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ORIGINAL ARTICLE

Ten-year trend in prevalence and outcome of Down syndrome with congenital heart disease in a middle-income country

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Abstract

Limited data are available on the survival of patients with Down syndrome and congenital heart disease (CHD) from middle-income countries. This retrospective cohort study was performed to determine the trends in the prevalence and survival of such patients born from January 2006 to December 2015 in Malaysia. Among 754 patients with Down syndrome, 414 (55%) had CHD, and no significant trend was observed during the 10 years. Of these 414 patients, 30% had lesions that closed spontaneously, 35% underwent surgery/intervention, 9% died before surgery/intervention, and 10% were treated with comfort care. The overall mortality rate was 23%, the median age at death was 7.6 months, and no significant changes occurred over time. The early and late post-surgery/intervention mortality rates were 0.7% and 9.0%, respectively. Most deaths were of non-cardiac causes. The overall 1-, 5-, and 10-year survival rates were 85.5%, 74.6%, and 72.9%, respectively. Patients with severe lesions, persistent pulmonary hypertension of the newborn, atrioventricular septal defect, and pulmonary hypertension had low survival at 1 year of age.

Conclusion: The prevalence of CHD in patients with Down syndrome is similar between Malaysia and high-income countries. The lower survival rate is attributed to limited expertise and resources which limit timely surgery.

What is Known:
- *The survival of patients with Down syndrome with congenital heart disease (CHD) has improved in high-income countries. However, little is known about the survival of patients with Down syndrome with CHD from middle-income countries.*
- *In the Caucasian population, atrioventricular septal defect is the most common type of CHD associated with Down syndrome.*

What is New:
- *In middle-income countries, the prevalence of CHD is the same as in high-income countries, but with a lower survival rate.*
- *In the Asian population, ventricular septal defect is the most common type of CHD in patients with Down syndrome.*

Keywords Congenital heart disease · Down syndrome · Middle-income country · Mortality · Prevalence · Survival

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Abbreviations

ASD	Atrial septal defect
AVSD	Atrioventricular septal defect
CHD	Congenital heart disease
CI	Confidence interval
HSAJB	Hospital Sultanah Aminah Johor Bahru
IQR	Interquartile range
LMICs	Low- and middle-income countries
PDA	Patent ductus arteriosus
PHT	Pulmonary hypertension
PPHN	Persistent pulmonary hypertension of the newborn
PS	Pulmonary stenosis
UMMC	University Malaya Medical Centre
VSD	Ventricular septal defect

Introduction

The World Health Organization has listed Down syndrome as one of the most common serious congenital disorders worldwide, and increased research and care are focusing on this condition [32]. However, most studies of Down syndrome are performed in high-income countries with good resources. Minimal data are available on the survival of children with Down syndrome from low and middle-income countries (LMICs).

In children with Down syndrome, the most common associated structural defect is congenital heart disease (CHD), which occurs in 45 to 55% of cases. Data from the Caucasian population show that the most common type of CHD is atrioventricular septal defect (AVSD) [1, 11, 23]. In contrast, recent regional studies from Asian countries have revealed ventricular septal defect (VSD) as the most common type of CHD [17, 22, 28]. These contradictory results indicate the need for further studies in the Asian population.

CHD is a major factor that determines the outcome for children with Down syndrome. In the USA, Kucik et al. [15] showed that children with both Down syndrome and CHD are five times more likely to die than those with Down syndrome without CHD. However, Fudge et al. [6] showed that Down syndrome does not significantly increase the mortality risk among patients with CHD. In high-income countries with excellent resources and expertise, timely cardiac surgery and effective pre-operative and post-operative care have allowed children with Down syndrome and CHD to achieve significant survival at 1 year of age, reaching a post-cardiac survival rate of > 90% in some series [7, 11, 14].

