DOI: https://doi.org/10.53350/pjmhs22161152

ORIGINAL ARTICLE

Infective Endocarditis in Children with Isolated VSD: A Single Center Study

TEHMINA KAZMI, SAFIA KHAN, S. SALMAN A SHAH, UZMA KAZMI, MAISAM KAZMI, SYED NAJAM HYDER
Department of Pediatric Cardiac Surgery. Children's Hospital and Institute of Child Health Lahore,
Correspondence to Dr. S. Salman A Shah, Assistant Professor, Email: salman1997@yahoo.com, Ph:92-042-321-498-2220 92-042-36617024

ABSTRACT

Aim: To determine the characteristics of isolated ventricular septal defect (VSD) in association with infective endocarditis (IE) among children with isolated VSD and its outcome.
Method: This was cross-sectional study. Data was collected prospectively from infective endocarditis patients with isolated ventricular septal defect (VSD), admitted in pediatric cardiology ward of The Children's hospital and Institute of Child Health, Lahore. Study period was from September 2018 till March 2021. The data was analyzed by using SPSS-26.
Result: Sixty patients of ventricular septal defect (VSD) with infective endocarditis (IE), fulfilling the inclusion criteria, were included in the current study. Mostly about 60% were male. Transthoracic Echocardiography was done for all the patients. Single vegetation was found among 68.3%, rest were having multiple vegetations. seen. Approximately 57% were having small size vegetations while remaining 43% were with moderated – large vegetations. Complications were reported in only 18% of the study population. Regarding outcome majority of the patients (90%) were successfully treated with medical management alone, while only 8.3% required surgical intervention as well. Only 1 out of 60 patients included in the study was expired. Characteristic of VSD, size of vegetation, and number of vegetations have significant influence on development of complications (p = <0.05).
Conclusion: Risk of complications among infective endocarditis with isolated VSD is comparatively greater with large vegetation and multiple number of vegetations as compared to single or small vegetation. Medical management is main stay of treatment while surgical intervention is usually required among infective endocarditis patients with DCSA-VSD & subaortic-VSD.
Key words: Ventricular septal defect (VSD), DCSA (doubly committed sub-arterial) VSD, Infective endocarditis (IE).

INTRODUCTION

The most prevalent reason for infective endocarditis (IE) in children in developing countries is congenital heart defect (CHD). A large population-based cohort study has been reported high risk of infective endocarditis in children with congenital heart defect that is about 6.1 per1000 from birth to 18 years of age, corresponding to 4.1 among 10,000 person per year[1].

In comparison with adult infective endocarditis patients, epidemiological profile is different among children. Incidence of IE is comparatively lower in pediatric age group. The estimated annual incidence of IE in children the United States has been reported 3.3 per 100,000 per year among children[2].

Despite modern investigation procedures, early diagnosis of definite, possible, and probable cases of infective endocarditis in children with underlying CHD remains difficult. The incidence of infective endocarditis in children with CHD has increased because of availability of advanced surgeries for complex cardiac lesions and improved survival. Ventricular septal defect is the most frequently seen congenital heart defect almost 20-30% in pediatric cardiology clinics. Although it is difficult to find the exact incidence, but estimates range from 2 to 5 out of every 1000 babies born[3-5].

According to AHA guidelines and NICE guidelines VSD is considered as moderate to low risk for developing infective endocarditis, as per that only good dental hygiene and skin care rather antibiotic prophylaxis is sufficient to prevent IE. On the other hand, a study conducted in Lahore, Pakistan reported significant risk of IE with small VSD and recommended use of prophylactic antibiotics in patients with even small VSD[6].

The study is conducted to determine the characteristics of isolated ventricular septal defect (VSD) in association with infective endocarditis (IE) among children with isolated VSD and its outcome in term of treatment modalities used, response to treatment, and complications.

MATERIAL AND METHOD

After approval from IRB, data of this causal and cross-sectional study was collected prospectively from infective endocarditis patients with isolated ventricular septal defect (VSD) as congenital cardiac defect, admitted in pediatric cardiology ward of The Children hospital and Institute of Child Health, Lahore. Study period was from September 2018 till March 2021. All the information regarding this study was collected on pre-designed proforma, after taking informed written consent from the parents. Diagnosis of Infective endocarditis (IE) was made based on duke's criteria. Patients who fulfilled two major criteria or one major and three minor criteria or five minor criteria as per Duke's criteria, were labeled as IE. All patient of IE with VSD, up to the age of 13 years of both genders were included in the study. Patients older than 13 years of age, having underlaying congenital cardiac defects except isolated VSD, and/or having any inherited or acquired chronic illness like metabolic disorder, chronic diarrhea, chronic liver or renal disease, were excluded from the study. Trans thoracic Echo-cardiography was performed in all patients with vivid-9-ge machine. Transesophageal echo was done only if needed.

