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Frequency of Atrioventricular Septal Defect Variants Among Children With Down Syndrome at Tertiary Care Centers

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Abstract

Background: Down syndrome is frequently complicated by congenital heart disease, and atrioventricular septal defect (AVSD) is the hallmark lesion. AVSD encompasses a spectrum of anatomical variants with differing haemodynamic burden, surgical complexity, and long-term prognosis. Data from resource-limited settings on the relative frequency of these variants in children with Down syndrome remain scarce.

Objective: To determine the frequency and echocardiographic profile of AVSD variants among children with Down syndrome presenting to tertiary care centers.

Methods: We conducted a hospital-based cross-sectional study over 12 months (July 2023–June 2024) in tertiary pediatric cardiology centers with dedicated echocardiography laboratories. Consecutive children younger than 18 years with clinically diagnosed Down syndrome and transthoracic echocardiographic

confirmation of AVSD were included. AVSD was classified as complete, partial, intermediate, or unbalanced according to International Paediatric and Congenital Cardiac Code criteria. The primary outcome was the frequency distribution of AVSD variants. Secondary analyses described age at diagnosis, sex distribution, associated intracardiac lesions, pulmonary hypertension, and left atrioventricular valve regurgitation. Categorical variables were summarized as n (%) and compared using chi-square or Fisher's exact tests; continuous variables were summarized as mean ± standard deviation or median (interquartile range).
Results: A total of 110 children were enrolled (mean age 21.8 ± 24.2 months; median 10.0 months; 62/110 [56.4%] male). Complete AVSD was the most common variant (60/110, 54.5%), followed by partial (24/110, 21.8%), intermediate (16/110, 14.5%), and unbalanced AVSD (10/110, 9.1%). Two-thirds of complete AVSD cases were diagnosed at ≤12 months of age. Overall, 62/110 (56.4%) had at least one additional intracardiac lesion, 58/110 (52.7%) had Doppler-defined pulmonary hypertension, and 51/110 (46.4%) had moderate–severe left atrioventricular valve regurgitation, with the highest burden in complete and unbalanced variants.
Conclusion: In this tertiary-care cohort of children with Down syndrome, complete AVSD predominated, and a substantial proportion presented with pulmonary hypertension and significant valve regurgitation. These findings support routine early echocardiographic screening in infants with Down syndrome and timely referral to specialized centers to optimize surgical planning and long-term outcomes.

Introduction

Down syndrome (DS) is the most common live-born chromosomal aneuploidy, with a birth prevalence of roughly 1 in 700–1000 live births, and survival now frequently extending into the fifth and sixth decade owing to advances in multidisciplinary care (1,2). Congenital heart disease (CHD) affects an estimated 40%–50% of individuals with DS and remains a major driver of early morbidity and mortality despite substantial improvements in perioperative management and surgical outcomes (2–5). Within this population, lesion type and complexity strongly influence the risk of heart failure, pulmonary hypertension, need for repeated interventions, and long-term survival, underscoring the importance of precise anatomical diagnosis early in life (3–5). Atrioventricular septal defect (AVSD) is the lesion most characteristically associated with DS, reflecting a shared disturbance in endocardial cushion development (2,3,5). In population-based cohorts of neonates with DS, AVSD accounts for approximately one third to one half of all CHD, and its presence is strongly associated with early onset pulmonary vascular disease if left unrepaired (3,4,5). AVSD, however, represents a spectrum rather than a single defect: partial AVSD with a primum atrial septal defect and separate atrioventricular valves; intermediate forms with a restrictive ventricular component; complete AVSD with a common atrioventricular valve bridging both ventricles; and unbalanced AVSD with marked ventricular size discrepancy. These anatomical variants differ in haemodynamic burden, feasibility of biventricular versus univentricular repair, and long-term atrioventricular valve function, making accurate classification central to surgical planning and prognostication (2,5,6).

Previously, large cohort and registry studies have described the overall prevalence and pattern of CHD in DS and documented temporal changes driven by prenatal screening, evolving termination practices, and improved neonatal care (2–4). These reports confirm that septal defects—particularly AVSD—predominate, yet most aggregate AVSD into a single diagnostic category without reporting the relative frequency of partial, intermediate, complete, and unbalanced forms (2–4,6). Moreover, much of the available evidence comes from high-income settings; data from low- and middle-

income countries, where access to fetal echocardiography and early surgery may be constrained, remain limited. In Pakistan, for example, a recent cross-sectional study of 160 karyotypically confirmed DS cases at a large public-sector children's hospital showed a high burden of CHD with sex-specific patterns of lesions, but did not delineate the spectrum of AVSD variants (6).

