

# Surgical Outcomes of Pediatric Patients with Ventricular Septal Defects in a Tertiary Referral Center in Pakistan: A Retrospective Cohort Study

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## Abstract

**Background:** The nature of complications and outcomes for Ventricular septal defect (VSD) repair differ between developed and developing countries. Understanding these differences can help optimize patient management according to geographical location.

**Objective:** The purpose of this study was to investigate the risk factors associated with in-hospital peri- and post-surgical complications of VSD repair in a developing country.

**Design:** A retrospective cohort study.

**Setting:** A tertiary referral center.

**Participants:** 117 patients under 18 years of age admitted for surgical closure of ventricular septal defect between July 1998 and June 2008.

**Main Outcomes:** Only patients with isolated VSD or VSD associated with acyanotic congenital heart disease were included. Outcomes were defined as in-hospital minor and major complications and mortality.

**Results:** Adverse complications occurred in 35.9% (42/117) and death in 3.4% (4/117) of cases. Age >12 months (OR 0.17 13 months-5 years; 0.10 5-18 years), weight >10 kg (OR 0.24 11-20 kg; 0.13>21 kg), and absence of pulmonary artery hypertension (OR 0.43) were all significantly associated with a reduced rate of adverse events. A longer stay in intensive care unit/semi-intensive care unit (OR 11.6 5-7 days; OR 6.1 >8 days) and larger size of ventricular septal defect (OR 5.4 medium size; 3.9 large size) were associated with an increased risk of adverse events. Infection (20%) and pneumonia (10%) were the commonest complications.

**Conclusions and relevance:** Age under one year, weight less than ten kilograms, pulmonary artery hypertension, and moderate to large size ventricular septal defect are more likely to be associated with adverse outcomes after surgical repair of ventricular septal defect. Infection and pneumonia comprise almost one third of the total complications, compared to higher arrhythmic events in developed countries. Developing countries have a distinct spectrum of complications that may be avoidable and treatable.

**Keywords:** Congenital heart surgery; Ventricular septal defects; Surgical repair

**Abbreviation:** VSD: Ventricular Septal Defect; AKUH: Aga Khan University Hospital; ASD: Atrial Septal Defect; PDA: Patent Ductus Arteriosus; MS: Mitral Stenosis; MR: Mitral Regurgitation; PS: Pulmonary Stenosis; AS: Aortic Stenosis; AR: Aortic Regurgitation; COA: Coarctation of the Aorta; PAH: Pulmonary Artery Hypertension; AVP: Aortic Valve Prolapsed; PVR: Pulmonary Vascular Resistance; CHF: Congestive Heart Failure; OR: Odd Ratio

## Introduction

Ventricular septal defect (VSD) is the most common congenital abnormality of the heart, accounting for 25% to 29% of all cases of congenital heart disease in Pakistan [1,2]. Spontaneous closure of VSDs occurs in 8.8% to 48% of children, depending on age [3-5], but surgical correction is required in 32% of cases, of which 91% are the Perimembranous VSD (PmVSD) type [6]. Although surgical mortality and morbidity have reduced significantly in developed countries, especially with the use of less invasive diagnostic procedures [7,8]; surgical outcomes remain poor for patients in a younger age group and with low weight at the time of surgery [9]. In spite of these data, age and weight remain controversial risk factors for adverse surgical outcome for children with VSD, with some studies suggesting that these factors are less important, particularly in developing countries [10,11]. The types of anatomic defects and hemodynamic factors in VSD in relation

to operative outcome have not been studied for patients treated in Pakistan. Therefore the purpose of this study was to comprehensively evaluate the demographic, morphologic, and hemodynamic aspects of VSD and their associations with surgical outcome, and assess the spectrum of complications occurring in a developing country tertiary referral center.