Type of VSD was recorded like peri-membranous VSD, subaortic VSD, doubly communicated subaortic (DCSA) VSD, muscular VSD; size of VSD was categorized as small <5mm, Moderate 5-11mm, and large 12mm or more; and characteristic of VSD (restricted, partially restricted, and not restricted) was classified based on shunt across VSD and degree of restriction was evaluated on color and spectral Doppler. Detail evaluation of vegetation was done including site, size, and number of vegetations. Size of vegetations was labeled as small <5mm, moderate 5-9mm, and Large >10mm. Treatment given was recorded as medical management in the form of antibiotics & anti-failure therapy and surgical intervention. Complications like pulmonary and systemic embolization, perforation of valve, abscess formation, sever tricuspid regurgitation, and aortic regurgitation were recorded.

The data was analyzed by using SPSS-26. Descriptive analysis was done to measure frequencies of qualitative and quantitative parameters like gender, VSD-size, VSD-type, VSD-character, Vegetation-size, vegetation-site, and number of vegetations.

Durbin-Watson test was applied to assess the autocorrelation or common method biasedness. Multiple regression analysis was run to assess the effect of VSD-size, VSD-type, VSD-character, Vegetation-size, vegetation-site, and number of vegetations, on development of complications and mode of treatment in term of medical & surgical management to

Received on 24-07-2021
Accepted on 13-12-2021

cure, and death during management. p-value of <0.05% was taken as threshold, keeping confidence interval of 95%.

RESULTS

During study period 106 patients of infective endocarditis with congenital heart disease were admitted in the pediatric cardiology ward of the children's Hospital and institute of child health; out of them 60 patients with isolated VSD fulfilling the inclusion and exclusion criteria were included in the study. Sixty patients of ventricular septal defect (VSD) with infective endocarditis (IE) diagnosed as per duke's criteria, were included in the current study i.e., 56.6% of all congenital cardiac defects with IE, admitted during study period.

Males were predominant among the study group as 60% (36 out of 60) were male and 40% (24 out of 60) were females. Majority of patients in study group, approximately 62%, were older than 5 years. Minimum and maximum age reported was 1.6 year and 13 years respectively. Most of the patients, 42 out of 60 (70%), were having moderate to large VSD. Maximum, 78% (47 out of 60) were having peri membranous VSD, while 6 (10%) patients had DCSA-VSD, 6 (10%) patients had subaortic-VSD and 1 (1.7%) had Muscular VSD. Similarly, 70% (42 out of 60) were having restricted VSD while rest 30% (18 out 60) were with partially restricted or unrestricted VSD. Trans thoracic Echocardiography was done for all the patients as per duke's criteria that reported single vegetation among 68.3% (41 out of 60) and remaining 31.7% (19 out of 60) were having multiple vegetations. Isolated tricuspid valve involvement with vegetations was documented in 43.3% (26 out of 60); isolated pulmonary valve, aortic valve, and right ventricular side of VSD were affected with vegetations in 5% (3 out of 60), 8.3% (5 out of 60), and 23.3% (14 out of 60) respectively. Only about 40% (24 out of 60) of the patients were having large size vegetations while most of the patient, approximately 57% (34 out of 60), were having small size vegetations (Table 1).

As per Hair et al. (2014), Durbin-Watson <4 indicates that there is no autocorrelation or common method biasedness. At R square = 0.253 in Model-1, it is concluded that 25.3% variation in outcome is caused by size of vegetation, size of VSD, type of VSD, number of vegetations, characteristic of VSD, site of vegetation. Model-2 at R square = 0.384, concluded that 38.4% variation in outcome is caused by size of vegetation, size of VSD, type of VSD, number of vegetations, characteristic of VSD, site of vegetation. (Table-2)

Regarding complications in 82% patients no complication of disease was reported, while remaining 18% (11 out of 60) developed different complications including sever tricuspid regurgitation (2 out of 60), aortic regurgitation (3 out of 60), and pulmonary embolism (6 out of 60) in about 3%, 5%, and 10% respectively.

Regarding outcome majority of the patients (90% i.e., 54 out of 60) were successfully treated with medical management alone, while 5 patients (8.3%) required surgical intervention as well. Only 1 out of 60 patients included in the study was expired due to pulmonary embolism.

Significant impact of VSD-type on mode of treatment with p of 0.005 and standardized coefficient beta =.360, it is applied that chances of IE resolution are higher with medical management alone in peri-membranous and muscular VSD as compared to DSCA and subaortic-VSD. On the other hand, p=.029 along with standardized coefficient beta = -.327 for mode of treatment with site of vegetation is indicating downward sloping of regression line, which means surgical management is highly needed when vegetations are involving isolated tricuspid valve either septal leaflet or anterior leaflet and least required in case of aortic valvular vegetations.

