Original Article

# Bicuspid Aortic Valve among Children Presenting in Two Health Institutions in Enugu, South-East Nigeria

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**Received:** 02-Oct-2024;
**Revision:** 10-Oct-2024;
**Accepted:** 16-Dec-2024;
**Published:** 27-Mar-2025

**Abstract**

**Background:** Bicuspid aortic valve (BAV) is the most common congenital heart defect. However, this is under-reported. It is not without associated cardiac anomalies. **Aim:** This study was aimed at documenting the prevalence of BAV in two referral health institutions and to determine the various types and associated cardiac anomalies. **Methods:** This was a descriptive study carried out in two referral health institutions. One thousand and five echocardiography was carried out in children with suspected cardiac diseases over a nine-year period. **Results:** Data was analyzed with IBM statistical software version 20. The prevalence of children with BAV is 1.7%. The most common type of BAV is the presence of left coronary and non-coronary sinuses. The most common associated lesion among children with BAV is atrial septal defect 7 (41.2%), followed by significant tricuspid regurgitation three (17.7%) and aortic stenosis three (17.7%). The mean cardiac structure diameters were not different when compared with age- and gender-matched controls (Children without BAV). **Conclusion:** Though BAV is the most common congenital heart disease, its rarity is proven in this study. It is also noteworthy that the cardiac defect is associated with valvar anomalies.

**Keywords:** *Bicuspid aortic valve, cardiac disease, children, congenital, echocardiography*

## Background

There is a rising prevalence of congenital heart disease in Nigeria.[1] This could be due to improved diagnostic facilities and increased manpower training in the field of pediatric cardiology.[2] Hitherto, left to right shunt defects such as ventricular septal defect (VSD) were observed as the most common acyanotic congenital heart defect, and tetralogy of Fallot (TOF) was the most common cyanotic heart defect.[3] Currently, the bicuspid aortic valve (BAV) has emerged as the most common congenital heart lesion worldwide.[4] Its non-recognition in Nigeria could be due to under-diagnosis.It may also present with one or more cardiac lesions resulting in a complex cardiac anomaly.[5,6] This lesion has accounted for several untimely deaths than all congenital heart diseases put together.[6,7]

Ideally, the aortic valve is usually tricuspid, but BAV contains two cusps instead of three. This could lead to degeneration of the valve with attendant dilatation of the aortic valve annulus. This lesion occurs with several forms of malformation of the valve, from the complete absence of the commissure to poor development of one or two commissures and adjacent cusps.[8] In the pediatric population, BAV may be asymptomatic and may occur with no sequel. However, over time, it becomes complicated with different degrees of valvular dysfunction such as aortic valve regurgitation, aortic valve stenosis, aortic dissection, and aortic aneurysm.[9-12] There are several theories propounded on the aethio-pathogenesis of BAV.[12] For instance, BAV is known to be caused by an abnormal blood flow

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_687_24

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**How to cite this article:** Chinawa JM, Chinawa AT, Ogbuka FN, Uwaezuoke NA, Chukwu BF, Yusuf PN. Bicuspid aortic valve among children presenting in two health institutions in Enugu, South-East Nigeria. Niger J Clin Pract 2025;28:167-73.

across the valve during embryogenesis resulting in an incomplete separation of the valve.[13] Kappetein *et al.*[13] documented abnormal neural crest migration with early fusion of the valve cushions as the underlying cause of BAV. The absence of endothelial nitric oxide synthetase has been implicated.

Literature has shown that about 50–75% of children with coarctation of the aorta have a BAV.[14-17] It is also documented that 30% of children with Turner and William syndrome present with various forms of BAV. The BAV is also observed in Shone syndrome, Kabuki syndrome, Marfan syndrome, and other genetic mutations.[15-17]

There is a paucity of data on BAV in Nigeria in particular and sub-Saharan Africa as a whole. Attention is given so much to other congenital heart diseases, and the diagnosis of BAV is often missed. This has resulted in several complications and death. Besides, due to limited data on children with BAV, there may be difficulty in assessing the true risk of complications related to the disease.[16]

This study was aimed at determining the prevalence of BAV and associated syndromes. It also elicited associated cardiac lesions in children with BAV and the presence of aortopathies (aortic regurgitation, stenosis, or coarctation) in children with BAV. The current study also compared the z-scores of cardiac structures and function of children with BAV with that of the normal population. This work also classified different types of BAV. This will be the first study in our locale and in Nigeria that describes the BAV in the pediatric population. In the near future, it will form a database for other studies in our setting.

