Natural history of ventricular septal defects in Nigerian children

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Introduction. Ventricular septal defect (VSD) is a common congenital heart disease (CHD). Spontaneous closure of the VSD may occur, depending on the type and size of defects. This study was conducted to determine the natural history of VSD in a group of Nigerian children.

Subjects and methods. Sixty-one children diagnosed with VSD were prospectively studied at a tertiary centre in Nigeria until they were 2 years old. They had regular two-dimensional (2D) and Doppler echocardiography evaluations for the VSD size and closure.

Results. Most (35 – 57.4%) of the patients were female, their mean age at presentation was 11.2±5.2 months, and the most common type of VSD was the perimembranous (39 – 63.9%). Almost half (28 – 45.9%) of the patients had spontaneous closure. The spontaneous closure rate was highest in muscular VSD (82.4%) and in small defects (95.0%). Incidental presence of a murmur, absence of heart failure and bronchopneumonia were good clinical predictors of closure. Only 3 (4.9%) patients had surgery abroad. There were 2 (3.3%) deaths from bronchopneumonia and bacterial endocarditis.

Conclusion. Spontaneous closure readily occurs in small-sized defects and muscular VSDs. However, most patients with moderate to large VSDs are confined to long-term medical management, highlighting the need for indigenous surgical capacity in Nigeria.

The global incidence of ventricular septal defect (VSD) is 1.5 - 3.5/1 000 live births, and represents about 20% of all congenital heart disease (CHD).[1,2] The prevalence of VSD among all CHD in hospital-based audits in Nigeria ranges between 35 - 55% of CHD.[3-5] A similar prevalence, with a range of 28 - 46% of CHD, has been reported from audits of echocardiography laboratories in Nigeria.[6,7] In all the studies, VSD is the most common CHD and also the most common CHD causing heart failure in childhood.[8,9]

The advent of two-dimensional (2D) and Doppler echocardiography has aided the early diagnosis and classification of the types and sizes of VSD. While this has been accompanied in developed countries by timely surgical or transcatheter closure of haemodynamically significant VSDs, this is not the case in resource-constrained countries such as Nigeria where, having made the diagnosis, the majority of patients are confined to long-term medical management because of the high cost of surgery (which is usually done outside the country).

Spontaneous closure of some of small and medium-sized defects within the first 2 years of life is the expected natural history in VSD.[10,11] The likelihood of spontaneous closure is also dependent on the type of VSD; muscular types close spontaneously more readily than other types.[12,13]

Since the cost of surgery is high, it is important to evaluate the natural history of VSD in our patients and identify the characteristics that are associated with spontaneous closure. This study was therefore conducted to determine the types, sizes, rates of spontaneous closure and possible predictors of spontaneous closure at the paediatric cardiology unit of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria.

Subjects and methods

Consecutive children, who were previously or recently diagnosed with VSD in the paediatric cardiology unit of the UBTH between September 2006 and February 2009, were recruited for the study. They were followed up until 2 years of age. The diagnosis was based on typical historical and physical findings. Further evaluation comprised a plain chest radiograph, an electrocardiogram using the Schiller AT-1 model, and a 2D and colour flow Doppler echocardiogram performed with a SIUI Apogee 3500 by the investigator. The VSD size was determined to be the widest diameter in any of the standard views (long and short axis parasternal, subcostal and apical views) and the size was related to the aortic root diameter. VSDs ≤5 mm were classified as small,[14] those from 6 mm to less than the size of the aorta were classified as moderate, and those the size of the aorta or larger were classified as large. The VSD type in terms of the site of the defect was also determined, using the classification of Soto *et al.*,[15] grouping them into the perimembranous, muscular, inlet and outlet types. Associated cardiac defects were noted. Only patients with an isolated VSD were finally analysed.