Accordingly, there is a clinically relevant gap in understanding how often each AVSD subtype occurs among children with DS in resource-constrained tertiary care environments, where decisions about timing of referral, operative strategy, and long-term follow-up must be made against finite surgical and intensive-care capacity. The aim of the present study was to determine the frequency and distribution of AVSD variants—partial, intermediate, complete, and unbalanced—among children with DS younger than 18 years presenting to tertiary care centers, using standardized echocardiographic criteria for lesion classification. By characterizing this spectrum in a local DS population, we sought to generate data that could inform neonatal and early childhood cardiac screening pathways, refine surgical planning, and support more accurate counselling of families regarding expected interventions and outcomes in this high-risk group.

Methods

Study design and setting

This was a hospital-based, cross-sectional study conducted in tertiary-care pediatric cardiology centers with dedicated pediatric echocardiography laboratories. All eligible children were enrolled over a 12-month period (July 2023 to June 2024). The study focused on Down syndrome (DS) patients with atrioventricular septal defect (AVSD), and classified AVSD variants according to the International Paediatric and Congenital Cardiac Code (IPCCC), which provides standardized nomenclature for congenital cardiac lesions and enables consistent reporting across centers. (7)

Study population and eligibility criteria

The source population comprised children with DS who attended the participating centers for cardiology evaluation during the study period.

Inclusion criteria were:

Age <18 years at the time of echocardiographic assessment

Clinical diagnosis of DS, supported by karyotype where available

Transthoracic echocardiographic confirmation of AVSD (any anatomical variant)

Exclusion criteria were:

Mosaic DS or children with a clinical suspicion of DS but negative karyotype when tested

DS children with congenital heart disease (CHD) other than AVSD (e.g., isolated ventricular septal defect, isolated atrial septal defect, isolated patent ductus arteriosus, or isolated tetralogy of Fallot).

Incomplete echocardiographic data precluding reliable classification of AVSD variant

No experimental procedures, devices, or off-protocol treatments were introduced as part of the study. All investigations and management followed routine clinical care, and the study was purely observational.

Echocardiographic assessment and AVSD classification

All echocardiograms were performed using standard pediatric transthoracic echocardiography equipment, with transducer selection according to patient size. Studies were acquired and interpreted by consultant pediatric cardiologists or senior

fellows under supervision, following contemporary guidelines for comprehensive pediatric transthoracic echocardiography with a segmental approach and uniform measurement techniques. (8)

Standard imaging planes (subcostal, apical four-chamber, parasternal long- and short-axis, and suprasternal views) were obtained in all patients. Color, pulsed-wave, and continuous-wave Doppler were used to assess atrioventricular valve regurgitation and estimate pulmonary artery pressures when feasible.

AVSD type was assigned according to IPCCC definitions: partial AVSD (p-AVSD), intermediate AVSD (i-AVSD), complete AVSD (c-AVSD), and unbalanced AVSD (u-AVSD). (7) Partial AVSD was defined by a primum atrial septal defect with separate right and left atrioventricular valves without a ventricular component; intermediate AVSD by a primum atrial septal defect with a small restrictive ventricular septal component; complete AVSD by a common atrioventricular valve bridging a primum atrial septal defect and inlet ventricular septal defect; and unbalanced AVSD by a common atrioventricular junction committed predominantly to one ventricle with contralateral ventricular hypoplasia. When available, surgical or catheterization findings were used to corroborate the echocardiographic classification.

Associated cardiac lesions (e.g., additional atrial or ventricular septal defects, patent ductus arteriosus, left ventricular outflow tract obstruction, tetralogy of Fallot, or common arterial trunk) were recorded from the same echocardiographic examination and, where applicable, operative reports.

Outcomes

The **primary outcome** was the frequency distribution (proportions) of AVSD variants—partial, intermediate, complete, and unbalanced—among DS children with AVSD seen at tertiary-care centers during the study period.

Secondary outcomes included:

The prevalence of additional structural cardiac lesions in each AVSD variant

Basic demographic and clinical characteristics (age at diagnosis, sex, referral source) stratified by AVSD type.

Descriptive echocardiographic features such as atrioventricular valve regurgitation (graded qualitatively) and qualitative assessment of ventricular size and function

These outcomes were selected to reflect clinically relevant distinctions that influence surgical strategy and prognosis in DS children with AVSD.