## Patients and Methods

### Study population

Aga Khan University Hospital (AKUH), Karachi, Pakistan, is a tertiary referral center for pediatric surgery. We performed a

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**Received** July 15, 2013; **Accepted** September 17, 2013; **Published** September 20, 2013

**Citation:** Bushra O, Muneer AM, Mehnaz A (2013) Surgical Outcomes of Pediatric Patients with Ventricular Septal Defects in a Tertiary Referral Center in Pakistan: A Retrospective Cohort Study. J Clin Exp Cardiol 4: 269. doi:10.4172/2155-9880.1000269

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retrospective cohort study of 117 consecutive pediatric patients admitted for surgical closure of a VSD. Patients aged from birth to 18 years of age were identified in the ten-year period between July 1998 and June 2008. Approval for the study was granted from the ethics committee and institutional review board of AKUH.

### Eligibility

All patients diagnosed with isolated VSD or VSDs associated with acyanotic heart disease-like atrial septal defect (ASD), patent ductus arteriosus (PDA), mitral stenosis (MS), mitral regurgitation (MR), pulmonary stenosis (PS), aortic stenosis (AS), aortic regurgitation (AR) or coarctation of the aorta (COA), and who subsequently underwent surgery, were included in the study. Patients with VSDs associated with complex cardiac lesions such as double-outlet ventricle, tetralogy of fallot, transposition of the great arteries, pulmonary atresia, tricuspid atresia, truncus arteriosus or single ventricle were excluded from the study.

### Data collection procedures

The patient records of AKUH were queried in order to collect data on patients meeting the stated criteria. For each patient the number of VSD, type of VSD, size of VSD, associated diagnosis with VSD, and outcomes were collected.

### Diagnostic criteria and variables

All patients were diagnosed using transthoracic echocardiography performed by a pediatric cardiologist. For this study, VSD was classified as PmVSD, muscular, inlet, and doubly committed subarterial/supracristal VSD. If a patient had more than one type of VSD, then only the larger-sized VSD was considered in the analysis. The size of the VSDs were categorized as small, moderate, and large if the VSD was less than 1/3, between 1/3 and 2/3, or more than 2/3 of the aortic root size, respectively. If a patient had multiple VSDs, then the sizes were added. The transthoracic echocardiography report was available in 115 out of 117 patients, and the size of VSD could not be categorized according to aortic root size in 22 out of 117 patients. Cardiac catheterization is done in 43 patients. No of patients with available information for demographic and morphologic data are mentioned in Table 3.

A pediatric cardiologist and cardiac surgeon preformed the preoperative clinical evaluation and laboratory tests. The pediatric cardiologist assessed pulmonary artery hypertension (PAH) using a combination of echocardiography and cardiac catheterization, which was also performed to investigate potential reversibility of PAH and to rule out complex cardiac morphology in selected cases. If infection was identified, patients received antibiotics and surgery was delayed for four weeks.

### Main outcome measures

Outcomes were determined in the time between surgery and discharge from hospital. Minor and major complications and death were considered as a single category of "adverse outcome". In-hospital complications included significant residual lesion, ventricular dysfunction, pericardial effusion, pericarditis, pericardial tamponade, right bundle branch block, transient heart block, transient rhythm abnormalities, insertion of permanent pacemaker for complete heart block, pleural effusion, pneumonia, lung collapse, pneumothorax, need for redo-surgery, neurological complications (such as seizures), renal insufficiency, infection, re-intubation, cardiopulmonary resuscitation, and gastrointestinal bleeding. A favorable outcome was defined as a patient discharged with no complications as defined above. Mortality

was defined as peri-operative or post-operative death before discharge from hospital.

