

## Short-term outcomes following congenital heart surgery in children with Down syndrome

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### Abstract

**Background** Children with Down syndrome (DS) differ from typical children because of many genetic-related aspects that may affect outcomes after congenital heart surgery. To date, there have been no studies on outcomes after congenital heart surgery on pediatric DS patients in Indonesia.

**Objective** To determine outcomes and mortality in DS patients who underwent heart surgery at Dr. Cipto Mangunkusumo Hospital, Jakarta.

**Methods** A prospective and retrospective cohort study was conducted in DS patients aged <15 years who underwent heart surgery from July 2007 to April 2015. The control group were patients in the same age range without DS who underwent heart surgery for various types of heart defects.

**Results** There were 57 DS and 43 non-DS patients during study period. The types of heart defects found in DS patients were atrioventricular septal defect (AVSD) and ventricular septal defect (VSD) in 18/57 (31.6%) patients each, tetralogy of Fallot (12/57; 21%), atrial septal defect (ASD) (4/57; 7%), patent ductus arteriosus (PDA) (4/57; 7%) and transposition of the great arteries with VSD (TGA-VSD) (1/57; 1.8%). DS patients showed an increased incidence of preoperative PH (63.1%) compared to non-DS patients (25.6%). Median duration of surgery was longer in DS [2.9 (range 0.5-5.8) hours] than in non-DS [2.2 (range 0.7-4.7) hours]. DS patients have a longer mean cardiopulmonary bypass duration [79.5 (SD 33.9) minutes] compared to non-DS [59.9 (SD 23.6) minutes], longer mean aortic cross-clamp duration [45.3 (SD 23.7) minutes] compared to non-DS [34.8 (SD 15.7)]. There were significant differences in the incidence of preoperative pulmonary hypertension, surgical time, duration of cardiopulmonary bypass (CPB), and length of the aortic cross-clamp in DS patients compared to non-DS ( $P < 0.05$ ). Median length of ICU stay was 1.9 (range 0.6 to 34) days in DS and 1 (range 0.3 to 43) day in non-DS patients ( $P = 0.373$ ). Median duration of mechanical ventilation [19.9 (range 3-540) vs. 8 (range 3-600) hours ( $P = 0.308$ )], rate of pulmonary complications [14/57 (24.6%) vs. 6/43 (14%) patients ( $P = 0.216$ )], and incidence of sepsis [16/57 (28.1%) vs. 6/43 (14%) patients ( $P = 0.143$ )] were not significantly different between DS and non-DS patients. However, complete atrioventricular (AV) block only occurred in DS patients [6/57

(10.5%)]. In the DS group, 5/57 (8.8%) patients died. There was no mortality in the non-DS group.

**Conclusion** Morbidity and mortality after cardiac surgery in were higher in DS than in non-DS patients. DS patients may have problems related to preoperative PH, AV block, longer surgical time, duration of CPB, and aortic cross-clamp compared to non-DS. [Paediatr Indones. 2023;63:181-8; DOI: <https://doi.org/10.14238/pi63.3.2023.181-8>].

**Keywords:** Down syndrome; congenital heart disease; cardiac surgery; cardiac surgery outcomes

Down syndrome (DS) is a chromosomal disorder associated with intellectual disability, characteristic facial features, and hypotonia during infancy. Children with this condition are at risk for heart defects and other disorders such as gastroesophageal reflux, celiac disease, deafness, leukemia, and hypothyroidism.<sup>1</sup> About 40-60% of cases have congenital heart

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disease (CHD), such as atrioventricular septal defect (AVSD), ventricular septal defect (VSD), atrial septal defect (ASD), tetralogy of Fallot (TF), or mitral valve prolapse.<sup>2</sup> Almost 50% die in the first year if corrective or palliative surgery is not performed for complex defects such as AVSD.<sup>3</sup> Children with DS and CHD are at risk for pulmonary complications, such as pulmonary hypertension (PH), which are inversely related to disease prognosis and associated with high perioperative and long-term mortality rates. The recommended ideal age for immediate cardiac AVSD correction is 3-4 months in DS patients who are at risk of early PH onset.<sup>3</sup> Infections are another possible complication, due to a genetic immune defect that makes children with DS susceptible to pneumonia and sepsis. The use of cardiopulmonary bypass (CPB) equipment in CHD corrective surgery also increases the risk of post-operative inflammatory stress, which may affect outcomes.<sup>4,5</sup>

