Study of clinical profile and outcome of ventricular septal defects diagnosed in infancy

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ABSTRACT

Objective: The objective of the study was to study the clinical profile and outcome of isolated ventricular septal defect (VSD) among infants visiting the departments of pediatrics and pediatric cardiology of the government hospital of South India. Infants with newly detected VSD were registered. Data regarding age at presentation, mode of detection, antenatal, natal and postnatal history, and development and growth were collected. Relevant investigations including echocardiography were done. Babies were followed up 6 monthly. At least one follow-up was done for each child with a maximum of three follow-ups unless VSD closed spontaneously. The data were analyzed using R statistical language and conclusions were drawn. **Results:** Almost equal gender ratio was observed. Gestational diabetes mellitus was seen in 23% of mothers. Family history of congenital heart disease was seen in 12% of patients and 5% had syndromic association. Perimembranous type of VSD was found to be the most common (52%). Small VSDs were seen in 62% of patients among which most were muscular (61%). Among the large VSDs, 57% were perimembranous. Overall, 46.2% of VSD closed spontaneously and nearly 10% reduced in size. Spontaneous closure rate was 80% for muscular VSD and 25% for perimembranous VSD. **Conclusion:** The moderate to large perimembranous defects and inlet and subpulmonic types of VSD are unlikely to close. These defects if detected moderate to large might be advised for early surgical closure. During parental counseling, the excellent long-term natural history of small VSDs, both muscular and perimembranous, could be emphasized, whereas those with moderate VSDs need to be kept under close follow-up and might require surgical closure.

Key words: *Natural history, Spontaneous closure, Surgical closure, Ventricular septal defects*

Ventricular septal defect (VSD) is the most common congenital heart disease among infants and children with the incidence of 20% [1]. Perimembranous VSD is the most common type of ventricular defect. The major determinant of the physiologic state of the patient as well as natural history of VSD is the size of the defect. Pulmonary vascular resistance determines the magnitude of shunt in infancy [1]. A large number of small defects close spontaneously. Moderate-sized defects might also close spontaneously, though to a lesser extent and might develop large left to right shunt in infancy with resultant risk of heart failure. Large defects usually do not close and result in heart failure in infancy itself. A number of other complications such as failure to thrive (FTT), recurrent respiratory infections, and development of pulmonary vascular occlusive disease are more likely with large defects.

Complete evaluation of natural history is important to decide the management of VSD. Larger defects with uncontrolled heart failure, FTT, and recurrent respiratory infections need early surgery, irrespective of the age of the child. If symptoms are controlled with drugs, they could be kept under close medical follow-up as there is always a chance of a spontaneous closure for perimembranous and muscular VSD. Inlet and outlet VSD would not close spontaneously and, hence, should be considered for early surgery if they are moderate-large. While under follow-up, frequent review is needed, especially in large VSD due to the risk of the development of dreaded complication of Eisenmenger syndrome. Even small VSD needs follow-up as they are at risk of developing infective endocarditis and aortic cusp prolapse which are indications of surgical closure of these VSDs.

The natural history of VSD has been earlier studied inpatient cohorts using cross-sectional echocardiography and color flow mapping. It has been observed that spontaneous closure is unlikely to occur in large VSDs, inlet and outlet VSDs, and those associated with Down syndrome. Small and muscular defects tend to close spontaneously more frequently than others [2,3]. The primary objective of the study was to assess the natural history of isolated VSD among infants visiting the departments of pediatrics and pediatric cardiology at a government hospital of South India.

MATERIALS AND METHODS

This is a prospective cohort study conducted at the departments of pediatrics and pediatric cardiology at a government Hospital of South India. The study was conducted during February 2012-October 2013. It included infants with newly diagnosed isolated VSD. The exclusion criteria were VSD in more than 1 year of age and associated with other major/complex cardiac malformations.

The sample size was calculated using the "Epicalc Package" from R statistical language. We assumed that 30% of VSDs close in the normal course within 1 year. Using a precision of 10%, design effect =1, and α=0.05, sample size obtained was 80. The study was started after getting the clearance from the research and ethical committee of the institution. A write-up was given to the parents stating the purpose and importance of the study and their consent was taken.

