

## Resolution of left heart dilation and degree of mitral regurgitation after surgical closure of ventricular septal defect

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### Abstract

**Introduction:** The most common form of congenital heart disease in childhood is the VSD, occurring in 50% of all children with congenital heart disease and in 20% as an isolated lesion, the incidence of VSDs has increased dramatically with advances in imaging and screening of infants, ranges from 1.56 to 53.2 per 1000 live births.

**Objective:** To evaluate improvement in LV function, LV dimensions, degree of MR, and LA dimensions post-surgical correction of congenital VSD in pediatric age group.

**Patients and Methods:** study was carried on 60 children with congenital ventricular septal defect presenting to NHI as candidates for surgical closure of VSD. Transthoracic echocardiography was done preoperatively, early postoperatively, and after 1 month and 3 month of discharge for evaluation of left ventricular function, left atrial diameter, LVEDD, degree of mitral regurgitation.

**Results:** Preoperative LVEDD, LAD and degree of mitral regurgitation were significantly increased in patients with VSD specially moderate and large defects, which showed significant reduction after closure of VSD without additional surgical repair of mitral valve.

**Conclusion:** The echocardiographic parameters of left heart dilation and degree of mitral regurgitation improved significantly after surgical closure of VSD without additional mitral valve repair.

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## Introduction

The size of the VSD, the pressure in the right and left ventricular chambers, and pulmonary resistance are factors that influence the hemodynamic significance of VSDs. A VSD may not be apparent at birth because of the nearly equal pressures in the right and left ventricles and a lack of shunting. With increasing shunt corresponding to the increasing pressure difference between the ventricles these defects become clinically apparent.

It is known that left-to-right shunting in ventricular septal defects (VSD) increases pulmonary arterial blood flow and pulmonary venous return to the left heart leading to volume overload of the left atrium (LA) and left ventricle (LV), and subsequent LV enlargement, mitral annular dilation, mitral regurgitation (MR), and consequent LA enlargement to allow for the homeostatic balance of LA pressure (Kizer et al., 2006, Senzaki et al., 2009, Ueda et al., 1996).

In the natural course of these changes after surgical closure, it has been demonstrated that the left ventricular end-diastolic volume (LVEDV) returns to normal within the first 2 years of life. However, the left atrial volume (LAV) remains elevated (Cordell et al., 1976).

The natural course of MR in children with VSD has also been studied, and it is believed that MR in children with a normal mitral valve (MV) apparatus and hemodynamically large VSD resolves spontaneously after the surgical closure of VSD (Mahadin et al., 2011). However, limited information is available on the relationship between MR and left heart volume overload. A higher degree of MR is supposed to be associated with more severe left heart dilation, and the reversibility of the myocardium damage might take a longer period with a more severe degree of left heart dilation.

## Objective

To evaluate improvement in LV function, LV dimensions, degree of MR, and LA dimensions post-surgical correction of congenital VSD in pediatric age group.

## Patients and Methods

In this prospective single center study seventy three children with congenital ventricular septal defect presenting to NHI as candidates for surgical closure of VSD were screened for possibility of recruitment after meeting Inclusion criteria; 13 patients were excluded and 60 patients were included in the study.

### *Inclusion criteria*

- All pediatric patients presenting with isolated congenital VSD who were suitable for surgical correction were included.
- Patients with associated PFO were also included.

### *Exclusion criteria*

- 1- Patients older than 18 years.
- 2- Patients with associated complex congenital cardiac defects.
- 3- Patients not suitable for surgical closure (e.g. having PVOD).
- 4- Patients with other non cardiac debilitating disease that would make follow up unsuitable.
- 5- Patients whose guardians didn't accept to comply with follow up visits.

All patients were subjected to:

- I. **Full history taking:** a full history was taken for each patient including:
  - a. Personal history: age, sex, race, parental consanguinity, maternal drug intake were specially targeted.
  - b. Surgical history: prior surgeries performed were recorded especially cardiac surgeries.
  - c. Associated anomalies and drug intake were also sought.
  - d. Presenting complaint: repeated chest infection, dyspnea, tachypnea, tachycardia, sweating, difficult feeding, milestones, and cyanosis.
- II. **Clinical examination:** all patients were subjected to full clinical examination including:
  - a. General examination: Weight, height, ABP (bilaterally), pulse (rate, rhythm, equality, peripheral pulse and special character), neck veins, and special facies were recorded, for assessment of shunt, and diagnosis of associated genetic anomalies especially down syndrome.
  - b. Local cardiac examination:
    - I. Inspection and palpation: for cardiac apex site, and character. Presence of thrills, and additional precordial pulsations (e.g. diastolic shock) was also sought, for assessment of ventricle enlargement pulmonary hypertension.
    - II. Auscultation: every patient was thoroughly auscultated for heart sounds, additional sounds and murmurs and full data regarding each was recorded, to diagnose the presence of holosystolic murmur and its degree, exclusion of other associated cardiac anomalies.
- III. **ECG:** for detection of heart rhythm, regularity, p wave, P-R interval, QRS axis and width, ST segment, QT interval.
- IV. **Echocardiography:**

Transthoracic echocardiography was done preoperatively, early postoperatively, and after 1 month and 3 month of discharge by GE- Vivid 5 machine using a 6 MHz probe and 3 MHz probe where the following views were taken for each patient:

  - parasternal long axis view: left atrial diameter, aortic root diameter, mitral valve (2-D and color flow mapping), ejection fraction by M-mode, and presence of perimembraeous VSD were assessed, exclusion of other anomalies.

- parasternal short axis view:
- apical 4 chamber: mitral valve assessment (exclusion of rheumatic or myxomatous affection by 2D, degree of regurgitation by CFM), perimembraneous and muscular VSD, the maximal shunt flow areas were measured by color Doppler echocardiography from frame by frame search of the video tape, tricuspid valve morphology, regurgitation by CFM, estimated pulmonary artery systolic pressure by CWD, exclusion of other anomalies.
- apical 5 chamber: mitral valve assessment, subaortic VSD, aortic valve morphology, including prolapsing aortic valve into VSD by 2-D, aortic regurgitation by CFM and CWD, exclusion of other anomalies.
- suprasternal long axis view: to exclude other cardiac anomalies as aortic arch anomalies, PDA.
- PDA view: pulmonary artery and both branches
- Subcostal long and short axis views:

Small VSDs (defined as VSD dimension less than half the size of the aortic annulus diameter), Large VSDs (defined as defect size equal to the diameter of the aortic annulus) typically have left atrial and left ventricular dilation with normal left ventricular systolic function. Dilation of the main and branch pulmonary arteries also is common. (Ooshima et al., 1995)

Two-dimensional (2D) imaging, M-mode, color flow Doppler (across valves and septae), pulsed and continuous wave Doppler were done in all relative views **preoperatively** with:

- 1- Full ***description of VSD***: type, number, size, direction of shunt and pressure gradient across).
- 2- Search for any ***associated cardiac anomalies***.
- 3- ***LV internal dimensions*** (ESD, and EDD) and ***LV ejection fraction*** (by M-mode and 2D eyeballing) and ***fractional shortening***. (*Those were also measured prior to patient discharge, one month and three months postoperative*).
- 4- ***LA dimensions***. (*measured prior to patient discharge, one month and three months postoperative by M-mode* ).
- 5- ***Degree of MR***: patients were classified into 3 groups according to the degree of MR based on qualitative color flow mapping as follows:
  - *Group 1*: no MR.
  - *Group 2*: trivial to mild MR.
  - *Group 3*: moderate, or severe MR.