The prevalence of DS in Indonesia is quite high. Based on 2004 data, there are approximately 298,000 individuals with DS living in Indonesia, which in 2010 had a population of 237 million, with 3.5 to 4 million births annually.<sup>6</sup> The incidence of DS is estimated to be 1 in 800 live births, translating to 4,000-5,000 newborns with DS annually in Indonesia. The incidence of CHD in DS infants is 40-60%, thus translating to 2,000-2,500 DS infants with CHD in Indonesia each year. DS infants should undergo heart screening and early treatment for any CHD present.<sup>7</sup>

Post-cardiac surgery outcomes in DS differ from those in non-DS patients. Variables such as length of stay, length of ventilator use, and complications are important parameters to determine the success of treatment in DS patients.<sup>3</sup> Post-operatively, DS patients have been reported to stay longer in the ICU and in the hospital in general, as well as require ventilatory assistance for longer than non-DS patients; however, the differences were not always significant across studies. One study reported a mortality rate of 4.5% in the DS group and 5.4% in the non-DS group.<sup>8</sup> In another study, length of hospital stay in the VSD, ASD, and TF groups were significantly different.<sup>8</sup> Differences in the rate of complications, such as systemic infection, lung infection, PH, and atrioventricular (AV) block, have also been reported.<sup>9</sup>

Peri-operative care and post-operative cardiac correction have undergone many improvements, as

well as surgical and interventional methods. All of these have a significant impact on post-operative cardiac outcomes, which will ultimately reduce post-operative morbidity and mortality as well as improve survival and quality of life of DS patients with CHD.<sup>10</sup> To the best of our knowledge, there has been no research on post-operative outcomes of CHD correction in DS patients at cardiac service centers in Indonesia to date, thus, we aimed to determine short-term outcomes and mortality in DS patients who underwent surgery in our tertiary referral center.

## Methods

This retrospective and prospective cohort study was done to assess short-term outcomes in DS and non-DS subjects with CHD. We recorded the length of ICU stay, duration of ventilator use, and complications, including PH crisis, pulmonary complications, sepsis, complete AV block requiring a pacemaker, and mortality. Subjects were DS and non-DS patients with CHD aged < 15 years who underwent heart surgery at DR. Cipto Mangunkusumo Hospital Cardiac Center, Jakarta from July 2007 to April 2015. Exclusion criteria were post-cardiac surgery patients with other syndromes in the non-DS group and/or incomplete medical records. Down syndrome was diagnosed by clinical signs including thick neck skinfolds, drooping mouth margins, generalized hypotonia, flat facies, dysplastic ears, epicanthic folds of the eyes, wide space between the first and second toes, and macroglossia. Non-DS patients were children with no clinical signs of DS. CHD was evaluated by trans-thoracic echocardiography using *Philips Affiniti 60* (*Philips*, Amsterdam) performed by a pediatric cardiologist. Data analysis results were expressed as distribution of frequencies, proportions, means, or medians. We compared the mean length of ICU stay and duration of post-operative ventilator use using the independent t-test or the appropriate non-parametric test. The chi-square test was used to compare categorical variables, such as the occurrence of complications (PH crisis, complete AV block, pulmonary complications, and sepsis). A P values of <0.05 was considered statistically significant.

## Results

There were 100 post-cardiac surgery patients in our study: 57 subjects with clinical DS and 43 non-DS patients who met the inclusion criteria. Both groups had CHD abnormalities and were similar in age range, but the number of controls (non-DS) was less than the number of DS patients, due to the difficulty of finding non-DS patients with isolated CHD.

The most common type of CHD abnormalities in DS were AVSD and VSD, found in 18/57 (31.6%) patients each. Of the DS patients with AVSD, 13 had complete AVSD (CAVSD) and five had partial AVSD. AVSD and VSD were followed by TF [12/57; (21%)], ASD [4/57 (7%)], patent ductus arteriosus (PDA) [4/57 (7%)], and transposition of the great arteries with VSD (TGA-VSD) [1/57 (1.8%)]. The complete list of CHDs, as well as other basic subject characteristics, are listed in **Table 1**.