The age at presentation and the age at onset of illness were documented. The presenting complaints, findings on clinical examination and complications associated with the VSD were noted. The morbidities/reasons for referral were classified into symptoms and signs of congestive cardiac failure (CCF), of bronchopneumonia, failure to thrive (FTT), dyspnoea only, fast breathing only, easy fatiguing, incidental finding of a murmur, and delay or loss of motor milestones. The weight of the patients at presentation was taken, using a scale. The Z scores were then determined using the World Health Organization (WHO) weight-for-age chart.[16] Socio-economic

status (SES) of patients was evaluated using the method described by Olusanya *et al*.[17]

Antibiotics were given for bronchopneumonia. Patients with pulmonary oedema and congestive cardiac failure were placed on diuretics, digoxin and captopril (angiotensin-converting enzyme inhibitor) as appropriate. Patients with moderate to large VSDs were advised to have surgery especially if they were decompensated; those who could not afford surgery and were decompensated were placed on hydrochlorothiazide, spironolactone and captopril and followed up in the paediatric cardiology clinic. Children with well-compensated small to moderate VSDs were also followed up in the clinic.

Patients were seen in the clinic monthly if they were on medication or 3 - 6-monthly if they were not on medication. At each visit they were evaluated for evidence of decompensation, clinical evidence of closure of the defect (initial increase in the loudness of the pansystolic murmur and later absence of the murmur) and for drug refill. A 2D and colour flow Doppler echocardiogram was done 6-monthly to assess the current size of the VSD and to confirm a suspected spontaneous VSD closure. The time of spontaneous closure of the VSD was noted.

Permission for the study was obtained from the UBTH Ethical Committee.

Statistical analysis

Data were entered into Microsoft Excel and imported into SPSS version 13.0 in which analysis was done. Mean and standard deviations (SDs) were determined for variables such as age and time of closure. The relationship between variables was evaluated by the chi-square or Fisher's exact test as appropriate. The level of significance at 95% confidence interval was set at $p<0.05$.

The sensitivity and specificity of the clinical features in predicting spontaneous closure were calculated respectively as the ratio of true positive/sum of true positive and false negative and the ratio of true negative/sum of true negative and false positive. True positive was the number of patients with the feature whose VSD closed, true negative was the number of patients without the feature whose VSD did not close, false positive was the number of patients without the feature who had a closed VSD, and false negative was the number of patients with the feature whose VSD did not close.

Results

There were 110 patients referred to the paediatric cardiology unit of UBTH who were diagnosed to have VSD either alone, in combination with other heart defects, or as a component of a complex congenital heart anomaly. Of the 110 patients with VSD, 66 (60.0%) had isolated VSD, and 44(40.0%) had VSD in combination with other defects (Table I). Five (8.2%) of those with isolated VSD were lost to follow-up before attaining 2 years of age, therefore 61 (92.4 %) of the patients were analysed.

Of the 61 patients analysed, there were 35 (57.4%) females and 26 (42.6%) males, giving a male:female ratio of 1:1.35. The mean age at onset of illness was 5.1±4.2 (range 1 - 22) months. The mean age at presentation in the clinic was 11.2±5.2 (range 2 - 24) months. There were more patients (33 – 55%) whose symptoms started on or before 6 months than those whose onset of symptoms was between 7 and 12 months (13 – 21.3%), and those whose onset of symptoms was after 12 months (2 – 3.3%). Their mothers were aged between 21 and 45 years with a mean of 30.8±5.4 years. There were more patients of low SES (26 – 42.6%) than middle (24 – 39.3%) or high SES (11 – 18.0%).

TABLE I. DISTRIBUTION OF VSD IN THE STUDY POPULATION

Characteristics	N	%
Isolated VSD	66	60.0
VSD + patent ductus arteriosus	3	2.7
VSD + atrial septal defect	12	10.9
VSD + tetralogy of Fallot	27	24.6
VSD + truncus arteriosus	2	1.8
	110	100.0

The presenting complaints/morbidities of the 61 children studied are shown in Table II. More than half of the patients (33 – 54.1%) presented with symptoms of bronchopneumonia (cough, fever and breathing difficulty), and about a third complained of easy fatiguing. Ten (16.4%) were referred because of the incidental finding of a murmur only. Some of the patients (15 – 24.6%) presented because of fast breathing alone. Body weight was not determined for 6 (9.8%) patients. Of the 55 whose weights were determined, almost half (27 – 49.1%) weighed less than 2 SD for their age, while 28 (50.9%) had normal weight for age.