## Methods

### Study area

This study was carried out in two hospitals located in Enugu metropolis, namely the Blessed Children Specialist Hospital and Triple Care Specialist Hospital. The hospital of study provides pediatric cardiology services and general pediatric services and reviews children with different types of cardiac maladies.

### Study population

A total of 1005 echocardiography was performed between 2016 and 2024 among children aged one day to 13 years. Children with BAV with or without associated cardiac lesions were included in the study while children with other forms of congenital heart disease, acquired heart diseases, or children with normal echocardiographic findings were excluded from the study. The cardiac valve dimensions of children with BAV were compared with age and gender-matched controls (children with no cardiac lesion).

### Study design

This was a descriptive study carried out in two referral health institutions among children aged one day to 13 years. It is a multi-center, population-based study where 1005 echocardiography was carried out in children with suspected cardiac disease over a 9-year period, from 2016–2024. The subjects used for the study were examined, with their history and clinical findings documented before echocardiography was performed.

### Echocardiography of BAV

Echocardiography on the subjects who met the inclusion criteria was studied with emphasis on prevalence rates, types, and a number of raphes as well as the spatial orientation of raphes or cusps. This was ascertained using classification by Sievers *et al.*[6] Other parameters documented on echocardiography were valvar structural dimension and left ventricular function with associated aortopathy. Aortic valve aortopathy was defined as aortic annulus size with Z-score greater than and equal to 3 with or without the presence of coarctation. Trans-thoracic echocardiography of the BAV was performed with all views such as subxiphoid, para-sternal, apical, supra-sternal, and the modified four chamber views. Both 2D, color Doppler, what of PW and CW Doppler, and M-mode were performed with such views. This was in line with the American Society of Echocardiography guidelines.[16]

### Definition of terms

BAV was defined as an aortic valve with a complete or partial obliteration of the commissure between two adjacent cusps with or without a raphe.[18,19] Besides, bicuspid valves could be diagnosed as bicuspids if two raphes are detected with commissural obliteration between adjacent cusps. When BAV was detected, repeat echocardiography was performed, and the aortic valve anatomy was studied on about two occasions before final diagnosis was made. BAVs were then classified as stated above into the number of raphes (type 0, 1, or 2, with numbers indicating the number of raphes).[18,19] Furthermore, cardiac valve structure and function were ascertained for the mitral valves, tricuspid valves, pulmonary valves, aortic valves, main pulmonary artery, and branch pulmonary artery. Congenital aortic stenosis was defined as peak flow velocity greater than 2 m/s across the aortic valve.[18,19] Aortic regurgitation was registered as trivial, mild, moderate, or severe.[18,19]

### Z-score calculation

The Z-score of all the valves and left ventricular function of children with BAV were calculated and compared

with an equal number of age and gender-matched controls (children with no cardiac lesion). The Z-scores were calculated with a Z-score calculator (Z-scores of cardiac structures parameter 2009).

## Result

### Data analysis

Data was analyzed with IBM statistical software version 20. The means and standard deviation of continuous variables were analyzed. The comparison of means was analyzed using an independent sample *t*-test or one sample *t*-test for comparison of the study population and the general population. Significant probability (*P*) value was set at $P < 0.05$.

## Result

There were 17 patients with BAV and 17 children without bicuspid aortic valve who also had no cardiac lesion matched for age and gender. The gender and mean age of the study participant and control were comparable as shown in Table 1. Nine (53%) of the participants with BAV were males and among those from the general population, 8 (47%) were males (Chi-square test: $d = 1$, $P = 0.73$). The age of study participants ranged from one day to 13 years while the mean age was 23. 9 ± 48.6 months for the subject and control (*t*-test = 0.003, df = 32.0, $P = 0.9$). The prevalence of children with BAV in the study was (17/1001) 1.7%

Table 2 shows the classification of BAV based on raphe position and coronary sinuses. The most common type of BAV is the presence of left coronary and non-coronary sinuses.