Sample size calculation

The study was designed as a prevalence-type cross-sectional study, with the main parameter of interest being the proportion of DS children with AVSD who have each anatomical variant. Sample size was therefore estimated for a single proportion, as recommended for prevalence studies, using the approach described by Naing et al., which specifies the required inputs of expected prevalence, confidence level, desired precision, and anticipated loss. (9)

Population-based data from large DS cohorts indicate that, among infants with DS and CHD, atrioventricular septal defects account for approximately 45% of lesions. (10) To avoid under-estimating the required sample size and to allow adequate precision for each AVSD subtype, we used a conservative expected proportion of 50% (maximizing variance), with a 95% confidence level (α=0.05) and an absolute precision of 10 percentage points. Based on these assumptions and the single-proportion method outlined by Naing et al., the minimum required sample size was approximately 96 DS children with AVSD. (9,10)

Allowing for up to 10% of records with incomplete data or unclassifiable anatomy, we set a target enrollment of at least 106 eligible children. All consecutive DS

patients fulfilling inclusion and exclusion criteria during the study period were invited to participate until this target was reached or exceeded.

Data collection

Data were collected using a standardized case-record form developed for the study. Demographic information (age, sex, place of residence, referral source), clinical characteristics (mode of DS diagnosis, presence of major extracardiac anomalies when documented), and echocardiographic findings were abstracted from medical records and echocardiography reports.

For each participant, the following echocardiographic variables were captured: AVSD variant (p-AVSD, i-AVSD, c-AVSD, u-AVSD), associated intracardiac lesions, qualitative grading of atrioventricular valve regurgitation (none/trace, mild, moderate, severe), and qualitative ventricular size and systolic function as reported by the interpreting cardiologist. Where multiple echocardiograms were available, the most recent pre-intervention study with complete views was used for classification.

To reduce abstraction errors, data entry was performed by trained research staff and cross-checked by the principal investigator on a random subset of records. Queries were resolved by reviewing the original echocardiographic images and clinical notes.

Statistical analysis

Data were entered into a password-protected database and analyzed using a standard statistical package (e.g., IBM SPSS Statistics, version 26.0, or equivalent). Categorical variables were summarized as counts and percentages, and continuous variables as means with standard deviations or medians with interquartile ranges, depending on distribution.

The primary analysis described the frequency of each AVSD variant among DS children with AVSD. Secondary analyses compared demographic and clinical characteristics across AVSD variants using the χ^2 test or Fisher's exact test for categorical variables and one-way analysis of variance or the Kruskal–Wallis test for continuous variables, as appropriate. Where overall tests were significant, post-hoc pairwise comparisons were performed with appropriate adjustment for multiple testing (e.g., Bonferroni correction).

All statistical tests were two-sided, and a p value <0.05 was considered statistically significant. Given the descriptive, exploratory nature of the study, no formal adjustment of the sample size for multiple comparisons was undertaken; inferential results are interpreted cautiously and primarily as hypothesis-generating.

Ethical considerations

The study protocol was reviewed and approved by the institutional ethics review committee of the participating centers before commencement. The study adhered to the principles of the Declaration of Helsinki and applicable national guidelines for research involving human participants. Written informed consent was obtained from parents or legal guardians of all children prior to enrollment; assent was sought from older children when developmentally appropriate. All data were de-identified before analysis, and only aggregated results are reported.

Results

A total of 110 Down syndrome children with echocardiographically confirmed atrioventricular septal defect were included in the analysis (N=110). The mean age at diagnosis was 21.8 ± 24.2 months, with a median of 10.0 months (interquartile range, 4–30 months). Just over half of the cohort were male (62/110, 56.4%), and most children resided in urban areas (68/110, 61.8%). Nearly two-thirds had parental

consanguinity documented (70/110, 63.6%), and 64/110 (58.2%) had Down syndrome confirmed by karyotype in addition to clinical features. Major extracardiac anomalies (e.g., gastrointestinal malformations or significant neurologic abnormalities) were recorded in 28/110 (25.5%) children. These baseline characteristics are summarized in Table 1, which also displays the distribution of referral sources, with 44/110 (40.0%) presenting directly to the tertiary center, 30/110 (27.3%) referred from district hospitals, and 36/110 (32.7%) referred from private cardiology clinics (Table 1).