However, a common practice in middle-income countries is to prioritize cardiac surgery for patients without Down syndrome with good outcomes because of chronic understaffing and financial constraints [18]. To the best of our knowledge, no studies have focused on the survival and mortality among patients with Down syndrome with CHD in Malaysia. Because of the limited resources in all areas, we postulate that the survival of such patients is significantly lower than that in high-income countries.

Therefore, this study was performed to determine the prevalence and distribution of CHD among patients with Down syndrome and to estimate the survival rate and its trend over time in a middle-income country. We hope that the results of this study will help formulate health policies that favor the inclusion of these children in society with timely treatment of CHD.

Methods

This retrospective cohort study included all patients with phenotypically confirmed Down syndrome with CHD born from 1 January 2006 to 31 December 2015 at two tertiary centers in Malaysia: Hospital Sultanah Aminah Johor Bahru (HSAJB) and University Malaya Medical Centre (UMMC). Non-Malaysian patients with Down syndrome were excluded from this study.

HSAJB is a tertiary government hospital that provides pediatric cardiology services for the State of Johor in southern Malaysia, which has a population of 3.5 million and annual live birth rate of about 50,000 per year [17].

UMMC is a government-funded teaching hospital with pediatric cardiology services located in the capital city of Malaysia, Kuala Lumpur, with an estimated annual delivery rate of 5000 to 6000 per year.

Neither center has a written standard policy for the care and cardiac assessment of children with Down syndrome and CHD. Because neither center has a dedicated pediatric cardiac surgeon, open heart surgery and high-risk intervention are offered in the Institut Jantung Negara, which is the only dedicated pediatric and congenital cardiac center in Malaysia.

All patients who met the inclusion criteria were divided into three groups: group 1 comprised patients who required no surgery/intervention, group 2 comprised those who needed some form of surgery/intervention, and group 3 comprised patients selected for comfort care. The decision for comfort care in both centers was made according to standard criteria such as the presence of severe pulmonary hypertension (PHT), isomerism, and cardiac defects that are not suitable for biventricular repair such as unbalanced AVSD. The decision was made with parental discussion and acceptance.

Data were retrieved from the medical records and clinic database. Patients were regarded as having Down syndrome based on the presence of phenotypic features of Down syndrome with or without chromosomal analysis. All studied patients were followed up from birth until December 2017. The data collected included maternal age, gestational age (premature or term), sex, birth weight, chromosomal analysis, cardiac and non-cardiac malformations, the presence of persistent pulmonary hypertension of the newborn (PPHN) at birth, PHT, and outcome (alive or dead) at last follow-up. All causes of death were verified with the Malaysian National Registration Office.

We defined PPHN based on the echocardiographic finding of right-to-left shunting through the ductus arteriosus or foramen ovale without significant structural cardiac lesions [25, 27]. The diagnosis of PHT was made from an estimated right ventricular systolic pressure of ≥ 50% or other echocardiographic findings suggestive of PHT, such as septal flattening, a dilated main pulmonary artery, and dilated right cardiac chambers in the absence of pulmonary stenosis (PS) [5].

CHD was defined as a gross structural abnormality of the heart or intrathoracic great vessels that was of actual or potential functional significance, as previously described by Mitchell et al. [19]. The severity of CHD was divided into

mild, moderate, and severe as defined by Hoffman and Kaplan [10]. The diagnosis of CHD was made by a pediatric cardiologist using either echocardiography or other modalities (cardiac computed tomography/magnetic resonance imaging or catheterization). Patent foramen ovale, mild branch PS, isolated dextrocardia, isolated bilateral superior vena cava, isolated right arch, and patent ductus arteriosus (PDA) with spontaneous closure within the first 6 months in premature infants and within the first 3 months in term infants were considered non-CHD. In patients with multiple cardiac defects, the primary defect that required the first intervention or was of hemodynamic significance was regarded as the primary defect. The age at cardiac diagnosis was the date of the first confirmatory diagnosis.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23 (IBM Corp., Armonk, NY, USA). Groups were compared using Student's *t* test for normally distributed continuous data and using a non-parametric test for non-normally distributed continuous data. We used Pearson's chi-square test for categorical variables. A p value of < 0.05 was considered statistically significant. We used EpiCalc 2000 (Brixton Health, Llanidloes, Wales) to analyze the trend over time and Kaplan–Meier analysis to estimate survival.