## V. Follow up:

All patients were followed up at 1 and 3 months where TTE was repeated for:

- 1- Adequacy of VSD closure.
- 2- Left sided systolic function and internal dimensions.
- 3- LA dimensions.
- 4- Residual MR.

**Statistical analysis:** All data was collected, tabulated and subjected to proper statistical analysis using IBM SPSS version 21.

## Results

The present study was prospective study conducted on **60 patients** presenting to National heart institute and showed the following results.

**Table (1): Demographic data of the study group**

Demographic data	Frequency	Percent
Sex		
Female	31	51.7
Male	29	48.3
Age (years)		
<1 years	15	25.0
1-2 years	19	31.7
2-6 years	18	30.0
>6 years	8	13.3
Range	0.3-14	
Mean+/-SD	3.03 +/- 3.07	

Thirty one (51.7 %) of our patients were females, and 29 (48.3 %) were males. Fifteen (25 %) aged less than 1 year, 19 (31.7 %) aged 1- 2 years, 18 (30 %) aged 2-6 years, 8 (13.3 %) aged > 6 years.

**Table (2): History distribution of the study group**

History	Frequency	Percent
<b>Maternal drug intake</b>		
No	46	76.7
Yes	14	23.3
<b>Prior surgeries</b>		
No	57	95.0
Pulmonary artery banding	3	5.0
<b>Associated cardiac anomalies</b>		
No	52	86.7
PFO	8	13.3
<b>Associated other anomalies</b>		
Down	6	10.0
No	54	90.0

There was positive history of maternal drug intake in 14 (23.3 %) of studied patients. Eight patients had associated PFO, 3 patients underwent prior pulmonary artery banding, and 6 patients had mongloid facies.

**Table (3): Descriptive data of the TTE presurgery**

VSD	Statistics
Type [No. (%)]	
Muscular	2 (3.4%)
Inlet	2 (3.3%)
Malalignment	2 (3.3%)
Outlet	2 (3.3%)
Perimembraneous	47 (78.3%)
Subaortic	5 (8.3%)
Number	
1	57 (95%)
2	3 (5%)
Size (cm)	
Range	0.3-1.3
Mean+/-SD	0.7+/-0.2
Pressure gradient (mmHg)	
Range	24-100
Mean+/-SD	65.7±18.1

LV	
EF% (2D)	
Range	55-80
Mean+/-SD	69.2+/-5.3
ESD	
Range	1.1-30
Mean+/-SD	2.6±3.6
EDD	
Range	2.3-5.4
Mean+/-SD	3.6±0.7
FS	
Range	28-47
Mean+/-SD	38.2±4.2
LA	
Range	1.2-4.4
Mean+/-SD	2.8±0.6
PAP	
Range	20-90
Mean+/-SD	48.1+/-16
MR	
NO MR	18 (30%)
Trivial or mild MR	24 (40%)
Moderate MR	12 (20%)
Severe MR	6 (10%)

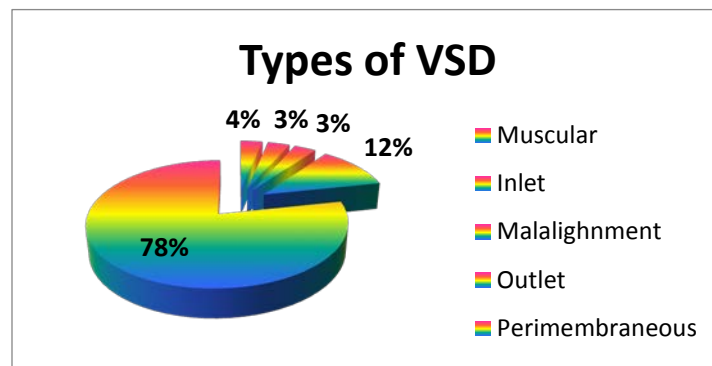


Fig.(1): distribution of patients as regards types of VSD.

Forty seven (78 %) patients had perimembraneous VSD, 2 (3.3 %) had outlet VSD, 2 (3.3 %) had malalignment VSD, 2 (3.3 %) had inlet VSD, 2 (3.3%) had muscular VSD. Twenty eight percent of patient had nonrestrictive VSD. Thirty percent had no mitral regurge, 40 % had trivial or mild mitral regurgitation, 20 % had moderate mitral regurgitation, 6 % had severe mitral regurgitation.

**Table (4): Descriptive data of the post surgical and predischarge echocardiography**

VSD	Statistics
LV	
EF% (2D)	
Range	40-80
Mean+/-SD	62.83±8.27
ESD	
Range	1.2-3.3
Mean+/-SD	2.06±0.45
EDD	
Range	1.8-4.8
Mean+/-SD	3.09±0.65
FS	
Range	20-44
Mean+/-SD	33.05+/-5.57
LA	
Range	1.3-4.20
Mean+/-SD	2.13±0.47
MR	
NO MR	38 (63.3%)
Trivial or mild MR	15 (25%)
Moderate MR	6 (10%)



Severe MR	1 (1.7%)
Residual VSD (mm))	
No	47 (78.3%)
Residual	13 (21.7%)

Predischarge echocardiography showed significant decrease in the degree of mitral regurgitation where 63.3 % had no mitral regurge, 25% had trivial or mild mitral regurge, 10% had moderate mitral regurge, and 1.7 % had severe mitral regurge, 21% had residual insignificant shunt.

**Table (5): Descriptive data of the follow up (1 month) of TTE**

VSD	Statistics
Adequacy of VSD closure	
No residual	51 (85%)
Residual defect	9 (15%)
LV	
EF% (M-mode)	
Range	45-76
Mean+/-SD	64.25+/-6.26
EF% (2D)	
Range	45-75
Mean+/-SD	63.77±6.19
ESD	
Range	1.2-2.9
Mean+/-SD	1.98±0.39
EDD	
Range	1.7-4.4
Mean+/-SD	2.94±0.58

FS	
Range	22-45
Mean+/-SD	33±3.99
LA	
Range	1.3-4
Mean+/-SD	2.02±0.47
MR	
NO MR	47 (78.3%)
Trivial or mild MR	9 (15%)
Moderate MR	3 (5%)
Severe MR	1 (1.7%)

One month post-operative echocardiography showed progressive decrease in the degree of mitral regurge except for severe mitral regurgitation (1.7%)

**Table (6): Descriptive data of the follow up (3 month) of TTE**

VSD	Statistics
Adequacy of VSD closure	
No	58 (96.7%)
Yes	2 (3.3%)
LV	
EF% (M-mode)	
Range	45-77
Mean+/-SD	65.02±6.14

