Thi-Qar Medical Journal (TQMJ):Vol.(27),No.(1),2024

Web Site: https://jmed.utq.edu Email: utjmed@utq.edu.iq

ISSN (Print):1992-9218

Outcome of VSD Surgery in Ibn Al-Nafees Teaching Hospital

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Abstract

Overview

The presentation of unrepaired VSDs is largely dependent on the presence of hemodynamically significant shunt. The murmur of VSD is typically pan-systolic best heard in the left lower sternal border; it is harsh and loud in small defects but softer and less intense in large ones. (TTE) is the most valuable tool for diagnosis due to its high sensitivity. Approximately 85% to 90% of small isolated VSDs close spontaneously during the first year of life. Surgical repair reduces the risk for endocarditis, might improve PAH, and overall, it increases survival.

Aim of the study: Is to evaluate the result of surgical closure of VSD in Ibn Al-Nafees teaching hospital.

Patients and methods: This is a retrospective study for surgically managed patients with ventricular septal defect in single center done in cardiac center, Ibn Al-Nafees teaching hospital during the period from January 2020 till December 2021. The documents of 50 patients were studied in our center during 2 years only. Patients who met the criteria of the study were included. The other patients were excluded from the study mainly those who had more complex cardiac anomalies, including tetralogy of Fallot, atrioventricular septal defect and coarctation of aorta.

Result: The youngest patient was 3 year while the oldest one was 28 years. The mean age group was 15 years. The lowest body weight was 13 kg while the highest was 80 kg. Only 15 patients had cardiac catheterization and most of them had other associated anomalies like ASD , aortic incompetence, subaortic ridge , PS , etc.

86% of patients have had pulmonary hypertension from mild to moderate to severe degree while those with PS protect the pulmonary circulation from pulmonary hypertension. The material of patch used was Dacron patch for all cases. The shortest cross clamp time was 19 minutes while the longest was 125 minutes. The shortest cardiopulmonary bypass time was 44 minutes while the longest time was 185 minutes. In our study aortic valve prolapse and regurgitation was the most common associated anomalies present in 20% of the patients. In our study 2 patients died.

Conclusion: Still we have adult congenital heart diseases like VSD or other congenital heart diseases which become very rare in developed countries. Mortality rate of 4%. Although it is high than the standard which is 0-1% in advanced cardiac centers.

Introduction

Ventricular Septal Defect (VSD)

Is the most common congenital cardiac anomaly in children and is the second most common congenital abnormality in adults, second only to a bicuspid aortic valve. An abnormal communication between the right and left ventricles and shunt formation is the main mechanism of hemodynamic compromise in VSD. While many VSDs close spontaneously, if they do not, large defects can lead to detrimental complications such as pulmonary arterial hypertension (PAH), ventricular dysfunction, and an increased risk of arrhythmias.[1][2][3] VSDs were first identified by Dalrymple in the year 1847.[4]

Etiology

VSD develops when there is a developmental abnormality or an interruption of the interventricular septum formation during the complex embryologic heart morphogenesis. VSDs are frequently isolated; however, they can occur in association with other congenital heart defects such as atrial septal defects, patent ductus arteriosus, right aortic arch, and pulmonic stenosis.
They are also found in cases of aortic coarctation and sub-aortic stenosis, and they are a frequent component of complex congenital heart disease such as Tetralogy of Fallot and transposition of great arteries. Several genetic factors have been identified to cause VSDs including chromosomal, a single gene, and polygenic inheritance. A TBX5 mutation was recently discovered to cause septal defects in patients with Holt-Oram syndrome. Non-inherited risk factors have been implicated in the development of VSDs; these include maternal infection (rubella, influenza, and febrile illness), maternal diabetes mellitus, and phenylketonuria. Exposure to toxins like alcohol, marijuana, cocaine, and certain medications such as metronidazole and ibuprofen are also linked to VSDs.[5][6]

Epidemiology

Isolated VSD accounts for 37% of all congenital heart disease in children.

The incidence of isolated VSD is about 0.3% of newborns. Because as many as 90% may eventually close spontaneously; the incidence is significantly lower in adults. VSDs have no gender predilection.[7]

Pathophysiology

The interventricular septum is an asymmetric curved structure due to the pressure difference in ventricular chambers. It is composed of five parts: the membranous, muscular (frequently referred to as trabecular), infundibular, atrioventricular, and the inlet.[8][9]

Failure of development or fusion of one of the above components during morphogenesis of the embryonic heart results in a VSD in the corresponding component. Different anatomic locations and histologic variations of VSDs have led to several classifications and nomenclature systems. Complexities in describing VSDs and multiple synonyms have been improved after a new unified classification was established and categorized VSDs into four major groups:

Type 1: (infundibular, outlet) This VSD is located below the semilunar valves (aortic and pulmonary) in the outlet septum of the right ventricle above the crista supraventricularis, which is why it is sometimes also referred to as supracristal. It is the most uncommon type representing only 6% of all VSDs with the exception being in the Asian population where it accounts for approximately 30%. Aortic valve prolapse and regurgitation are common because of loss of support of the right and/or the noncoronary cusps of the aortic valve. It is unusual for these defects to close spontaneously.