Data regarding age at presentation, mode of detection, antenatal, natal and postnatal history, and development and growth were collected. Physical examination findings were noted. Investigations of chest X-ray, electrocardiogram, and echocardiography were done. The echocardiographic evaluation was performed with a commercially available echocardiographic machine (Toshiba power vision 6000) using transducer with a frequency of 5 MHz. The treatment options were prescribed based on these findings.

Babies were followed up 6 monthly, and clinical examination and relevant investigations were done. At least one follow-up was done for every baby. No further follow-up was conducted for those VSDs which were found to have closed spontaneously during the first follow-up. VSDs were classified based on location as perimembranous, muscular, inlet, and outlet and according to size as small –<1/3rd aortic root, moderate –1/3–2/3rd aortic root, and large –>2/3rd aortic root.

RESULTS

Total infants who satisfied the inclusion criteria and were enrolled in the study were 84. Of the total cases, 47.62% (40) were male and 52.38% (44) females. The history of gestational diabetes was noted in 23.81% (20) of the mothers. Family history was reported in 11.9% (10) of cases. A total of 4.76% (4) of the cases were syndromic. Predominant age group was the neonatal group (< 28 days) coming to 67.86% (57) of the total cases. The diagnosis of 2.38% of the cases was done after 6 months of age. Figure 1 shows the frequency of various treatment modalities.

Most of the cases (84.52%) were detected when evaluated for an incidentally detected murmur. Remaining 15.48% of the cases were symptomatic [Table 1]. The most common type of VSD was perimembranous (52%) type followed by muscular (42%), subpulmonar (5%), and inlet VSD (1%) [Tables 2 and 3].

DISCUSSION

A total of 84 infants were enrolled and followed up at an interval of 6 months. At least one follow-up was done for every baby. No further follow-up was conducted when VSDs closed spontaneously. One baby expired before the first follow-up and another baby was lost for follow-up. Associated syndromes were seen in 4 patients (4.76%), of which three were Down and one was a case of congenital rubella syndrome. CRS patient had moderate subaortic VSD. In the study by Corone *et al.*, 11% of cases had syndromic association [4]. According to Nora *et al.*, the syndromic association was ~5% [5].

Of the 84 cases, 57 cases (67.86%) were detected in <28 days babies and 20 cases (23.80%) in postneonatal period within 3 months. Seven cases were detected after 3 months. Of the 84 cases, 71 cases (84.52%) were diagnosed during the evaluation of an incidentally detected murmur. Most of the babies detected in the neonatal period had only a murmur (95%). Babies with significant problems at presentation such as congestive cardiac failure (CCF), FTT, and bronchopneumonia presented within the first 3 months and this association was found to be significant. This might be attributed to the fall in pulmonary vascular resistance when the shunt across the defect increases. In the study by Hrahsheh *et al.*, the mean age at the time of diagnosis was 2.0 months ±15 days (Range: 1 day–3.0 months) [6].

The most common VSD was the perimembranous type (52.38%), next was muscular type (41.66%). Subpulmonic (4.76%) and inlet (1.19%) VSDs were rare. In the study by Van den Heuvel *et al.*, the most common defect was perimembranous (50%) followed by muscular (40%) and inlet and subpulmonic were rare [7]. Eroglu *et al.* reported 65.7% defects to be perimembranous, 30.8% muscular, 0.7% inlet, and 0.5% outlet VSDs [8]. According to Hrahsheh *et al.*, 67 patients had muscular (59.0%) and 46 had membranous VSDs (41.0%) [6]. According to Sadoh *et al.*, the most common