Results

In total, 754 patients with Down syndrome were identified during the study period, and 414 of these patients had CHD with a median follow-up of 2.7 years (interquartile range (IQR), 1.1–5.5). Therefore, the prevalence of CHD among patients with Down syndrome was 54.9% (95% confidence interval (CI), 51.3–58.5). Table 1 shows the trend analysis of CHD prevalence, management, and mortality across the 10-year study period. The trends in the prevalence of CHD in patients with Down syndrome, patients who received comfort care, and mortality during the study period were similar. However, there was a significant increase in the number of patients with Down syndrome with CHD who required surgery/intervention.

Of the 414 patients, 169 (40%) were in group 1, 204 (50%) were in group 2, and 41 (10%) were in group 3. In group 1, all patients had mild lesions, and 74% (68 PDAs, 36 VSDs, 16 atrial septal defects (ASDs), and 5 PSs) closed spontaneously during follow-up. The median age of follow-up in group 1 was 2.9 years (IQR 1.2–5.5).

In group 2, 37 (18%) patients died while waiting for surgery/intervention, 146 (72%) underwent surgery/intervention, and the remaining were still awaiting surgery/intervention at the time this study was conducted. The cause of death prior to surgery was pneumonia ($n = 11$), infection ($n = 10$), cardiac-related disease ($n = 8$), unknown cause ($n = 7$), and a motor vehicle accident ($n = 1$).

The median age at the surgery/intervention was 10.5 months (IQR, 4.9–23.7) with a median waiting time for surgery/intervention of 9 months (IQR, 4–22). Of the 146 patients who underwent surgery/intervention, 1 (who had a PDA) died of methicillin-resistant *Staphylococcus aureus* sepsis within 30 days. Thirteen patients (7 with PDAs, 3 with VSDs, 2 with AVSDs, and 1 with pulmonary atresia with AVSD) died 30 days after the surgery/intervention due to pneumonia ($n = 5$), infection ($n = 4$), leukemia ($n = 2$), cardiac-related disease ($n = 1$), and unknown cause ($n = 1$).

In group 3, the decision for comfort care was based on the presence of severe PHT (14 AVSDs, 5 VSDs, 3 ASDs, and 2 PDAs), a complex defect (7 unbalanced AVSDs, 1 double-outlet right ventricle, and 1 severe Ebstein anomaly), severe PPHN (5 AVSDs), severe prematurity with extremely low birth weight (1 AVSD), and refusal of surgery (1 VSD and 1 ASD).

Table 1 Trend analysis for the prevalence of congenital heart disease, management, and mortality among children with Down syndrome with congenital heart disease in Malaysia, 2006–2015

Variables	Total	Birth year										Chi-square test for trend, *p* value
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	
All DS	754	81	61	71	57	70	67	82	95	86	84	
DS with CHD	414 (54.9)	41 (50.6)	36 (59.0)	38 (53.5)	37 (64.9)	41 (58.6)	37 (55.2)	51 (62.2)	46 (48.4)	45 (52.3)	42 (50.0)	0.69, 0.41
Group 1	169 (40.8)	21 (51.2)	11 (30.6)	20 (52.6)	15 (40.5)	21 (51.2)	18 (48.7)	17 (33.3)	16 (34.8)	16 (35.6)	14 (33.3)	3.42, 0.06
Group 2	204 (49.3)	15 (36.6)	19 (52.7)	15 (39.5)	20 (54.1)	14 (34.1)	15 (40.5)	29 (56.9)	26 (56.5)	25 (55.5)	26 (61.9)	5.84, 0.02
Group 3	41 (9.9)	5 (12.2)	6 (16.7)	3 (7.9)	2 (5.4)	6 (14.7)	4 (10.8)	5 (9.8)	4 (8.7)	4 (8.9)	2 (4.8)	1.58, 0.21
Died	93 (22.5)	7 (17.1)	5 (13.9)	8 (21.1)	6 (16.2)	11 (26.8)	9 (24.3)	18 (35.3)	11 (23.9)	12 (26.7)	6 (14.3)	1.25, 0.25