Type 2: (membranous) This VSD is, by far the most common type, accounting for 80% of all defects. It is located in the membranous septum inferior to the crista supraventricularis. It often involves the muscular septum when it is commonly known as peri membranous. The septal leaflet of the tricuspid valve sometimes forms a “pouch” that reduces the shunt and can result in spontaneous closure.

Type 3: (inlet or atrioventricular canal) This VSD is located just inferior to the inlet valves (tricuspid and mitral) within the inlet part of the right ventricular septum. It only represents 8% of all defects. It is seen in patients with Down syndrome.

Type 4: (muscular, trabecular) This VSD is located in the muscular septum, bordered by muscle usually in the apical, central, and outlet parts of the interventricular septum. They can be multiple, assuming a “Swiss cheese” appearance. They represent up to 20% of VSDs in infants. However, the incidence is lower in adults due to the tendency of spontaneous closure.

The main pathophysiologic mechanism of VSD is shunt creation between the right and left ventricles. The amount of blood shunted and the direction of the shunted blood determine the hemodynamic significance of the VSD. These factors are governed by the size, location of the VSD, and pulmonary vascular resistance.

While VSDs are classified according to location, they can also be classified into size. The size is described in comparison to the diameter of the aortic annulus. They are considered small if they measure less or equal to 25% of the aortic annulus diameter, medium if they measure more than 25% but less than 75%, and large if they are greater than 75% of the aortic annulus diameter.

In the setting of long-standing large left-to-right shunts, the pulmonary vascular endothelium undergoes irreversible changes resulting in persistent PAH. When the pressure in the pulmonary circulation exceeds the pressure in the systemic circulation, the shunt direction reverses and becomes a right-to-left shunt. This is known as Eisenmenger syndrome occur in 10% to 15%.

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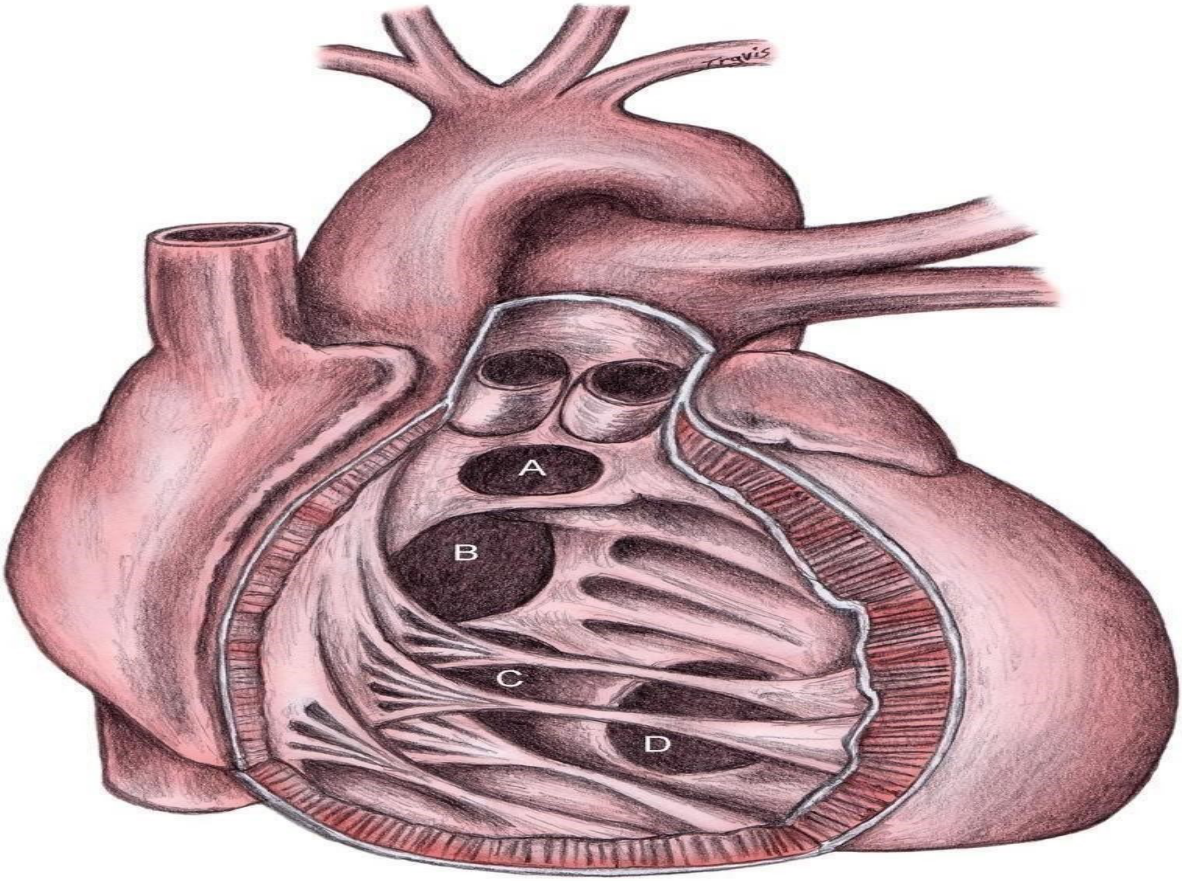

