Survival and outcomes of isolated neonatal ventricular septal defects: A population-based study from a middle-income country

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ABSTRACT

Background and Aims : **Limited data on the survival and outcomes of ventricular septal defect (VSD) in middle-income countries are available. Hence, this study aims to determine the survival and factors associated with mortality among neonatal VSD.**

Materials and Methods : **This is a retrospective, population based study of neonates with isolated VSD born between 2009 and 2019. Kaplan–Meier analysis was used to estimate the overall survival. Cox regression analysis was used to determine factors associated with mortality.**

Results : **There were 726 patients studied, with 82 (11%) of them having trisomy 21. The median age of diagnosis and follow-up was 5 days (interquartile range [IQR]: 2–10 days) and 2.3 years (IQR: 0.6–4.8 years), respectively. Of 726, 399 (55%) were perimembranous, 218 (30%) muscular, and 109 (15%) outlet VSD. VSD was small in 309 (42%), moderate in 337 (46%), and large in 80 (11%). Of 726 patients, 189 (26%) had congestive heart failure (CHF) and 52 (7.2%) developed pulmonary hypertension (PHT). Interestingly, one-third of CHF and PHT resolved over time during follow-up. Only 1 (0.1%) patient had infective endocarditis, 38 (5.2%) developed aortic regurgitation, and none had Eisenmenger syndrome. Overall, 149 (20%) needed surgery, 399 (55%) spontaneously closed, and 178 (25%) remained small. The mortality rate was 3.9% (28), 16 (57%) preoperatively, and 11 (39%) due to pneumonia. Trisomy 21, PHT, and birth weight <2.5 kg were independent factors for mortality with an adjusted hazard ratio of 6.0 (95% confidence interval [CI]: 2.1–16.9), 3.2 (95% CI: 1.2–8.4), and 3.6 (95% CI: 1.7–7.8), respectively. The overall survival at 1, 5, and 10 years was 96% (95% CI: 95–98), 95% (95% CI: 94–97), and 95% (95% CI: 94–97), respectively.**

Conclusions : **Despite limited pediatric and congenital cardiac services in middle-income countries, the overall survival of neonatal VSD is good, with poor outcomes in small infants, PHT, and trisomy 21.**

Keywords : Congestive heart failure, pulmonary hypertension, spontaneous closure, survival, ventricular septal defect

INTRODUCTION

Ventricular septal defect (VSD) is the most common congenital heart disease (CHD) in children, with an

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incidence ranging from 2 to 3 per 1000 live births.[1,2] Depending on its size and type, VSD may result in spontaneous closure, congestive heart failure (CHF), or pulmonary hypertension (PHT). A large VSD is commonly associated with CHF, and if left untreated, it may cause PHT, resulting in significant morbidity and mortality.[3] In contrast, small or muscular VSDs may close naturally over time, whereas moderate-sized VSDs can either progress into CHF or decrease in size over time.[4]

Advancements in echocardiography have made it possible to detect VSD accurately during *in utero* and early neonatal periods. In addition, early CHF- and PHT-related changes in echocardiography can be swiftly identified, enabling timely medical and surgical interventions. This leads to optimal management and better outcomes for children with VSD.[5-7]

Studies on the natural history of VSD have been conducted, but most were single-center, carried out many years ago in developed countries.[8-13] In addition, some studies only involved a small number of infants and children.[14,15] Furthermore, research on VSD in the neonatal population[16,17] and middle-income countries is lacking. Given limited resources in pediatric and congenital cardiac services, we assume that the survival rate of neonatal VSD may be lower compared to developed countries. In addition, to gain a more accurate understanding of the natural history of VSD, conducting a study from the neonatal period with longer follow-up is necessary. Therefore, this population-based study aims to estimate the survival rate of neonatal VSD at 1, 5, and 10 years and to determine factors associated with mortality.

MATERIALS AND METHODS

Study population

This population-based study was conducted in Johor, Malaysia, with a population of 3.4 million and an annual birth rate of 55,000. Malaysia is a middle-income country where government hospitals mainly provide health services with support from private hospitals. There is only one hospital providing pediatric cardiac services, and almost all CHD cases were referred here for diagnosis confirmation and follow-up.[2]

The study included all infants born in Johor from January 2009 to December 2019 diagnosed with isolated VSD during their first 28 days of life. Infants with VSD diagnosis beyond the neonatal period and those with other CHD, such as coarctation of the aorta, pulmonary stenosis, tetralogy of Fallot, or complex CHD, were excluded. However, neonates with VSD associated with closing patent ductus arteriosus, small atrial septal defect, or patent foramen ovale were included in the study.

All infants were followed until their VSD closed spontaneously; they were transferred to another center, reached adulthood, or passed away. Infants with lethal congenital malformations and those who had only one echocardiogram on review were excluded from the final analysis.

