rates of 60.4% and 29.1%, respectively, in DS patients in Pakistan.[4,5] Environmental factors like parental smoking, alcohol use during pregnancy, and gestational diabetes may also increase VSD risk.[6] This study aims to analyze the profiles and risk factors of infants with VSD at dr. Cipto Mangunkusumo Hospital (CMH), Indonesia, in 2020, addressing the gap in existing research on this patient population.

Methods

This case-control study was conducted in the Cardiology Division of the Department of Child Health, CMH, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, between October 2021 and June 2022. This study compares the profiles and risk factors of children with VSD to those without CHD from January to December 2020 in the Pediatric Cardiology Outpatient Clinic of CMH. Children with isolated VSD and an incomplete profile of the VSD were excluded from the study.

A total of 40 children with isolated VSD were randomly selected as subjects from 1,300 medical records utilizing a random number table. As controls, 40 children without VSD treated at the Pediatric General Polyclinic at CMH were randomly selected from 1,903 medical records using a random number table. Data were collected from medical records, and missing information was obtained by telephone interviews with the patients' parents. The sample size was determined using the single sample size formula for categorical descriptive statistics.

The baseline characteristics of the research participants were presented as percentages, medians, or means, as appropriate. The prevalence ratio was used to investigate the correlation between each risk factor and the incidence of isolated VSD. The data was then analyzed using Statistical Package for the Social Sciences (SPSS) version 20 for Windows (IBM Corporation, Armonk, New York, USA).

This research had received ethical approval from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia, No. KET-924/UN2.F1/ETIK/PPM.00.02/2021. The author received hospital approval before performing the data collection. Prior to data collection, all patients were informed about the study objectives.

Results

During the study, 40 participants were recruited into each group from medical records with informed consent. Because fewer toddlers were recruited for the control group, there were more toddlers with smaller body weight and height in the VSD group than in the control group (Table 1). The pulse rate, blood pressure, respiratory rate, and family size were comparable in both groups. Regarding oxygen saturation, about 30% of children with VSD had abnormal measurements, compared to 0% in the control group.

Table 1. Subjects' Characteristics of VSD (N=40) vs Control Group (N=40)

Characteristics	VSD	Control
Age (years), n (%)		
Infant	8 (20)	8 (20)
Toddler	24 (60)	12 (30)
Children	8 (20)	20 (50)
Body weight (kg), median (min-max)	8.4 (3.6-57)	16.5 (2.3-60)
Body height/length (cm), mean (SD)	85 (25.3)	104.8 (34.7)
Pulse rate (per minute), mean (SD)	112.2 (19.3)	101.8 (19.2)
Blood pressure (mmHg), mean (SD)		
Systolic	100.13 (11.9)	99.6 (13.9)
Diastolic	63.7 (8.8)	63.2 (8.6)
Mean	75.8 (8.9)	75.3 (9.4)
Respiratory rate (per minute), mean (SD)	24 (3.5)	21.5 (3.4)
Oxygen saturation, n (%)		
Normal	28 (70)	40 (100)
Abnormal	12 (30)	0
Family size, n (%)		
<5 people	27 (67.5)	25 (62.5)
≥5 people	13 (32.5)	15 (37.5)

Several VSD risk factors were compared with controls (Table 2). Children with VSD had a higher percentage of low birth weight (15% vs. 12.5%) and preterm birth (37.5% vs. 25%) compared to controls. Nutritional status was poorer in the control group (55% vs. 50%), and low socioeconomic status was more common in the control group (65.5% vs. 57.5%). A significant proportion of children with VSD had DS (12.5%). None of the mothers smoked or consumed alcohol during pregnancy. Advanced maternal age (>35 years) was similar in both groups (87.5% vs. 85%). More fathers in the VSD group smoked during pregnancy (52.5% vs. 42.2%). Gestational diabetes was present in 5% of mothers in the VSD group, compared to none in the control group.