Figure (1.1): Classification of VSD: Schematic representation of the location of various types of ventricular septal defects (VSDs) from the right ventricular aspect. A = Doubly committed sub arterial ventricular septal defect; B = Peri membranous ventricular septal defect; C = Inlet or atrioventricular canal-type ventricular septal defect; D = Muscular ventricular septal defect. [10]

History and Physical examination

The presentation of unrepaired VSDs is largely dependent on the presence of hemodynamically significant shunt; hence it is directly related to the size of the defect. Small VSDs only lead to the minimal left-to-right shunt without left ventricular (LV) fluid overload or PAH; they are usually asymptomatic or found incidentally on physical exam. Medium size VSDs result in a moderate LV volume overload and absent to mild PAH; they present late in childhood with mild congestive heart failure (CHF). Those with large defects develop CHF early in childhood due to the severe LV overload and severe PAH. The murmur of VSD is typically pan-systolic best heard in the left lower sternal border; it is harsh and loud in small defects but softer and less intense in large ones.

Handgrips increase afterload, increasing the strength of the murmur. Infundibular defects are best heard in the pulmonic area. A diastolic decrescendo murmur and wide pulse pressure can be detected in the setting of aortic regurgitation. Increased LV flow may result in the mid-diastolic rumble in the lower left sternal border. A systolic click of a septal aneurysm can be appreciated sometimes in membranous defects. Eisenmenger syndrome manifests in cyanosis, desaturation, dyspnea, syncope, secondary erythrocytosis, and clubbing; in such cases, the typical murmur of VSD can be absent and accentuated pulmonic component of the second heart sound may be heard.

Evaluation[11][12]

- **Color Doppler transthoracic echocardiography**

(TTE) is the most valuable tool for diagnosis due to its high sensitivity. Color Doppler TTE can detect up to 95% of VSDs, especially non-apical lesions larger than 5 mm; it provides morphologic information such as size, location, and the number of the defects as well as hemodynamic information such as jet size, severity, and estimation of pulmonary artery pressure. TTE is useful in detecting any associated aortic insufficiency and other associated congenital heart defects. Lastly, TTE is also helpful in evaluating the right and left ventricular chamber size and function. Limitations include operator dependence and poor acoustic window. When conventional TTE is equivocal, a trans-esophageal echo (TEE) is recommended.

- **Electrocardiography (ECG)**

Is entirely normal in half of the patients with VSD. When the ECG is abnormal, it may detect LV hypertrophy in those with large shunts. In patients with PAH, the ECG may show right bundle branch block, right axis deviation, and right ventricular (RV) hypertrophy and strain.

- **Chest radiography (CXR)**

s often normal in those with small defects. Enlarged cardiac silhouette can be observed in those with larger defects and increased LV size. RV enlargement and increased pulmonary diameter can be observed in those with PAH.

- **Cardiac magnetic resonance imaging(MRI)** and **computed tomography(CT)** Are useful in cases where anatomy is complex such as VSD accompanied with other congenital heart anomalies and in defects in unusual locations that are hard to visualize by conventional TTE.

- **Cardiac catheterization**

Gives accurate hemodynamic information regarding the pulmonary vascular resistance and response to vasodilators; this is particularly useful in those who are being evaluated for surgical closure. It provides more details on coexisting aortic regurgitation, in multiple VSDs, and when coronary artery disease is suspected.