Data are presented as *n* or *n* (%)

DS, Down syndrome; *CHD*, congenital heart disease; *Group 1*, children with DS who required no surgery or intervention; *Group 2*, children with DS who required surgery or intervention; *Group 3*, children with DS treated with comfort care

Table 2 shows the characteristics and outcomes of the patients with Down syndrome with CHD in this study. The median age at the time of cardiac diagnosis was 7 days (IQR, 1–60). One patient had Eisenmenger syndrome, 22% had PHT, and 16% had PPHN during the 10-year study period. Chromosomal analysis results were available in only 160 (39%) patients (155 non-disjunctions, 2 Robertsonian translocations, and 3 mosaics). Mortality was significantly high among patients with AVSD (45%), PPHN (40%), PHT (39%), and severe lesions (38%).

Table 3 shows the distribution and severity of lesions among patients with Down syndrome with CHD in our cohort. The most commonly observed lesions were VSD (32.1%), PDA (30.4%), and AVSD (18.4%). There were 171 (41%) mild lesions, 70 (17%) moderate lesions, and 173 (42%) severe lesions. Of the 173 severe lesions, 20% were

Table 2 Characteristics and outcomes of children with Down syndrome with congenital heart disease among Malaysian children, 2006–2015

Variable	Total, $n = 414$		Outcome				p value*
			Survived, $n = 321$		Died, $n = 93$		
Sex							
Male	189	(45.7)	149	(46.4)	40	(43.0)	0.56
Female	225	(54.3)	172	(53.6)	53	(57.0)	
Race							
Malay	317	(76.6)	243	(75.7)	74	(79.6)	0.73
Chinese	70	(16.9)	57	(17.8)	13	(14.0)	
Indian	21	(5.1)	17	(5.3)	4	(4.3)	
Others	6	(1.4)	4	(1.2)	2	(2.2)	
Gestational age							
Premature	62	(15.0)	44	(13.7)	18	(19.4)	0.16
Term	352	(85.0)	277	(86.3)	75	(80.6)	
PHT	92	(22.2)	56	(17.4)	36	(38.7)	< 0.001
PPHN	68	(16.4)	41	(12.8)	27	(29.0)	< 0.001
Duodenal atresia	25	(6.0)	18	(5.6)	7	(7.5)	0.49
Hirschsprung disease	8	(1.9)	7	(2.2)	1	(1.1)	0.49
Severity							
Mild/moderate CHD	241	(58.2)	214	(66.7)	27	(29.0)	< 0.001
Severe CHD	173	(41.8)	107	(33.3)	66	(71.0)	
Lesion							
AVSD	76	(18.4)	42	(13.1)	34	(36.6)	< 0.001
VSD	133	(32.1)	110	(34.3)	23	(24.7)	0.08
PDA	126	(30.4)	110	(34.3)	16	(17.2)	0.002
Birth year							
2006–2010	193	(46.6)	156	(48.6)	37	(39.8)	0.13
2011–2015	221	(53.4)	165	(51.4)	56	(60.2)	
Management							
No surgery/intervention (Group 1)	169	(40.8)	156	(48.6)	13	(14.0)	< 0.001
Surgery/intervention (Group 2)	204	(49.3)	153	(47.7)	51	(54.8)	
Comfort care (Group 3)	41	(9.9)	12	(3.7)	29	(31.2)	
Age at cardiac diagnosis, days	7 (1–60)		6 (0–73)		7 (1–36)		0.81
Age at last follow-up or death, years	2.7 (1.1–5.5)		3.8 (1.8–6.5)		0.6 (0.2–1.3)		< 0.001
Duration of follow-up, months	30.4 (11.9–63.6)		42 (20.8–73.4)		6.6 (2.2–13.8)		< 0.001
Maternal age, years	36.2 (30.0–40.0)		36.3 (30.2–40.5)		35.7 (28.8–39.2)		0.72