Table 2. Comparison of Subjects' Risk Factors between VSD (N=40) and Control (N=40)

Risk Factor	VSD N (%)	Control N (%)	p-value	OR (CI 95%)
Gender				
Male	19 (47.5)	19 (47.5)	1*	1 (0.42-2.41)
Female	21 (52.5)	21 (52.5)		
Birth weight				
Low birth weight	6 (15)	5 (12.5)	0.745*	1.24 (0.34-4.43)
Normal and high birth weight	34 (85)	35 (87.5)		
Gestational age				
Preterm	15 (37.5)	10 (25)		1.80 (0.69-4.70)
Term and post-term	25 (62.5)	30 (75)	0.228*	
Nutritional status				
Good and overweight	20 (50)	18 (45)	0.654*	1.22 (0.51-2.94)
Inadequate and bad	20 (50)	22 (55)		
Socio-economic status				
Low	23 (57.5)	26 (65)	0.491*	0.73 (0.29-1.80)
Middle and high	17 (42.5)	14 (35)		
Genetic syndrome				
Trisomy 21/ Down syndrome	5 (12.5)	0	0.02**	2.14 (1.68-2.73)
No Trisomy 21/ Down syndrome	35 (87.5)	40 (100)		
Maternal smoking during pregnancy				
Yes	0	0	1**	1 (0.02-51.63)
No	40 (100)	40 (100)		
Maternal age when pregnant				
≤ 35 years old	35 (87.5)	34 (85)	0.745*	1.24 (0.34-4.43)
> 35 years old	5 (12.5)	6 (15)		
Maternal alcohol intake in pregnancy				
Yes	0	0	1**	1 (0.02-51.63)
No	40 (100)	40 (100)		
Paternal smoking				
Yes	21 (52.5)	17 (42.5)	0.370*	1.49 (0.62-3.61)
No	19 (47.5)	23 (57.5)		
Gestational diabetes				
Yes	2 (5)	0	0.494**	2.05 (1.64-2.58)
No	38 (95)	40 (100)		

*Chi-square test; **Fisher's exact test

Table 3. Profile of Children with Isolated VSD (n=40)

VSD Profile	n (%)
Main complaint	
Hard to gain weight	23 (57.5)
Murmur	10 (25)
Short of breath	3 (7.5)
Fatigue easily	3 (7.5)
Recurrent upper respiratory tract infection	1 (2.5)
VSD size	
Small VSD	6 (15)
Moderate VSD	11 (27)
Large VSD	23 (57.5)
VSD classification	
Perimembranous VSD	26 (65)
Doubly committed sub-arterial VSD	9 (22.5)
Inlet VSD	3 (7.5)
Trabecular muscular VSD	2 (5)
Cardiomegaly	
Yes	3 (7.5)
No	37 (92.5)
Heart failure	
Yes	4 (10)
No	36 (90)
Pulmonary hypertension	
Yes	17 (42.5)
No	23 (57.5)
Failure to thrive	
Yes	7 (17.5)
No	33 (82.5)
Acute respiratory infection	
Yes	14 (35)
No	26 (65)
Eisenmenger syndrome	
Yes	0
No	40 (100)
Familial congenital heart disease, n (%)	
Yes	2 (5)
No	38 (95)
Intervention/Surgical Treatment, n (%)	
VSD closure operation	24 (60)
Transcatheter	9 (22.5)
No	7 (17.5)

In children with isolated VSD (Table 3), the most common complaint was an inability to gain weight (57.5%). Large VSD size (57.5%) and perimembranous type (65%) were prevalent, while cardiomegaly was rare (7.5%). Pulmonary hypertension was the most frequent complication (42.5%). Only 5% had a family history of CHD. Most children with VSD (60%) underwent VSD closure surgery, rather than transcatheter or no treatment.