Data source

The data were obtained from the Pediatric Cardiology Clinical Information System, a clinical registry that caters to children with CHD in Johor State, Malaysia.[2] The data retrieved encompass birth weight, gender, ethnicity, gestational age, maternal diabetes, family history of CHD, age of diagnosis, associated noncardiac malformations or syndromes, and the type and severity of VSD.

Case ascertainment and ventricular septal defect classification

Infants suspected of having VSD underwent a thorough two-dimensional (2D) echocardiography conducted by a trained echocardiographer. The examination utilized standard parasternal short- and long-axis, apical 4- and 5-chamber views to identify and classify the size and type of VSD accurately.[5] VSD was classified, according to Soto *et al.*, into perimembranous, muscular, and outlet VSD.[18] VSD severity was classified into three groups: small VSD for sizes <3 mm, moderate VSD for sizes between 3 mm and 5 mm, and large VSD for sizes >5 mm.[17] In patients with multiple VSDs, the primary lesion was determined to be one with the most significant hemodynamics. For instance, moderate perimembranous and small muscular VSDs were classified as moderate perimembranous VSDs.

Ventricular septal defect management

All VSDs were monitored based on clinical condition. For instance, in cases where the patient was asymptomatic and had a small VSD, follow-up appointments were scheduled every 3–4 months for up to 1 year of age and then yearly until the VSD closed naturally. However, moderate-to-large VSDs required early follow-up appointments.

Ventricular septal defect outcome

VSD outcomes measured were the rates of spontaneous closure, CHF, and PHT. Spontaneous closure was defined as no flow across the VSD using the color Doppler method. Patients were considered to have CHF if they displayed evidence of volume overload on the left side of the heart in 2D echocardiography, such as a dilated left atrium or ventricle and signs or symptoms of heart failure. PHT was defined based on changes observed during echocardiography.[7] These changes include bidirectional shunt across the VSD, dilated right atrium and ventricle, and septal flattening. Furthermore, other potential causes of PHT, such as pulmonary venous obstruction and lung disease, were carefully investigated. The rate of aortic regurgitation, infective endocarditis, and Eisenmenger syndrome were also sought.

Mortality

The occurrence of death was noted and categorized as either cardiac or noncardiac related. In addition, death was classified based on whether it occurred before, during, or within 30 days after the surgery. All deaths were verified with the National Registration Department.

Statistics

The Statistical Package for the Social Sciences version 23 (IBM Corp., Armonk, NY, USA) was utilized to analyze the data. Student's *t*-test and nonparametric tests were employed to analyze normal and nonnormal continuous data, respectively. Meanwhile, categorical data were analyzed using Pearson's Chi-square test. $P < 0.05$ was considered statistically significant. Kaplan–Meier survival analysis was employed to determine the cumulative VSD spontaneous closure and survival.

Cox regression analysis was conducted to identify the variable associated with mortality. The variables studied included sex, race, birth weight, gestational age, age diagnosis, maternal diabetes, presence of noncardiac malformation, trisomy 21, VSD size, VSD type, presence of PHT, and CHF. An adjusted hazard ratio (aHR) with a 95% confidence interval (CI) not including one was deemed significant.

RESULTS

There were 653,740 live births during the study, with 4449 new CHDs detected. Of 4449 CHDs, 1526 (34%) were isolated VSD, giving an incidence of 2.3 (95% CI: 2.2–2.4) per 1000 live births. Of 1526 VSDs, 800 (52%) were detected during the neonatal period, and 74 patients were excluded [Figure 1].

The median age at diagnosis of 726 included in the final analysis was 5 days, with 494 patients (68%) diagnosed within 1 week of life. Follow-up ranged from 13 days to 12.1 years, with a median of 2.3 years. The shorter follow-up was due to early neonatal death and discharge. Table 1 shows the demographic data of the study population.

The mean VSD size was 3.2 ± 1.7 mm, ranging from 1 mm to 12 mm. VSD size was small in 309 (42%), moderate in 337 (46%), and large in 80 (11%) patients. Perimembranous VSD was found in 399 (55%), muscular in 218 (30%), and outlet in 109 (15%) patients. Twenty-six (3.6%) patients had multiple defects. Overall, there were 130 (17.9%) patients who were associated with a noncardiac malformation (21, 2.9%) and syndrome (109, 15%). Of 109 syndromic infants, 82 (75%) were trisomy 21.