EF% (2D)	
Range	45-77
Mean+/-SD	64.73±5.95
ESD	
Range	1.1-2.8
Mean+/-SD	1.97±0.43
EDD	
Range	1.6-4.2
Mean+/-SD	2.9±0.59
FS	
Range	21-43
Mean+/-SD	33.15±4.39
LA	
Range	3.9-1.94
Mean+/-SD	1.94±0.54
MR	
NO MR	50 (83.33%)
Trivial or mild MR	8 (13.33%)
Moderate MR	1 (1.67%)
Severe MR	1 (1.67%)

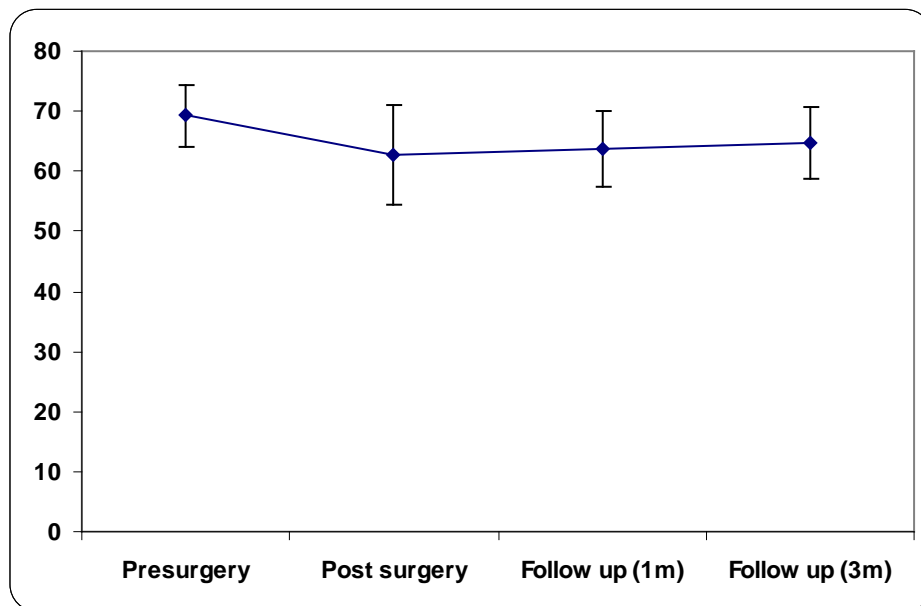
Three month post-operative echocardiography showed decrease in the degree of mitral regurgitation where 83.3% had no mitral regurgitation, 13.3% had trivial or mild mitral regurgitation, 1.6% had moderate mitral regurgitation, and 1.6% had severe mitral regurgitation, 3.3% had residual insignificant shunt.

**Table (7): Difference between presurgical and follow up echocardiography as regards EF (2D)**

TTE	EF (2D)		Paired Diff.		Paired Difference t-test	
	Mean	SD	Mean	SD	t	p-value
Presurgery	69.22	5.27				
Post surgery	62.83	8.27	6.38	9.47	5.220	<0.001
Follow up (1m)	63.77	6.19	5.45	8.32	5.075	<0.001
Follow up (3m)	64.73	5.95	4.48	7.99	4.346	<0.001

This table shows highly statistically significant difference between presurgical and postsurgical follow up as regard EF (2D).

There is postsurgical decrease in ejection fraction found in the predischarge echocardiography followed by increase in ejection fraction 1 month and three month postoperative echocardiography. Three patients had impaired systolic function, 2 patients showed restoration of normal systolic function in 1 and 3 month follow up.

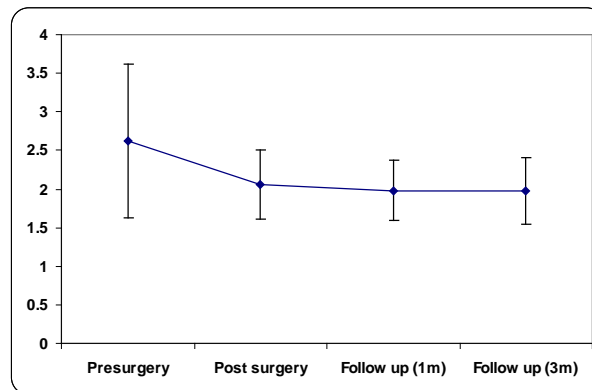


**Fig.(2): Difference between presurgical and postsurgical echocardiography as regard EF (2D).**

**Table (8): Difference between presurgical and follow up echocardiography as regards LVESD**

TTE	ESD		Paired Diff.		Paired Difference t-test	
	Mean	□SD	Mean	□SD	T	p-value
Presurgery	2.62	1.50				
Post surgery	2.06	0.45	0.56	3.67	1.189	0.239
Follow up (1m)	1.98	0.39	0.64	3.63	1.370	0.176
Follow up (3m)	1.97	0.43	0.65	3.66	1.381	0.173

This table shows no statistically significant difference between presurgical and postsurgical echocardiography as regard LVESD.

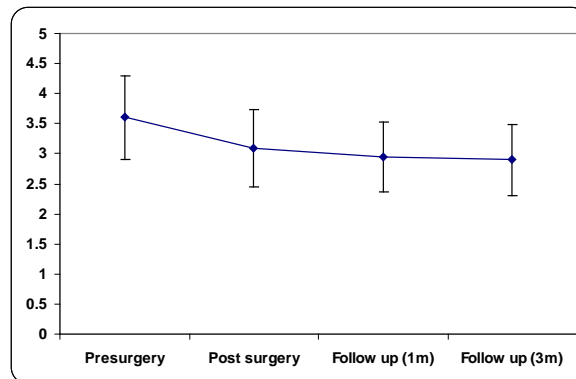


**Fig.(3): Difference between presurgical and postsurgical echocardiography as regard LVESD.**

**Table (9): Difference between presurgical and follow up echocardiography as regards LVEDD**

TTE	EDD		Paired Diff.		Paired Difference t-test	
	Mean	□SD	Mean	□SD	t	p-value
Presurgery	3.60	0.70				
Post surgery	3.09	0.65	0.51	0.46	8.580	<0.001
Follow up (1m)	2.94	0.58	0.66	0.37	13.811	<0.001
Follow up (3m)	2.90	0.59	0.70	0.37	14.519	<0.001

This table shows highly statistically significant difference between presurgery and other category as regard LVEDD.