Treatment / Management

Approximately 85% to 90% of small isolated VSDs close spontaneously during the first year of life. Patients with small, asymptomatic VSDs with the absence of PAH have an excellent prognosis without any intervention. Otherwise, the management approach includes VSD closure.[13]

Patients with Eisenmenger syndrome are usually managed in advanced centers due to the complexity of managing such cases. Historically, surgical repair of VSDs was the only option; however, recent advances in interventional techniques make percutaneous VSD closure possible. It is no longer recommended for patients with unrepaired ventricular septal defects to be routinely prescribed antibiotic prophylaxis for infective endocarditis.[13] Endocarditis prophylaxis is mainly indicated in cyanotic congenital heart disease, prior episodes of endocarditis, and in those who have prosthetic heart valves or had repair with prosthetic material. In general, VSD closure is indicated in medium to large defects with a significant hemodynamic compromise such as those who are symptomatic and have LV dysfunction. An intervention should be also considered in cases of progressive aortic insufficiency or after an episode of endocarditis. The indications of a surgical closure according to the ACC/AHA 2008 guidelines are summarized in the following:

- Those who suffered an episode of endocarditis.

- When the ratio of the pulmonary blood flow to the systemic blood flow (Qp/Qs) is equal to or more than 2 plus clinical evidence of LV fluid overload.
- In milder shunts such as those with Qp /Qs above 1.5, it is reasonable to intervene when there is evidence of LV systolic or diastolic dysfunction, or when the pulmonary artery pressure and pulmonary vascular resistance are less than two-thirds of systemic pressure and systemic vascular resistance, respectively

Surgical repair reduces the risk for endocarditis, might improve PAH, and overall it increases survival. Without PAH, the operative mortality rate is approximately 1%. Complications include residual or recurrent VSD, valvular incompetence such as tricuspid regurgitation and aortic insufficiency, arrhythmias, LV dysfunction, and progression of PAH. The arrhythmias which accompany VSD repair include atrial fibrillation, complete heart block, and uncommonly, ventricular tachycardia. The main contraindication for surgical VSD closure is the presence of

irreversible PAH; this is due to the high surgical perioperative mortality and pulmonary complications.[14]

Percutaneous device VSD closure is reserved for those whose surgery is very risky due to severe PAH, multiple comorbidities, and those who had prior cardiothoracic surgery such as residual or recurrent VSD. Muscular VSDs are the main type amenable to this procedure, the proximity of other defects to the inlet valves makes performing this technique challenging in such cases. Despite the fact that it is still unpopular in the United States, current data shows excellent outcomes with complete closure and low mortality. The most frequent complication is complete atrioventricular block mostly related to peri membranous defects.[15] In conclusion, VSD is the most common congenital anomaly at birth. Small defects are expected to close spontaneously in the first year of life; however, larger defects can result in severe complications. Surgical VSD closure and device closure are the main intervention for large defects.[16]

Prognosis

The prognosis is good for patients who have undergone VSD repair. However, they have a higher risk of arrhythmia, endocarditis, and congestive heart failure in the long run in comparison to the general population.[16]

Aim Of the Study

Is to evaluate the result of surgical closure of VSD in Ibn Al-Nafees teaching hospital.

Patients and Methods

This is a retrospective study for surgically managed patients with ventricular septal defect in single center done in cardiac center, Ibn Al-Nafees teaching hospital during the period from January 2020 till December 2021. The documents of 50 patients were studied in our center during 2 years only. All of them had echocardiography study and only 15 case had cardiac catheterization. 14 of them were isolated VSD while the other 36 cases were VSD with other associated congenital heart disease. Patients who met the criteria of the study were included. The other patients were excluded from the study mainly those who had more complex cardiac anomalies, including tetralogy of fallot, atrioventricular septal defect and coarctation of aorta. History taking, physical examination and laboratory finding were recorded for all the patients. After confirmation of diagnosis, patients were scheduled for intervention. The information of our patients were retrospectively collected from information recorded from patient's medical files or surgeon s notes with permission from the institution. The preoperative characteristics including age, sex, weight, type of VSD were examined. Depending on transthoracic echocardiography, VSD were divided into four group, perimemberanous, muscular, doubly committed and multiple. All the patient underwent median sternotomy and cardiopulmonary bypass. The used surgical technique, aortic cross clamp time and

bypass time were assessed. Surgical outcome and complications including bleeding, residual VSD, heart block, wound infection were assessed. Prior to discharge and during hospital stay transthoracic echocardiography had been done to assess the surgical outcome.