Spontaneous closure

Spontaneous VSD closure was observed in 399 (55%) patients, with the highest rate observed in infants with muscular (78%) and small (78%) VSD [Table 2]. The median age of spontaneous VSD closure was 6.9 months (interquartile range [IQR]: 3.3–14.8 months), ranging from 13 days to 6.9 years. The overall estimated spontaneous VSD closure was 26% (95% CI: 23%–29%) at 6 months, 43% (95% CI: 39%–47%) at 1 year, 56% at 2 years, 68% (95% CI: 64%–72%) at 5 years, and 73% (68%–78%) at 10 years [Figure 2a]. There was a significant difference in spontaneous closure in VSD type [Figure 2b] and size [Figure 2c]. The rate of spontaneous VSD closure showed a significant rise during the initial 2 years of life, eventually stabilizing around the age of 7 years. Further analysis revealed that muscular VSD (aHR 4.2 [95% CI: 2.7–6.5], $P < 0.001$), perimembranous VSD (aHR 3.4 [95% CI: 2.2–5.2] $P < 0.001$), small VSD (aHR 16.1 [95% CI: 5.1–50.7], $P < 0.001$), and moderate VSD (aHR 7.5 [95% CI: 2.4–23.5], $P < 0.001$) were the independent factors for spontaneous VSD closure.

Table 1: Characteristics, complications, and outcome of isolated ventricular septal defect presenting during the neonatal period

Characteristic	*n*=726
Age at diagnosis (days), median (IQR)	5 (2–10)
Birth weight (kg), median (IQR)	2.9 (2.4–3.3)
Sex, *n* (%)	
Male	364 (50.1)
Female	362 (49.9)
Ethnicity, *n* (%)	
Malay	533 (73.4)
Chinese	131 (18.0)
Indian and others	62 (8.5)
Preterm, *n* (%)	153 (21.1)
Family history of CHD, *n* (%)	22 (3.0)
Maternal diabetes, *n* (%)	163 (22.5)
Associated with a syndrome, *n* (%)	109 (15.0)
Trisomy 21, *n* (%)	82 (11.3)
Noncardiac malformation, *n* (%)	33 (4.5)
Complications during follow-up, *n* (%)	
Heart failure	189 (26.0)
Pulmonary hypertension	52 (7.2)
Aortic regurgitation	38 (5.2)
Infective endocarditis	1 (0.1)
Eisenmenger syndrome	0
Outcome at the last follow-up, *n* (%)	
Close spontaneously	399 (55.0)
Needs surgery	149 (20.5)
Small and hemodynamically not significant	178 (24.5)
Died, *n* (%)	28 (3.9)
Cardiac related, *n* (% of died)	2 (7.1)
Noncardiac, *n* (% of died)	20 (71.5)
Undetermined, *n* (% of died)	6 (21.4)

IQR: Interquartile range, CHD: Congenital heart disease

Congestive heart failure and surgery

CHF was observed in 189 (26%), with the majority associated with moderate and large VSD [Figure 3]. The median age of CHF diagnosis was 6.6 weeks (IQR: 3–11 weeks), ranging from 3 days to 2.5 years. Of 189 CHF, 66 (35%) had their CHF resolved over time (41 remained small and 25 closed spontaneously). Further

