Pattern of congenital heart disease among children presenting to the Uganda Heart Institute, Mulago Hospital: a 7-year review

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Abstract

Background: Congenital heart disease (CHD) is the most common congenital anomaly in children. Over half of the deaths due to CHD occur in the neonatal period. Most children with unrepaired complex heart lesions do not live to celebrate their first birthday. We describe the spectrum of congenital heart disease in Uganda.

Methods: We retrospectively reviewed the data of children with CHD who presented to the Uganda Heart Institute (UHI), Mulago Hospital Complex from 2007 to 2014.

Results: A total of 4621 children were seen at the UHI during the study period. Of these, 3526 (76.3%) had CHD; 1941(55%) were females. Isolated ventricular septal defect (VSD) was the most common CHD seen in 923 (27.2%) children followed by Patent ductus arteriosus (PDA) 760 (22%) and atrial septal defects (ASD) 332 (9.4%).

Tetralogy of Fallot (TOF) and Truncus arteriosus were the most common cyanotic heart defects (7% and 5% respectively). Dysmorphic features were diagnosed in 185 children, of which 61 underwent genetic testing (Down syndrome=24, 22q11.2 deletion syndrome n=10). Children with confirmed 22q11.2 deletion had conotruncal abnormalities.

Conclusion: Isolated VSD and Tetralogy of Fallot are the most common acyanotic and cyanotic congenital heart defects. We report an unusually high occurrence of Truncus arteriosus.

Keywords: Congenital heart disease; children; Uganda.

DOI: https://doi.org/10.4314/ahs.v20i2.26

Cite as: *Namuyonga J, Lubega S, Aliku T, Omagino J, Sable C, Lwabi P. Pattern of congenital heart disease among children presenting to the Uganda Heart Institute, Mulago Hospital: a 7-year review. Afri Health Sci. 2020; 20(2): 745-752. https://doi.org/10.4314/ahs.v20i2.26*

Introduction

Congenital heart disease (CHD) is the most prevalent congenital abnormality and a leading cause of childhood mortality[1]. The estimated prevalence of CHD is 8-12/1000 live births[2-4].

Without appropriate treatment, about one in three children born with significant congenital heart disease will die within the first month of life[5]. Unrepaired congenital heart disease is a major cause of heart failure among children in Africa[6]. We believe that this study is the largest in Africa to report on congenital heart disease amongst children. The aim of this study was to describe the spectrum of congenital heart disease among children who presented to the Uganda Heart Institute.

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Methods

We retrospectively reviewed 3526 echocardiography reports of patients with CHD that presented to the Uganda Heart Institute (UHI) between 2007 to 2014. The registry for congenital heart disease was established in 2007 by the pediatric cardiology division as part of the Ministry of Health reporting system and serves as the basis for this study. Makerere University School of Medicine Ethics and Research Committee approved the genetics component of the study.

Study site

The Institute is a 40 bed facility located within the Mulago Hospital complex and has been in existence for 28 years. The UHI has a fully functional operating theatre in addition to a catheterization laboratory. It performs paediatric and adult open-heart surgeries, diagnostic

and interventional catheterization procedures. Outpatient clinics run on a daily basis. Averagely, 60 to 80 paediatric open heart surgeries are conducted per year. A paediatric cardiology fellowship program has run since 2010.

Study procedure

Detailed transthoracic echocardiography was performed and interpreted by one of the two pediatric cardiologists (PL /SL) using standard guidelines[7] with a Sonos 5500 (Philips, Best, Netherlands) and a Philips IE 33 (Philips, Best Netherlands) for the periods 2007 to 2011 and 2012 to 2014 respectively.

Difficult cases were discussed and a final diagnosis made by consensus. Digital archiving enabled cases to be reviewed and discussed with colleagues (CS) from other centers. Re-evaluation of cases at follow up improved diagnostic accuracy.

Severe congenital Heart disease, CHD was defined as complex heart abnormalities that were life-threatening. For example, heterotaxy syndromes, anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) and univentricular heart. Patient demographics including age, sex, weight and type of congenital heart defect were entered into an Excel spreadsheet and analyzed using SPSS version 16. Pulse oximetry readings were available for only a small subset of children and not included in the analysis.