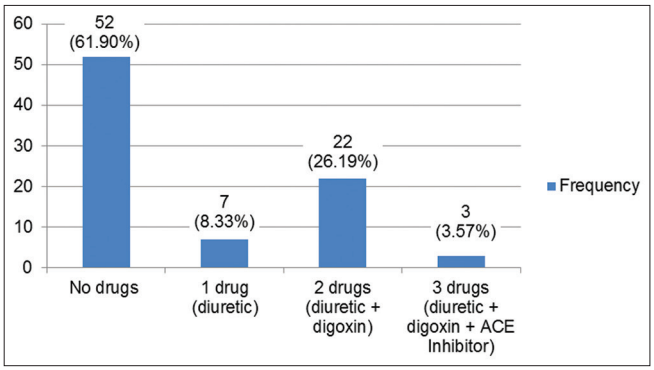

Figure 1: The frequency of various treatment modalities

Table 1: Clinical presentation of the study population

Clinical features	Frequency (%)
Incidental murmur	71 (84.52)
Bronchopneumonia	4 (4.76)
CCF	3 (3.57)
CCF+FTT	3 (3.57)
FTT	2 (2.38)
Bronchopneumonia+FTT	1 (1.19)

FTT: Failure to thrive, CCF: Congestive cardiac failure

Table 2: Ventricular septal defect status at final follow-up

Size	First follow-up	Second follow-up	Final follow-up
	Frequency (%)	Frequency (%)	Frequency (%)
No change	44 (54)	12 (37)	28 (33.33)
Decreased	4 (5)	6 (18)	8 (9.52)
Spontaneous closure	28 (34)	11 (33)	-
Surgical closure	6 (7)	4 (12)	7 (8.33)
Closed	-	-	39 (46.42)
Death	-	-	1 (1.19)
Lost follow-up	-	-	1 (1.19)
Total	82 (100)	33 (100)	84 (100)

Table 3: Site, size, and outcome of ventricular septal defect

Site	Size	Total	No change	Reduction of size	Spontaneous closure	Surgical closure
Perimembranous	Small	18	7	1	10	0
	Moderate	22*	10	6	1	3
	Large	4	1	0	0	3
Muscular	Small	32	4	0	28	0
	Moderate	2	1	1	0	0
	Large	1	1	0	0	0
Subpulmonic	Small	2	2	0	0	0
	Moderate	1	1	0	0	0
	Large	1	0	0	0	1
Inlet	Small	0	0	0	0	0
	Moderate	0	0	0	0	0
	Large	1	1	0	0	0

*Two cases no follow-up

type of VSD (39–63.9%) was perimembranous type followed by muscular (17–27.9%) and subarterial type (5–8.2%) [7].

Of the total subjects, 52 VSDs (61.90%) were small, 25 (29.76%) were moderate, and 7 (8.33%) were large VSDs. Among the small VSDs, 32 (61%) were muscular, next in frequency was perimembranous type. Most of the moderate and large VSDs were perimembranous defects. According to Eroglu *et al*., 76% were small VSDs, 18% moderate, and 6% large [8]. The moderate and large lesions were detected within the first 3 months. The statistical association was significant (Chi-square test, $p<0.04$). There were 68 patients (81%) who were asymptomatic. In the study by Corone *et al*., 71% of patients were asymptomatic [4]. Among the 16 symptomatic patients, six babies had large defects and nine babies had moderate defects. The statistical significance of this association was significant (Chi-square test, $p<0.001$).

There were 82 cases which were followed up. One baby expired due to severe pneumonia and another baby was lost for follow-up. The clinical problems encountered on follow-up were the development of CCF, FTT, bronchopneumonia, pulmonary hypertension, and right ventricular outflow tract obstruction. None of the cases developed aortic cusp prolapse, pulmonary vascular occlusive disease, or infective endocarditis. According to the observations by Corone *et al*., Halloran *et al*., and Plauth *et al*., the development of aortic regurgitation and infective endocarditis was rare in <2 years old [4,9,10]. CCF developed in nine patients on follow-up, of which three were large defects and remaining six moderate defects. Overall, during the entire study period, 2 (5.71%) of the 35 muscular VSDs and 10 (22.72%) of the 44 perimembranous VSDs developed CCF. Corone *et al*. observed that CCF is frequent in <1 year of age and complicates patients with large shunts [4]. In another study by Hiraishi *et al*., CCF developed in 2 (4%) of 46 patients with muscular VSD and in 12 (25%) of 47 patients with membranous VSD [11].