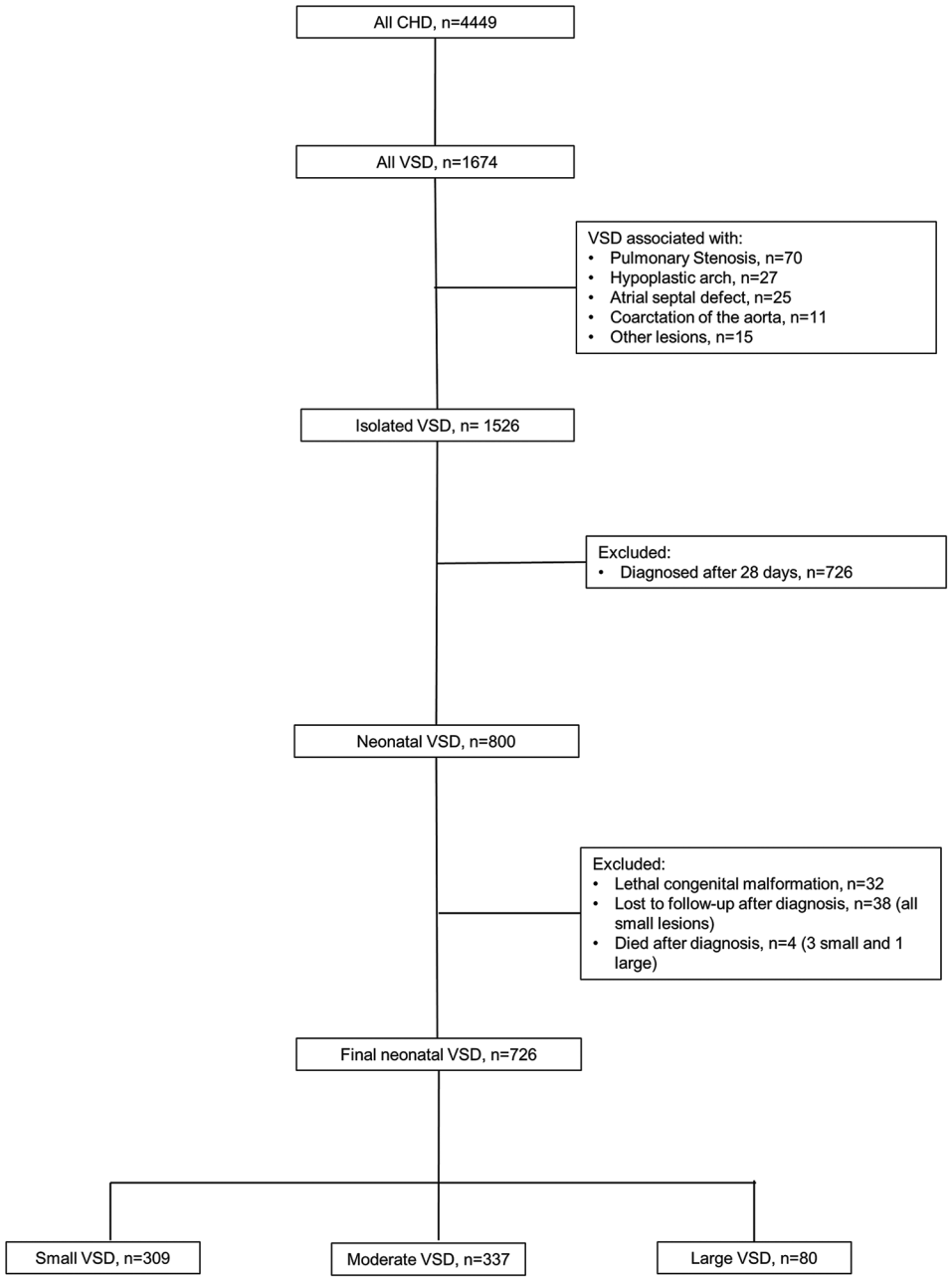

Figure 1: Study population

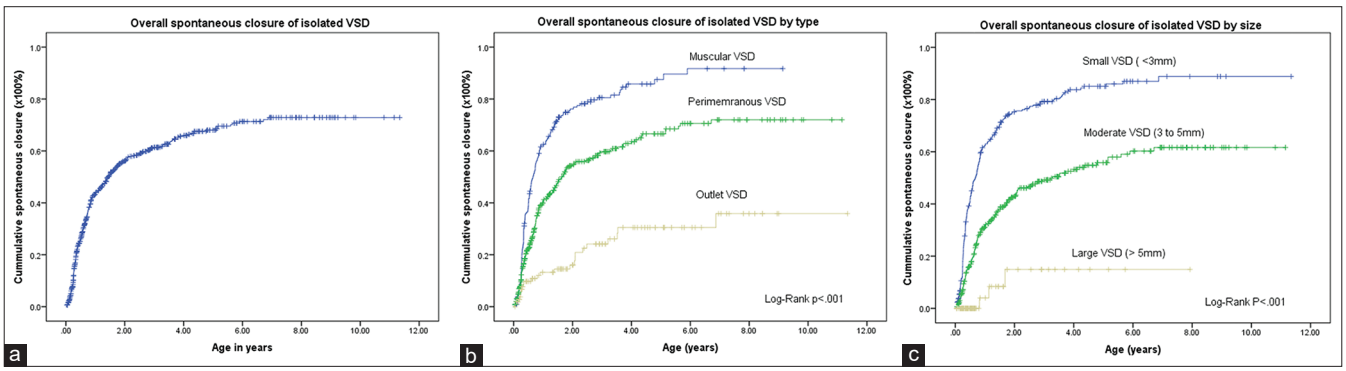

Figure 2: The overall estimated spontaneous closure of ventricular septal defect (a), by type (b), and by size (c)