Data are presented as n (%) or median (interquartile range)

*Comparison between children who survived and died; $p < 0.05$ is considered statistically significant

PHT, pulmonary hypertension; *PPHN*, persistent pulmonary hypertension of the newborn; *CHD*, congenital heart disease; *VSD*, ventricular septal defect; *PDA*, patent ductus arteriosus; *AVSD*, atrioventricular septal defect

Table 3 Frequency and severity of cardiac defects in children with Down syndrome with congenital heart disease among Malaysian children, 2006–2015

Specific cardiac lesion	Total, $n = 414$		CHD severity					
			Mild, $n = 171$		Moderate, $n = 70$		Severe, $n = 173$	
VSD	133	(32.1)	58	(33.9)	30	(42.9)	45	(26.0)
PDA	126	(30.4)	74	(43.3)	28	(40.0)	24	(13.9)
AVSD	76	(18.4)	0	(0.0)	0	(0.0)	76	(43.9)
ASD	44	(10.6)	32	(18.7)	12	(17.1)	0	(0.0)
TOF	17	(4.1)	0	(0.0)	0	(0.0)	17	(9.8)
PS	7	(1.7)	6	(3.5)	0	(0.0)	1	(0.6)
PAVSD	2	(0.5)	0	(0.0)	0	(0.0)	2	(1.2)
DORV	2	(0.5)	0	(0.0)	0	(0.0)	2	(1.2)
Ebstein's anomaly	2	(0.5)	0	(0.0)	0	(0.0)	2	(1.2)
Aortic stenosis	1	(0.2)	1	(0.6)	0	(0.0)	0	(0.0)
TGA	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.6)
TA	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.6)
PAIVS	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.6)
TAPVD	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.6)

Data are presented as *n* (%)

CHD, congenital heart disease; *VSD*, ventricular septal defect; *PDA*, patent ductus arteriosus; *AVSD*, atrioventricular septal defect; *ASD*, atrial septal defect; *TOF*, tetralogy of Fallot; *PS*, pulmonary stenosis; *DORV*, double-outlet right ventricle; *AS*, aortic stenosis; *TGA*, transposition of great arteries; *TA*, tricuspid atresia; *PAVSD*, pulmonary atresia with ventricular septal defect; *PAIVS*, pulmonary atresia with intact septum; *TAPVD*, total anomalous pulmonary venous drainage

treated with comfort care (27 AVSDs, 5 VSDs, 1 double-outlet right ventricle, 1 Ebstein anomaly, and 1 PDA).

A total of 93 patients (22.5%; 95% CI, 18.6–26.8) died during the 10-year study; among these patients, 62% died within the first year of life. The median age at death in groups 1, 2, and 3 was 3.5 months (IQR, 2.3–11.6), 9.4 months (IQR, 3.2–18.2), and 6.9 months (IQR, 2.0–16.8), respectively, with an overall median age at death of 7.6 months (IQR, 2.7–15.2). In total, 29 (31%) deaths were cardiac-related, 13 (14%) were of unknown cause, and 51 (55%) were non-cardiac-related (22 cases of pneumonia, 21 infections, 3 malignancies, and 5 others). The crude mortality rates for VSD, PDA, and AVSD were 17%, 13%, and 45%, respectively. The post-surgery/intervention mortality rate was highest for PDA at 19%, followed by VSD and AVSD at 6% each.