Subaortic VSD was seen in 2 patients (2.43%) and they developed infundibular pulmonary stenosis on follow-up. One baby had a small defect and the other had a moderate defect. One baby with moderate subaortic VSD expired at 3 months of age due to severe bronchopneumonia. Spontaneous closure was observed in 39 of the defects (47.56%).

Spontaneous closure was seen in 28 of the muscular defects (80%) and 11 of the perimembranous defect (25%) which included a moderate-sized defect also. None of the large defects or any of the subpulmonic or inlet VSD closed spontaneously or reduced in size. The frequency of spontaneous closure as observed by Hoffman *et al*. was 33%, Eroglu *et al*. 27% Keith *et al*. 21%, Mitchell *et al*. 35%, and Moe *et al*. 45% [12,8,13,14,15]. The

rate of spontaneous closure as reported in these studies varied from 21% to 45%. Our observation was at par with these reports. In the study by Hornberger *et al*., 75% of the muscular VSDs closed spontaneously [16]. According to Eroglu *et al*., 15% of perimembranous and 57% of muscular defects closed spontaneously [8]. Trowizsch *et al*. found a spontaneous closure rate of 37.9% for muscular defects and 4.7% for membranous defects within the first 13 months of life [17].

Wu *et al*. found that the expected probability of developing spontaneous closure of membranous VSDs was 35% [18]. The study by Hrashesh *et al*. has also shown that spontaneous closure of muscular VSDs is more frequent than that of perimembranous VSD (67.0% vs. 24.0%) [6]. In studies done by Shirali *et al*. and Turner *et al*. (on the natural history of VSD), both found a significantly higher spontaneous closure rate for muscular defects [2,19].

Mehta *et al*. studied 124 neonates with VSD and found the rate of closure of muscular VSD to be almost double that of perimembranous VSD (23% vs. 42%) by the end of the 1st year of life [20]. A much higher rate of spontaneous closure of muscular VSD has been reported, 78% had closed by 6 months of age[20] and 76% by 1 year [21]. According to Hrahsheh *et al*., 45 of the muscular defects closed spontaneously, 6 were closed surgically, and 16 remained open (59.0%, 8.0%, and 33.0%, respectively) [6]. Regardless of the type, 27 (64.0%) of moderate and large size defects needed medical and/or surgical treatment.

According to Li *et al*., the major determinants of spontaneous closure of isolated VSD were the diameter of the defect and location [22]. In addition, VSD location might also affect the incidence of spontaneous closure. According to Abbag *et al*., spontaneous closure is age dependent, occurring mainly in perimembranous and muscular VSDs [23]. Spontaneous closure of a large VSD is unusual.

Decrease in size was seen in 8 defects (9.52%) and all were moderate defects. There was no change in the size of 28 of the defects (33.33%). According to Eroglu *et al.,* the reduction in VSD size was 15% [8]. According to Heuvel *et al*., the probability of spontaneous closure was determined by morphology rather than size of the defect [24]. Surgical closure was done in seven of the defects which included three moderate perimembranous, three large perimembranous, and one large subpulmonic defect. According to the observations by Hrashesh *et al*., 64% of the moderate size and large VSDs required medical and/or surgical therapy in the first 2 years of life [10]. Medical and/or surgical therapy was needed in 6 (8%) patients with muscular VSDs and 46% of cases with perimembranous VSDs needed medical therapy and/or surgery during the 2-year follow-up. According to Turner *et al*., perimembranous VSDs are defects with a poor prognosis as in his study, 39% of membranous versus 3% of muscular VSDs required surgical closure, whereas 29% membranous and 69% muscular VSDs closed spontaneously by 6 years of age [19].

The study was limited by the short study period and small sample size. The study period was too short to study the natural history of VSD and longer duration of the study with more sample size is needed.

CONCLUSION

On follow-up, nearly 47% of VSD closed spontaneously and 10% reduced in size. Muscular VSD had a high chance of spontaneous closure (80%), and small and moderate perimembranous VSDs had 25% chance of spontaneous closure. None of the large inlet and outlet VSD closed spontaneously. The main complications seen were congestive heart failure and bronchopneumonia. VSDs are essentially remediable lesions with a normal life expectancy, and hence, there is a need for quick surgical access for moderate and large VSDs.

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