### Statistical analysis

The dependent variable was binary: adverse event or no adverse event. The following independent variables were used to identify risk factors for adverse events. Within each independent variable group, one subgroup was selected as the reference to calculate odds ratio (OR) for adverse events for the other subgroups relative to the reference group: age <12 months for "age", <5 kg for "weight", yes for "PAH", 1-1.5 for "Qp:Qs", 0.5-1.5 for "pulmonary vascular resistance (PVR)", 0-4 days for "duration of stay in Intensive care unit/semi-intensive care unit(ICU/SICU)", perimembranous for "VSD type", single for "number of VSDs", small for "size of VSD", and yes or ASD for "associated defect". Data for each group of variables are presented as OR comparing each subgroup to its respective reference subgroup; ORs were determined using the 2-way contingency table chi-square test. Bias was reduced by considering all patients within the study period, which also determined the study size. Missing data were excluded from the analysis. Values of  $p < 0.05$  were considered significant. Data were analyzed using SPSS for Windows (IBM Inc.) version 16.0.

### Results

A total of 117 patients underwent open-heart surgery for the repair of VSD. The baseline clinical characteristics of the patients are shown in Table 1.

The distribution of demographics, types of morphologic defect and hemodynamic factors are shown in Table 2. PmVSD was the most common type of defect, identified in 65% (75/115) of patients, followed by supracristal VSD (22%; 25/115), muscular VSD (9%; 10/115), and inlet-type VSD (3%; 4/115). One patient was diagnosed with a Gerbodes-type VSD. A single VSD was found in 94% of patients (108/115). The VSD was small in 24.2% (23/95), medium sized in 33.7% (32/95), and large in 42.1% (40/95) of patients. VSDs were associated with other congenital cardiac defects in 65% (76/117) of cases. The associated defects were PS (9%; 11/117), ASD (11%; 13/117), PDA

Variable	n
Age (year)	5 yr ± 4 (3 to 17 yr)
Age category	
Less than one year	25 (21%)
One to five years	52 (45%)
five to 18 years	40 (34%)
Gender (M:F)	1.3:1.0
Mean BSA(cm <sup>2</sup> )	0.6
Weight (Kg)	15.5 ± 10.93 (3.1 to 60)
Weight category	14 (12%)
Less than 5 kg	
6 to 10 kg	21 (18%)
11 to 20 kg	55 (47%)
More than 21 kg	13 (11%)
Genetic syndrome	15/117 (13%)
Down's syndrome	10/117 (8.5%)
Qp:Qs ratio	2.3 ± 1.3 (1.0 to 7.0)
Pulmonary vascular resistance index (Woods unit/m <sup>2</sup> )	3.4 ± 2.6 (0.5 to 11.3)
PA band before surgery	19/112 (17%)
Stay in ICU/SICU (days)	4 ± 4 (1 to 24)
Duration of intubation (Hours)	20 ± s34 (1 to 211)

Table 1: Clinical characteristics of the patients in this study.

Adverse outcome	n	%
Ventricular dysfunction	10	9
Pericardial effusion	6	5
Transient heart block	2	2
Transient rhythm abnormality	14	13
Permanent pace maker	1	1
Pleural effusion required chest tube	8	7
Pneumonia	12	10
Lung collapse	5	4
Need redo surgery	2	2
Seizures	7	6
Infections	22	20
Failure to extubate on planned day	5	4
CPR	9	8
GIT bleeding	1	1
Intraoperative complications	7	6
Clot in mediastinum	1	1
Total	112	

**Table 2:** Details of the peri- and post-operative complications observed in this study.

(13%; 15/117), MR (17%; 20/117), and MS in one patient, COA in two patients, AS in two patients, AR (26%; 30/117), and aortic valve prolapsed (AVP) (30%; 35/117). Cardiac catheterization was performed in 37% (43/117) of cases, and 50% (58/117) of patients had PAH. 16% (19/117) of patients had undergone pulmonary artery banding (PA band) prior to VSD repair.

Overall, 35.9% (42/117) patients had adverse complications and death occurred in 3.4% (4/117) of cases. 18% (21/117) of patients had more than one complication (Table 2). Infections (including pneumonia) were the most common complication, occurring in 30% of patients. Transient rhythm abnormalities were the next frequent complication, occurring in 13% patients.