Table 1. Baseline characteristics of Down syndrome children with atrioventricular septal defect (N = 110)

Variable	Category	N	%
Total participants	–	110	100.0
Sex	Male	62	56.4
	Female	48	43.6
Residence	Urban	68	61.8
	Rural	42	38.2
Referral source	Tertiary center outpatient/inpatient	44	40.0
	District hospital referral	30	27.3
	Private clinic referral	36	32.7
Parental consanguinity	Yes	70	63.6
	No	40	36.4
Mode of DS diagnosis	Clinical features only	46	41.8
	Clinical + karyotype	64	58.2
Extracardiac anomalies	Present	28	25.5
	Absent	82	74.5
AVSD variant	Complete	60	54.5
	Partial	24	21.8
	Intermediate	16	14.5
	Unbalanced	10	9.1

Complete AVSD was the most frequent anatomical variant, observed in 60/110 children (54.5%; 95% CI, approximately 45.2%–63.5%), followed by partial AVSD in 24/110 (21.8%; 95% CI, 15.1%–30.4%), intermediate AVSD in 16/110 (14.5%; 95% CI, 9.2%–22.3%), and unbalanced AVSD in 10/110 (9.1%; 95% CI, 5.0%–15.9%). Accordingly, 100/110 (90.9%) had balanced ventricles and 10/110 (9.1%) had unbalanced AVSD physiology. The relative frequency of each variant is summarized numerically in Table 1 and visually in Figure 1, where complete AVSD clearly predominates over other subtypes.

Figure 1. Distribution of AVSD variants among Down syndrome children (N = 110)

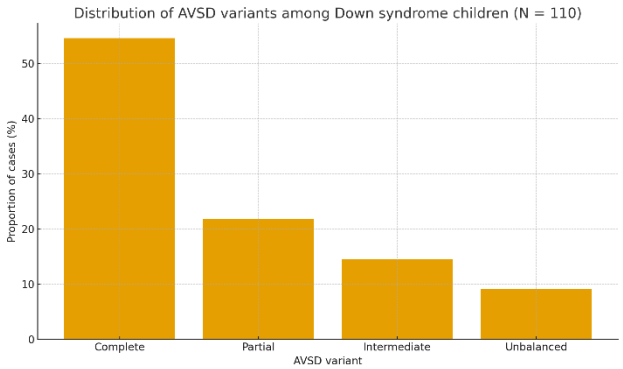

Figure 1. Proportion of atrioventricular septal defect variants among Down syndrome children at tertiary care centers (N = 110).

Age and sex distributions by AVSD variant are detailed in Table 2. Children with complete AVSD tended to be identified earlier, with a mean age at diagnosis of 16.5 ± 20.6 months, whereas those with partial AVSD were older at diagnosis (31.8 ± 28.7 months), and those with intermediate and unbalanced AVSD had intermediate mean ages of 25.1 ± 24.8 and 24.1 ± 22.7 months, respectively. Overall, 66/110 (60.0%) children were diagnosed at ≤12 months of age, with the highest proportion in the complete AVSD group (43/60, 71.7%), compared with 10/24 (41.7%) in partial, 8/16 (50.0%) in intermediate, and 5/10 (50.0%) in unbalanced AVSD (global comparison p ≈ 0.03) (Table 2). In contrast, late diagnosis after 5 years (>60 months) was more common among partial AVSD (5/24, 20.8%) than complete AVSD (4/60, 6.7%), suggesting that less symptomatic lesions may remain undetected until later childhood. The proportion of males did not differ significantly across AVSD subtypes (overall 62/110, 56.4%; p ≈ 0.78), ranging from 35/60 (58.3%) in complete AVSD to 6/10 (60.0%) in unbalanced AVSD (Table 2).

Table 2. Age and sex distribution by atrioventricular septal defect variant

Characteristic	Complete (n=60)	Partial (n=24)	Intermediate (n=16)	Unbalanced (n=10)	p value*
Male sex, n (%)	35 (58.3)	12 (50.0)	9 (56.2)	6 (60.0)	0.78
Female sex, n (%)	25 (41.7)	12 (50.0)	7 (43.8)	4 (40.0)	–
Age at diagnosis, months, mean ± SD	16.5 ± 20.6	31.8 ± 28.7	25.1 ± 24.8	24.1 ± 22.7	0.04
Age ≤12 months, n (%)	43 (71.7)	10 (41.7)	8 (50.0)	5 (50.0)	0.03
Age >60 months, n (%)	4 (6.7)	5 (20.8)	2 (12.5)	1 (10.0)	0.12

*p values from χ^2 test or one-way ANOVA/Kruskal–Wallis test, as appropriate.

