

## Natural History of isolated Ventricular Septal Defects in the first two years of life

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### الخلاصة

تقييم نتائج الفتحات المنفردة بين البطينين بالنسبة للانسداد التلقائي او صدغ الحجم في السنتين الاولى من العمر.

تمريضاً لخمسة وستين (56) طفلاً لديهم فتحة قلبية ولادية منفردة بين البطينين والمراجعين لمستشفى بابل للنسائية والاطفال التعليمي وتمت دراستهم مستقبلياً من كانون 2008 الى كانون 2010 لدراسة لظهور الفتحات المنفردة بين البطينين. وبينت النتائج كما يلي:-

معظم المرضى كانت فترة المراجعة خلال الاشهر الثلاثة الاولى من العمر (90%).

• ان غالبية الفتحات من النوع الغشائي (68%) كانت الفتحات المتوسطة الحجم 56% من عدد الفتحات الكلي.

• الضغط الشرياني الرئوي يعتمد على حجم وليس على النوع للفتحة القلبية. الانسداد الكلي خلال السنتين الاولى من العمر كان 64% من عدد الكلي لصدغ الحجم في الفتحات 20%.

اغلقت الفتحات من الذوع الغشائي في السنتين الاولى من العمر بنسبة 73.5% وصدغرت بالحجم بنسبة 26.5% ما اغلقت الفم من الذوع العضلي في السنتين الاولى من العمر بنسبة 70% وصغررت بالحجم بنسبة 10%.

اسدنتج اذا انسداد ذات الطبع في لفتحة القلوب المنفردة ما بين البطينين خلال السنتين الاولى بالنسبة للذوع الغشائي والعضلي بينما ما لا يدت الانسداد بالنسبة للنوع الداخلي والخارجي. الكلمة المرجعية:

التاريخ الطبيعي ، الفتحة بين البطينين ، العلاج الطبي ، الانسداد الجراحي .

### Abstract

**Objective:** To evaluate the natural history of isolated ventricular septal defects in the first two years of life.

**Patients and Methods:** We prospectively studied a total of 50 infants diagnosed as isolated ventricular septal defect between january 2008 -january 2009.

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Infants aged less than three months, with isolated ventricular septal defects were followed for two years. Infants with Down syndrome, other types of ventricular septal defect and those who had an additional hemodynamic significant heart defects were excluded.

**Results:** A total of 50 infants 30 males vs. 20 females (60% vs. 40%) were followed up for 24 months. The mean age at the time of diagnosis was forty days  $\pm$ 5 days (Range: 1 day-3.0 months). 34 patients (68.0%) had membranous, 10 patients (20.0%) had muscular, 4 patients (8.0%) had inlet and 2 patients (4.0%) had outlet ventricular septal defects. There were 16(32.0%) small, 28(56.0%) moderate, and 6(12.0%) large size defects. 7 of muscular defects closed spontaneously, 2 were closed surgically and 1 remained open but decrease in size (70.0%, 20.0%, and 10.0% respectively). On the other hand 25 of membranous defects closed spontaneously and 9 defects remained open by the end of the study ((74.0%),(26.%) respectively). Regardless of type all small 16(32.0%) not required medical treatment, 34(68.0%) of moderate and large size defects needed medical and/or surgical treatment in the first two years of life but by the end of follow up 16(32.0%) defect closed spontaneously and 10(20.0%) defects had their size decreased, all of them of moderate size.

**Conclusion:** Infants with muscular ventricular septal defects have better prognosis in the 1<sup>st</sup> year but spontaneous closure with membranous is more in the 1<sup>st</sup> 2 years and infants with moderate and large ventricular septal defects usually need medical and/or surgical treatment.

Key Words: Natural history, Ventricular Septal Defects,, Medical Therapy, Surgical Closure.

### **Introduction**

Ventricular septal defect (VSD) is the most common congenital cardiac abnormality found in children, if one

excludes a bicuspid aortic valve from consideration(2% of population)<sup>1-7</sup>.

A definitive diagnosis and localization of ventricular septal defect by Doppler color flow mapping in infancy is important for prognosis, counseling and from surgical point of view.<sup>3-5</sup>

VSD classified anatomically into *perimembranous VSD*(80%),*muscular VSD*(5-20%),*inlet VSD* (5-8%),*outlet VSD*(5-7%) also classified according to defect size large (>10mm); moderate(5-10mm); small(<5mm)<sup>2,7,8</sup>.