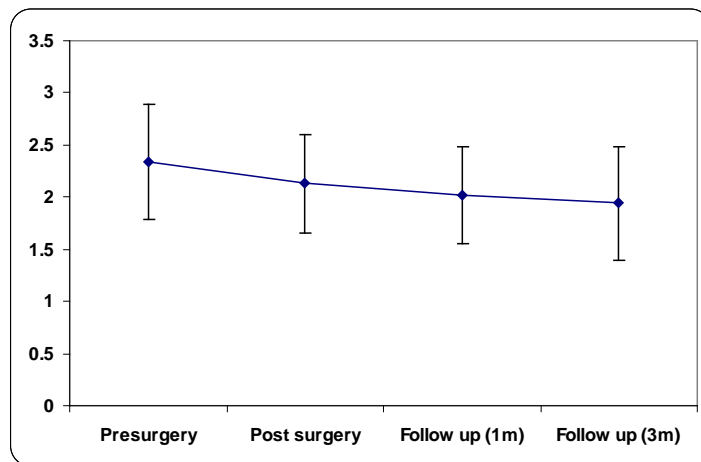
**Fig.(4): Difference between presurgical and postsurgical echocardiography as regard EDD.**

Significant progressive reduction in left ventricular end diastolic diameter in pre-discharge, 1 month, 3 month echocardiography.

**Table (10): Difference between presurgical and follow up echocardiography as regards left atrial diameter**

TTE	LA		Paired Diff.		Paired Difference t-test	
	Mean	□SD	Mean	□SD	t	p-value
Presurgery	2.34	0.55				
Post surgery	2.13	0.47	0.21	0.28	5.853	<0.001
Follow up (1m)	2.02	0.47	0.33	0.35	7.285	<0.001
Follow up (3m)	1.94	0.54	0.41	0.40	7.868	<0.001

This table shows highly statistically significant difference between presurgery and other category as regard left atrium. Significant progressive reduction in left atrial diameter in predischarge, 1 month, 3 month echocardiography.

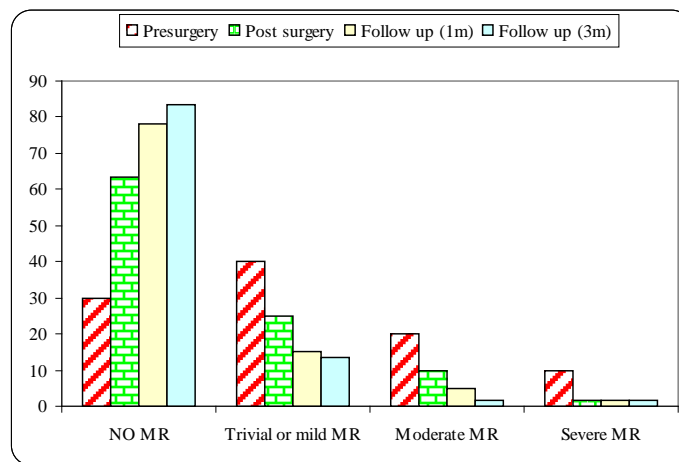


**Fig. (5): Difference between presurgical and postsurgical echocardiography as regard left atrial diameter.**

**Table (11): Difference between presurgical and follow up echocardiography as regards mitral regurgitation**

MR	Presurgery	Post surgery	Follow up (1m)	Follow up (3m)	p-value
NO MR	18 (30%)	38 (63.3%)	47 (78.3%)	50 (83.3%)	<0.001
Trivial or mild MR	24 (40%)	15 (25%)	9 (15%)	8 (13.3%)	
Moderate MR	12 (20%)	6 (10%)	3 (5%)	1 (1.7%)	
Severe MR	6 (10%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard MR. Degree of mitral regurgitation decreased significantly postoperatively.



**Fig.(6): Difference between presurgical and postsurgical echocardiography as regard mitral regurgitation.**



**Table (12): Difference between presurgery and follow up echocardiography as regards EF in patient < 6years**

Age <6 years	EF		Paired Diff.		Paired Difference t-test	
	Mean	□SD	Mean	□SD	t	p-value
Presurgery	69.51	5.47				
Post surgery	63.63	8.91	5.88	10.71	3.923	0.000
Follow up (1m)	64.20	6.42	5.31	9.41	4.035	0.000
Follow up (3m)	64.86	6.46	4.65	8.69	3.819	0.000

This table shows statistically high significant difference between presurgical and postsurgical echocardiography as regard EF in patients younger than 6 years.

**Table (13): Difference between presurgical and follow up echocardiography as regards EF in patient >6years**

Age >6 years	EF(M-mode)		Paired Diff.		Paired Difference t-test	
	Mean	□SD	Mean	□SD	t	p-value
Presurgery	70.67	5.52				
Post surgery	66.89	7.52	3.78	5.14	2.204	0.059
Follow up (1m)	64.56	5.57	6.11	5.06	3.623	0.007
Follow up (3m)	65.89	4.08	4.78	4.02	3.562	0.007

This table shows statistically high significant difference follow up one ,month and three month between presurgical postsurgical echocardiography as regard EF in the patients older than 6 years, no significant difference in pre-discharge.

**Table (14): Difference between presurgical and follow up echocardiography as regards EF in small VSD**

Small VSD	EF (M-mode)		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	70.00	4.30				
Post surgery	65.80	6.61	4.20	6.53	1.437	0.224
Follow up (1m)	66.60	4.16	3.40	8.02	0.948	0.397
Follow up (3m)	66.80	3.03	3.20	4.87	1.470	0.216

This table shows no statistically significant difference between presurgical and postsurgical echocardiography as regard EF.

**Table (15): Difference between presurgical and follow up echocardiography as regards EF in large VSD**

Large VSD	EF (M-mode)		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	69.65	5.57				
Post surgery	63.96	8.94	5.69	10.36	4.073	0.000
Follow up (1m)	64.04	6.40	5.62	8.98	4.641	0.000
Follow up (3m)	64.85	6.34	4.80	8.39	4.244	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard EF in large VSD.

**Table (16): Difference between presurgical and follow up echocardiography as regards ESD in patients < 6 years**

Age (years) = <6 years	ESD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.61	3.93				
Post surgery	1.98	0.41	0.64	3.98	1.140	0.260
Follow up (1m)	1.90	0.36	0.71	3.94	1.284	0.205
Follow up (3m)	1.87	0.39	0.74	3.96	1.329	0.190

This table shows no statistically significant difference between presurgery and other category as regard ESD.

**Table (17): Difference between presurgical and follow up echocardiography as regards ESD in patients > =6 years**

Age (years) >=6 years	ESD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.67	0.41				
Post surgery	2.51	0.39	0.16	0.24	1.941	0.088
Follow up (1m)	2.40	0.29	0.27	0.21	3.881	0.005
Follow up (3m)	2.50	0.21	0.17	0.30	1.644	0.139

This table shows statistically high significant difference follow up one month between presurgical and postsurgical echocardiography as regard ESD in patients older than 6 years, no significant difference in predischarge follow up three month.

**Table (18): Difference between presurgical and follow up echocardiography as regards ESD in small VSD**

Small VSD	ESD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	1.88	0.40				
Post surgery	1.66	0.11	0.22	0.44	1.108	0.330
Follow up (1m)	1.60	0.25	0.28	0.38	1.633	0.178
Follow up (3m)	1.66	0.25	0.22	0.47	1.056	0.351

This table shows no statistically significant difference between presurgical and postsurgical echocardiography as regard ESD.