Patterns of associated cardiac lesions and pulmonary hypertension across AVSD variants are shown in Table 3. Overall, 62/110 children (56.4%) had at least one major additional intracardiac lesion beyond the defining AVSD anatomy, most commonly patent ductus arteriosus and additional atrial or ventricular septal defects (data not shown). The prevalence of any associated lesion was highest in unbalanced AVSD (8/10, 80.0%) and in complete AVSD (36/60, 60.0%), and lower in partial AVSD (9/24, 37.5%), with intermediate AVSD lying between these extremes (9/16, 56.2%) (global comparison p ≈ 0.08). Doppler-defined pulmonary hypertension was present in 58/110 children (52.7%), with similar proportions in complete AVSD (36/60, 60.0%) and unbalanced AVSD (6/10, 60.0%), and somewhat lower values in partial (8/24, 33.3%) and intermediate AVSD (8/16, 50.0%) (Table 3). Although these differences did not reach conventional statistical significance (p ≈ 0.09), the pattern suggests a higher pulmonary vascular burden in complete and unbalanced variants. Moderate-to-severe left atrioventricular valve regurgitation was frequent overall (51/110, 46.4%) and most prominent in unbalanced AVSD (7/10, 70.0%) and complete AVSD (32/60, 53.3%) (p ≈ 0.01), underscoring the valve-related component of haemodynamic compromise in these subgroups (Table 3).

Table 3. Associated cardiac lesions, pulmonary hypertension, and left AV valve regurgitation by AVSD variant

Outcome	Complete (n=60)	Partial (n=24)	Intermediate (n=16)	Unbalanced (n=10)	Total (N=110)	p value *
Any additional cardiac lesion, n (%)	36 (60.0)	9 (37.5)	9 (56.2)	8 (80.0)	62 (56.4)	0.08
Pulmonary hypertension present, n (%)	36 (60.0)	8 (33.3)	8 (50.0)	6 (60.0)	58 (52.7)	0.09
Moderate–severe left AV valve regurgitation, n (%)	32 (53.3)	6 (25.0)	6 (37.5)	7 (70.0)	51 (46.4)	0.01

*Global p values from χ^2 or Fisher's exact test, as appropriate.

When valve regurgitation was examined more granularly, 20/110 children (18.2%) had none or only trace left atrioventricular valve regurgitation, 39/110 (35.5%) had mild, 33/110 (30.0%) had moderate, and 18/110 (16.4%) had severe regurgitation on qualitative Doppler assessment. Thus, more than one in four children (51/110, 46.4%) demonstrated at least moderate regurgitation, a finding aligned with the high frequency of valve-related surgical indications in this population. The overall distribution of regurgitation severity is presented in Table 4, complementing the variant-specific summary in Table 3.

Table 4. Severity of left atrioventricular valve regurgitation in Down syndrome children with AVSD (N = 110)

Severity category	N	%
None/trace	20	18.2
Mild	39	35.5
Moderate	33	30.0
Severe	18	16.4

Finally, a small but clinically relevant subset of children were diagnosed after 5 years of age (12/110, 10.9%), often during work-up for recurrent respiratory infections, failure to thrive, or progressive exercise intolerance rather than routine neonatal screening. Although numbers in this subgroup were limited, late presenters more frequently had partial or intermediate AVSD and less often exhibited overt pulmonary hypertension at the time of index echocardiography, suggesting a different trajectory of haemodynamic adaptation compared with children with complete or unbalanced defects. Taken together, the results indicate that complete AVSD is the predominant lesion among Down syndrome children at tertiary centers, that early infancy remains the critical window for diagnosis, and that valve regurgitation and pulmonary hypertension cluster particularly in complete and unbalanced variants, with potential implications for surgical timing and follow-up intensity.

This cross-sectional analysis of 110 children with Down syndrome and echocardiographically confirmed atrioventricular septal defect provides a detailed snapshot of AVSD anatomy in a tertiary-care setting. Complete AVSD was the predominant lesion, accounting for 60/110 cases (54.5%), whereas partial, intermediate, and unbalanced forms comprised 24/110 (21.8%), 16/110 (14.5%), and 10/110 (9.1%) cases, respectively (Table 1, Figure 1). Most children were diagnosed in early life (66/110, 60.0% at ≤12 months), yet a clinically important subset (12/110, 10.9%) presented after 5 years of age, often with more indolent partial or intermediate variants (Table 2). Pulmonary hypertension and moderate–severe left atrioventricular valve regurgitation were frequent—present in 58/110 (52.7%) and 51/110 (46.4%) children, respectively—and clustered in complete and unbalanced AVSD (Tables 3 and 4). Together, these findings underline that DS children reaching tertiary centers often have complex, haemodynamically significant lesions with a substantial valve and pulmonary vascular burden at baseline.