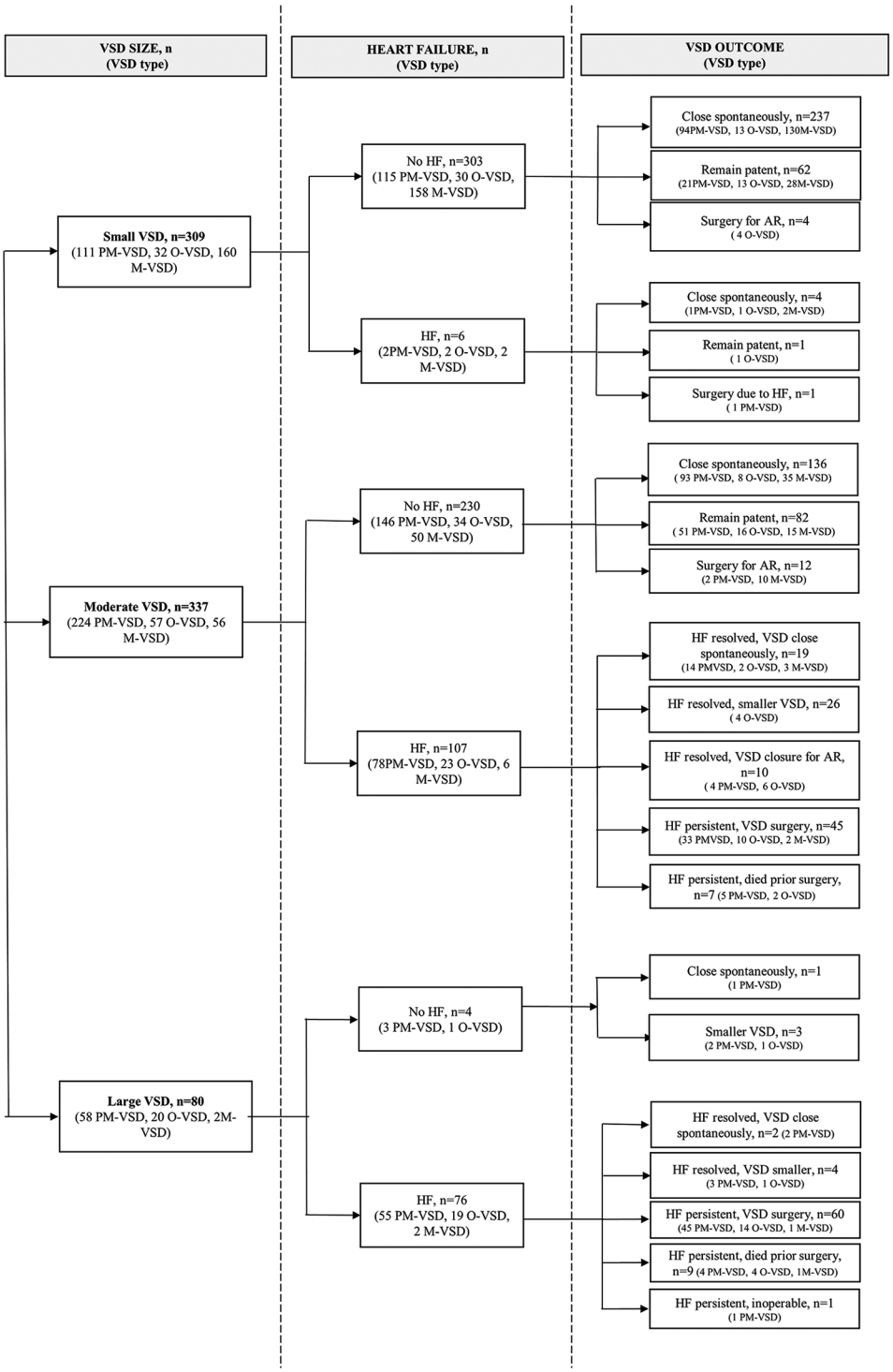

Figure 3: The outcome of congestive heart failure by ventricular septal defect size and type. PMVSD: Perimembranous ventricular septal defect, O-VSD: Outlet ventricular septal defect, M-VSD: Muscular ventricular septal defect

analysis showed significant CHF resolution in small or moderate VSD compared to large VSD (60/113 [53%] vs. 6/76 [8%], $P < 0.001$), in VSD without PHT compared to VSD with PHT (61/157 [39%] vs. 5/32 [16%], $P = 0.012$), and in nontrisomy 21 VSD versus trisomy 21 infants (62/149 [42%] vs. 4/36 [10%], $P < 0.001$).

Of the remaining 123 (65%) patients with persistent CHF, 104 had surgical closure (median age of 7.3 months, ranging from 1.2 months to 5.2 years), 16 (13%) died before surgery, two were still waiting for surgery, and one patient was treated with comfort care. Four patients (3.3%) had permanent heart block postoperatively, whereas 12 (10%) had a significant chylothorax that

Table 2: The rate of spontaneous closure of ventricular septal defect by size and type

VSD size	All VSD		Muscular VSD		PMVSD		Outlet VSD	
	Total (*n*)	SC	Total (*n*)	SC	Total (*n*)	SC	Total (*n*)	SC
Small (<3 mm)	309	241 (78.0)	160	132 (82.5)	111	95 (81.2)	32	14 (43.8)
Moderate (3–5 mm)	337	155 (46.0)	56	38 (67.9)	224	107 (47.8)	57	10 (17.5)
Large (>5 mm)	80	3 (3.8)	2	0	58	3 (5.2)	20	0
All	726	399 (55.0)	218	170 (78.0)	399	205 (51.4)	109	24 (22.0)

VSD: Ventricular septal defect, PMVSD: Perimembranous VSD, SC: Spontaneous closure

required medical therapy. In addition, there was no device closure in this cohort.