**Table (19): Difference between presurgical and follow up echocardiography as regards ESD in large VSD**

Large VSD	ESD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.69	3.78				
Post surgery	2.09	0.45	0.59	3.83	1.151	0.255
Follow up (1m)	2.01	0.38	0.67	3.79	1.320	0.192
Follow up (3m)	2.00	0.43	0.69	3.82	1.343	0.185

This table shows no statistically significant difference between presurgical and postsurgical echocardiography as regard ESD.

**Table (20): Difference between presurgical and follow up echocardiography as regards EDD in patients < 6 years**

Age (years) = <6 years	EDD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	3.43	0.59				
Post surgery	2.95	0.57	0.48	0.47	7.313	0.000
Follow up (1m)	2.79	0.47	0.64	0.39	11.814	0.000
Follow up (3m)	2.76	0.49	0.67	0.38	12.517	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard EDD in patients < 6 years.

**Table (21): Difference between presurgical and follow up echocardiography as regards EDD in in patients >= 6 years**

Age (years) >=6 years	EDD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	4.56	0.55				
Post-surgery	3.90	0.47	0.66	0.37	5.298	0.001
Follow up (1m)	3.77	0.40	0.79	0.25	9.574	0.000
Follow up (3m)	3.71	0.41	0.84	0.27	9.233	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard EDD in patients >= 6 years.

**Table (22): Difference between presurgical and follow up echocardiography as regards EDD in small VSD**

Small VSD	EDD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	T	p-value
Presurgery	3.22	0.72				
Post-surgery	2.60	0.24	0.62	0.73	1.901	0.130
Follow up (1m)	2.66	0.25	0.56	0.68	1.840	0.140
Follow up (3m)	2.68	0.25	0.54	0.69	1.737	0.157

This table shows no statistically significant difference between presurgical and postsurgical echocardiography as regard EDD in small VSD.

**Table (23): Difference between presurgical and follow up echocardiography as regards EDD in large VSD**

Large VSD	EDD		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	3.63	0.70				
Post-surgery	3.14	0.66	0.50	0.44	8.489	0.000
Follow up (1m)	2.97	0.59	0.67	0.34	14.671	0.000
Follow up (3m)	2.92	0.61	0.71	0.34	15.700	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard EDD in large VSD.

**Table (24): Difference between presurgical and follow up echocardiography as regards left atrial diameter in patients < 6 years**

Age(years) <6 years	LA		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.22	0.46				
Post surgery	2.05	0.44	0.17	0.25	4.900	0.000
Follow up (1m)	1.93	0.44	0.29	0.34	6.181	0.000
Follow up (3m)	1.84	0.51	0.38	0.40	6.733	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard LA in patients < 6years.

**Table (25): Difference between presurgical and follow up echocardiography as regards left atrial diameter in patients >= 6 years**

Age (years) = >=6 years	LA		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	3.04	0.51				
Post surgery	2.59	0.34	0.46	0.35	3.861	0.005
Follow up (1m)	2.52	0.34	0.52	0.36	4.397	0.002
Follow up (3m)	2.49	0.37	0.56	0.37	4.531	0.002

This table shows statistically significant difference between presurgical and postsurgical echocardiography as regard left atrial diameter in patients >= 6years.

**Table (26): Difference between presurgical and follow up echocardiography as regards left atrial diameter in small VSD**

Small VSD	LA		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.28	0.22				
Post-surgery	1.98	0.15	0.30	0.16	4.243	0.013
Follow up (1m)	2.12	0.48	0.16	0.53	0.673	0.538
Follow up (3m)	1.94	0.13	0.34	0.19	3.900	0.018

This table shows statistically significant difference in pre-discharge and follow up three month as regard left atrial diameter in patients with small VSD, no significant difference in follow up one month..

**Table (27): Difference between presurgical and follow up echocardiography as regards left atrial diameter in large VSD**

Large VSD	LA		Paired Diff.		Paired Difference t-test	
	Mean	±SD	Mean	±	t	p-value
Presurgery	2.35	0.57				
Post-surgery	2.14	0.48	0.21	0.29	5.246	0.000
Follow up (1m)	2.01	0.47	0.34	0.33	7.713	0.000
Follow up (3m)	1.94	0.56	0.41	0.41	7.383	0.000

This table shows highly statistically significant difference between presurgical and postsurgical echocardiography as regard left atrial diameter in patients with large VSD.



## Discussion

The most common form of congenital heart disease in childhood is the VSD, occurring in 50% of all children with congenital heart and in 20% as an isolated lesion disease (Kidd et al., 1993). The incidence of VSDs, which has increased dramatically with advances in imaging and screening of infants, ranges from 1.56 to 53.2 per 1000 live births (Wu et al., 1993).

A defect in the interventricular septum allows communication between the systemic and pulmonary circulations. As a result, flow moves from a region of high pressure to a region of low pressure leading to LV volume overload, Excessive pulmonary blood flow, Reduced systemic cardiac output.

The present study was a prospective study conducted on **60 patients** presenting to National heart institute who met the inclusion criteria aiming at determining the effect on degree of MR preoperatively and improvement of echocardiographic parameters after surgical closure of VSD.

### **The demographic characteristics of the study were as follows**

*In the present study*, mean age of patients was 3 years  $\pm$  3 SD ranging from 3 months to 14 years (Table (1)), weight ranges from 5 to 40 Kg. This is in concordance with the study by Cordell et al., 1976 who studied Left heart volume characteristics following ventricular septal defect closure in infancy in 13 patients with VSD, also in concordance with Jian et al., 2014 who studied 465 children with age 3 to 12 years with perimembranous VSD, and in concordance with the study by Arthur et al., 1965 who studied mitral valve disease and its association with VSD in patients with mean age of 10 years, also in concordance with the study by Hisatomi et al., 1996 who studied the effect of mitral valve repair at the time of VSD surgical closure in 25 patients with VSD mean age  $2.6 \pm 2.3$  years, and the study by Ootaki et al., 2003 who studied closure of trabecular ventricular septal defects by sandwiching technique without ventriculotomy on 11 patients with mean age was 4.7 years.

This is not in concordance with the study by Agarwal et al., 2002 who studied the mortality, morbidity and long-term follow-up of patients undergoing corrective surgery for ventricular septal defect and congenital mitral valve repair in 69 consecutive patients aged 2 months to 45 years, also not in concordance with Mongeon et al., 2010 who studied the indications and outcomes of surgical closure of ventricular septal defect retrospectively 46 adult patients who underwent surgical VSD closure, mean age  $33.6 \pm 11.2$  years.

In the present study, 78% of our patients had perimembranous VSD 3.3% had outlet VSD, 8.3 % had subaortic VSD, 3.4% had muscular VSD, 3.3% had malalignment VSD, and 3.3% had inlet VSD (Table (3), figure (1)). In the study by Hwa et al., 2014 who studied the effect of severity of MR on the speed of improvement of echo parameters after VSD closure on 40 patients, 82.5% of the patients had perimembranous VSD, 15 % had subarterial VSD and 2.5% had muscular VSD. In the study by Jian et al., 2014 all patients had perimembranous VSD.