The natural history of VSD has a wide spectrum, ranging from spontaneous closure or reduction in size to congestive heart failure (CHF) and recurrent respiratory tract infections to death in early infancy.<sup>2,4</sup>

Spontaneous closure usually occurs by age 2 years and uncommon after age 4 years although spontaneous closure has been reported in adults, closure is most frequently observed in muscular defects (80%), followed by perimembranous defects (35-40%) and more in small defect(30-50%) than others, outlet ventricular septal defects have a low incidence of spontaneous closure, and inlet ventricular septal defects do not close,<sup>2,4,9-13</sup>.Diagnosis in early life is a prerequisite for early surgery in children with pulmonary hypertension at risk for the development of pulmonary obstructive disease.

Closure may occur by means of hypertrophy of the septum, formation of fibrous tissue, sub aortic tags, apposition of the septal leaflet of tricuspid valve, or (in rare cases) prolapsed of a leaflet of the aortic valve.<sup>(4,14-16)</sup>

A small ventricular septal defect that does not spontaneously close is generally associated with a good prognosis, risk for infective endocarditic, risk of prolapsed of the aortic cusp over time(per membranous) and small risk of arrhythmia were reported.<sup>5, 17- 21</sup>

### **Aims of the Study**

To evaluate the prognosis of our patients with isolated VSDs at their first Two years of life .

### **Patients and Methods**

Between: January2008 to January2009, we diagnosed a total of 50 infants with isolated ventricular septal defect as their primary cardiac lesion. All infants had been referred to pediatric cardiology clinic, Babylon maternity and children teaching hospital for cardiac evaluation. The causes of referral were: heart murmur found during routine neonatal examination, tiring on feeding, tachypnea, dyspnea, and poor weight gain ,those infants were referred from in patients or out patients . Infants included in the study are those who have isolated ventricular septal defect and less than three months at the time of diagnosis .Infants with ventricular septal defects with other cardiac lesions, infants with Down syndrome and those who don't fulfill the inclusion criteria were excluded from the study.

All patients had a complete history and physical examination by pediatric cardiologist, performed at a mean age of (40 ± 5days ) range: 1 day -3 months . The echocardiogram examination was performed using sonosite machine. Two sub-costal views, parasternal long-and short-axis, and apical four chamber-views, with 8 & 12-MHz transducer focused appropriately for the size of the infant, were performed in all patients. Color Doppler flow mapping was also performed in each view and continuous-wave interrogation of flow velocity was obtained from abnormal jets.

Defect size was often given in terms of the size of the aortic root. Defects that were about the size of the aortic root were classified as large(>10mm), those one third to two thirds of the diameter of the aortic roat are moderate(5-10mm), and

those less than one third of the aortic root diameters were regarded as small defect(<5mm).

The pulmonary artery pressure was regarded as normal between 20-25mm Hg, mild pulmonary hypertension between 25-40mm Hg, moderate pulmonary hypertension between 40-60mm Hg and severe pulmonary hypertension above 60mm Hg. It assessed by Doppler echocardiography which allow estimation of

pulmonary artery pressures by measuring tricuspid regurgitation velocity and pulmonary regurgitation velocity .

Pulmonary artery pressure = RV systolic pressure = 4 (peak velocity )<sup>2</sup> + RA pressure (RA pressure normal value = 8-10mm Hg ) .

VSDs were classified as muscular or membranous according to their location and relation to the tricuspid annulus and semilunar valves. Patients were followed at approximately 6 months peroid till 24 months of age. The VSD was considered spontaneously closed if echocardiogram of the ventricular septum was normal, and the characteristic murmur was no longer heard.

The following statistical methods were used:

1-Descriptive statistics (Mean , Graphics) .

2- Statistical tests (Chi – square test) .

3- SPSS(version 10) .

P\_value >0.05 means no significant difference , p\_value ≤ 0.05 means significant difference<sup>27</sup>.

## **Results**

A total of 50 infants were included in the study all of them were followed up for 24 months. There were 30 males and 20 females (60 % vs. 40%) with male to female ratio 1.5:1 , P-value< 0.05. The mean age at the time of diagnosis was forty days ±5 days (range 1 day- 3.0 months). Thirtyfor(68%) patients had membranous type VSD, 10 (20%)patients had muscular VSDs ,4(8%) and 2(4%) patients had inlet and outlet VSDs respectively (P- value< 0.05) –Fig. 1.