Age >12 months (OR 0.17 13 months-5 years; 0.10 5-18 years), weight >10 kg (OR 0.24 11-20 kg; 0.13 >21 kg), and absence of PAH (OR 0.43) were all significantly associated with a reduced rate of adverse events (Table 3). A longer stay in ICU/SICU (OR 11.6 5-7 days; 6.1>8 days) and larger size of VSD (OR 5.4 medium size; 3.9 large size) were significantly associated with an increased rate of adverse events (Table 3). The inlet type of VSD (OR 15.8) and very high PVR (OR 21.7) demonstrated a trend towards association with adverse events, although not quite reaching statistical significance.

Patients with VSDs associated with ASD or PDA had an adverse outcome in 54% and 53% of cases, respectively, followed by AR, MR, and aortic valve prolapse in 33%, 30%, and 29% of cases, although these associations were not significant due to small sample sizes.

## Discussion

We have shown that patients under one year old, under ten kilograms, with PAH and moderate to large sized VSDs were more likely to have an adverse outcome after surgery for repair of VSD. Infection and pneumonia comprised almost one third of total complications. The inlet type of VSD had the worst outcomes.

In terms of overall outcomes, our in-hospital mortality of 3.4% was higher than recent published mortality rates for VSD repair in developed countries. Mortality has been reduced to between 0.5% and 1.7% [7-9] in Western healthcare systems, which has fallen from

8.2% only two decades ago [8], and much lower than the mortality rates shown for the same procedure in the Indian subcontinent [10-13].

Variable	n	Adverse event (n)	Rate of adverse event (%)	Odds ratio (95% CI; p-value)
<b>Age</b>				
<12 months	25	19	76	1
13 months-5 years	52	18	35	0.17 (0.06-0.49; 0.0012)
5-18 years	40	10	25	0.10 (0.03-0.34; 0.0001)
<b>Weight</b>				
<5 kg	14	11	79	1
6-10 kg	21	10	48	0.24 (0.05-1.15; p=0.08)
11-20 kg	55	18	33	0.13 (0.03-0.53; p=0.005)
>21 kg	13	8	62	0.12 (0.03-0.53; p=0.0053)
<b>PAH</b>				
Yes	58	30	52	1
No	54	17	31	0.43 (0.20-0.93; p=0.03)
<b>Qp:Qs</b>				
1-1.5	12	5	42	1
1.6-2.0	10	2	20	0.35 (0.05-2.4; p=0.28)
2.1-4.0	15	6	40	0.93 (0.19-4.4; p=0.93)
4.1-6.0	2	1	50	1.4 (0.07-28.1; p=0.83)
>6.1	1	1	100	4 (0.13-120.7; p=0.41)
<b>PVR</b>				
0.5-1.5	7	1	14	1
1.6-3.0	6	1	17	1.2 (0.05-24.5; p=0.91)
3.1-4.5	9	3	33	3 (0.24-37.7; p=0.85)
4.6-6.0	3	1	33	3 (0.24-37.7; p=0.85)
>6.0	2	2	100	21.7 (0.64-730.1; p=0.09)
<b>Duration of stay in ICU/SICU</b>				
0-4 days	81	20	23	1
5-7 days	24	19	79	11.6 (3.83-35.1; p<0.0001)
>8 days	12	8	67	6.1 (1.7-22.4; p=0.0065)
<b>VSD Type</b>				
Perimembranous	75	27	36	1
Muscular	10	5	33	1.7 (0.47-6.70; p=0.39)
Inlet	4	4	100	15.8 (0.82-306.0; p=0.07)
Supracristal VSD	25	9	36	1 (0.39-2.57; p=1.0)
Gerboodes	1	0	0	0.58 (0.02-14.9; p=0.74)
<b>Number of VSDs</b>				
Single	108	44	41	1
Multiple	7	3	43	1.1 (0.23-5.11; p=0.11)
<b>Size of VSD</b>				
Small	23	4	17	1
Medium	32	17	53	5.4 (1.5-19.4; p=0.01)
Large	40	18	45	3.9 (1.11-13.5; p=0.03)
<b>Associated defects</b>				
Yes	76	28	37	1
No	41	19	46	1.5 (0.68-3.1; p=0.32)
PS	11	5	45	1
ASD	13	7	54	1.4 (0.27-7.0; p=0.68)
PDA	15	8	53	1.37 (0.39-6.6; p=0.69)
MR	20	6	30	0.51 (0.11-2.4; p=0.39)
MS	1	0	0	0.39 (0.01-11.8; p=0.59)
COA	2	1	50	1.2 (0.06-24.5; p=0.12)
AS	2	0	0	0.24 (0.009-6.0; p=0.38)
AR	30	10	33	0.60 (0.15-5.6; p=0.48)
Prolapse of coronary cusp	35	10	29	0.48 (0.12-1.94; p=0.30)