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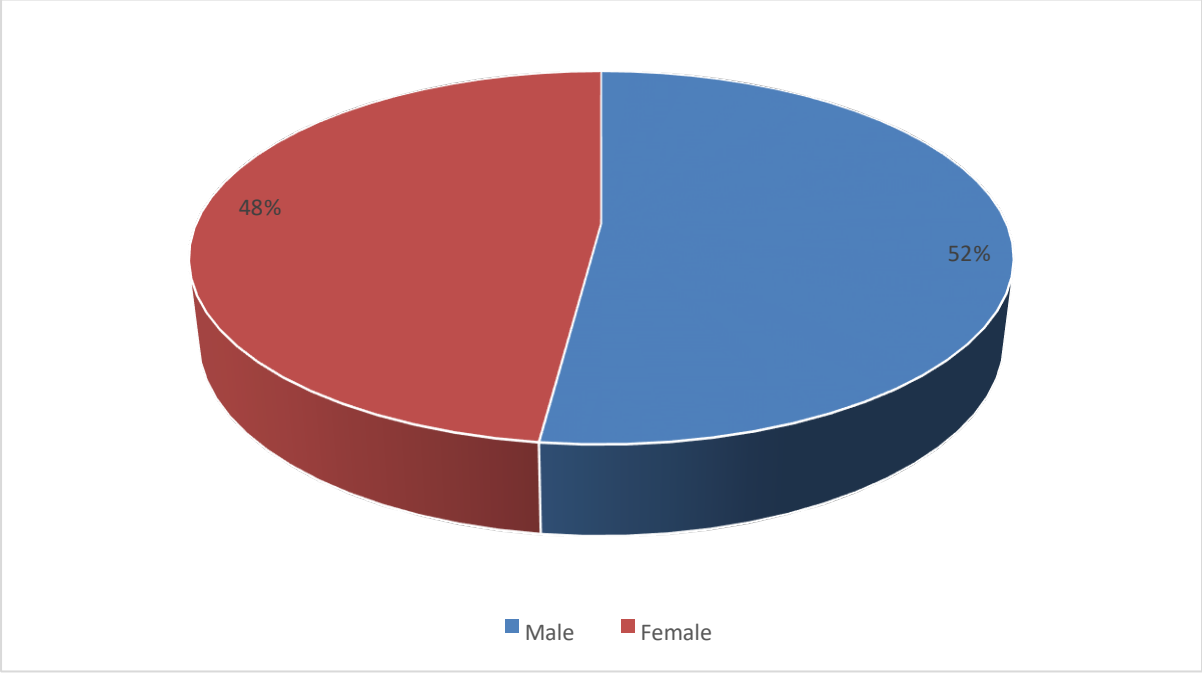
ISSN (Print):1992-9218

:RESULTS

Table 3.1: Age distribution

Age	NO.	Percentage
5-3	12	%24
10-5	18	%36
15-10	10	%20
20-15	7	%14
25-20	2	%4
30-25	1	%2

The youngest patient was 3 year while the oldest one was 28 years. The mean age group was 15 .years



FIGUREe :Sex Distribution **3.1S** .

Body weight :**3.2**

Body weight	Number of cases	percentage
Kg 15-13	5	%10
Kg 20-15	14	%28
Kg 25-20	19	%38
Kg 30-25	4	%8
Above 30 Kg	8	%16

The lowest body weight was 13 kg while the highest was 80 kg.

Table 3.3: Cardiac Catheterization

	Number of cases	percentage
With catheterization	15	%30
Without cathterizatiom	35	%70

Only 15 patients had cardiac catheterization and most of them had other associated anomalies like ASD , aortic incompetence, subaortic ridge , PS , etc.

Table 3.4: Types of VSD

Type of VSD	Number of cases	Percentage
Conoventricular defect (perimembranous (defect	40	%80
Subaortic subpulmonic defect (outlet defect)	3	%6
Inlet septal defect (atrioventricular canal type defect)	5	%10
Muscular defect (trabecular defects)	2	%4

3.5: VSD with or without pulmonary hypertension

	Number of cases	**Percentage**
VSD without PS	**43**	**%86**
VSD with PS	**7**	**%14**

86% of patients have had pulmonary hypertension from mild to moderate to severe degree while those with PS protect the pulmonary circulation from pulmonary hypertension

Table 3.6: Associated anomalies

Associated anomalies	**Number of cases**	**percentage**
Pulmonary stenosis	**7**	**%14**
Aortic valve prolapse	**10**	**%20**
Aortic regurgitation	**10**	**%20**
Subaortic ridge	**2**	**%4**
Atrial septal defect	**7**	**%14**

Table 3.7: Surgical approach

Surgical approach	**Number of cases**	**percentage**
Transatrial (right atrium)	**35**	**%70**
Transventricular (right ventricle)	**13**	**%26**
Transpulmonic	**2**	**%4**

Types of closure :**3.8**

Type of closure	Number of cases	percentage
Patch	**45**	**%90**
Direct closure	**5**	**%10**

The pericardial patch was used in all cases.