According to size and irrespective of type 28 (56%) had moderate size defect, followed by small and large defects, 16 (32%) and 6 (12%) respectively with no significant difference ( $P\text{-value} > 0.05$ ) -Fig.2.

Table I: show that Perimembranous type VSD had presented as small size in 9 (26.5%), moderate size 25 (73.5%) and there is no large size. Muscular type VSD had presented as small size in 7 (70%), moderate size 1 (10%) and large size 2 (20%). Inlet type had presented as moderate and large size in 2 (50%) for each of them. Outlet had presented only as large size 2 (100%).

Table 2: show that pulmonary blood pressure was normal in small size VSDs while in moderate size rang from normal 22(78.5%), mild 3(10.7%) to moderate 1(3.6%) to sever2(7.1%) and moderate to sever in large VSDs 4(66.7%),2(33.3%).Also it display that pulmonary blood pressure in perimembranousVSDs defects it vary from normal 31(91.2%)- to mild3(8.8%) while in muscular from normal 7(70%) to moderate 2(20%) to sever 1(10%) and in inlet and out let from moderate to sever{1(25%),3(75%)} in inlet and 1(50%) for each in out let.During follow-up 3(30.0%) patients of those with muscular defects need medical treatment, two of them referred for surgical closure of the defect to control symptoms of heart failure and severe pulmonary hypertension and 1(10%) remained open and need medical treatment but became of smaller size at the end of the study. On the other hand among patients with membranous VSDs no surgical closure were clinically indicated during period of fallow up, 25(74.0%) patients required medical treatment, 16 grow out of their treatment before end of study and in 9(26%) patients medical therapy (furosemide and digoxin) were continued beyoned end of the study. For patients of inlet and outlet all of them required medical and surgical treatment.

The remaining VSDs were either closed spontaneously or decreased in size. In case of muscular VSDs, 7(70.0%) had closed spontaneously. Twenty five infants (74.0%) with

membranous defects had their defects closed spontaneously and in 9(26%) defects remained open but decrease in size by the end of the study .For inlet and outlet non of them closed spontaneously or decrease in size during our study and 2 (30.0%) of them were dead.

According to size and irrespective of type,there were a total of 16(.32%) infants with small VSDs and 34(68.0 %) with moderate size or large VSDs. All patients with small VSDs closed with out medical treatment while all moderate and large VSDs required medical therapy (furosemide and digoxin) to control their symptoms of heart failure or pulmonary hypertension at some time after the age of four weeks. Medical treatment continue and needed in 18(36.0%) patients with moderate and large defects by the end of the study , eight(44.0%) of them referred to surgical therapy .

*Table 3* show No. of closed VSDs during the first 2 year of life ,it was 32 (64%) and total No. of decreased VSDs size was 10 (20%) . 18 (36%) Patients with VSDs which had not been closed developed complications in form of heart failure 10(20%), aneurysm 4(8%) , aortic regurgitaion 2(4%) , and death 2(4%).

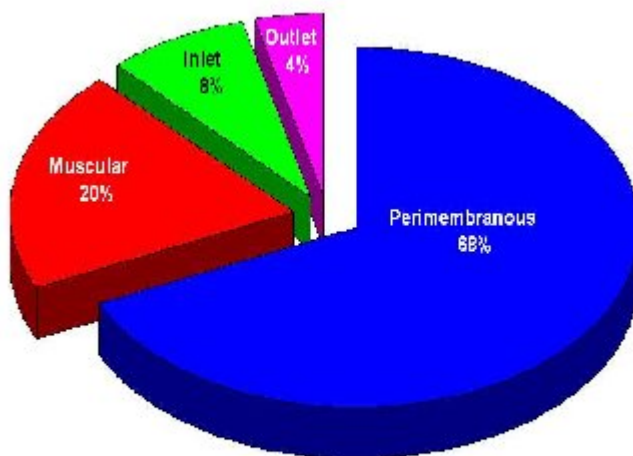
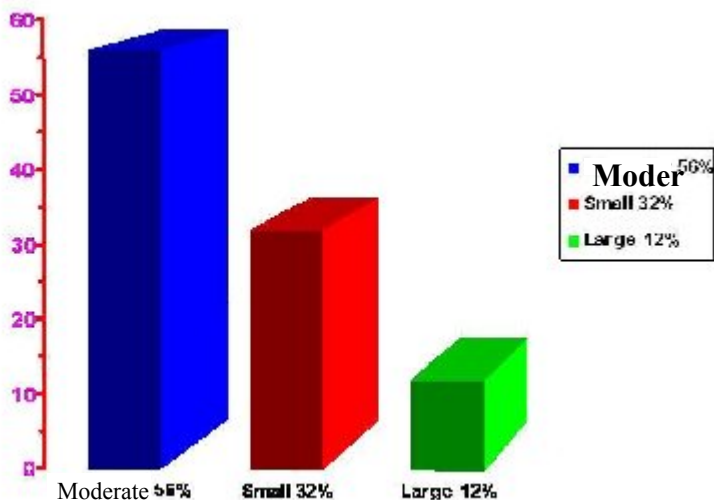