Aortic regurgitation and surgery

Aortic regurgitation was observed in 38 (5.2%) patients. Of 38, 12 (32%) were related to CHF (seven perimembranous VSDs and five outlet VSDs), and 26 (68%) were without CHF (six perimembranous VSDs and 20 outlet VSDs). The median age of aortic regurgitation detection associated with CHF was 1.1 years, ranging from 5 days to 3.7 years, and without CHF was 3.9 years, ranging from 3 months to 11 years. Of 26 AR without CHF, 16 had successful VSD closure at a median age of 5.4 years, ranging from 1.3 to 11 years. Overall, 120 patients had successful surgery (104 due to CHF and 16 due to AR) with no death within 30 days of surgery.

Pulmonary hypertension

Of 726 patients, 52 (7.2%) had 2D echocardiography features of PHT. Of these patients, 24 were diagnosed with persistent PHT of the newborn within 72 h of birth, whereas five were diagnosed between days 3 and 7, 15 between days 8 and 28, and eight beyond the neonatal period. Of 52 PHT, 45 (86%) were associated with moderate-to-large VSD, and 41 (79%) were associated with trisomy 21. Overall, 19 (36%) patients with PHT resolved within 6 weeks of life, 7 (13%) resolved within 6 weeks to 3 months of life, and 26 (50%) remained persistent. Of 52 patients with PHT, 13 (25%) died with a median death age of 96 days, ranging from 25 days to 24.8 months.

Trisomy 21

There were 82 (11%) infants with trisomy 21, with 16 having small, 47 moderate, and 19 large VSDs. Nineteen (23%) infants in the group had persistent PHT of the newborn, of which 8 had persistent features of PHT beyond 6 weeks of life. CHF was observed in 40 infants, with 27 having successful surgery and 7 dying while waiting for surgery.

Mortality and survival

The mortality rate was 3.9% (28), with a median age of death being 2.9 months (IQR: 1.9–8.3 months) ranging from 16 days to 2.9 years. Of 28 deaths, 16 (57%) occurred preoperatively and 2 (7.1%) after 30 days of surgery. There is no death occurring within 30 days of surgery. Most deaths were related to severe pneumonia (11/28, 39%) and infection (7/28, 25%).

Univariate analysis showed that death was significant in large VSD compared to small or moderate VSD (11/80 [14%] vs. 17/646 [2.6%], $P < 0.001$), in VSD with CHF compared to those without CHF (18/189 [9.5%] vs. 10/537 [1.9%], $P < 0.001$), in trisomy 21 compared to nontrisomy 21 (16/82 [19%] vs. 12/644 [1.9%], $P < 0.001$), VSD with PHT compared to without PHT (13/52 [25%] vs. 15/674 [2.2%], $P < 0.001$), and in patients with birth weight <2.5 kg compared to more than 2.5 kg (15/214 [7%] vs. 13/512 [2.5%], $P = 0.004$). However, multivariate analysis showed that trisomy 21, PHT, and birth weight <2.5 kg were independent factors for mortality with aHR of 6.0, 3.2, and 3.6, respectively [Table 3].

The overall estimated survival of isolated VSD at 1, 5, and 10 years was 96% (95% CI: 95–98), 95% (95% CI: 94–97), and 95% (95% CI: 94–97), respectively [Figure 4a]. Significantly low survival was noted in infants with birth weight <2.5 kg, PHT, and trisomy 21 compared to their counterparts [Figure 4b-d].

DISCUSSION

In this study, the first from a middle-income country, the natural and unnatural history of VSD presenting during the neonatal period was examined through a population-based approach. In addition to VSD size and type, it was found that small infants, trisomy 21, and PHT played a significant role in determining the complications and outcomes associated with this condition.

Spontaneous closure

The study found that the overall spontaneous closure rate for VSDs was 55%, with an estimated 42% closed within the 1st year and 70% by age 6 years. Our estimated closure rate was slightly lower than other neonatal studies, which reported rates ranging from 59%–61% at 1 year to 82%–92% at 6 years.[16,17] This could be attributed to a higher percentage of perimembranous and outlet VSDs in our cohort. However, the closure rate for muscular VSDs was consistent with recent studies, ranging between 60% and 90%.[5,16,17,19]

This study revealed that perimembranous and outlet VSDs have a higher spontaneous closure rate than previous studies.[17,20-22] The findings indicate that one out of every five outlet VSDs and one out of every two