**Table 1: Characteristics of the respondents**

| Variable | BAV (*n*=17) | (*n*=17) | *P* |
|---|---|---|---|
| Age of respondents in years | | | |
| Mean±SD | 23.9±48.6 | 23.9±48.6 | 0.9 |
| Gender | | | |
| Male | 9 (53) | 8 (47) | |
| Female | 8 (47) | 9 (53) | |

$X^2$, $P$=0.73

**Table 2: Prevalence of hypertension among the respondents**

| Variable | Frequency (*n*=135) | Percent (%) |
|---|---|---|
| Classification of hypertension | | |
| The presence of left coronary and Non-coronary sinuses | 15 | 88.2 |
| Presence of right coronary and left coronary sinuses | 2 | 11.8 |
| Presence of right coronary and non-coronary sinuses | 0 | 0 |

The most common associated lesion among children with BAV is atrial septal defect 7/17 (41.2%), followed by tricuspid regurgitation 3/17 (17.7%) and aortic stenosis 3/17 (17.7%) [Table 3].

The mean cardiac structural diameter of the subjects and control were shown as in Table 4, and they were comparable. The mean diameter of the mitral valve among those with BAV was 13.47 ± 6.41 mm compared with 13.12 ± 5.1 mm among those without bicuspid valve (*t*-test = 0.17, $P = 0.9$). Also, the mean of main pulmonary artery diameter of those with BAV (10.83 ± 5.73 mm) was comparable with those without bicuspid valve (10.36 ± 5.4 mm), (*t*-test = 29.8, $P = 0.8$).

We also compared the cardiac function parameters between children with a bicuspid aortic valve and

**Table 3: Associated cardiac anomalies of children with BAV**

| Ass anomalies Frequency | Percent (%) |
|---|---|
| ASD 7 | 41.2 |
| Tricuspid regurgitation 3 | 17.7 |
| Aortic Stenosis 3 | 17.7 |
| PDA 1 | 5.9 |
| TOF 1 | 5.9 |
| Right arch 1 | 5.9 |
| VSD 1 | 5.9 |
| Hypoplastic RPA 1 | 5.9 |
| Aneurysm of the AA 1 | 5.9 |
| Pulmonary regurgitation 1 | 5.9 |
| Syndromic Correlates 0 | 0 |
| Consanguinity 0 | 0 |

**Table 4: Mean diameter of cardiac structures of subjects (*n*=17) and control (*n*=17)**

| Variable | Type of valve | Mean (mm) | Std. deviation | *P* |
|---|---|---|---|---|
| Mitral valve | BAV | 13.47 | 6.4 | 0.9 |
| | Control | 13.12 | 5.1 | |
| Tricuspid valve | BAV | 12.66 | 4.9 | 0.2 |
| | Control | 15.60 | 7.2 | |
| Aortic valve | BAV | 8.69 | 3.7 | 0.6 |
| | Control | 9.53 | 4.5 | |
| Pulmonary valve | BAV | 9.83 | 4.9 | 0.6 |
| | Control | 9.05 | 3.9 | |
| Main pulmonary artery | BAV | 10.83 | 5.7 | 0.8 |
| | Control | 10.36 | 5.4 | |
| Right pulmonary artery | BAV | 6.44 | 2.8 | 0.5 |
| | Control | 7.18 | 3.6 | |
| Left pulmonary artery | BAV | 7.55 | 3.2 | 0.7 |
| | Control | 7.21 | 3.5 | |