The DS group were slightly older than the non-DS group at the time of surgery [median age 1.5 (range 0.3 to 13.2) *vs.* 1.2 (range 0.08 to 14.9) years] but had lower body weight [median 7.5 (range 3.5 to 23) *vs.*

8.3 (range 2.8 to 23) kg]. The DS group had a lower proportion of subjects with good nutritional status than the non-DS group [27/57 (47.4%) *vs.* 23/57 (53.5%)]. Palliative action in the DS group was mostly for TF in five patients with the Blalock-Taussig (BT) shunt; one patient underwent the Rastelli procedure. Other palliative actions were for one patient with CAVSD undergoing bidirectional cavo-pulmonary shunt (BCPS) surgery and one patient with TGA-VSD who underwent BT shunt surgery.

On the evaluation of pre- and intraoperative characteristics, we found an increased incidence of PH in DS (63.1%) compared to non-DS (25.6%) ( $P < 0.0001$ ). Median duration of surgery was longer in DS [2.9 (range 0.5-5.8) hours] than in non-DS patients [2.2 (range 0.7-4.7) hours] ( $P = 0.003$ ), as was mean duration of CPB [79.5 (SD 33.9) *vs.* 59.9 (SD 23.6) minutes] ( $P = 0.002$ ), longer mean aortic cross-clamp duration [45.3 (SD 23.7) *vs.* 34.8 (SD 15.7) minutes] ( $P = 0.015$ ). Significant differences were also found in the incidence of preoperative PH, median surgical time, mean length of CPB time, and mean length of the aortic cross-clamp in DS patients

**Table 1.** Basic characteristics of subjects

| Variables                      | DS<br>(n=57)   | Non-DS<br>(n=43) |
|--------------------------------|----------------|------------------|
| Median age (range), years      | 1.5 (0.3-13.2) | 1.2 (0.08-14.9)  |
| Median body weight (range), kg | 7.5 (3.5-23)   | 8.3 (2.8-23)     |
| Sex, n (%)                     |                |                  |
| Female                         | 36 (63.2)      | 27 (62.8)        |
| Male                           | 21 (36.8)      | 16 (37.2)        |
| Nutritional status, n (%)      |                |                  |
| Good                           | 27 (47.4)      | 23 (53.5)        |
| Low                            | 19 (33.3)      | 11 (19.3)        |
| Severe                         | 11 (25.6)      | 9 (20.9)         |
| Type of surgery, n (%)         |                |                  |
| Definitive                     | 49 (86)        | 36 (83.7)        |
| Palliative                     | 8 (14)         | 7 (16.3)         |
| Type of CHD, n (%)             |                |                  |
| AVSD                           |                |                  |
| CAVSD                          | 13 (22.8)      | 7 (16.3)         |
| Partial AVSD                   | 5 (8.8)        | 1 (2.3)          |
| VSD                            | 18 (31.6)      | 18 (41.9)        |
| TF                             | 12 (21)        | 9 (20.9)         |
| ASD secundum                   | 4 (7)          | 4 (9.3)          |
| PDA                            | 4 (7)          | 4 (9.3)          |
| TGA-VSD                        | 1 (1.8)        | 0 (0)            |

AVSD=atrioventricular septal defect, CAVSD=complete atrioventricular septal defect, VSD=ventricle septal defect, TF=tetralogy of Fallot, ASD=atrial septal defect, PDA=patent ductus arteriosus, TGA=transposition of great arteries

compared to non-DS. The complete comparison of pre- and intraoperative characteristics can be seen in **Table 2**.

**Table 3** shows that the median length of ICU stay and ventilator use in DS subjects was longer than that of non-DS subjects, but the difference was not statistically significant. None of our subjects had PH crisis. Pulmonary complications were found in 14/57 (24.6%) of DS patients and only 6/43 (14%) of non-DS patients, but the difference was not significant ( $P=0.216$ ). The most common types of pulmonary complications were unilateral or bilateral pleural effusion and pulmonary atelectasis. Other pulmonary complications included chylothorax, acute respiratory distress syndrome, pneumothorax, and bronchiolitis. Sepsis was higher in the DS group than in the non-DS group [14/57 (28.1%) vs. 6/43 (14%), respectively], but the difference was not statistically significant ( $P=0.143$ ). Of patients with sepsis, four had positive blood cultures. Six patients in the DS group (10.5%) had complete AV block, compared to none in the non-DS group ( $P=0.036$ ). The DS group had five

deaths (8.8%); there were no deaths in the non-DS group ( $P=0.068$ ).