Discussion

This study revealed that children with DS have about twice the risk of having an isolated VSD compared to those without DS. Parents of children with congenital heart disease (PCCHD) often face mental health challenges due to the extensive care their children require, including frequent cardiac procedures and hospitalizations, which significantly impact their emotional and financial well-being.[6] Consequently, these families tend to have fewer children, often prioritizing the needs of their sick child. Thus, it is common for VSD-affected families to have no more than five members.[6,7]

Gender did not appear to influence the prevalence of VSD, which is consistent with findings by Nembhard et al,[8] which showed no association between VSD and gender. Given that ventricular septum formation takes place prior to

fetal sexual differentiation and is thus unaffected by chromosomes or sex hormones, this implies that sex is not a significant risk factor.[9] Low birth weight, often associated with VSD, was not linked to higher VSD risk in this study. Although previous research in Sudan and China reported higher rates of low birth weight among VSD patients, an American study found that many CHD patients had normal birth weights. Thus, our findings suggest that low birth weight is not always a risk factor for VSD.[10,11]

Premature birth (PTB) has been considered a risk factor for VSD. However, some studies suggest that CHDs contribute to PTB, rather than PTB leading to CHDs. CMH, as a national referral center, receives many referred cases with various medical conditions, which may result in a higher proportion of term births. This could explain the absence of a significant association between gestational age and VSD in this study.[12] Nutritional status was assessed based on the most recent body weight in the medical records. It is possible that some children had lower body weight at the time of referral, but their nutritional status improved following treatment at the hospital. As a result, low nutritional status is not a risk factor for VSD in this study.[13] Increased metabolic demands and feeding challenges put children with VSD at high risk for malnutrition; in Ethiopia, 38.6% of those children experienced wasting and 43.1% were underweight.[14] A study conducted in 23 low and middle income countries found that 46% of children with VSD were not underweight and 54% of them did not have wasting, indicating that nutritional intervention and the severity of the defect play significant roles. As a result, low nutritional status is not always present and is dependent on systemic and clinical factors.[14,15]

Genetic factors play a crucial role in the development of VSD, with several studies highlighting a strong association between DS and an increased risk of VSD.[16] Atrioventricular septal defects (AVSD), which frequently include or develop into VSD, account for nearly 45% of CHDs in infants with DS.[17] The high prevalence of AVSD and VSD in people with DS is further highlighted by data from China and Japan, demonstrating the importance of early cardiac screening and immediate intervention in this population.[17,18] This finding is supported by this study's result of an association between DS and VSD in the patient group.[16-18]

Maternal health and lifestyle factors including age, smoking, alcohol consumption, and gestational diabetes, were also evaluated. The incidence of VSD was not associated with maternal age, which is consistent with results from population-based studies conducted in Europe between 1995 and 2015. This lack of association may be because VSD is a multifactorial condition, meaning that early embryonic environmental exposures, sporadic genetic mutations, and epigenetic factors may be more important in disrupting cardiac septation than maternal age alone.[19] Smoking and alcohol consumption during pregnancy has been identified as a potential risk factor. However, in this study, smoking and drinking alcohol were not reported among the mothers, which may reflect the low prevalence of smoking among women in Indonesia. This supports the conclusion that maternal age over 35, alcohol consumption, and smoking does not increase the risk of VSD in this population.[20]

Household socioeconomic status, while often linked to health outcomes, did not significantly impact on VSD prevalence in this study. Both VSD patients and controls primarily came from low-income families, with most relying on government-supported insurance. This indicates that socioeconomic status did not statistically increase VSD risk.[21] The study also detailed the profile of VSD patients, highlighting weight gain difficulties as the most common complaint, large VSD size, and perimembranous type as prevalent characteristics. Pulmonary hypertension emerged as the most frequent complication, associated with the large size of VSDs seen in many patients. Familial CHD was not commonly linked to VSD, and most patients underwent surgical VSD closure, consistent with treatment practices for larger defects.[2,12]

Several limitations were noted in this study, including data gaps in medical records and reliance on parental recall, which may not always be accurate. The case-control design also posed challenges in distinguishing between cause and effect. Despite these limitations, the study provides

valuable insights into the risk factors and profiles of children with VSD at CMH.

Conclusion

Children with Down syndrome were about twice as likely to have isolated VSD. Further studies are needed to strengthen evidence and explore population-level risk factors, ideally in hospitals with fewer referral cases for broader evaluation.

Conflicts of Interest

The author declares that there are no conflicts of interest.

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