Out of 5 patients who underwent surgical removal of vegetation and closure of defect 3 had DCSA-VSD, and 2 had Subaortic-VSD. Characteristic of VSD, size of vegetation, and number of vegetations have significant influence on development of complications with p-value of .002, .012, .042 and standardized coefficient beta reported -.404, -.286, -.255 respectively, that is reflecting downward slopping of regression line in their relationship. It is concluding that risk of complications is higher with multiple and/or large size vegetations as compared to single and/or small to medium size vegetations; at the same time unrestricted-VSD is having higher probability of complications than restricted and partially restricted-VSD

Table-1 Demographic Features and Echo Findings

	Frequency	%age
Gender:		
Male	36	60
Female	24	40
Age:		
<2 years	8	13.3
2-5 years	15	25
5.1-10 years	23	38.3
>10 years	14	23.3
Type of VSD:		
Peri membranous	47	78.3
subaortic VSD	6	10
Muscular VSD	1	1.7
DCSA VSD	6	10
Size of VSD:		
Small	18	30
Moderate	21	35
Large	21	35
Characteristic of VSD:		
Restricted	42	70
Partially restricted	9	15
Not restricted	9	15
Site of vegetations:		
Tricuspid valve septal leaflet	23	38.3
Tricuspid valve anterior leaflet	3	5
Right ventricular side of VSD	14	23.3
Pulmonary valve	3	5
Tricuspid valve and pulmonary valve	5	8.3
Tricuspid valve and right ventricular side	3	5
of VSD Aortic valve	5	8.3
Size of vegetations:		
Small	34	56.7
Moderate	2	3.3
Large	24	40
Number of vegetations:		
Single	41	68.3
Multiple	19	31.7

Table-2: Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Durbin-Watson
1	.503[a]	.253	.169	.33959	1.534
2	.620[a]	.384	.314	.96529	1.589

{***Predictors:*** (constant), Size of vegetation, Size of VSD, Type of VSD, Number of vegetation's, Characteristic of VSD, Site of vegetation.
Dependent variable: Mode of treatment in Model-I and complication in Model-II}

Table 3: Outcome

Outcome	No. of patients	Percentage
Responded to medical management and discharged	54	90
Required surgery	5	8.3
Mortality	1	1.7

Table-4: Statistical evaluation of Impact on Outcome

	Mode of Treatment			Complications		
	Standardized Coefficient Beta	t	sig	Standardized Coefficient Beta	t	sig
Type of VSD	.360	2.905	.005	-.112	-.995	.324
Size of VSD	.079	.568	.572	-.052	-.412	.682
Characteristic of VSD	.173	1.256	.215	-.404	-3.235	.002
Site of vegetations	-.327	-2.245	.029	.246	1.861	.068
Size of vegetations	.128	1.062	.293	-.286	-2.614	.012
No. of vegetations	.043	.322	.749	-.255	-2.088	.042

DISCUSSION

In this study we found that about 56.6% of IE with CHD were having VSD as underlaying cardiac defect. In our study group male children predominated female 60% vs 40%. In the study, Majority of children belonged to more than 5 year of age i.e 62% and 38 %children were less than 5 year. In our study, 30% VSDs were categorized as small VSDs and 35% were moderate and 35% were large defects but out of them 70% defects were restricted by some mechanism.

The commonest site of vegetation in our patients was septal leaflet of tricuspid valve (38%) and RV side of interventricular septum (23%). Results has indicated that surgical management was highly needed when vegetation involved tricuspid septal or anterior leaflet in our study group also when vegetation is causing severe tricuspid regurgitation (2 out of 60 patients 3 %) and right heart failure and when associated with pulmonary embolism (6 out of 60 i.e., 10%). Risk of pulmonary embolism was high when vegetation was on tricuspid valve and pulmonary valve.

Hussain et al. in a study on tricuspid valve endocarditis has reported that surgery is primarily considered for unsuccessful medical treatment, large vegetations and serious septic pulmonary embolism, it is less often required for TV regurgitation and heart failure[12].

According to AHA guidelines surgical treatment of tricuspid valve IE is reserved for patients with the following:[15].

- TV vegetation > 2cm with septic pulmonary emboli.
- Persistent bacteremia for one week despite adequate treatment.
- Severe tricuspid regurgitation with right-sided heart failure

Our study also concluded that rate of complications and need of surgery was also high in patients with multiple vegetations and large vegetations (>10mm) (25.3% variation in outcome due to number, site and size of vegetation)[16]. Five patients required surgical removal and closure of defects. in two patients' severe regurgitation of tricuspid valve was leading to heart failure. In two patient's pulmonary embolism was indication for surgery and in one patient aortic regurgitation led to heart failure. In this patient removal of vegetation and closure of septal defect along with aortic valve repair was performed. This fact has also been supported by a multicenter prospective cohort study including 384 patients with infective endocarditis, it was observed in this cohort that a vegetation size of >10 mm along with severe vegetation mobility were predictors of new embolic events[9,17].