Other short-term outcomes during hospitalization are shown in **Table 4**. There was a significant difference in median duration of inotropic use between the DS and non-DS groups [2 (range 0.02-15) vs. 1 (range 0.1-4.8) days, respectively; ( $P=0.004$ )]. There were no significant differences between the two groups in length of hospital stay, inotropic scores at 24 and 48 hours, the presence of residual heart lesions, or rate of re-operation.

Short-term post-cardiac surgery outcomes by type of CHD abnormality (VSD, CAVSD, and TF) in the DS and non-DS groups are shown in **Table 5**. In TF patients, those with DS had significantly longer ICU stay and duration of ventilator use, as well as more sepsis cases. The patient who stayed the longest in the DS group had sepsis and chylothorax in the mediastinal drain, and underwent pleurodesis. In the non-DS group, the longest-stay patients were there due to complications of diaphragmatic paralysis. Data analysis could not be carried out in patients with

**Table 2.** Preoperative and intraoperative characteristics of DS and non-DS groups

| Variables                                | DS<br>(n=57)  | Non-DS<br>(n=43) | P value |
|--|---------------|------------------|---------|
| Preoperative infection, n (%)            | 3 (5.2)       | 4 (9.3)          | 0.785   |
| Extended preoperative care, n (%)        | 10 (17.5)     | 6 (14)           | 0.455   |
| PH, n (%)                                | 36 (63.1)     | 11 (25.6)        | <0.0001 |
| Mean TR PG, mmHg (SD)                    | 47.9 (18.6)   | 49.9 (21)        | 0.793   |
| Median surgery time, hours (range)       | 2.9 (0.5-5.8) | 2.2 (0.7-4.7)    | 0.003   |
| Mean length of CPB (SD), min             | 79.5 (33.9)   | 59.9 (23.6)      | 0.002   |
| Mean length aortic cross clamp, min (SD) | 45.3 (23.7)   | 34.8 (15.7)      | 0.015   |
| Delayed sternal close, n (%)             | 4 (7)         | 1 (2.3)          | 0.391   |

PH=pulmonary hypertension, TR=tricuspid regurgitation, PG=pressure gradient, CPB=cardiopulmonary bypass

**Table 3.** Outcomes in DS and non-DS groups post-surgery

| Variables                                 | DS<br>(n=57) | Non-DS<br>(n=43) | P value |
|---|--------------|------------------|---------|
| Median ICU length of stay (range), days   | 1.9 (0.6-34) | 1 (0.3-43)       | 0.373   |
| Median duration ventilator (range), hours | 19.9 (3-540) | 18 (3-600)       | 0.308   |
| PH crisis, n (%)                          | 0            | 0                | -       |
| Pulmonary complication, n (%)             | 14 (24.6)    | 6 (14)           | 0.216   |
| Sepsis, n (%)                             | 16 (28.1)    | 6 (14)           | 0.143   |
| Complete AV block, n (%)                  | 6 (10.5)     | 0                | 0.036   |
| Mortality in hospital, n (%)              | 5 (8.8)      | 0                | 0.068   |

other CHDs due to the small number of subjects. DS subjects with CAVSD and TF experienced the highest rate of pulmonary complications: 35.7% and 45.5%, respectively. Of the five patients who died, two had CAVSD, all of whom underwent definitive correction surgery; the remaining three had TF, who had undergone TF correction surgery, Rastelli procedure, and BT shunt, respectively.

**Table 6** shows the analysis of durations of surgery, aortic cross clamp, and CPB based on the type of cardiac abnormality in DS and non-DS patients. In VSD patients, the mean duration of surgery was significantly higher in DS than in non-DS subjects [2.6 (0.5) vs. 2.2 (0.4) hours, respectively (P=0.040)]. There were no significant differences between DS and non-DS groups in mean duration of aortic cross-clamp and CPB.