**Table 3:** Association of demographics, morphology, and hemodynamic factors with outcome.

Between 1976 and 1996, perioperative morbidity reduced significantly from 29% to 15% in children who underwent large VSD repairs; however, changes in post-operative morbidity have remained static (approximately 40%; 8). This is comparable to the postoperative mortality seen in this study, but different in that cardiac dysrhythmia is the most common complication in developed countries [8], while infection and pneumonia were most common in our study. Anderson et al. identified transient or complete heart block, re-operation, and pleural effusion as the main complications [9], while another study from the Indian subcontinent also showed infection and pneumonia to be the most common complication (17%) in the developing country setting, slightly less than our rate of 31%. These data suggest that the nature of post-operative complications is different in developing countries, and may be avoidable and easily treatable.

In our study, other complications were transient heart block (2%), need for permanent pacemaker (1%), and re-do surgery (2%). This compares with 3.5% for transient heart block, 2.1% for permanent pacemaker, and 4.9% for re-do surgery in developed countries [9]. The need for a chest tube for pleural effusion in 7% of patients and seizures in 6% of patients compares to 3.5% and 1.7% in developed countries, respectively [9]. Another study reported a reoperation rate of 2.8% after surgical closure of an isolated single VSD, and none of these patients had post-operative heart block, rhythm abnormality, or a neurologic event [7].

Restrictive VSD is not usually referred for percutaneous or surgical closure due to the usual natural history of spontaneous closure or reduction in size. Miyake et al. studied spontaneous closure of VSD in infants under three month of age, and found spontaneous closure occurred in 72% of cases without congestive heart failure (CHF), but in only 19% of infants with CHF [5]. Backer et al. evaluated outcomes of surgical repair for restrictive VSD in a low risk population with a Qp:Qs ratio of less than 2, no PAH, and no symptoms of congestive cardiac failure. They reported no mortality and no complications such as heart block, redo surgery, or wound infection [14] in this low risk population.

In our study, complications of VSD repair were higher in patients with moderate and large VSDs. We did not evaluate confounding risk factors for adverse outcome according to different sizes of VSD. Since we followed standard indications for referring patients for surgery, we assumed that the indication for surgery in restrictive or small to moderately sized VSDs would be either high Qp:Qs ratio, high PVR, AVP with regurgitation, or deteriorating clinical condition despite medical therapy.

We compared our data with the risks and benefits shown for the operative results of restrictive VSD from Backer et al, and natural spontaneous closure of VSD without CHF [5,14]. Our data allow us to conclude that if we repair restrictive or moderately-sized VSDs before patients develop a high Qp:Qs ratio, higher PVR, or clinical symptoms, we can reduce the rate of post-operative complications.

