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ORIGINAL ARTICLE

Clinical features and echocardiographic findings in children with ebstein's anomaly: A descriptive case-series of 48 cases.

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ABSTRACT... Objective: To determine the clinical features and echocardiographic findings among children presenting with Ebstein's anomaly (EA). **Study Design:** Descriptive Case-series. **Setting:** Department of Pediatric Cardiology, National Institute of Cardiovascular Diseases (NICVD), Karachi Pakistan. **Period:** July 2021 to June 2022. **Material & Methods:** Children of both genders aged above 1 month up to 18 years, having echocardiographic confirmed EA were analyzed. Demographic data along with clinical features, presenting symptoms and echocardiographic findings were noted in all case. **Results:** In a total of 48 cases of EA, 38 (79.2%) were female. The mean age was 8.4±4.21 years. Cyanosis, exertional dyspnea, easy fatigue ability and exercise intolerance were the most frequent symptoms reported in 31 (64.6%), 27 (56.3%), 26 (54.2%) and 24 (50.0%) patients respectively. Arrhythmias and heart failure were the most frequent clinical features noted in 29 (60.4%) patients each. Small atrial septal defect (ASD) was noted in 27 (56.3%) patients while ventricular septal defect in 19 (39.6%) cases. There were 11 (22.9%) patients who presented timely with diagnosis of EA while 37 (77.1%) patients had late diagnosis. **Conclusion:** Majority of the patients with Ebstein's anomaly were female. Cyanosis, exertional dyspnea, easy fatigue ability and exercise intolerance were the most frequent symptoms whereas arrhythmias and heart failure were the most frequent clinical features observed. ASD was the most commonly noted associated CHDs observed in almost half of the Ebstein's anomaly case. Almost 3/4th of the patients had late diagnosis.

Key words: Arrhythmia, Dyspnea, Ebstein's Anomaly, Exercise Intolerance, Heart Failure.

INTRODUCTION

Ebstein's anomaly (EA) is a rare disease and described as a congenital malformation depicted as tricuspid valve pathology with right heart enlargement.[1] The incidence of EA is estimated to be around 1/200,000 live-births while its share is below 1% in all types of congenital heart diseases (CHDs).[2,3] The EA was initially detailed by Wilhelm Ebstein in 1866.[4] The EA can vary widely in severity, anatomy and presentation.

The exact genetic etiology of EA is still not full uunderstood.[5] Diagnosis of EA is predominantly dependent upon echocardiographic findings but it is important to develop a proper understanding of anatomy and physiology, as well as, clinical features of EA. Clinical features of EA are generally dependent upon anatomic severity while majority of the cases present during early years of life while there have been reported incidents of delayed presentation of EA in the adulthood.[6,7] Manuel V and colleagues from Angola analyzing 1362 patients of CHDs over a period of 37 months noted 8 (0.6%) cases of EA.[8] Among cases with EA, most frequently presenting symptoms were congestive heart failure (CHF) and cyanosis noted in 5 cases (62.5%) each.[8]

The EA usually presents with cyanosis, heart failure, arrhythmia or paradoxical embolism but most of these findings are derived from isolated case reports or small case-series studies.[9,10]

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No study has been specifically conducted in Pakistan to determine clinical features and patterns of echocardiographic findings among children with EA so the present study was planned. The objective of this study was to determine the clinical features and echocardiographic findings among children presenting with EA. This study is the first of its kind and describes our one-year experience about EA at a leading tertiary cardiac care hospital of the country.

MATERIAL & METHODS

This case-series study was conducted at department of pediatric cardiology, "National Institute of Cardiovascular Diseases (NICVD)", Karachi Pakistan from July 2021 to June 2022. Ethical Clearance was acquired from Institutional Ethical Committee of NICVD (certificate number ERC005/2022, dated 14-12-2021). Informed and written consents were sought from parents/guardians. Inclusion criteria were children of both genders aged above 1 month up to 18 years, having echocardiographic confirmed EA were analyzed. Exclusion criteria were parents/guardians unwilling to let their children be part of this study.

Confirmation of EA was done on the basis of transthoracic echocardiography and Doppler studies as per the recommendations of the "American College of Cardiology/American Heart Association".[11] The EA was labeled as displacement of the septal and posterior leaflets of the tricuspid valve > 8 mm/m^2 body surface area in relation to the position of the mitral valve anterior leaflet.[12,13]

Demographic data along with clinical features, presenting symptoms and echocardiographic findings were noted in all case. A special proforma was made to record all study data. Data was entered and analyzed in "Statistical Package for Social Sciences (SPSS)" version 26:00. Descriptive statistics were applied for expressing our results. Mean and standard deviation were calculated for numeric data. Frequency and percentages were shown for categorical data.