**Table 5: Comparison of the mean cardiac function parameters between the subjects (*n*=17) and control (*n*=17)**

| Variable | Subjects | Mean (mm) | Std. deviation | *P* |
|---|---|---|---|---|
| IVSD | BAV | 5.92 | 2.7 | 0.5 |
| | Control | 5.27 | 2.5 | |
| LVIDd | BAV | 20.01 | 7.5 | 0.8 |
| | Control | 20.81 | 10.4 | |
| LVPWd | BAV | 5.21 | 2.3 | 0.9 |
| | Control | 5.19 | 3.1 | |
| IVSs | BAV | 6.08 | 4.0 | 0.7 |
| | Control | 5.61 | 3.2 | |
| LVIDs | BAV | 12.31 | 5.6 | 0.3 |
| | Control | 14.33 | 6.8 | |
| LVPWs | BAV | 6.79 | 3.6 | 0.7 |
| | Control | 6.40 | 4.1 | |
| EF | BAV | 72.13 | 13.8 | 0.1 |
| | Control | 65.05 | 11.0 | |
| FS | BAV | 37.98 | 10.1 | 0.5 |
| | Control | 35.58 | 9.6 | |

normal children without a bicuspid valve and observed no difference in these parameters between the two groups. Table 5 shows the mean cardiac function parameters between the study population and the general population.

## Discussion

This study was aimed at determining the prevalence of BAV and associated factors. The prevalence of children with BAV in this study was 1.7%. Studies on autopsy have documented prevalence values of between 0.5% and 1.37%.[20,21] Panayotova *et al.*[21] identified BAV as the most common congenital heart defect, with a prevalence rate of less than 1% of the population.[22] In addition, Sillesen *et al.*[22] also noted that BAV affects 0.5% to 1.4% of the population. These similar prevalence rates observed in our reportage and that stated above could be due to the large sample size used for the study.

Male predominance was noted among children with BAV. It is interesting to note that several studies have documented more males presenting with BAV than females.[23-26] The high prevalence of males concerning lesions of cono-truncal origin may explain the high prevalence.[27] Kong *et al*.[28] also noted that BAV is three to four times more frequent in males than in females. They attributed this to be due to reduced concentration of X-chromosome genes among males. The issues of low penetrance, multi-factorial inheritance, valvar dilatation, and degenerative disease in males have also been adduced as the cause of the male preponderance.[7] Michelena *et al.,*[26] however, noted that though specific gender-specific implications of BAV have not been fully documented, higher risks of complications are seen in males compared to females.[28]

Majority of our entries presented with type 1 variety of BAV based on the number of raphes. A large cohort has reported the distribution of BAV sub types from a very large population.[29] Besides, Sievers *et al.*[27] also reported that 88% of their subjects with BAV presented with the type 1 variety which included 71% of them showing features of right–left coronary raphe, 15% with right coronary–non-coronary raphe, 3% with left coronary–non-coronary raphe. Their study, however, was based on pathological findings in BAV surgical specimens using 304 subjects.[29] Furthermore, another study has documented type 1/type 2 in 89% of patients with BAV and type 0 in 11% using 2118 subjects with a mean age of 47 ± 18 years.[31]

Associated cardiac anomalies were identified in children with BAV in the current study. The cardiac anomalies included atrial septal defect (ASD) with the prevalence of 41.2%, tricuspid regurgitation with the prevalence of 17.7%, aortic stenosis with the prevalence of 17.7%, patent ductus ateriosus (PDA) with the prevalence of 5.9%, tetralogy of Fallot (TOF) with the prevalence of 5.9%, right arch with the prevalence of 5.9%, VSD with a prevalence of 5.9%, hypoplastic right pulmonary artery (RPA) with the prevalence of 5.9%, aneurysm of the ascending aorta with the prevalence of 5.9%, and pulmonary regurgitation with the prevalence of 5.9%. Some studies have documented a low prevalence of associated cardiac anomalies in children with BAV.[32-34] Szöcs *et al.*[33] in their meta-analysis on BAV and associated features noted 0.5% of children with BAV presented with atrial and VSD each, 1.5% with mitral valve prolapse, 11.8% with aortic coarctation, 3.7% with coronary anomalies, 3.3%, with patent ductus arteriosus, and 5.9% with VSD. Sillesen *et al.*[22] noted that though the aortic valve of newborn subjects with BAV was non-obstructive, the higher flow velocities across the valve showed a smaller functional valve orifice size than in those without BAV. Spaziani *et al.*[30] also noted trivial or mild aortic valve regurgitation among subjects with BAV. Incomplete coaptation, redundancy, or prolapse of the leaflets could explain these associated lesions observed in children with BAV.[33] The right aortic arch and aneurysm of the ascending aorta observed among children with BAV in the current study is corroborated by Zhao *et al.*[31] They noted a rare case of BAV combined with a right-sided aortic arch aneurysm in their reportage. They also documented the presence of an aberrant left subclavian artery and Kommerell's diverticulum as associated findings. Nevertheless, the patient was followed up routinely since the findings were