Table 3.9: Aortic cross clamp time

Time	Number of cases	percentage
45minutes-30	**15**	**%30**
minutes 60-45	**19**	**%38**
minutes 75-60	**7**	**%14**
minutes 90-75	**5**	**%10**
Above 90 minutes	**4**	**%8**

The shortest cross clamp time was 19 minutes while the longest was 125 minutes.

Table 3.10: Cardiopulmonary bypass time

Time	Number of cases	percentage
Below 60 minutes	**14**	**%28**
minutes6 90-60	**23**	**%46**
minutes 120-90	**5**	**%10**
Above 120 minutes	**8**	**%16**

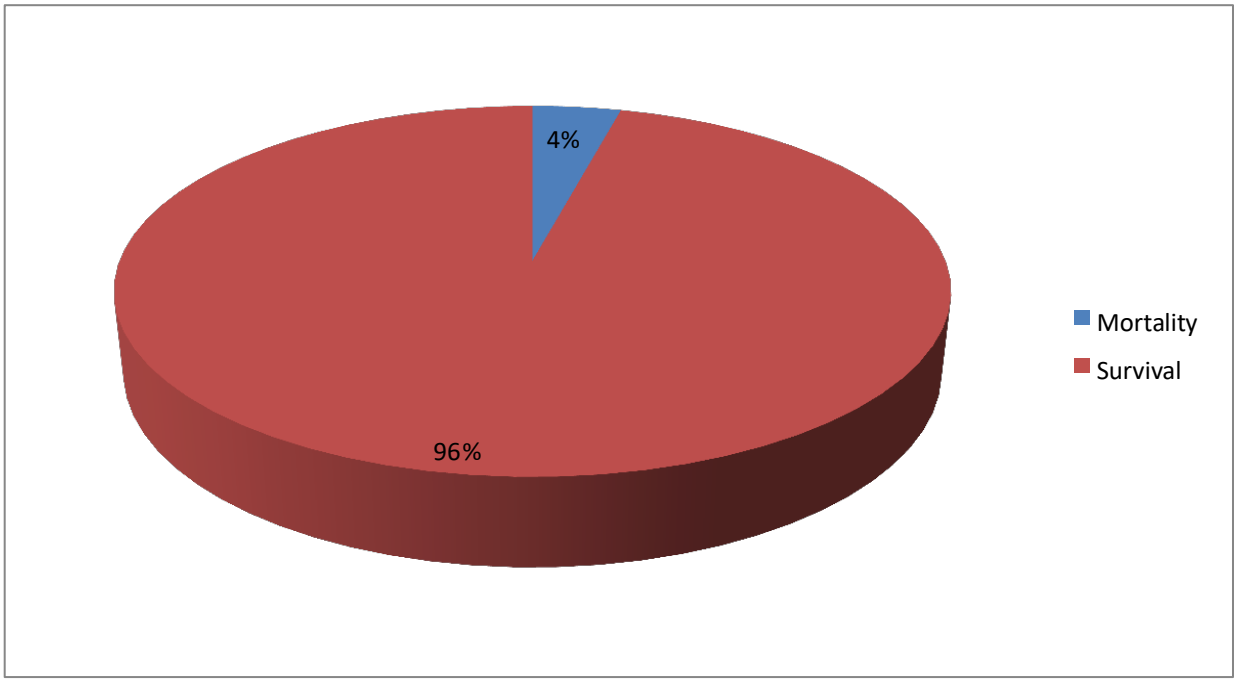
The shortest time was 44 minutes while the longest time was 185 minutes.

Table 3.11: Additional surgeries

Additional surgery	Number of cases	percentage
Pulmonary valvotomy	3	%6
Outflow patch for RVOT	4	%8
Closer of Atrial septal Defect	7	%14
Excision of subaortic Ridge	2	%4
Aortic valve replacement	2	%4

Table 3.12: Complication of surgeries

Complication	Number of cases	percentage
Atelectasis	15	%30
Arrhythmias	10	%20
Heart block	8	%16
Low cardiac output syndrome	7	%14
Pulmonary hypertension	6	%12
Renal impairment	4	%8
Bleeding	3	%6
Wound infection	3	%6
Encephalopathy	2	%4
Residual leak	2	%4