Table 3: Factors associated with mortality

Variables	Total	Died, *n* (%)	Crude HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
Race						
Malay	533	22 (4.1)	1.34 (0.54–3.29)	0.530	1.17 (0.47–2.93)	0.736
Non-Malay	193	6 (3.1)	Reference		Reference	
Sex						
Male	364	18 (4.9)	1.75 (0.81–3.78)	0.158	1.45 (0.66–3.18)	0.349
Female	362	10 (2.8)	Reference		Reference	
Birth weight <2.5 kg						
Yes	214	15 (7.0)	2.98 (1.42–6.27)	0.004	3.62 (1.67–7.85)	0.001
No	512	13 (2.5)	Reference		Reference	
CHF						
Yes	189	18 (9.5)	4.45 (2.05–9.66)	<0.001	0.99 (0.31–3.20)	0.989
No	537	10 (1.9)	Reference		Reference	
Pulmonary hypertension						
Yes	52	13 (25.0)	11.77 (5.60–24.73)	<0.001	3.22 (1.23–8.45)	0.018
No	674	15 (2.2)	Reference		Reference	
Trisomy 21						
Yes	82	16 (19.5)	10.68 (5.05–22.58)	<0.001	6.03 (2.15–16.91)	0.001
No	644	12 (1.9)	Reference		Reference	
VSD size						
Large	146	16 (11.0)	4.72 (2.23–9.99)	<0.001	2.72 (0.93–7.98)	0.068
Small/moderate	580	12 (2.1)	Reference		Reference	
VSD type						
PM	399	17 (4.3)	2.82 (0.83–9.62)	0.098	1.01 (0.27–3.80)	0.990
Outlet	109	8 (7.3)	4.56 (1.21–17.2)	0.025	4.08 (0.99–16.64)	0.050
Muscular	218	3 (1.4)	Reference		Reference	

Analyzed with Cox regression analysis, corrected for race and sex. A *P* value is considered significant if a 95% CI does not include 1. HR: Hazard ratio, CI: Confidence interval, VSD: Ventricular septal defect, PM: Perimembranous, CHF: Congestive heart failure

perimembranous VSDs tend to close spontaneously. This higher closure rate could be attributed to early diagnosis of VSD and longer follow-up duration in this cohort.

One of the key factors affecting the spontaneous closure of VSD is the size of the defect.[4,23] In this study, small VSDs were significantly associated with spontaneous closure, with small VSDs being 16 times more likely to close than large VSDs. Similar to findings from Xu *et al.*,[4] nearly 80% of small VSDs (with a diameter of <3 mm) were observed to close spontaneously, whereas only 50% of moderate VSDs (3–5 mm) and hardly any large VSDs (over 5 mm) were found to close spontaneously.

Congestive heart failure

CHF usually develops in moderate and large VSDs due to increasing systemic to pulmonary shunts. This study showed that one in four VSDs developed CHF at a median age of 6 weeks of life. Interestingly, one-third of these infants improved over time and escaped surgical closure. Our study indicates that VSDs that are small-to-moderate in size, not linked to chromosome anomalies, and lacking PHT characteristics are strongly associated with the resolution of CHF. Therefore, this finding supports the current practice of trial of medical treatment for this group of patients.[3] In contrast, for large VSDs, early surgical closure should be prioritized, especially if accompanied by CHF, PHT, and trisomy 21. However, this can be a considerable obstacle in lower- and middle-income countries with limited resources and expertise.[24] It is apparent from this study that a considerable number of patients passed away while awaiting surgery, especially those with PHT.

Pulmonary hypertension

It has been established that the causes of PHT are multifactorial.[25] In a large VSD that goes untreated, persistent high blood flow to the lungs can result in PHT, which carries a high risk of morbidity and mortality.[26] On the other hand, even small defects may have PHT due to primary PHT or in conjunction with chromosomal abnormalities.[27] This study is the first to examine the prevalence of PHT and its immediate effects on neonates with VSD. Nearly 10% of VSD patients demonstrated PHT, especially in infants with trisomy 21 and moderate-to-large VSD. While some of these PHT may have improved over time, the health-care system is still significantly burdened by the need to monitor these patients closely. Thus, making timely decisions regarding surgery is crucial to prevent heart failure from worsening and the development of Eisenmenger syndrome.

Device closure and infective endocarditis

Our study found that none of the small or moderate VSDs required device closure and had good outcomes. Furthermore, one-third of the patients with CHF resolved spontaneously over time, especially those with small or moderate VSDs. In addition, we observed a low incidence of infective endocarditis in our cohort, which can be attributed to the prophylaxis for subacute bacterial endocarditis, which is still practiced at the time of the study. Therefore, this finding provides further evidence against surgical or catheter closure for patients with small VSDs.[28] Rushing for device closure should be avoided in this group of infants.