RESULTS

In a total of 48 cases of EA, 38 (79.2%) were female. The mean age was 8.4±4.21 years while 22 (45.8%) cases were aged between 6 to 10 years. The mean body weight was calculated to be 17.6±6.3 kg. Residential status was rural in 33 (68.8%) patients of Ebstein's anomaly. Socioeconomic status was 32 (66.7%) patients was middle. Majority of the patients, 37 (77.1%) were presented in emergency department. Analysis of "New York Heart Association (NYHA) classification was found to be NYHA-IV in 18 (37.5%) patients (Table-I).

Characteristics		Number (%)
Gender	Male	10 (20.8%)
	Female	38 (79.2%)
Age Groups (years)	<1	4 (8.3%)
	1-5	5 (10.4%)
	6-10	22 (45.8%)
	>10	17 (35.4%)
Weight (kg)	<5	5 (10.4%)
	5-10	8 (16.7%)
	11-20	18 (37.5%)
	>20	17 (35.4%)
Residence	Urban	15 (31.3%)
	Rural	33 (68.8%)
Socio-Economic Status	Lower	12 (25.0%)
	Middle	32 (66.7%)
	Upper	4 (8.3%)
Place of Enrollment	Outpatient Department	11 (22.9%)
	Emergency Department	37 (77.1%)
NYHA functional Class	I	4 (8.3%)
	II	11 (22.9%)
	III	15 (31.3%)
	IV	18 (37.5%)

Table-I. Socio-Demographic and clinical characteristics of patients with ebstein's anomaly (n=48)

Cyanosis, exertional dyspnea, easy fatigue ability and exercise intolerance were the most frequent symptoms reported in 31 (64.6%), 27 (56.3%), 26 (54.2%) and 24 (50.0%) patients respectively. Evaluation of clinical features revealed that arrhythmias and heart failure were the most frequent, noted in 29 (60.4%) patients each (Figure-1).

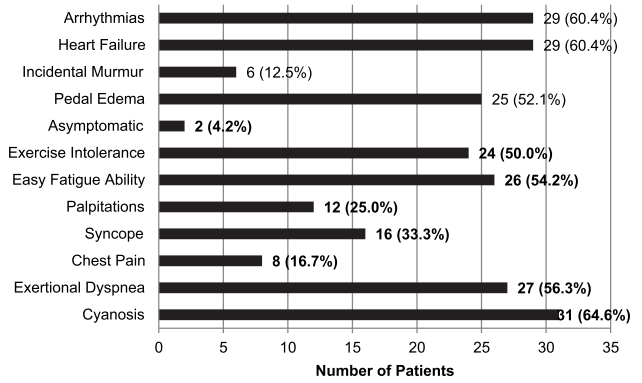

Figure-1. Frequency of presenting symptoms and clinical features (n=48)

Displacement index was between 16-30 mm/m^2 in 23 (47.9%) patients. Celermajor Index was noted to be Grade-3 and Grade-4 in 22 (45.8%) and 15 (31.3%) cases. Left ventricular compaction was observed among 5 (10.4%) cases while left ventricular dysfunction was shown in 17 (35.4%) patients. Half of the patients, 24 (50.0%) were having severe tricuspid regurgitation. Small atrial septal defect (ASD) was noted in 27 (56.3%) patients while ventricular septal defect in 19 (39.6%) cases. Mild pulmonary valve stenosis was observed in 11 (22.9%) cases. Echocardiographic features and associated CHDs among patients of EA patients are shown in Table-II.

There were 11 (22.9%) patients who presented timely with diagnosis of EA while 37 (77.1%) patients had late diagnosis. Enquiry from parents/guardians about the causes of late diagnosis of EA revealed "lack of education/understating of the disease on the part of the patient/guardian" to be the most prevalent cause observed in 11 (22.9%) cases. "Limited access to healthcare facility" was the cause behind late diagnosis among 10 (20.8%) EA cases diagnosed late. "Inadequate counseling by the doctor" were reported by 8 (16.7%) patients to be the cause behind late presentation of EA while "Social factors" and the patients being asymptomatic were the cause behind late diagnosis in 6 (12.5%) and 2 (4.2%) respectively. Knowledge of the disease was found to be good, average and poor in 6 (12.5%), 14 (29.2%) and 28 (58.3%) parents/guardians respectively.