life-threatening. Some studies have reported an increasing prevalence of ascending aorta abnormalities in children with BAV when compared with controls.[35-39] These anomalies were attributed to increased hemodynamic stress on BAV valve leaflets. There was no associated coarctation of the aorta in our reportage. On the other hand, Lim *et al.*[37] in a cohort of 532 subjects who had isolated BAV noted 4.3% of coarctation of the aorta among children with BAV. The surgical repair was mainly due to aortic regurgitation or aortic stenosis.[39]

This study showed no difference between children with BAV and normal children matched for age and gender. This suggests a relatively absence of valvar abnormalities among the subjects with BAV. However, this was not in keeping with the study of van Rensburg *et al.*[38] who noted congenital mitral valve abnormalities in their reportage. They concluded that mitral valve abnormalities occur more commonly in children with BAVs than in control. This shows that associated anomalies of BAV in children extend beyond the aorta.[39]

This study showed zero prevalence of associated consanguinity among children born with BAV. This is expected as consanguineous marriage is very rare in South East Nigeria. Glotzbach *et al.*[39] using a very large population of 3,812,588 subjects noted familial hazard risk of first-degree relatives of patients with BAV.[39] Several studies have noted a strong association between consanguineous marriage and high prevalence of BAV.[39]

The majority of the subjects with BAV in the current study were asymptomatic. Those who presented with breathlessness had associated lesions. In childhood, BAV is usually asymptomatic with one in 50 children presenting with clinical symptoms.[39] However, in adulthood, clinical presentation varied from mild to severe disease.[39] Clinical features are often associated with aortopathy and endocarditis.[39] Shear stress with attendant valve calcification is noted as trigger of clinical symptoms of BAV in adulthood.[39]

There were no associated syndromes in children with BAV as seen in this study. Some studies have documented associated syndromes in children with BAV implicating autosomal dominant inheritance, variable expressivity, and incomplete penetrance, as possible triggers.[39] This could also be due to the complex genetic model seen in the cardiac anomaly which includes high genetic heterogenicity.[39] The zero prevalence of syndromic correlate documented in this study could be explained by the fact that chromosomal analysis was not performed for any of the children with BAV due to financial constraints. Syndromic features were ascertained using phenotypic and clinical features alone.

### Limitation

Though this article is strengthened by the large number of sample size (1005 echocardiographic examination), a nationwide and cohort study design may be needed to validate the findings obtained from this study.

## Conclusion

Though BAV is the most common congenital heart disease, its rarity is proven in this study. It is also noteworthy that the cardiac defect is associated with valvar anomalies.

### Ethical approval and consent to participate

The approval of the Health Research Ethics Committee of the University of Nigeria Teaching Hospital, Enugu was obtained. (IRB number of 00002323). A verbal oral informed consent was obtained from the patients and parents/caregivers of all study participants while an assent was obtained in participants aged 7 years and older.

### Author contributions

JMC conceived and designed this study while ATC, BCC, NUA, FON, and NYP helped in the critical revision of the article. JMC and BFC also did the data analysis/interpretation. All authors have read and approved the manuscript.

### List of abbreviation

ASD: Atrial Septal Defect

BAV: Bicuspid Aortic Valve

CW: Continuous Wave

EF: Ejection Fraction

FS: Fractional shortening

IVSd**:** Interventricular septum diameter in diastole

IVSs: Interventricular septum diameter in systole

LVID: Left ventricular internal diameter in systole

LVIDd: Left ventricular internal diameter in diastole

LVPWs: Left ventricular posterior wall diameter in systole

PDA: Patent ductus ateriosus

PW: Pulse wave

RPA: Left pulmonary artery

TOF: Tetralogy of Fallot

VSD: Ventricular septal defect

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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