Fig. 1 Distribution of patients according to types of VSD.





**Fig. 2** Distribution of patients according to size of VSD .

**Table (1)** Distribution of cases according to type and size of VSDs .

Type of VSD	Size of VSD			Total No.
	small	Moderate	Large	
	No. (%)	No. (%)	No. (%)	
Perimembranous	9 (26.5%)	25 (73.5%)	0 (0%)	34
Muscular	7 (70%)	1 (10%)	2 (20%)	10
Inlet	0 (0%)	2 (50%)	2 (50%)	4
Outlet	0 (0%)	0 (0%)	2 (100%)	2

**Table (2)** Changes in pulmonary blood pressure of the cases according to type and size of VSDs.

Type of VSD	Pulmonary blood pressure				Total No.
	Normal	Mild	Moderate	Severe	
	No. (%)	No. (%)	No. (%)	No. (%)	
perimembranous	31 (91.2%)	3 (8.8%)	0 (0%)	0 (0%)	34
Muscular	7 (70%)	0 (0%)	2 (20%)	1 (10%)	10
Inlet	0 (0%)	0 (0%)	1 (25%)	3 (75%)	4
Outlet	0 (0%)	0 (0%)	1 (50%)	1 (50%)	2
Size of VSD					
Small	16(100%)	0(0%)	0(0%)	0(0%)	16



Moderate	22(78.5%)	3(10.7%)	1(3.6%)	2(7.1%)	28
Large	0(0%)	0(0%)	4(66.7%)	2(33.3%)	6

**Table (3) Time (age)of closure and changes in size of VSDs according to its type and size .**

Type of VSD	Closure <1year	Closure 1-2year	Total No.(%)	DecreaseIn size(%)
	No. (%)	No. (%)		
perimembranous	14 (41.2%)	11 (32.3%)	25(73.5%)	9(26.5%)
muscular	5 (50%)	2 (20%)	7(70%)	1(10%)
inlet	0 (0%)	0 (%0)	0	0
outlet	0 (0%)	0 (0%)	0	0
Total	19(59.37%)	13(40.6%)	32(64%)	10(20%)
<b>Size of VSD</b>				
Small	14(87.5%)	2(12.5)	16(100%)	-
Moderate	5(17.85%)	11(39.28)	16(57.3)	10(35.7)
Large	0	0	0	0

**Discussion**

The natural history of ventricular septal defects (VSDs) showed that these defects rarely close after the age of two years and the closure depends to a large degree on the size of the defect, in addition in the presence of a large ventricular septal defect early diagnosis and early successful surgical repair is the only way of preventing the development of pulmonary obstructive disease<sup>1-3</sup>. Successful surgical repair of large and moderate ventricular septal defects in the first two years of life will result in complete recovery of left ventricular function and geometry to normal levels when compared to repair after age of two years.<sup>3,4</sup> Hence first two years of life are crucial in a patient with isolated ventricular septal defects.

The results of our study are in agreement with other studies, regarding time of first presentation, (93% )of our patients present in the 1<sup>st</sup> 3months of age more common between 1- 3 months (60%) , this related to hemodynamic changes due to changes in pulmonary resistance which doesn't occur until 4-6 weeks of age so the auscultatory turbulence of VSDs flow will be apparent<sup>1-5</sup>. Also for type of VSDs Our

study show that the perimembranous type VSD was the most common type followed by muscular type , inlet type and least common type was outlet type (68% ,20%8% 4%) respectively this finding compatabile with others.<sup>1,4-13</sup>

But in our study, there was significant difference regarding gender with predominance of male (60% vs.(40%)for female . This was differ from others.<sup>2,4,6</sup> *Rasheed A.R. study* showed female preponderance (54%) vs. male (46%) with no significant difference , our finding might be related to sample size and to care of some families which more for male than female so they bring him early.