**Table 4.** Outcomes of length stay in hospital, use of inotropes, residuals and re-operation after cardiac surgery in DS and non-DS

| Variables                                      | DS<br>(n=57) | Non-DS<br>(n=43) | P value |
|--|--------------|------------------|---------|
| Median duration of inotropic use, days (range) | 2 (0.02-15)  | 1 (0.1-4.8)      | 0.004   |
| Median 24-hour inotropic score (range)         | 10 (0-28)    | 5 (0-50)         | 0.334   |
| Median 48-hour inotropic score (range)         | 0 (0-28)     | 0 (0-10)         | 0.335   |
| Residual, n (%)                                | 11 (19)      | 3 (7)            | 0.144   |
| Re-operative, n (%)                            | 2 (3.4)      | 0 (0)            | 0.506   |
| Median length of hospital stay, days (range)   | 8.4 (3-58)   | 6 (3.6-73)       | 0.335   |

**Table 5.** Short-term post-cardiac surgery outcomes in DS and non-DS based on type of CHD

| Variables                                    | VSD (n=36)        |                   |         | Complete AVSD (n=20) |                    |         | TF (n=19)         |                 |         |
|--|-------------------|-------------------|---------|----------------------|--------------------|---------|-------------------|-----------------|---------|
|  | DS<br>(n=18)      | Non-DS<br>(n=18)  | P value | DS<br>(n=13)         | Non-DS<br>(n=7)    | P value | DS<br>(n=11)      | Non-DS<br>(n=8) | P value |
| Median ICU length of stay (range), days      | 1.7<br>(0.6-5.9)  | 0.9<br>(0.6-10.6) | 0.946   | 5<br>(0.6-34)        | 1.25<br>(0.8-12.7) | 0.231   | 4.75<br>(0.6-26)  | 0.83<br>(0.7-3) | 0.038   |
| Median duration of ventilator (range), hours | 17.1<br>(3-114.9) | 18<br>(5.1-168)   | 0.647   | 96<br>(10-540)       | 18<br>(7.9-264)    | 0.217   | 90<br>(3.8-329.1) | 12.48<br>(6-51) | 0.017   |
| PH crisis, n (%)                             | 0                 | 0                 | -       | 0                    | 0                  | -       | 0                 | 0               | -       |
| Pulmonary complication, n (%)                | 1 (5.6)           | 2 (11.1)          | 1       | 5 (38.5)             | 0                  | 0.123   | 5 (45.5)          | 1 (12.5)        | 0.177   |
| Sepsis, n (%)                                | 2 (11.1)          | 3 (16.7)          | 1       | 7 (53.8)             | 1 (14.3)           | 0.174   | 5 (45.5)          | 0               | 0.045   |
| AV block, n (%)                              | 1 (5.6)           | 0                 | 1       | 2 (15.3)             | 0                  | 0.533   | 0                 | 0               | -       |
| Mortality, n (%)                             | 0                 | 0                 | -       | 2 (15.3)             | 0                  | 0.533   | 3 (27.3)          | 0               | 0.228   |

**Table 6.** Duration of surgery, aortic cross clamp, and CPB by type of CHD abnormality

| Variables           | Mean duration of surgery, hours (SD) |            |         | Mean duration of aortic cross clamp, hours (SD) |             |         | Mean duration of CPB, hours (SD) |             |         |
|---------------------|--------------------------------------|------------|---------|---|-------------|---------|----------------------------------|-------------|---------|
|                     | DS                                   | Non-DS     | P value | DS  | Non-DS      | P value | DS                               | Non-DS      | P value |
| Left to right shunt |                                      |            |         |   |             |         |                                  |             |         |
| VSD (n=36)          | 2.6(0.5)                             | 2.2 (0.4)  | 0.040   | 33.6 (13.3)                                     | 30 (7.7)    | 0.324   | 59.5 (20.5)                      | 50.7 (8.4)  | 1       |
| CAVSD (n=20)        | 3.6(0.5)                             | 3.1(0.9)   | 0.102   | 69.1 (14.4)                                     | 57.3 (11.4) | 0.101   | 103.6 (20)                       | 85.7 (17.5) | 0.082   |
| ASD (n=8)           | 2.3(0.3)                             | 2.1(1)\1.2 | 0.781   | 15.3 (11.9)                                     | 12.5 (7.9)  | 0.713   | 44.5 (7.8)                       | 30 (16.9)   | 0.191   |
| PDA (n=8)           | 1(0.7)                               | (0.6)      | 0.788   | -   | -           | -       | -                                | -           | -       |
| Partial AVSD (n=6)  | 3.2(0.6)                             | 3(-)       | 0.732   | 45.8 (26.6)                                     | 50 (-)      | 0.892   | 77.6 (21.1)                      | 94 (-)      | 0.518   |
| Right to left shunt |                                      |            |         |   |             |         |                                  |             |         |
| TF (n=19)           | 3.6(1.4)                             | 2.6 (0.9)  | 0.106   | 54.2 (24.9)                                     | 42.7 (2.3)  | 0.468   | 123 (42)                         | 92.7 (9.3)  | 0.279   |