In the study by Agarwal et al., 2002 75% of the patients had perimembranous and subarterial ventricular septal defects. Mongeon et al., 2010 studied the indications and outcomes of surgical closure of ventricular septal defect retrospectively on 46 adult patients who underwent surgical VSD closure where 72% of patients had membranous VSD, 26% had subarterial VSD. In the study by Hijazi et al., 2000 the location of the VSD was mid muscular in 4 patients, anterior in 2, apical in 1, and posterior in 1 patient.

*In the present study*, most patients had preoperative elevated left ventricular end diastolic diameter, there were highly significant reduction in LVEDD in patients in all age group due to restoration of hemodynamics in the form of decrease in the preload and afterload after removal of shunt burden, except for patients with small VSD who showed no significant reduction in LVEDD in pre-discharge, 1 month, 2 months and three months follow up echocardiography, this is attributed to absence of preoperative elevation of LVEDD in this group of patients (table (9, 20-23), figure (4)) .

This is in agreement with the study by Cordell et al., 1976 who showed that transcatheter preoperative values for LVEDV were elevated in every patient, LVEDV fell to within or just above the normal range following closure of the defect in all except one patient, whose postoperative LVEDV was mildly elevated. The postoperative end-diastolic volumes are not significantly different from normal. The results of the previous study is also in agreement with the study by Jarmakani et al., 1971 who studied the effect of corrective surgery on left heart volume and mass in children with ventricular septal defect through quantitation of left ventricular and left atrial volume, left ventricular ejection fraction and muscle mass in 23 patients an average of 2 years after successful closure of a ventricular septal defect, postoperative Left ventricular end-diastolic volume was significantly decreased from the preoperative value but remained significantly greater than normal , most probably due to partially irreversible changes in the myocardium associated with long-term hypertrophy as none of these patients were less than four years of age at the time of VSD closure. The study of Roos-Hesselink et al., 2004 found that Left ventricular dimensions were normal in 96% of the patients as they followed up 176 consecutive patients 20 to 34 years after surgical closure of isolated ventricular septal defect which was done at young age. Similar results were also found by Hwa et al., 2014 who evaluated the effect of severity of MR on the speed of improvement of echo parameters after VSD closure on 40 patients, the reduction in LVEDV was associated with the severity of MR; where the no MR group showed no significant decrease in the LVEDV index, at any time following closure of the VSD. The mild MR group demonstrated a significant reduction in the LVEDV index at one month, three months, and 12 months postoperatively. The moderate to severe MR group demonstrated a significant reduction in the LVEDV index only at 12 months postoperatively. Pacileo et al., 1998 studied the influence of size of the VSD and age at surgical repair on left ventricular mechanics after closure of ventricular septal defect in 20 patients, it was shown that in the presence of a large ventricular septal defect, early successful surgical repair <2 years of age results in complete recovery of left ventricular mechanics in the postoperative follow-up. These results were not in agreement with the results of our study which showed significant

reduction in LVEDD in all age groups as long as the patient is still operable, this study showed that surgical closure at > 2 years of age, even for a moderately sized ventricular septal defect, deleteriously affects postoperative left ventricular geometry and shape, since prolonged volume overload may be detrimental to myocardial function. Also in agreement with the study by Pawelec et al., 2005 who showed significant reduction in the left ventricular diameter after closure of perimembranous VSD either by catheter or by surgery, the study was carried on 11 children treated with perimembranous VSD occluder implantation and 12 children with surgical repair.

*In the present study*, there was postsurgical decrease in ejection fraction in the pre-discharge echocardiography but most patients were within normal range followed by increase in ejection fraction 1 month and three month postoperative echocardiography most probably due to cardioplegia. Except for patients with small VSD who showed non-significant change in postoperative EF, and three patients had impaired systolic function, 2 patients showed restoration of normal systolic function in 1 and 3 month follow up (table (7, 12-15), figure(2)). This could be attributed to improvement of hemodynamics, reduced volume overload and reverse remodeling as ejection fraction is a useful parameter for measuring cardiac performance, if preload and afterload are constant. Both increased preload and decreased afterload tend to elevate the ejection fraction. The presence of both increased preload, (i.e. LVEDV), and decreased afterload, via ejection across the VSD into the pulmonary circuit, likely contribute to the normal preoperative values for ejection fraction in our patients. Following closure of the defect, both preload and afterload tend to normalize and any intrinsic depression of left ventricular function should become manifest as an abnormally low ejection fraction.

This is in agreement with the study by Cordell et al., 1976 where Left ventricular ejection fraction (LVEF) was close to or within normal limits in all patients preoperatively. Only one patient had a decline in ejection fraction after repair, but her postoperative value remained within normal limits. The postoperative values for LVEF were not significantly different from the preoperative values or from normal.

These results are in agreement with the study of Jarmakani et al., 1971 who reported persistent abnormalities in left ventricular size and pump function in children who had VSDs closed at ages ranging from 3 to 12 years, follow up of these patients confirmed the presence of decreased left ventricular contractility in postoperative VSD patients who had had left to right shunts in excess of 40%, this may be due to the diffuse cardiac sclerosis reported by Krymsky et al., 1965 in various forms of congenital heart disease (including VSD) they reported finding areas of sclerosis in young people, even infants, but reported that "The older a patient is, i.e., the longer the duration of disease, the larger was the degree of cardiac sclerosis." It could be suggested that the better functional status of the infants reported in the study by Jarmakani et al., 1971 is related to the shorter length of time that their hearts were subjected to abnormal work requirements. Other factors should be considered, perhaps the major one is operating room procedure. The patients who made up Jarmakani's study had their VSDs closed in the early and middle 1960s. Operative technique has changed considerably over the past decade with far

greater appreciation being given to the possible permanent effects of myocardial ischemia produced during intra-cardiac manipulation. Our patients had their defects closed using cardiopulmonary bypass and surface cooling with intermittent cross-clamping of the aorta. It is conceivable that the intraoperative procedures used in our patients served to protect their hearts to a greater degree than was possible ten years ago, and that this factor contributed to the better functional result. Another factor that should be considered is the lack of hypertrophy as compared to dilatation. Old methods of cardioplegia and the long time taken to perform the surgery.

The results of the present study are not in agreement with Myrthe et al., 2015 who investigated clinical outcome 30 years after surgical VSD closure on 174 patients during childhood between 1968 and 1980, patients were reexamined every 10 years, the Left ventricular systolic function was impaired but stable in 21% of patients.

In the study by Pawelec et al., 2005 left ventricular EF was significantly lower after surgery than in children treated with the occluder follow-up after 3 and 18 months showed that left ventricular EF was higher in patients after Membr VSDO occluder implantation than after surgical repair of VSD, as there is no cardioplegia during transcatheter closure, in our study the follow up started immediately postoperatively. The results of the present study were not in agreement with the study by Pedersen et al., 2008 who studied 26 children who underwent surgical closure of a ventricular septal defect 11 +/- 2 years postoperatively by use of conventional and tissue doppler echocardiography, comparing the findings to those obtained from a control group to determine the long-term significance of right bundle branch block on left ventricular systolic and diastolic function in children who underwent surgical closure of ventricular septal defect, systolic long axis function was significantly reduced in children after surgical closure of ventricular septal defects, irrespective of the presence of right bundle branch block.