Our study show the frequency of VSD defects is moderate, small , large size VSD ( 56% ,32%, 12%) respectively, this differ fom other studies as Eroglu-A G et al study in which reported small, moderate and large size (76%,18%,6%) respectively .This study and others shows that large size defect was lower incidence as our study and show small size defect were higher incidence than moderate which differ from our finding<sup>4,5,9-14-19</sup> . This lowe frequency of small VSD in our study migt be explained on base of that some Patients with small defects did not seeking medical advice because they are asymptomatic .

In our study we found pulmary pressure is affected by size of VSD defects rather than type this in agreement with *other sudies*<sup>1,2,5,15-20</sup> . Normal pulmonary artery pressure was recorded in all Paients with small and most of moderate size VSDs, and moderate to severe pulmonary hypertension was recorded in moderately large and large size VSDs this can be explained by small and moderate VSD restricted the left to right shunts , while in large defects , there is essentially no resistance to flow across VSD with systemic pressure in both ventricles and pulmonary artery so early indication of surgical correction of large VSD to prevent progressive pulmonary vascular obstruction<sup>20,21</sup> .

Membranous ventricular septal defect often achieve partial closure with a layer of tissue underneath the tricuspid valve

that form over the membranous ventricular septal defect, adherent septal leaflet of tricuspid valve and high tendency of aneurysmal transformation while all muscular type VSD was closed by end to end mechanism and this is similar to the result reported by *Anderson et al*<sup>14</sup>.

Spontaneous closure of ventricular septal defect varies directly with their size and location. The overall spontaneous closure rate for VSDs defects in the 1<sup>st</sup> two years of life, in our study was 64.0%, these findings are in conformity with the observation by other authors.<sup>4,5,9,17,20,21</sup> Our study has also showed that spontaneous closure rate for membranous defects was (73.5%), for muscular type was (70%), but the closure of muscular is more frequent in the 1<sup>st</sup> year (50.0% vs 41.0% in membranous). While none of the other defects were closed, this finding is not in agreement with other studies which show higher rate of closure for muscular defects as study by *Eroglu-A G et al*<sup>1</sup> show that spontaneous closure in the first 2 year of life in perimembranous was 18%, muscular type 52%<sup>21,22,23</sup>. This difference might be explained on small sample size besides that in our study the membranous VSD, the defects were small (26.6%) and moderate (73.5%) in size and no large defects and the closure in small and moderate type are high<sup>1,2,4,5,21-24</sup>.

Our study also shows that medical and/or surgical therapy was needed in 3 (30.0%) patients with muscular while a higher percentage 25 (74%) of those with perimembranous VSDs needed medical therapy and/or surgery and all 6 (100.0%) patients of those with inlet and outlet VSDs needed medical therapy and/or surgery during the two-year period of follow-up and our results showed that all small size 16 (100%) patients closed during follow-up while 16 (57.1%) defect of moderate size closed spontaneously and the remaining patients with the moderate defects 12 (42.8%) were remained open and need medical treatment (digoxin + furosemid) but 10 of them became of smaller size by the end of the study and none of large size (6) defects closed or showed change in size (2 of

them were dead near the end of the study) this finding in *agreement with other studies*<sup>20-26</sup>.

In the second natural history study of congenital heart defects (NHS-2), 23% of moderate size VSDs closed spontaneously while among the 14 who had severe VSDs on entry to the study, were managed medically. Only one VSD apparently closed spontaneously and eight patients (57.1%) developed Eisenmenger syndrome.<sup>26</sup> In Turner et al. group of patients only one large ventricular septal defect closed spontaneously.<sup>12</sup>

### **Conclusion**

In infants

- muscular VSDs close spontaneously at a rate higher than perimembranous VSDs in 1<sup>st</sup> year and carry a better prognosis.
- But In the first two years of life perimembranous muscular VSDs close spontaneously at a rate little bit higher than muscular VSDs .
- All small VSDs closed spontaneously non of them need medical and /or surgical treatment while Majority of moderate and large VSDs need medical and /or surgical treatment in infancy.

### **Recommendation**

All infants should be examined in the 1<sup>st</sup> 3 months of age . Clinicians should be alerted to the presence of murmur & refer them to the nearest hospital for further evaluation.

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