## Discussion

Children with Down syndrome and CHD or complete AVSD have the greatest risk for developing pulmonary vascular disease that persists, even in the first year of life. The presence of upper airway obstruction due to anatomic abnormalities in DS leads to hypoxia and CO<sub>2</sub> retention, which, together with high pulmonary flow resulting from an AVSD shunt, triggers the acceleration of irreversible pulmonary vascular disease. Hence, cardiac correction surgery is recommended before the age of 6 months.<sup>5</sup>

The most common types of CHD in our DS subjects were AVSD and VSD (18; 31.6% for both), followed by TF (12; 21%). In contrast, A US study noted that most DS patients had AVSD (45%), followed by VSD (35%), ASD, PDA, TF, and other defects.<sup>5</sup> A study in Poland showed that AVSD (50%) was the most common disorder, followed by VSD (24%).<sup>9</sup> Studies in Saudi Arabia and Sudan also showed a higher number of AVSD than others.<sup>10,11</sup> An India study reported the highest frequency in VSD (41%), AVSD (28%), and TF (15%).<sup>12</sup> A large number of AVSD patients in DS is due to the role of chromosome 21 genes in growth and endocardial cushion adhesion.<sup>13</sup>

We found that the durations of surgery, aortic cross-clamp, and CBP [median (range) 2.9 (0.5-5.8) hours, 45.3 (23.7) hours, and 79.5 (33.9) hours, respectively] were significantly longer in the DS group than in the non-DS group. A study reported similar aortic cross-clamp and CBP times to our findings in DS/VSD patients [median (range) 46 (35-59) minutes and 77 (60-95) minutes, respectively]. Systemic inflammatory response syndrome (SIRS) after CPB can be initiated through several mechanisms, including contact of blood with foreign bodies/surfaces of the CPB circuit, emergence of ischemic reperfusion injury due to secondary aortic cross-clamp, and the presence of endotoxemia. There was a positive correlation between the magnitude of interleukin-6 response to CPB and the duration of CPB. In severe conditions, this inflammatory reaction may increase capillary permeability, peripheral vasoconstriction, fever, myocardial edema, diffuse cerebral edema, and diffuse bleeding, all of which are related to outcomes in DS patients after surgery.<sup>8</sup>

The median length of ICU stay and duration

of ventilator use were longer in DS patients [1.9 (range 0.6-34) days and 19.9 (range 3-54) hours, respectively] than in non-DS patients [1 (range 0.3-43) days and 18 (range 3-60) hours, respectively], but these differences were not significant. Another study also reported no significant differences between groups with regards to median length of ICU stay or duration of ventilator use.<sup>10</sup> However, we found that DS/TF patients had significantly longer ICU stay and use of a ventilator compared to non-DS/TF subjects (Table 5). This finding was partly due to complications of pulmonary atelectasis, bilateral pleural effusion, superior vena cava syndrome (SVC syndrome) and re-opening procedure in the left lung branch due to stenosis. Among non-DS patients with TF, only one had complications of pleural effusion. In our study, DS/CAVSD subjects used ventilation for longer than non-DS/CAVSD subjects, but the difference was not significant. A study reported a mean length of ICU stay of 6.9 (SD 5.68) days and mean duration of ventilator use of 63.2 (SD 100.45) hours in the DS group, but these were not significantly different with non-DS subjects. When viewed separately, in the AVSD subtype of CHD, the same study found a significant difference in mean length of ventilator use [68.2 (SD 46.0) hours in the DS group vs. 37.4 (SD 29.0) hours in the non-DS group].<sup>12</sup>