Survival analysis

The overall 1-, 5-, and 10-year survival rates for patients with Down syndrome with CHD in our cohort were 85.5%, 74.6%, and 72.9%, respectively (Fig. 1). Survival at 1 year of age was higher for patients who did not than for those who did require surgery/intervention (93.8% vs. 85.9%, respectively). Further analysis showed no significant difference in overall 1-year survival from 2006 to 2010 (87%) versus 2011 to 2015 (84%). However, a significantly low survival rate at 1 year of age was observed in patients with PPHN (70% vs. 88%, $p < 0.0001$), AVSD (72% vs. 86%, $p < 0.0001$), severe lesions (76% vs. 93%, $p < 0.0001$), and PHT (79% vs. 87%, $p < 0.0001$) compared with their counterparts.

Discussion

The prevalence of Down syndrome with CHD in this study was 55% with no significant changes over 10 years. This is consistent with a recent publication from high-income

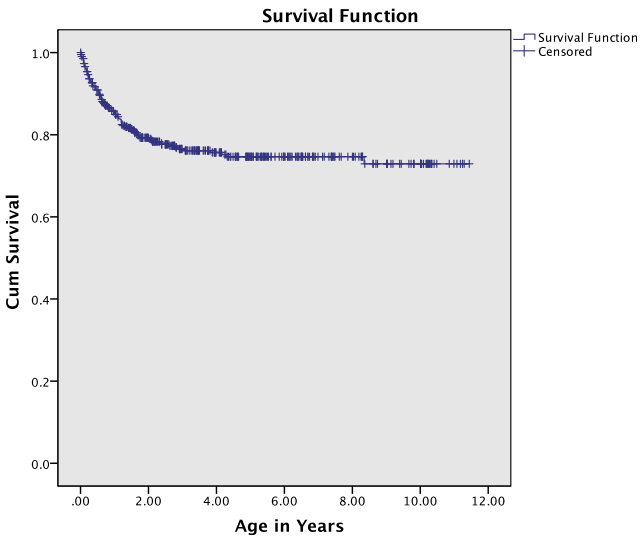

Fig. 1 Survival probabilities of 414 patients with Down syndrome with congenital heart defects born from 2006 to 2015. Cum, cumulative

countries showing a prevalence of 42 to 54% [1, 11, 23]. However, our study showed that VSD rather than AVSD was the most frequent cardiac defect in patients with Down syndrome with CHD. Recent studies from the Asian population showed that VSD was the most common cardiac defect among patients with Down syndrome, with a prevalence of 39% in Singapore [28]; 34% in Johor, Malaysia [17]; and 28% in Kerala, India [22]. Hence, our result supports VSD as the most common cardiac defect among children with Down syndrome in the Asian population. This variability of CHD types observed in different geographical areas has been well described [30, 33] and could be due to genetic variation [24].

To the best of our knowledge, this is the first study in Malaysia to examine the survival of patients with Down syndrome with CHD. Our study showed a difference in estimated survival among the three groups. Good survival at 1 year (94%) was noted in group 1, followed by groups 2 (86%) and 3 (51%). The overall survival rate was 85%, which is similar to the rates published 20 years ago from Ireland at 80% [8] and the UK at 90% [12]. However, it is lower than recently published rates: 97% in Germany [14], 95% in Norway [2], and 92% in Australia [7]. The low survival rate in our study is due to the inclusion of those with comfort care (1 in 10 patients). Furthermore, pediatric and congenital cardiac surgery is highly costly. Because of our relative lack of resources in both expertise and facilities required for surgery for CHD, complex cardiac surgery is prioritized to patients with no associated congenital abnormalities or other comorbidities with a better prognosis [18].