All patients were initially given first line intravenous antibiotics i.e. Benzyl penicillin, Amikacin and oral Rifampicin. Majority of patients responded to it. In few patients second line antibiotic injection cephradime, Vancomycin was given due to persistent or recurrent fever and after surgery. Our 90% patients were discharged after 4-6 weeks completing treatment. Patients who underwent surgery were also discharged after completing six weeks of medical treatment. One patient (1/60 1.8%) expired due to complication of recurrent pulmonary embolism.

CONCLUSION

Need for surgical intervention in management of IE is higher in DCSA-VSD, subaortic-VSD, and when tricuspid valves are involved with vegetation as compared to other types of VSD and other sites of vegetations. Risk of complications is higher with large vegetation and multiple number of vegetations.

Conflict of interest: Nil

REFERENCES

1. Dinela Rushani, Jay S. Kaufman, Raluca Ionescu-Ittu, Andrew S. Mackie, Louise Pilote, Judith Therrien, and Ariane J. Marelli. Infective Endocarditis in Children with Congenital Heart Disease Cumulative Incidence and Predictors. 2013;128:1412–141HomeCirculationVol. 128, No. 13.
2. Kosger P, Keskin T, Kiztanir H, Ucar B. Clinical Characteristics, Treatment Approaches, and Complications in Children with Infective Endocarditis: A Single Center Experience from Turkey, Osmangazi Journal of Medicine, 2020;42(2):231- 239 Doi: 10.20515/otd. 569875 231.
3. S Di Filippo, B Semiond, M Celard, F Sassolas, F Vandenesch, J Ninet, J Etienne, A Bozio Characteristics of infectious endocarditis in ventricular septal defects in children and adults. Arch Mal Coeur Vaiss 2004 May;97(5):507-14.
4. Braz. J. Cardiovasc. Surg., ahead of print Epub Sep 18, 2020, infective endocarditis in childhood: a single-center experience of 18 years5 brazilian journal of cardiovascular surgeryprint version issn 0102-7638on-line version issn 1678.
5. Di Filippo S, Delahaye F, Semiond B, et al. Current patterns of infective endocarditis in congenital heart disease. Heart. 2006;92(10):1490-1495. Doi:10.1136/hrt.2005.085332.
6. Hyder N, Kazmi U, Kazmi T. Small Ventricular Septal Defects considering not requiring surgical closure: The frequency of developing complications in our centre. Heart Res Open J.2016 2(5) ;144-149.
7. Soufflet V, Van de Bruaene A, Troost E, Gewillig M, Moons P, Post MC, et al. Behavior of unrepaired perimembranous ventricular septal defect in young adults. Am J Cardiol 2010; 105:404-7.
8. Robert W Elder, Robert S Baltimore The Changing Epidemiology of Pediatric Endocarditis. Infect Dis Clin North Am 2015 Sep;29(3):513-24.
9. Di Filippo S, Delahaye F, Semiond B, et al. Current patterns of infective endocarditis in congenital heart disease. Heart. 2006;92(10):1490-1495. doi:10.1136/hrt.2005.085332
10. Ashkenazi S, Levy O, Blieden L Trends of childhood infective endocarditis in Israel with emphasis on children under 2 years of Age. pediatr Cardiol 1997;18(6):419-24.
11. Gabriels C, De Backer J, Pasquet A, Paelinck BP, Morissens M, Helsen F, et al. Long-term outcome of patients with perimembranous ventricular septal defect: Results from the Belgian registry on adult congenital heart disease. Cardiology 2016; 136:147-55.
12. Hussain ST, Witten J, Shrestha NK, Blackstone EH, Pettersson GB. Tricuspid valve endocarditis. Ann Cardiothorac Surg. 2017;6(3):255-261. doi:10.21037/acs.2017.03.09
13. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; ACC/AHA Task Force Members. 2014 15. 15 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: Circulation. 2014 Jun 10;129(23): e650. PMID: 24589852.
14. kelechi e. Okonta and Yahaya b. Adamu what size of vegetation is an indication for surgery in endocarditis. . Interact Cardiovasc Thorac surg. 2012 Dec;15(6):1052-6.
15. Saxena a, Aggarwal n, Gupta p, Juneja r, kothari ss, Math r. Predictors of embolic events in pediatric infective endocarditis. Indian heart j. 2011 may-jun;63(3):237-40. Pmid: 22734342.