We also found no significant differences in the DS and non-DS groups with regards to PH crisis or pulmonary complications. The incidence of sepsis was higher in the DS group (28.1%) than in the non-DS group (14%), but this difference did not reach statistical significance ( $P=0.143$ ). Mokryk *et al.*<sup>10</sup> similarly noted that 28.6% of DS subjects had sepsis, while Kabbani *et al.*<sup>14</sup> reported a notably smaller incidence of sepsis (10%). However, the two studies did not include a comparison to non-DS patients. In our study, among subjects with TF, 5/12 subjects with DS had sepsis, while no non-DS subjects in this group had sepsis. Our DS/TF subjects had relatively difficult anatomical malformations (TF-CAVSD, PA-VSD), and other comorbidities such as hypothyroidism, post-colostomy atresia ani, and cholestasis. A previous study reported that the occurrence of post-operative cardiac complications in VSD, such as infection, pulmonary complications, PH, and complete AV block were all significantly different. They also noted that TF subjects with and without DS

had significantly different pulmonary complications. The presence of a deficiency of underlying primary immunological factors and anatomic factors such as airway abnormalities, ear anatomy, macroglossia, and airway hypersecretion resulted in increased susceptibility to infection in this group.<sup>8</sup>

None of our subjects had PH crisis. The mean gradient pressures of tricuspid regurgitation (TR) before surgery were 47.9 (SD 18.6) in the DS group and 49.9 (SD 21) in the non-DS group, which were considered to be medium grade PH category. Post-CPB pulmonary vasoconstriction has been demonstrated with severity of vasoconstriction correlated to the duration of CPB and related to pulmonary vascular endothelial injury.<sup>15</sup> Similar results in previous study noted no significant difference in incidence of PH crisis between the DS and comparison groups. Some patients were treated with preoperative sildenafil, intraoperative NO<sub>2</sub>, and postoperative sildenafil, in combination with inhaled *Iloprost*® a prostacyclin analogue.<sup>12</sup> These medications are believed to be the best modalities to prevent a PH crisis. Management of PH, pre-, intra-, and post-operatively was one reason there were no PH crises in either group.<sup>16</sup>

Pulmonary complications were not significantly different between the two groups, be it in the general DS grouping or specific to CHD abnormalities. The problem of airway obstruction due to anatomical abnormalities can be found in DS patients in the form of small nasal passages, excessive nasal secretions, small nasopharynx, mid-facial and mandibular hypoplasia, relative adenotonsillar hypertrophy, macroglossia, or respiratory muscle hypotonia, further predisposing them to pulmonary complications. Toth *et al.*<sup>17</sup> showed similar results, with 20.7% of the DS group having pulmonary complications.

Complications of complete AV block were significantly different between the DS and non-DS groups. Of those six DS patients who experienced complete AV block, four had AVSD and one patient each had VSD and ASD. Fudge *et al.* reported that VSDs with complete AV block requiring a permanent pacemaker postoperatively were significantly more frequent in DS (2.9%) than in non-DS (0.8%).<sup>8</sup>

Mortality in our subjects was 8.8% in the DS group, while none of the non-DS subjects died. Several other studies reported mortality rates of 10.5%,<sup>2</sup> 4.5%, and 2.5%.<sup>18</sup> In conclusion, morbidity and mortality

were higher after cardiac surgery in DS vs non-DS. DS patients may have problems related to preoperative PH, AV-block, a longer length of stay in ICU, duration of CPB, and duration of aortic cross-clamp compared to non-DS, all of which can affect postoperative morbidity and mortality after pediatric cardiac surgery.

We conclude that children with CHD and DS who undergo heart surgery have more complex problems compared to children with CHD without DS. In DS patients, early cardiac screening is needed in DS patients to prevent preoperative complications and postoperative workup warranted to prevent sepsis and arrhythmia problems, to ultimately reduce morbidity and mortality.

## Conflict of interest

None declared.