The financial limitations in Malaysia contribute to the problem because other pediatric diseases are prioritized. This leads to long waiting times for surgery/intervention and therefore significant mortality before surgery (1 in 5 patients in our study died while waiting for surgery; most died of pneumonia and infection). Ideally, all patients with Down syndrome with CHD with significant lesions should undergo early surgery/intervention to avoid complications such as severe heart failure, PHT, and recurrent infection. Unfortunately, this is not feasible in Malaysia because of the lack of dedicated pediatric cardiac surgeons. During the study period, only 5 dedicated pediatric cardiac surgeons in Malaysia were available to cover a population of almost 34 million. Unfortunately, this is a common problem facing LMICs [20, 21]. Hence, a multipronged approach is necessary to improve congenital cardiac surgery services in LMICs. Providing optimal nutrition, ensuring good infection control, optimizing heart failure therapy, and providing well-equipped intensive care are critical to improve the outcomes [13].

Surgery in patients with Down syndrome, particularly those with AVSD, was historically associated with significant mortality and morbidity. However, with advances in surgical techniques and improvements in post-operative care in the current era, many studies have shown no significant difference in mortality between children with and without Down syndrome [6, 9, 16, 29]. In our cohort, the overall surgical/intervention mortality rate was 9.6%, and most were late deaths unrelated to the procedure. This low mortality rate in the early post-surgery/intervention period was partly due to selection bias (comfort care in patients with severe lesions and PHT) and the fact that many children died before surgery.

Chromosomal analysis results were available for only 40% of patients, and non-disjunction was the most common cause of Down syndrome. This low percentage of chromosomal results highlights a major problem in the genetic services in LMICs. In LMICs, genetic conditions are not considered priorities because of other numerous pressing health issues such as control of communicable diseases and other preventable health conditions. Fear of stigmatization and cultural and religious factors contributed to parents' refusal of genetic testing.

An interesting finding in our study is a high percentage of PPHN (16%) compared to studies from high-income countries with rates ranging from 1.2 to 13% [3, 4, 26, 31]. There are two reasons for this finding. Firstly, in LMICs with limitations in human resources and expertise, the incidence of PPHN is high compared to high-income countries. Infection, meconium aspiration, and hypoxic-ischemic encephalopathy are common problems in our country leading to a high rate of PPHN. Secondly, the high rate could be due to the inclusion of mild PPHN which required supplemental oxygen in our study.

Limitations

This study has several limitations related to its observational and retrospective nature. First, the lack of confirmatory chromosomal results for the diagnosis of Down syndrome in our study may have led to overdiagnosis of Down syndrome. However, because Down syndrome has a characteristic phenotype that is easily differentiated, overdiagnosis of Down syndrome is minimal. The second limitation is the lack of post-mortem data on the cause of death in our cohort because post-mortem examinations are not compulsory. Our study showed a significant number of unknown causes of death. This may have led to incorrect information about the actual cause of death. There is also a need to change the legislation to obligatory post-mortem examinations in all cases of unknown causes of death. The third limitation is the lack of detailed surgical and intervention data. This is unavoidable because the surgeries and some interventions were performed in another cardiac center. A national registry for Down syndrome or CHD is required to overcome these issues. However, development and maintenance of a national registry is very costly, particularly in LMICs.

Conclusion

The prevalence of CHD in patients with Down syndrome has remained static over time, with VSD as the most common cardiac defect. Overall, a significant number of patients died of pneumonia and infection before surgery. The lower survival rate of patients with Down syndrome probably reflects the challenges faced by families and the healthcare system to cope with the disease burden in the context of LMICs. Further studies are needed to identify methods to overcome this limitation in middle-income countries.

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Authors' contributions Dr. HR was involved in data entry and analysis and drafted the initial manuscript.

Dr. NZ conceptualized and designed the study, carried out the echocardiogram, and revised the manuscript.

Dr. MNMB conceptualized and designed the study, carried out the echocardiogram, analyzed the data, and revised the manuscript.

Prof TMK reviewed the manuscript for important intellectual content and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all the aspects of the work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the clinical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Medical Research and Ethics Committee of Ministry of Health Malaysia (NMRR-17-957-35260(IIR)) and University Malaya Medical Centre (MREC ID NO: 201723-4886).

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