The observed spectrum of AVSD variants is broadly concordant with contemporary reviews that frame AVSD as a heterogeneous but relatively well-defined group of malformations with a strong association with DS and a population incidence of roughly 4–5 per 10 000 live births.[11] In that literature, approximately half of AVSD cases occur in children with DS, supporting the view that trisomy 21 and endocardial cushion dysregulation are tightly linked to this phenotype.[11] Genome-wide association work further suggests that DS-associated AVSD is not simply a dosage effect of chromosome 21 but reflects additional, polygenic modifiers that differ from those seen in non-syndromic AVSD.[12] Against this mechanistic background, our findings of a high proportion of complete defects and a non-trivial fraction of unbalanced lesions are consistent with the expectation that DS confers both a higher risk of AVSD and a tendency toward more complex anatomy.

Population-based data from a nationwide Norwegian cohort have shown that AVSD is disproportionately represented among DS infants and that complete forms dominate the spectrum, while unbalanced AVSD represents a smaller but clinically challenging minority.[13] Similarly, an analysis of a large US inpatient database reported that, among hospitalised children with AVSD, those with DS most often have complete defects and frequently require early intervention.[14] The proportions of complete (54.5%) and unbalanced (9.1%) AVSD in our cohort align closely with those reports,[13,14] despite important differences in health-system context and referral pathways. However, the relatively high share of partial and intermediate AVSD in older children in our series suggests that milder lesions may remain undetected longer in resource-constrained settings, where routine neonatal echocardiographic screening for DS is not uniformly implemented.

Our age-at-diagnosis pattern also resonates with surgical outcome series in which earlier repair is associated with improved survival and less pulmonary vascular disease. Large cohort studies of AVSD repair now report early mortality generally below 5% and 10–15-year survival exceeding 90%, but emphasise that delayed referral, pre-existing pulmonary hypertension, and complex anatomy adversely influence outcome.[15–17] In one single-center series of middle- to long-term outcomes, most patients underwent repair in early infancy, and late presenters were more likely to have residual pulmonary hypertension and significant left atrioventricular valve regurgitation.[17] Compared with those experiences, our median diagnostic age of 10 months and the substantial proportion of children with Doppler-defined pulmonary hypertension (more than half overall, and 60.0% in complete and unbalanced AVSD) suggest that many DS children in our setting may already be at or beyond the optimal window for surgery by the time they are fully evaluated (Tables 2 and 3).

Valve function is a central determinant of both perioperative risk and long-term reintervention after AVSD repair. Recent multicenter and single-center studies have highlighted that moderate or greater regurgitation of the left atrioventricular valve, particularly when present at discharge or early follow-up, is a strong predictor of reoperation and reduced event-free survival.[15,16,18] Our finding that nearly one in two children had at least moderate left atrioventricular valve regurgitation at baseline, and that this burden was highest in complete (53.3%) and unbalanced (70.0%) variants, is therefore clinically worrisome (Tables 3 and 4). It implies that a substantial proportion of patients are entering the surgical pathway with significant valve dysfunction already established, potentially limiting the durability of primary repair. This observation dovetails with data showing that complex valve morphology, unbalanced ventricles, and incomplete commissural or cleft closure are key substrates for persistent or recurrent regurgitation after repair.[18,19]

Recent series focusing specifically on left-sided atrioventricular valve regurgitation after complete AVSD repair demonstrate that late moderate–severe regurgitation remains common, frequently necessitating valve re-repair or replacement during childhood or adolescence.[18,19] Hoashi and colleagues, for example, reported that residual regurgitation after repair was most often observed in patients with intrinsically dysplastic valves or significant ventricular imbalance.[19] The high prevalence of moderate–severe regurgitation in our unbalanced subgroup is consistent with these mechanistic insights and suggests that surgical strategies in such patients may require particular attention to valve geometry, leaflet tissue adequacy, and the feasibility of long-term biventricular circulation. Our data, although pre-operative, reinforce the message that unbalanced AVSD in DS is a high-risk phenotype from both haemodynamic and valve perspectives.

Beyond anatomical description, state-of-the-art reviews of AVSD emphasise the importance of meticulous echocardiographic assessment and standardized nomenclature to inform operative planning and longitudinal care.[11,20] In our cohort, classification was based on comprehensive transthoracic echocardiography in line with current pediatric echocardiographic standards and IPCCC terminology, allowing us to separate partial, intermediate, complete, and unbalanced forms in a reproducible way. Such granularity is not merely academic; it is directly relevant to decisions about the timing of repair, choice between biventricular and single-ventricle strategies, and anticipated need for reintervention.[20] The high frequency of additional intracardiac lesions (56.4% overall, with the highest proportion in unbalanced AVSD) in our sample further underscores the need for detailed segmental analysis in DS children, as concomitant lesions may alter the surgical approach and postoperative course (Table 3).