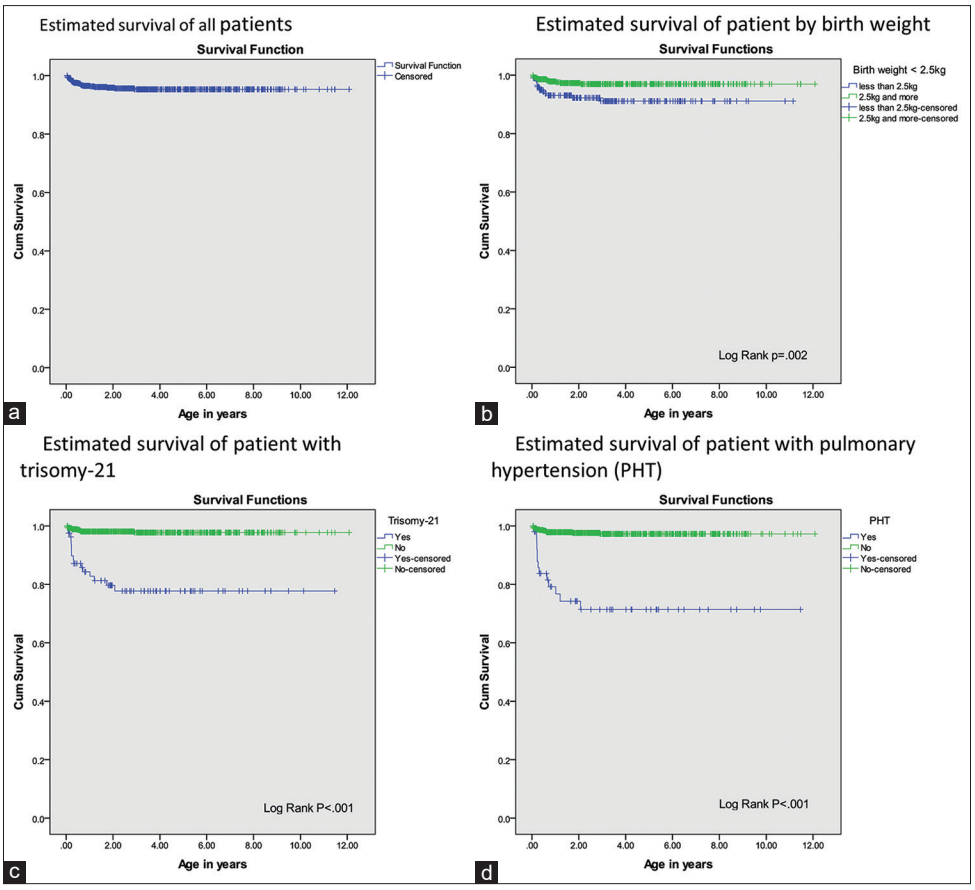

Figure 4: The estimated survival rate of all neonates with isolated ventricular septal defect (a), by birth weight (b), trisomy 21 (c), and pulmonary hypertension (d)

Mortality and survival

Compared to high-income countries, our study showed a slightly higher overall mortality rate,[29] which is not unexpected given the lack of resources and expertise in pediatric congenital cardiac services in our country. The primary cause of the high mortality rate in this study was preoperative mortality resulting from infection and pneumonia, especially infants with low birth weight, trisomy 21, and PHT. Therefore, early surgery in this group of neonates is needed to improve the outcomes.

However, despite the limitations of congenital cardiac surgery services, we observed no deaths during surgery, and the postoperative complication rate was low, aligning with studies conducted in high-income countries. Furthermore, the overall survival of neonatal VSD remains good, with 95% survival at 10 years.

Limitation of the study

There are a few limitations in this study. First, some patients may have been diagnosed with VSD in other states of Malaysia or may have passed away before receiving a diagnosis, leading to underreporting of VSD. Second, the involvement of multiple centers and echocardiographers could have caused interobserver variability, especially when measuring and evaluating the size and type of VSD. Third, apart from trisomy 21, we acknowledge that other genetic disorders might have an impact on our cohort's outcome. Unfortunately, due to a small number of cases, we could not include this factor in the final analysis. Another limitation was that 38 patients with small VSDs (4%) were excluded since they only had one echocardiogram. It is possible that these patients are still alive or have passed away, and we are unable to trace them back as they did not come for follow-up. This is a reality in clinical practice, especially in our country. Finally, PHT was defined based on 2D echocardiography, and only a small percentage underwent cardiac catheterization to determine pulmonary resistance.

CONCLUSIONS

This population-based study with a larger and longer follow-up showed that the prognosis of isolated VSD presenting during the neonatal period in Malaysia is good, with 1 in 2 spontaneously close and 1 in 5 needing surgery. Neonates who have a low birth weight, trisomy 21, or PHT are at a higher risk for poor outcomes.

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Conflicts of interest

There are no conflicts of interest.

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