Discussion

A total of 50 patients underwent surgical closure of VSD. The youngest patient was 3 year while the oldest one was 28 years. The mean age group was 15 years. This is different from the study done in Utrecht University Netherlands where the median age at operation was 168 days. [17] In our study 52% of patients were male. The male to female ratio was 1.1:1. This is comparable to the study done in Netherland where the male to female ratio was 1:1. The lowest body weight was 13 kg and the highest was 80 kg. This is different from Utrecht university study where the median weight at operation was 6 kg. This difference regarding the body weight and age can be attributed to deficiency in our center to deal with patients less than 10 kg in weight. Only 15 patients had cardiac catheterization and most of them had other associated anomalies like ASD, aortic incompetence, subaortic ridge, pulmonary stenosis, etc. cardiac catheterization is recommended when there is suspicion of pulmonary hypertension and increased pulmonary vascular resistance and also in complex cardiac anomalies. In our study the most common type of VSD was the perimembranous defect (80%) and the less common type was the muscular (4%). This is comparable to the study done in Freeman hospital in the UK northern region. This is due to the fact that perimembranous defects are larger than muscular defect and even when they are small they have less chance to close spontaneously at age of six years. [18] Pulmonary stenosis was present in 14% and this protect against pulmonary hypertension which present in 86% of patients. In our

study aortic valve prolapse and regurgitation was the most common associated anomalies present in 20% of the patients. All the patients underwent median sternotomy and cardiopulmonary bypass. VSD was closed by taransatrial approach in 70% of the patients, transventricular approach in 26% and transpulmonic approach was needed in the remaining. Based on their own experience the surgeons decided whether to use patch or close the defect with direct stiches. In our study 90% of VSD were closed by pericardial patch and direct closure was used in only 10%. While in the

Utrecht University study, patch was used in 80%. [17] Due to associated pulmonary stenosis, pulmonary valvotomy was needed in 6% and outflow patch for RVOT in 8%. Associated atrial septal defect was closed in 14 % and excision of subaortic ridge in 4%. Aortic valve replacement was needed in 2 patients due to aortic valve prolapse and combined aortic regurgitation.

The shortest aortic cross clamp time was 19 minutes and the longest was 125 minutes. The shortest cardiopulmonary bypass time was 44 minutes and the longest time was 185 minutes.

In our study atelectasis was the most common complication seen in 30%. Most of them were treated by expectorant and proper chest physiotherapy. While in Utrecht university study atelectasis was seen in 14%.[17]

Arrhythmias was seen in 20% in the form of sinus tachycardia, ventricular ectopic, sinus bradycardia and right bundle branch block while in the study done in turkey arrhythmia was seen in 8.1%. [19]

Heart block was seen in 8 patients (16%). 7 patients (14%) needed only temporary pacemaker lasting for few days and permanent pacemaker was needed in only one patient (2%). while in Utrecht university study transient block was seen in
4.9% and permanent block in 0.8%.[17]

Low cardiac output syndrome was seen in 7 patients (14%). Most of them were treated by supportive medical treatment.

3 patients (6%) developed wound infection who were treated by proper antibiotic and daily dressing while in Utrecht university study the incidence of wound infection was 4%.[17]

Bleeding was seen in 2patients (4%). One patient was treated conservatively and re exploration is needed in the second patient.

Residual VSD which is defined as flow across the ventricular septum assessed by echocardiography after operation was seen in 2 patients (4%). The leak was small and

hemodynamically insignificant. While in Utrecht university study re exploration for residual VSD was needed in 2.1%. [17]

Renal impairment was seen in 4 patient (8%). All of them were treated conservatively.

In our study 2 patients died. One in the 6thpostoperative day due to hypertensive pulmonary crisis and the second one due to encephalopathy so the operative mortality was 4% while in Utrecht university study the operative mortality was 0%.[17]

Conclusions

1. Still we have adult congenital heart diseases like VSD or other congenital heart diseases which become very rare in developed countries.
2. Mortality rate of 4%. Although it is high than the standard which is 0-1% in advanced cardiac centers.
3. The majority of cases were diagnosed only by echocardiography unlike years ago when for every case catheterization was done.
4. The earlier surgery done for VSD yield better outcome to prevent pulmonary hypertension.

Recommendations

1. More experience is needed to deal with small babies with congenital heart disease whose body weight less than 10 kg.
2. More facilities are needed to deal with surgery of congenital heart disease for example intraoperative (TEE) transesophageal echocardiography which is used routinely now all over the world.