The implications for practice in similar resource-limited environments are several. First, the predominance of complete AVSD and the substantial burden of pulmonary hypertension and valve regurgitation at diagnosis argue for structured early cardiac screening in all infants with DS, ideally within the first months of life. Second, our variant-specific data highlight that complete and unbalanced AVSD represent particularly high-risk subgroups in which delays in referral may have disproportionate consequences for operability and long-term outcomes. Third, the high prevalence of moderate–severe left atrioventricular valve regurgitation suggests that preoperative optimization, careful surgical technique, and close postoperative surveillance of valve function should be prioritized, with a low threshold for re-evaluation if clinical status worsens. Finally, the observed pattern of referrals—from district hospitals and private clinics as well as direct presentations—suggests that strengthening primary- and secondary-level awareness of DS-associated CHD could shorten diagnostic pathways and support earlier transfer to specialized centers.

Our findings also point to several directions for future research. Prospective, longitudinal follow-up of this cohort through and beyond surgical repair would clarify how baseline variant, associated lesions, pulmonary hypertension, and valve regurgitation translate into survival, functional status, and reintervention rates in this setting. Comparative studies across regions with differing access to early echocardiography and pediatric cardiac surgery could help disentangle the contributions of health-system factors versus inherent anatomical complexity. In addition, integration of genetic analyses—building on existing genome-wide studies of DS-associated AVSD[12]—might reveal whether particular genetic backgrounds are over-represented among children with unbalanced anatomy or severe valve disease in South Asian populations. Such work could ultimately refine risk stratification and inform family counselling.

Limitations

Several limitations merit consideration when interpreting these data. The cross-sectional design restricts inference to descriptive associations and does not allow assessment of causal relationships between AVSD subtype, pulmonary hypertension, valve regurgitation, and clinical outcomes. Because the study was conducted in tertiary-care centers, the cohort likely over-represents children with more complex or symptomatic lesions, and the distribution of AVSD variants may differ from that in community-level DS populations. Echocardiographic classification, although grounded in contemporary standards, is inherently operator-dependent; subtle distinctions between intermediate and complete forms or between balanced and mildly unbalanced ventricles may have been misclassified in a minority of cases. Pulmonary hypertension was assessed qualitatively using Doppler-based estimates rather than invasive hemodynamics, introducing some measurement uncertainty. Finally, the sample size, though adequate for descriptive purposes, limits power for more granular subgroup analyses, particularly within the relatively small unbalanced AVSD group.

Conclusion

In a cohort of 110 children with Down syndrome and atrioventricular septal defect evaluated at tertiary-care centers, complete AVSD emerged as the dominant variant, with partial, intermediate, and unbalanced forms comprising smaller but clinically important proportions. Most children were diagnosed in infancy, yet a notable minority presented after 5 years of age, particularly those with partial and intermediate defects. Pulmonary hypertension and moderate–severe left atrioventricular valve regurgitation were common and concentrated in complete and unbalanced AVSD, signaling a high preoperative haemodynamic and valve burden. These findings suggest that, in resource-constrained environments, DS children with AVSD frequently reach specialist care later than ideal and with advanced disease. Strengthening early cardiac screening pathways for DS, ensuring timely referral to pediatric cardiology services, and tailoring surgical planning to AVSD variant and valve status may help mitigate downstream morbidity. Future prospective and genetic studies are needed to define long-term outcomes and refine risk stratification for this high-risk group.

References

Balistreri CR, Ammoscato CL, Scola L, Fragapane T, Giarratana RM, Lio D, et al. Cardiac defects and genetic syndromes: old uncertainties and new insights. Genes (Basel). 2021;12(7):1047. doi: 10.3390/genes12071047.

Versacci P, Di Carlo D, Digilio MC, Marino B. Cardiovascular disease in Down syndrome. Curr Opin Pediatr. 2018;30(5):616–622. doi: 10.1097/MOP.0000000000000661.

Santoro SL, Steffensen EH. Congenital heart disease in Down syndrome – a review of temporal changes. J Congenit Cardiol. 2020;4(1):1–14. doi: 10.1186/s40949-020-00055-7.

Weijerman ME, van Furth AM, van der Mooren MD, van Weissenbruch MM, Rammeloo L, Broers CJM, et al. Prevalence of congenital heart defects and persistent pulmonary hypertension of the neonate with Down syndrome. Eur J Pediatr. 2010;169(10):1195–1199. doi: 10.1007/s00431-010-1200-0.