The chest radiographs of 28 (84.8%) of the 33 patients with congestive heart failure and/or bronchopneumonia showed increased cardiothoracic ratio and increased pulmonary vascular markings. Their ECGs similarly demonstrated evidence of left ventricular hypertrophy (LVH) and left atrial hypertrophy (LAH). Three (9.1%) of them had right bundle branch block. The chest radiograph and ECG findings were unremarkable in patients with small VSDs. The commonest type of VSD (39 – 63.9%) was the perimembranous type; others were the muscular type (17 – 27.9%) and the subarterial type (5 – 8.2%). Most of the VSDs (26 – 42.6%) were medium-sized, while 20 (32.8%) were small and 15 (24.6%) were large VSDs.

During follow-up of the 61 patients, 28 (45.9%) had spontaneous closure of the VSD. Of these, 15 (53.6%) were male and 13 (46.4%) female. The mean age at spontaneous closure was 15.5±5.8 (range 6 - 24) months. Eight (28.6%) closed within the first year of life, and 20 (71.4%) closed in the second year of life. Significantly more of the muscular compared with the other types of VSD closed spontaneously ($p=0.003$) and significantly smaller defects closed spontaneously compared

TABLE II. DISTRIBUTION OF PRESENTING FEATURES/MORBIDITIES IN THE STUDY POPULATION

Features	N	%
Bronchopneumonia	33	54.1
Easy fatigue	20	32.8
Murmur	18	29.5
Respiratory difficulty only	17	27.9
Fast breathing only	15	24.6
Congestive cardiac failure	15	24.6
Delayed developmental milestone	12	19.7

Most patients had multiple features.

with moderate and large defects (p=0.0001). Spontaneous VSD closures were highest in patients of highest SES (72.7%, 50.0%, and 29.2% for high, middle and low SES respectively, p=0.048) (Table III). Gender did not significantly affect closure. Spontaneous closure occurred in 8 (29.6%) of the 27 patients whose weights were ≤3 SD; this rate was lower in those whose weight was ≥2 SD (19 (67.9%) of 28). This was, however, not statistically significant (p=0.104). All 10 patients referred on account of murmur only had spontaneous closure. Only 20% and 27.3% of patients who presented with congestive heart failure and bronchopneumonia respectively had spontaneous closure. Regarding features that predicted likelihood of spontaneous closure, the incidental presence of a murmur only always predicted closure within 2 years, while the absence of congestive heart failure and bronchopneumonia were also good predictors (Table IV).

Two (3.3 %) patients died during the follow-up period from severe bronchopneumonia and bacterial endocarditis, which were both confirmed on autopsy. Only 3 (4.9%) of patients with large VSD could afford surgical closure before 2 years of life.

Discussion

Spontaneous closure of VSD occurs in its natural history, and various closure rates have been reported. The overall spontaneous closure rate of 45% in our study is lower than Jordanian and American studies,[18,19] in which there was a higher proportion of muscular VSD in the studied populations than in our study. The overall closure rate was, however, higher than that of the study conducted by Moe *et al.*[20] in which the proportion of patients with membranous VSDs was higher than that in our study. The differences in closure rates could be due to the fact that spontaneous closure is reported to be higher in muscular than perimembranous VSDs.[18,21] Hrahsheh and co-worker followed up 117 infants, and spontaneous closure occurred in 67% of the muscular VSDs and 24% of the perimembranous VSDs.[18] Al-Hakim *et al.* found a spontaneous closure of 15% of perimembranous VSDs compared with 37% of muscular VSDs in a study of 118 patients with VSD.[11]

There is a higher prevalence of small muscular VSDs in early infancy than the membranous type.[21,22] These higher values were mostly reported in studies where neonates were screened for VSD using 2D and Doppler echocardiographic examination.[21,22] These small muscular VSDs tend to close early,[22] thereby making the perimembranous type that tends to close later more prevalent later in infancy and in the older age group. The mean age of presentation of 11.2 months in this study would be in keeping with a preponderance of perimembranous VSDs as was observed in the study. The finding of a smaller proportion of muscular VSDs in this study may be due to the fact that most babies in our environment are born outside health facilities and would not receive medical attention until they become sick. It is possible that babies in this category with small muscular VSDs would have experienced spontaneous closure before detection in a health facility. It is interesting that about a fifth each of medium- and large-sized VSDs in this study closed spontaneously despite their initial symptoms. This finding is, however, in keeping with other reports in which a small proportion of the moderate or large-sized VSDs closed spontaneously.[18,23]

The patients referred on account of a murmur only in this study were asymptomatic and all had spontaneous closure, which is consistent with the presence of a small muscular VSD. This finding agrees with earlier work of Freedom *et al.*[24] and Gabriel *et al.*[25] One important value of diagnosing small VSD (and indeed all VSDs), as most close spontaneously, would be in preventing bacterial endocarditis. Although the risk is reported to be small,[1,11] it can be fatal, as shown in one of 2 deaths due to bacterial endocarditis, in our study.