Echocardiographic Features		Number (%)
Displacement Index (mm/m^2)	8-15	8 (16.7%)
	16-30	23 (47.9%)
	>30	17 (35.4%)
Celermajor Index	Grade 1 (<0.5)	3 (6.3%)
	Grade 2 (0.5-0.99)	8 (16.7%)
	Grade 3 (1-1.49)	22 (45.8%)
	Grade 4 (≥1.5)	15 (31.3%)
Left Ventricular Compaction		5 (10.4%)
Left Ventricular Dysfunction		17 (35.4%)
Tricuspid Regurgitation	Mild	3 (6.3%)
	Moderate	13 (27.1%)
	Severe	24 (50.0%)
	Free	8 (16.7%)
Right Ventricular Size	Normal	2 (4.2%)
	Borderline Small	19 (39.6%)
	Hypoplastic	27 (56.3%)
Atrial Septal Defect	Patent Foramen Ovale	10 (20.8%)
	Small	27 (56.3%)
	Moderate	9 (18.8%)
	Large	2 (4.2%)
Pulmonary Valve Stenosis	Mild	11 (22.9%)
	Moderate	7 (14.6%)
	Pulmonary Atresia	1 (2.1%)
	No Pulmonary Stenosis	29 (60.4%)
Ventricular Septal Defect		19 (39.6%)
Patent Ductus Arteriosus		8 (16.7%)
Atrioventricular Septal Defect		13 (27.1%)
Mitral Valve Prolapse		11 (22.9%)
Coarctation of the Aorta		10 (20.8%)

Table-II. Echocardiographic features and associated congenital heart diseases among patients with Ebstein's Anomaly

DISCUSSION

Being a relatively rare CHD type, research on Ebstein's anomaly is largely limited to case reports from Pakistan.[14,15] To the best of our knowledge, present is the first study exploring presentation and echocardiographic features of patients with EA. We noted that 79.2% of patients with EA were female. Our findings are in agreement with a single center study from Angola where the authors shared 75% patients with EA to female.[8] Our findings are in contrast to Anderson HN et al[16] and da Silva JP et al[17] where they noted a slight male predominance in EA patients. Some others have also reported almost equal gender

distribution in EA cases[18-20] so present study's findings in terms of a clear female predominance are not definite and needs to be further verified in larger multicenter studies.

The mean age was 8.4±4.21 years in this study. Manuel V et al[8] found mean age among EA patients to be 69±59 months which was higher than what we reported here. Data from developed countries report that CHDs are diagnosed in the fetal period on during neonatal period in majority of the cases[18,20,21] but studies from the developing nations still show that many CHD cases are still reported in the later years of childhood.[8,19,22] In this study, 77.1% EA cases had late diagnosis which is a matter of concern in our population. Patients with delayed diagnosis of CHDs often have developed complications which worsen the prognosis.[23,24]

Cyanosis (64.6%), exertional dyspnea (56.3%), easy fatigue ability (54.2%) and exercise intolerance (50.0%) were the most frequent symptoms reported in this study while arrhythmias (60.4%) and heart failure (60.4%) were the most common clinical features observed. The literature reports that cyanosis, dyspnea and poor exercise tolerance to be key symptoms among patients with EA.[25] Cyanosis is reported in almost half of EA patients while studies have reported that severe cyanosis is further related to poor exercise intolerance.[26,27] Chest pain and syncope are the other commonly reported symptoms by other researchers in the past.[28] Palpitations are also a common presentation among cases of EA as these are usually related to arrhythmias.[29,30]

We found that 68.8% patients belonged to NYHA functional class-III or IV. A study from Sudan reported almost same findings about NYHA functional class findings among patients with EA.[19] Timely access to quality healthcare services is a challenge for most patients of CHDs in our part of the world so emphasis should be made in neonatal screening and early diagnosis of CHDs. There needs to be a national registry for CHD patients so that these patients can be tracked and taken care off after leaving early diagnosis period.

Being a single center study performed on a relatively small sample size are some limitations of this study. We were unable to report management strategies and treatment outcomes in studied cases.

CONCLUSION

Majority of the patients with Ebstein's anomaly were female. Cyanosis, exertional dyspnea, easy fatigue ability and exercise intolerance were the most frequent symptoms whereas arrhythmias and heart failure were the most frequent clinical features observed. ASD was the most commonly noted associated CHDs observed in almost half of the Ebstein's anomaly case. Almost 3/4th of the patients had late diagnosis.

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2	Shahnawaz Sathio	Methodology, Discussion.	
3	Arshad Sohail	Data analysis.	
4	Mujeeb Ur Rehman	Data collection, Literature search.	
5	Fazal Ur Rehman	Data collection, Literature review.	
6	Abdul Sattar Shaikh	Literrature review, Discussion.	
7	Najma Patel	Methodology, Discussion.	