Baban A, Olivini N, Cantarutti N, Calì F, Vitello C, Valentini D, et al. Differences in morbidity and mortality in Down syndrome are related to the type of congenital heart defect. Am J Med Genet A. 2020;182(6):1342–1350. doi: 10.1002/ajmg.a.61586.

Haider A, Khan S, Tafweez R, Yaqoob M. Gender and its association with cardiac defects in Down syndrome population at Children Hospital & Institute of Child Health, Lahore, Pakistan. Pak J Med Sci. 2024;40(3):371–375. doi: 10.12669/pjms.40.3.7346.

Jacobs JP, Franklin RCG, Béland MJ, Spicer DE, Colan SD, Walters HL, et al. Nomenclature for pediatric and congenital cardiac care: unification of clinical and administrative nomenclature – the 2021 International Paediatric and Congenital Cardiac Code (IPCCC) and the Eleventh Revision of the International Classification of Diseases (ICD-11). Cardiol Young. 2021;31(7):1057–1188. doi: 10.1017/S104795112100197X.

Lopez L, Saurers DL, Barker PCA, Cohen MS, Colan SD, Dwyer J, et al. Guidelines for performing a comprehensive pediatric transthoracic echocardiogram: recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2024;37(2):119–170. doi: 10.1016/j.echo.2023.11.015.

Naing L, Nordin RB, Abdul Rahman H, Naing YT. Sample size calculation for prevalence studies using Scalex and ScalaR calculators. BMC Med Res Methodol. 2022;22(1):209. doi: 10.1186/s12874-022-01694-7.

Wang X, Ji X. Sample size estimation in clinical research: from randomized controlled trials to observational studies. Chest. 2020;158(1 Suppl):S12–S20. doi: 10.1016/j.chest.2020.03.010.

Calkoen EE, Hazekamp MG, Blom NA, Elders BBLJ, Gittenberger-de Groot AC, Haak MC, et al. Atrioventricular septal defect: from embryonic development to long-term follow-up. Int J Cardiol. 2016;202:784–795. doi: 10.1016/j.ijcard.2015.09.081.

Ramachandran D, Zeng Z, Locke AE, Mulle JG, Bean LJH, Rosser TC, et al. Genome-wide association study of Down syndrome–associated atrioventricular septal defects. G3 (Bethesda). 2015;5(10):1961–1971. doi: 10.1534/g3.115.019943.

Nordklev CB, Gjesdal O, Gunnes N, Holmstrøm H, Morken NH, Vangen S, et al. Down syndrome and associated atrioventricular septal defects in a nationwide Norwegian cohort: prevalence, time trends, and outcomes. Acta Obstet Gynecol Scand. 2024;103(10):2024–2030. doi: 10.1111/aogs.14932.

Aly S, Qattea I, Othman H, Nguyen HH, Aly HZ. Outcomes of atrioventricular septal defects with and without Down syndrome: analysis of the national inpatient database. Cardiol Young. 2024;34(3):614–623. doi: 10.1017/S1047951123003116.

Schumacher K, Marin Cuartas M, Meier S, Hörer J, Schreiber C, Vogt M, et al. Long-term results following atrioventricular septal defect repair. J Cardiothorac Surg. 2023;18(1):250. doi: 10.1186/s13019-023-02355-6.

Schleiger A, Miera O, Peters B, Heinemann M, Berger F, Mertins L, et al. Long-term results after surgical repair of atrioventricular septal defect. Interact Cardiovasc Thorac Surg. 2019;28(5):789–796. doi: 10.1093/icvts/ivy334.

Cai Y, Chen R, Chen G, Liu F, Chen H, Lu Z, et al. Middle- to long-term outcomes of surgical repair for atrioventricular septal defect: a single-center study. J Thorac Dis. 2022;14(10):3920–3932. doi: 10.21037/jtd-22-790.

Ozturk M, Tongut A, Sterzbecher V, Bechtold C, Westhofen S, Schneider H, et al. Repair of the complete atrioventricular septal defect – impact of postoperative moderate or more regurgitation. Interdiscip Cardiovasc Thorac Surg. 2024;38(4):ivae053. doi: 10.1093/icvts/ivae053.

Hoashi T, Hirano A, Hosoda R, Yazaki S, Murakami A, Shiraishi I, et al. Left-sided atrioventricular valve regurgitation after the repair of complete atrioventricular septal defect. Pediatr Cardiol. 2024;online ahead of print. doi: 10.1007/s00246-024-03707-2.

Taqatqa AS, Vettukattil JJ. Atrioventricular septal defects: pathology, imaging, and treatment options. Curr Cardiol Rep. 2021;23(9):93. doi: 10.1007/s11886-021-01523-1.