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## References

1. Parker P. Down syndrome. A 3-in-1 medical reference. A bibliography and dictionary for physicians. Las Vegas: Icon Group International Inc.; 2007. ISBN: 978-0497113698. p.3-82.
2. Martínez-Quintana E, Rodríguez-González F, Medina-Gil JM, Agredo-Muñoz J, Nieto-Lago V. Clinical outcome in Down syndrome patients with congenital heart disease. *Cir Cir.* 2010;78:245-50. PMID: 20642908.
3. Sheehan A, Ward OC, Duff DF, Denham B, Neligan M, Wood A. Cardiac surgery in Down syndrome. *Ir Med J.* 1990;83:67-9. PMID: 2143995.
4. Reller MD, Morris CD. Is Down syndrome a risk for poor outcome in after repair of congenital heart defects? *J Pediatr.* 1998;132:738-41. DOI: [https://doi.org/10.1016/S0022-3476\(98\)70372-5](https://doi.org/10.1016/S0022-3476(98)70372-5).
5. Seale A, Shinebourne EA. Cardiac problems in Down syndrome. *Paediatrics and Child Health.* 2004;14:33-8. DOI: <https://doi.org/10.1016/j.cupe.2003.09.005>.
6. Badan Pusat Statistik. Data Sensus Penduduk 2010. [cited

- 2017 April 2015]. Available from: <https://sensus.bps.go.id/main/index/sp2010>.
7. Irwanto WH, Aini Airefa, Sunny Mariana Samosir. A-Z Sindrom Down. Surabaya: Universitas Airlangga; 2009. p.1-32.
  8. Fudge Jr JC, Li S, Jagers J, O'Brien SM, Peterson ED, Jacobs JP, et al. Congenital heart surgery outcomes in Down syndrome: analysis of a national clinical database. *Pediatrics*. 2010;126:315-22. DOI: <https://doi.org/10.1542/peds.2009-3245>.
  9. Malec E, Mroczek T, Pajak J, Januszewska K, Zdebska E. Results of surgical treatment of congenital heart defects in children with Down's Syndrome. *Pediatr Cardiol*. 1999;20:351-4. DOI: <https://doi.org/10.1007/s002469900483>.
  10. Kabbani MS, Giridhar S, Elbarbary M, Elgamal MA, Najm H, Godman M. Postoperative cardiac intensive care outcome for Down syndrome children. *Saudi Med J*. 2005;26:943-6. PMID: 15983679.
  11. Sulalfa KM Ali. Cardiac abnormalities of Sudanese patients with Down's syndrome and their short-term outcome. *Cardiovasc J Afr*. 2009;20:112-5. PMID: 19421645.
  12. Lal PS, Chavan B, Devendran VR, Varghese R, Murmu UC, Kumar RS. Surgical outcome of congenital heart disease in Down's syndrome. *Asian Cardiovasc Thorac Ann*. 2013;21:166-9. DOI: <https://doi.org/10.1177/0218492312450701>.
  13. Bruneau BG, Burn J, Srivastava D. Aetiology of congenital cardiac disease. In: Anderson RH, Baker EJ, Penny D, Redington AN, Rigby ML, Wernovsky G, eds. *Paediatric cardiology*. 3<sup>rd</sup> ed. Philadelphia: Churchill Livingstone Elsevier; 2010. p. 161-71.
  14. Mokryk I, Koval O, Novack A, Kartashova O, Muzychin O, Bordyugova O, et al. Cardiac surgical aspects of Down syndrome. *J Cardiothorac Surg*. 2013;8:96. DOI: <https://doi.org/10.1186/1749-8090-8-S1-P96>.
  15. Antoniou T, Theodoraki K. Perioperative management of pulmonary hypertension. In: Narin C, ed. *Perioperative considerations in cardiac surgery*. London: IntechOpen; 2012. p.109-24. ISBN: 978-953-51-0147-5.
  16. Park M, Simon MA. Ask the expert: perioperative management of pulmonary hypertensive crisis. *Adv Pulm Hypertens*. 2013;12:38-9. DOI: <https://doi.org/10.21693/1933-088x-12.1.38>.
  17. Tóth R, Szántó P, Prodán Z, Lex DJ, Sági E, Szatmári A, et al. Down syndrome and postoperative complications after paediatric cardiac surgery: a propensity-matched analysis. *Interact Cardiovasc Thorac Surg*. 2013;17:691-7. DOI: <https://doi.org/10.1093/icvts/ivt267>.
  18. Atz AM, Hawkins JA, Lu M, Cohen MS, Colan SD, Jagers J, et al. Surgical management of complete atrioventricular septal defect: associations with surgical technique, age, and trisomy 21. *J Thorac Cardiovasc Surg*. 2011;141:1371-9. DOI: <https://doi.org/10.1016/j.jtcvs.2010.08.093>.