Moderate to large VSDs may be better managed surgically as they are more prone to congestive heart failure and lower respiratory tract infections because of left to right shunting of blood, causing pulmonary overcirculation. Thirty-three (80.5%) of the 41 subjects with medium and large-sized VSDs in our study presented with bronchopneumonia and/or heart failure, and should have had surgery. Cost prevented

TABLE III. PATIENT DEMOGRAPHICS, VSD CHARACTERISTICS AND VSD CLOSURE

Characteristics	N	N closed (%)	p
Gender			
Male	35	15 (2.9)	0.612
Female	26	13 (50.0)	
Socio-economic status			
High	11	8 (72.7)	0.048
Middle	24	7 (29.2)	
Low	26	13 (50.0)	
Nutritional status			
Malnutrition	27	8 (29.6)	0.104
Normal nutrition	28	19 (67.9)	
VSD type			
Muscular	17	14 (82.4)	0.003
Perimembranous	39	14 (35.9)	
Subaortic	5	0	
VSD size			
Small VSD	20	19 (95.0)	0.0001
Medium VSD	26	6 (23.1)	
Large VSD	15	3 (20.0)	

TABLE IV. PREDICTIVE VALUES OF VSD CHARACTERISTICS FOR SPONTANEOUS CLOSURE

Characteristics	Sensitivity	Specificity	PPV	NPV
Absence of CCF	66.7	88.0	88.9	68.8
Absence of bronchopneumonia	42.9	52.6	66.7	29.4
Absence of malnutrition	44.4	51.4	29.6	65.5
Murmur only	100.0	-	∞	-
Dyspnoea	18.5	35.3	18.5	35.3
Fast breathing only	24.3	25.0	33.3	17.6
Easy fatiguability	25.0	39.4	25.9	38.2

PPV = positive predictive value; NPV = negative predictive value.

most of the patients from having surgery; only 3 patients underwent surgery. Being confined to medical treatment only, VSD patients may be predisposed to pulmonary hypertension and subsequent Eisenmenger syndrome over time. Meanwhile, the cost of managing recurrent infections and heart failure adds to the burden of health care.

Spontaneous closure readily occurs in small-sized defects and muscular VSDs.

The prevalence of VSD in our study is least among the high SES group and highest among the low SES group. While there is no obvious reason for this, it is possible that mothers of low SES are more likely to use unorthodox antenatal medications consisting of herbs and other mixtures which could be teratogenic. The finding in relation to SES, however, suggests that most patients with VSD are unlikely to have the means for surgical intervention. Spontaneous closure irrespective of the type of VSD was more common among children of high SES, and again there is no clear reason for this. Our findings about SES need to be evaluated in a multi-centre study with a larger sample size.

Spontaneous closure of a VSD is gratifying news to the patient, family and physician in an environment where surgery is not readily available. Although the use of 2D and Doppler echocardiography is best for predicting VSD closure,[21,26] the use of less favourable and less sensitive clinical features may be resorted to in resource-poor settings where the availability and affordability of imaging devices is low. The finding of a murmur in an asymptomatic infant, and the absence of congestive heart failure and pneumonia, have good sensitivity and positive predictive value in predicting closure of VSD within 24 months, according to this study.

Conclusion

In the natural history of VSD, perimembranous VSDs are most common, the majority of small VSDs close spontaneously, while only about a fifth of the medium and large defects close spontaneously. Heart failure and chest infections are common among those with medium and large defects. Infective endocarditis and mortality were limited in our study but this finding may change with a larger number of participants. Surgery was not affordable for most patients, who were consequently exposed to more complications. This emphasises the urgent need to establish affordable, functional cardiac centres in Nigeria to make surgery accessible and to improve patient care. Long-term follow-up and larger studies will elucidate the true outcome of VSD in our population.

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