References

1- Ghosh S, Sridhar A, Solomon N, Sivaprakasham M. Transcatheter closure of ventricular septal defect in aortic valve prolapse and aortic regurgitation. Indian Heart J. 2018 Jul - Aug;70(4):528-532. [PMC free article] [PubMed]

2- Hopkins MK, Goldstein SA, Ward CC, Kuller JA. Evaluation and Management of Maternal Congenital Heart Disease: A Review. Obstet Gynecol Surv. 2018 Feb;73(2):116-124. [PubMed]

3- Kenny D. Interventional Cardiology for Congenital Heart Disease. Korean Circ J. 2018 May;48(5):350-364. [PMC free article] [PubMed]

4- Ammash NM, Warnes CA. Ventricular septal defects in adults. Ann Intern Med. 2001 Nov 06;135(9):812- [PubMed] .24

5- Muthialu N, Balakrishnan S, Sundar R. Single patch closure of multiple VSDs through right atrial approach. .Indian Heart J. 2018 Jul - Aug;70(4):578- 579
[PMC free article] [PubMed]

6- Durden RE, Turek JW, Reinking BE, Bansal M. Acquired ventricular septal defect due to infective endocarditis. -Ann Pediatr Cardiol. 2018 Jan
Apr;11(1):100-102. [PMC free article] [PubMed]

7- Pinto NM, Waitzman N, Nelson R, Minich LL, Krikov S, Botto LD. Early

Childhood Inpatient Costs of Critical Congenital Heart Disease. J Pediatr. 2018 Dec; 203:371- 379.e7. [PubMed]

8- Patel ND, Kim RW, Pornrattanarungsi S, Wong PC. Morphology of intramural ventricular septal defects: Clinical imaging and autopsy correlation. Ann Pediatr Cardiol. 2018 Sep-Dec;11(3):308-311. [PMC free article] [PubMed]

9- Lopez L, Houyel L, Colan SD, Anderson RH, Béland MJ, Aiello VD, Bailliard F, Cohen MS, Jacobs JP, Kurosawa H, Sanders SP, Walters HL,

10- Weinberg PM, Boris JR, Cook AC, Crucean A, Everett AD, Gaynor JW, Giroud J, Guleserian KJ, Hughes ML, Juraszek AL, Krogmann ON,

11- Maruszewski BJ, St Louis JD, Seslar SP, Spicer DE, Srivastava S, Stellin G, Tchervenkov CI, Wang L, Franklin RCG. Classification of Ventricular Septal Defects for the Eleventh Iteration of the International Classification of Diseases-Striving for Consensus: A Report From the International Society for Nomenclature of Paediatric and Congenital Heart Disease. .Ann Thorac Surg. 2018 Nov;106(5):1578-1589

12- Szkutnik; et al. (2007). "Use of the Amplatzer muscular ventricular septal defect occluder for closure of perimembranous ventricular septal defects". .Heart. 93: 355–358

13- Maagaard M, Heiberg J, Eckerström F, Asschenfeldt B, Rex CE, Ringgaard S, Hjortdal VE. Biventricular morphology in adults born with a ventricular septal defect. .Cardiol Young. 2018 Dec;28(12):1379-1385

14- Hadeed K, Hascoët S, Karsenty C, Ratsimandresey M, Dulac Y, Chausseray G, Alacoque X, Fraisse A, Acar P. Usefulness of echocardiographic-fluoroscopic fusion imaging in children with congenital heart disease. Arch .Cardiovasc Dis. 2018 Jun - Jul;111(6-7):399-410

15- Sendi P, Hasse B, Frank M, Flückiger U, Boggian K, Guery B, Jeger R, Zbinden S, Agyeman P, Knirsch W, Greutmann M. Infective endocarditis: prevention and antibiotic prophylaxis. Swiss Med Wkly. 2021 Feb .w20473:151;15

16- Garg N, Nayyar M, Khouzam RN, Salem SA, Ardeshna D. Peri- procedural antibiotic prophylaxis in ventricular septal defect: a case study to re-visit guidelines. Ann Transl Med. 2018 Jan;6(1):18.

17- Cresti A, Giordano R, Koestenberger M, Spadoni I, Scalese M, Limbruno U, Falorini S, Stefanelli S, Picchi A, De Sensi F, Malandrino A, Cantinotti M. Incidence and natural history of neonatal isolated ventricular septal defects: Do we know everything? A 6-year single-center Italian experience follow-up. Congenit Heart Dis. 2018 .Jan;13(1):105-112

18- Cantinotti M, Assanta N, Murzi B, Lopez L. Controversies in the definition and management of insignificant left-to-right shunts. .Heart. 2014 Feb; 100(3):200-5

19- Maartje Schipper, Martijn G. Slieker, and Johannes M. P. J. Breur. Surgical repair of ventricular septal defect; Contemporary results and risk factors for complicated course.

20- S W Turner, S Hunter, J P Wyllie. The natural history of ventricular septal defects.

21- Erkut Ozturk,Hasan Candas Kafali Yakup Ergul Turkish journal of thoracic and cardiovascular surgery.