*In the present study*, there was highly significant difference between preoperative and postoperative LAD in the form of reduction in left atrial diameter in patients younger than 6 years, and patients with large VSD, significant difference in patients more than 6 years, pre-discharge and 3 month postoperative follow up. No significant difference in 1 month postoperative follow up (table 10, 24-27, figure (5)). This is in agreement with the study by Hwa et al., 2014 where the no MR group showed a significant decrease in the LA volume index only at three months following closure of the VSD. The mild MR group demonstrated a significant reduction in the LA volume index at one month, three months, and 12 months postoperatively. The moderate to severe MR group demonstrated a significant decrease at three months and 12 months. There was also a significant intergroup difference between the no MR group and the moderate to severe MR group, and between the mild MR group and the moderate to severe MR group.

This is not fully in agreement with the study by (Cordell et al., 1976) where maximal left atrial volume (LAm<sub>ax</sub>) was grossly elevated in all but one patient, whose value was within normal limits, this patient was found to have an atrial level left to right shunt across a patent foramen oval. Although LAm<sub>ax</sub> decreased appreciably following operative repair, the postoperative values remain

mildly, but significantly elevated above normal. Perhaps this is due to permanent changes in elasticity of left atrium occurred preoperatively as a result of marked degree of dilatation, overstretching of the relatively thin-walled atrial chamber could produce such an effect which could prevent a return to a normal volume following relief of the volume load. Same results were conducted in the study by (Jarmakani et al., 1971) where the left atrial maximal volume also was significantly decreased from the preoperative value.

*In the present study*, thirty percent of our patients had no mitral regurgitation, 40% had mild mitral regurgitation, 20% had moderate mitral regurgitation, and 10% had severe mitral regurgitation (table (11), figure (6)).

Degree of mitral regurgitation decreased significantly post-surgery at all grades of pre-surgical mitral regurgitation. Pre-discharge echocardiography showed significant decrease in the degree of mitral regurgitation where 63.3% had no mitral regurgitation, 25% had trivial or mild mitral regurgitation, 10% had moderate mitral regurgitation, and 1.7% had severe mitral regurgitation. One month post-operative echocardiography showed progressive decrease in the degree of mitral regurgitation except for severe mitral regurgitation (1.7%). Three months post-operative echocardiography showed decrease in the degree of mitral regurgitation where 83.3% had no mitral regurgitation, 13.3% had trivial or mild mitral regurgitation, 1.7% had moderate mitral regurgitation, and 1.7% had severe mitral regurgitation (table 11), This can be attributed to reduction in LV volumes and reduction of mitral annular dilatation degree.

The results our study are in agreement with the study by Hwa et al., 2014 where 40% of the patients had no MR, 37.5% had mild MR, and 22.5% of the patients had moderate or severe MR, the study showed that the group which did not have MR preoperatively did not progress to new-onset MR after surgical closure of the VSD. All patients improved regarding the degree of MR. In the mild MR group (n = 15), at one month postoperatively 12 patients had their mitral regurgitation resolved and three patients improved to a trivial degree of MR; only one patient remained with trivial MR until 12 months after surgery. In the moderate to severe MR group (n = 9), at one month postoperatively, MR had resolved in three patients, improved to trivial MR in three patients, decreased from severe to moderate in two patients, and one patient remained with moderate MR. At three months, four patients improved to trivial and three patients remained without MR. At 12 months, MR remained trivial in two patients which supports our results.

The results of the present study are also in agreement with the study by Pawelec et al., 2005 who showed that mitral regurgitation decreased significantly after closure of VSD with the Membranous VSDO. MR was significantly smaller in patients treated with the occluder than in those after surgery.

The results of the present study is not in agreement with the study by Roos-Hesselink et al., 2004 who reported no significant change in mitral regurgitation, the study by Hisatomi et al., 1996 examined the intermediate and long-term follow-up of 25 patients who initially underwent conservative mitral valve repair for mitral regurgitation associated with ventricular septal defect, preoperative degree of mitral regurgitation was mild in 3, moderate in 17, and severe in 5 patients,



Postoperative color Doppler flow imaging was performed 12 years after operation in 22 of the 23 survivors, showed no mitral regurgitation in 4, mild regurgitation in 14, and moderate regurgitation in 4 patients. Four patients had mitral stenosis most probably iatrogenic due to overcorrection, with a mean transmitral pressure gradient greater than 10 mm Hg. The residual lesion of moderate mitral regurgitation developed in 6 of 11 patients in whom bilateral mitral annuloplasty was applied after the initial operation, this is attributed to tight annuloplasty which is avoidable as our study showed significant decrease in degree of functional mitral regurgitation without repair of mitral valve

*In the present study*, no postoperative mortality neither reoperation occurred. This is in agreement with the study by Gan et al., 2008 where there was no mortality perioperatively or during the entire follow-up period. This is not in agreement with the study by Agarwal et al., 2002 where 3 patients died due to pulmonary arterial hypertensive crisis and 1 due to residual mitral stenosis. One death was due to intractable congestive heart failure. Another patient died due to persistent low cardiac output, Reoperation was required in 22 patients, mainly for recurrent/residual mitral valve dysfunction. The results of the present study are not in agreement with the study by Mongeon et al., 2010 although no early death, yet late mortality was 5% (mean follow-up: 10.3 +/- 12.4 years) due to arrhythmia, heart failure, endocarditis, during valvular surgery, noncardiac causes, and unknown causes. The results of the present study are not in agreement with those reported by Khan et al., 2006 where overall early mortality was 6.25% due to pulmonary hypertensive crisis, there have been no late deaths.

*In the present study*, twelve patients had residual VSD at pre-discharge echocardiography, 7 patients had insignificant residual shunt at 1 month follow-up, 4 patients had residual shunt at 3 month follow-up. The results of the present study are also in agreement with the study by Mongeon et al., 2010 where residual VSD was found in 7 patients, late residual VSDs were more common after suture closure (6 of 8 patients). The use of intraoperative transesophageal echocardiography was associated with fewer residual VSDs. Our results were also in agreement with the study by Ootaki et al., 2003 where no residual shunt was found in 3 patients, and a minimal residual shunt was observed in 5 patients, Mild residual shunt was observed in 3 patients. Our results are also in agreement with Hijazi et al., 2000 they reported that 6 patients had trivial residual shunt, which disappeared completely within 24 hour in five and at 6-month follow-up in the sixth patient. The results of the present study is not in agreement with those reported by Stellin et al., 2000 where no significant residual shunt at ventricular level was detected by postoperative two-dimensional and Doppler echocardiography.