PmVSDs were observed in 65% of patients, followed by supracristal VSD in 22% of cases. Associated AR and AVP were present in 26% and 30% of patients, respectively, and one third of patients with AR and AVP suffered an adverse outcome. VSD is known to be associated with AVP in 8.6% of cases and AR in 6.4% of cases [4]. Eroglu et al. found that none of the VSDs with AVP close spontaneously [4], and therefore these lesions require surgical intervention. Spontaneous closure of PmVSD without CHF is 74%, while for supracristal VSD only 23%, with the remaining VSDs either being small or not requiring surgery [5]. Backer et al. found AR and AVP in 18% and 45% of cases,

respectively, in a low risk population who underwent VSD repair, with no adverse outcomes [14]. In another study, AR and AVP were found in 72% and 44% of patients with supracristal VSD undergoing surgical repair, respectively; this study also showed that the early closure of the supracristal VSD reduces the progression of AR [15]. These data suggest that early surgery before the development of AR or AVP not only reduces the chance of aortic valve replacement, but also reduces post-operative complications.

A study from India demonstrated that operative weight was not associated with the length of hospital stay, but that younger age and preoperative pneumonia required longer post-operative care [10]. In one study from Pakistan, operations in children under five and younger age were associated with adverse outcomes [12]. Another study from a developing country hospital reported no association between age and post-operative morbidity, but did suggest that this group requires longer post-operative care [11]. In contrast, Anderson et al determined that infants under six month of age, and each kilogram decrease in weight increased composite risk of surgery 1.8 fold [9]. In our study, age less than one year and weight less than ten kilograms were significantly associated with higher peri- and post-surgical complications. Anderson et al. also found that age over six months and higher weights were associated with reduced incidence of heart block and post-operative hemorrhage, respectively [9].

More than half of patients had PAH, which was significantly associated with adverse outcome. Several studies have shown the association between PAH and higher mortality and morbidity in patients undergoing VSD repair [12,16]. Surgical repair of small to moderately size shunts without PAH were the most frequent indication for surgical repair in the current era and is associated with significantly lower mortality and morbidity [8].

VSD was associated with ASD and PDA in 10 and 12% of cases respectively, and more than half of these cases had an adverse outcome, although these relationships were not statistically significant due to small subgroup sizes. Other studies have also identified ASD as an important risk factor for surgical outcome of VSD [17].

Most of the surgical morbidity in our study was due to infection and pneumonia, which is related to patients' immune status and preoperative health. This study helps doctors to counsel families of high-risk patients about likely post-operative complications. Surgical or percutaneous repair of moderately sized VSD, regardless of symptoms and PAH, should be emphasized as a risk and re-evaluated. These data help doctors understand the need for follow up for medical therapy, compliance with medication in developing countries, SBE prophylaxis, reducing loss to follow up, the role of PAH, and factors to help reduce hospital stays and complications.

## Limitations

There are several limitations in this study. First, this is a retrospective study that depended on the written documentation of several doctors, and therefore there were some missing data that might be difficult to evaluate. Second, over the ten year of period covered in this analysis, three different surgeons performed the surgery, with a cardiac surgeon specialized in pediatric cardiac surgery only starting in 2007. Third, this study did not differentiate between the high risk and low risk populations in different sizes and types of VSD repair, and therefore the question of which complications contribute to high risk moderately size VSD population remains unanswered. However, overall this study

provides a comprehensive overview of the problem of risk factors and outcome in VSD, allowing more focused evaluation in future studies.

## Conclusion

Patients aged less than one year, weight under 10 kilograms, PAH, and moderate to large size VSDs are more likely to develop adverse outcomes after surgical repair. Infection and pneumonia comprise almost one third of the total complications in this population treated in a developing country.

## Competing Interest

There is no competing interest in writing this article.

## Author contributions

**Bushra Omair:** She worked as a primary author, design data, collected data, did statistical analysis, interpreted, drafted, and analyze manuscript critically, and prepare for final submission.

**Muhammad Muneer Amanullah:** He worked as a co-author, helped in designing this article and did critical analysis.

**Mehnaz Atiq:** She concept/design data, analyses critically, and review/correct it before final submission.

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