*In the present study*, postoperative arrhythmias occurred in 4 patients who had immediate postoperative complete heart block requiring transient pacemaker, 3 patients return to normal sinus rhythm within 7 days this is due to tissue edema during surgical manipulation and only 1 patient require permanent pacemaker most probably due to injury of conduction system . The results of the present study are also in agreement with the study by Mongeon et al., 2010 where high-grade atrioventricular block requiring permanent pacemaker occurred in 1 patient. Our results are also in agreement with the study by Gan et al., 2008 where 3 patients developed

arrhythmia in the form of incomplete right bundle branch blocks early and at 6 months follow-up. Also Hijazi et al., 2000 reported transient junctional rhythm occurred in 1 patient.

*In the present study*, there were marked relief of symptoms in all our patients during follow-up. Similar results were conducted by Stellin et al., 2000 they reported that all the patients were asymptomatic and growing well at a mean follow-up of 18 months. This is due to decreased remodeling and significant restoration of nearly normal hemodynamics after closure of VSD.

## Conclusion

From the present study we conclude that surgical closure of VSD in infancy results in improvement of Left ventricular ejection fraction and reduction of left ventricular and atrial dimensions, and this was shown with all degrees of preoperative mitral regurgitation.

With lower degrees of preoperative mitral regurgitation, improvement in left ventricular systolic function and dimensions is more rapid and significant.

There is improvement of degree of mitral regurgitation after surgical correction of ventricular septal defect.

**Study limitations:** This study was a single center study, number of patients recruited was limited, patients with associated defects were excluded due to relatively small number of patients so the effect of associated defects was not studied.

## References

- Agarwal S and Airan B, et al. Ventricular septal defect with congenital mitral valve disease: long-term results of corrective surgery. *Indian Heart J.* 2002 Jan-Feb; 54(1):67-73.
- Arthur Hollman and Hamedt et al. mitral valve disease with ventricular septal defect. *Brit. Heart J.*, 1965, 27, 274.
- Clark EB and Driscoll DJ et al. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents Including the Fetus and Young Adult.* Philadelphia, Pa: Lippincott Williams & Wilkins; 2001; 1: 64–79.
- Cordell D and Graham Jr et al. Left heart volume characteristics following ven-tricular septal defect closure in infancy. *Circulation.* 1976; 54:294-8.
- Fu YC and Bass J et al. Transcatheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occlude. *J Am CollCardiol.* Jan 17 2006; 47(2):319-25.
- Gan C and Lin K et al. Periventricular device closure of ventricular septal defects. *Ann Thorac Surg.* 2008 Jul; 86(1):142-6

- Hijazi ZM and Hakim F et al. Transcatheter closure of single muscular ventricular septal defects using the amplatzer muscular VSD occluder: initial results and technical considerations. *Catheter Cardiovasc Interv.* 2000 Feb; 49(2):167-72.
- Hisatomi K and Isomura T et al. Mitral valve repair for mitral regurgitation with ventricular septal defect in children. *Ann Thorac Surg.* 1996 Dec;62(6):1773-7.
- Hwa Jin Choa and Jae Sook Maa et al. Timing in resolution of left heart dilation according to the degree of mitral regurgitation in children with ventricular septal defect after surgical closure. *Pediatr (Rio J).* 2014;90(1):71--77.
- Jarmakani J and Graham TP et al. The effect of corrective surgery on left heart volume and mass in children with ventricular septal defect. *Am J Cardiol* 27: 254, 1971.
- Jian Yang and Lifang Yang et al. Transcatheter Versus Surgical Closure of Perimembranous Ventricular Septal Defects in Children, the American College of Cardiology, 2014, Foundation ISSN 0735-1097 Vol. 63, No. 12.
- Roos-Hesselink JW and Meijboom FJ et al. Outcome of patients after surgical closure of ventricular septal defect at young age: longitudinal follow-up of 22–34 years. *European heart, 2004- Eur Soc Cardiology*
- Khan IU and Mufti WA et al. Ventricular septal defect in infants and children with increased pulmonary vascular resistance and pulmonary hypertension--surgical management: leaving an atrial level communication, *J Ayub Med Coll Abbottabad.* 2006 Oct-Dec; 18(4):21-5.
- Kidd L and Driscoll DJ et al. Second natural history study of congenital heart defects. Results of treatment of patients with ventricular septal defects. *Circulation.* Feb 1993; 87(2 Suppl):I38-51.
- Kizer J and Bella JN et al. Left atrial diameter as an independent predictor of first clinical cardiovascular events in middle-aged and elderly adults: the Strong Heart Study (SHS). *Am Heart J.* 2006;151:412-8.
- Mahadin DR and Srivastava S et al. Outcomes of mitral regurgitation associated with large ventricular septal defect and a normal mitral valve apparatus: does intact atrial septum have an impact? *Pediatr Cardiol.* 2011; 32:1128-31.
- Matsuhisa H and Yoshimura N et al. Ventricular septal dysfunction after surgical closure of multiple ventricular septal defects, *Ann Thorac Surg.* 2013 Sep;96(3):891-7.
- Moller JH and Moodie DS et al. Symptomatic heart disease in infants: comparison of three studies performed during 1969–1987. *Pediatr Cardiol.* 1995; 16: 216–222.
- Mongeon FP and Burkhart HM et al. Indications and outcomes of surgical closure of ventricular septal defect in adults, *JACC Cardiovasc Interv.* 2010 Mar; 3(3):290-7.
- Myrthe E. and Judith A.A.E. et al. Unnatural History of the Ventricular Septal Defect Outcome Up to 40 Years after Surgical Closure *J Am Coll Cardiol.* 2015;65(18):1941-195.
- Ootaki Y and Yoshimura N et al. Surgical management of trabecular ventricular septal defects: the sandwich technique, *J Thorac Cardiovasc Surg.* 2003 Mar; 125(3):508-12.



- Pacileo G1 and Pisacane C et al. Left ventricular mechanics after closure of ventricular septal defect: influence of size of the defect and age at surgical repair. *Cardiol Young*. 1998 Jul; 8(3):320-8.
- Pawelec-Wojtalik and Wojtalik M et al. Closure of perimembranous ventricular septal defect using transcatheter technique versus surgical repair. *Pol*. 2005 Dec; 63(6):595-602; discussion 603-4.
- Pedersen TA and Andersen NH et al. The effects of surgically induced right bundle branch block on left ventricular function after closure of the ventricular septal defect, *Cardiol Young*. 2008 Aug; 18(4):430-6.
- Senzaki H and Kumakura R et al. Left atrial systolic force in children: reference values for normal children and changes in cardiovascular disease with left ventricular volume overload or pressure overload. *J Am Soc Echocardiogr*. 2009;22:939-46.
- Stellin G and Padalino M et al. Surgical closure of apical ventricular septal defects through a right ventricular apical infundibulotomy. *Ann Thorac Surg*. 2000 Feb; 69(2):597-601.
- Ueda Y and Fukushige J et al. Congestive heart failure during early infancy in patients with ventricular septal defect relative to early closure. *Pediatr Cardiol*. 1996; 17:382-6.
- Wu MH and Wu JM et al. Implication of aneurysmal transformation in isolated perimembranous ventricular septal defect. *Am J Cardiol*. Sep 1 1993; 72(7):596-601.