Syndromic children

If the child had an obvious syndromic condition based on clinical examination, they were sent for genetics assessment. Genetics testing was done by a highly experienced genetics specialist from Washington DC, United States together with the Ugandan team and the paediatric cardiologist (CS) during some missions. Genetics diagnosis was based on clinical presentation of the common genetics syndromes with associated complications. These were matched with the echocardiogram diagnosis. We secured Institutional Ethical approval from the Makerere School of Medicine as well as from the National Institute of Health (NIH) laboratory in Washington DC, United States to run detailed microarray and DNA sequencing for the genetics study but blood samples were not taken off or sent for analysis. The team relied on clinical diagnosis by a highly skilled genetics specialist. Syndromes such as Down's syndrome, 22q11 deletion syndrome, Holt Oram and Williams syndrome were diagnosed. Children with Holt Oram syndrome had upper limb abnormalities in addition to the CHD. A genetics syndrome was diagnosed based on clinical evaluation, the results were given to the family, and was counseled by our team, a geneticist and genetic counselor.

Congenital Rubella Syndrome

Congenital Rubella syndrome, CRS was diagnosed based on clinical features of cataracts, microphthalmia, microcephaly and hearing impairment. Retrospective data was obtained from the World Health Organization -Congenital Rubella (WHO- CRS) Surveillance that was conducted at the UHI in 2014. CRS was confirmed by blood samples obtained from the child and mother. Serum was tested at Uganda Virus Research Institute (UVRI) for evidence of active rubella virus infection through identification of rubella-specific IgM antibodies. UVRI is a government parastatal certified by the American College of Pathologist to conducts research, surveillance and diagnostics linked to viral etiology and provides expert advice[8].

Results

Overall, 4621 charts were reviewed during the study period. A diagnosis of congenital heart disease was made in 3526 (76.3%) children. The majority 1941(55%) were females. Most patients presented during infancy (range 1 day -18 years).

VSD was the most prevalent defect (921) of which 702 children (76%) had perimembranous VSD, and 79 (8.5%) had muscular VSD. PDA was the second most commonly occurring defect seen in 760 cases (22%). ASD was present in 332 children (9.4%) with the Ostium secundum type occurring in 293 (88%) followed by the sinus venosus defect, 23 (6.9%).

Tetralogy for Fallot and persistent Truncus arteriosus were the most common cyanotic heart diseases. Some defects occurred in small percentages and have been reported. Children with syndromes in the study were examined for specific genetic abnormalities.

Table 1: Acyanotic heart diseases

	Number	Overall Percentage in CHD (%) N=3526	Mean age (months)/years	Female n (%)
Isolated VSD	921	26	25(2)	484 (52)
PDA	760	22	19(1.6)	478 (62)
ASD	332	9.4	51(4)	188 (56)
ECD	265	8	17(1)	164(62)
Pulmonary valve stenosis	226	6	38(3)	99(44)
Mitral valve prolapse	63	2	90(7.5)	44(69)
Aortic valve stenosis	35	0.9	100(8)	14(40)
PAPVC	17	0.5	46 (4)	5(29)
COA	14	0.4	80(6.5)	7(50)

***ECD**- endocardial cushion defects**, VSD-** Ventricular septal defect**, ASD-**Atrial septal defect, **PDA-** Patent ductus arteriosus**, PAPVC**- partial anomalous pulmonary connections, **COA-** coarctation of the aorta*

Among the cyanotic defects, Tetralogy of Fallot (TOF) was the most common, 247 cases (7%) were seen with a male preponderance.

Table 2: Cyanotic heart diseases

Lesion	Numbers	Mean age Years (months)	Female Number (%)	Overall percentage in CHD (N=3526)
Tetralogy of Fallot	247	4(50)	110(44)	**7**
Truncus arteriosus	165	0.4 (5)	92(56)	**5**
DORV	104	1.4(16.5)	56(53)	**3**
Pulmonary atresia	71	2.6(32)	38(53)	**2**
Tricuspid atresia	62	1.6(20)	31(50)	**1.8**
D TGA	53	0.7(9.5)	21 (40)	**1.5**
A PVR	8	0.5(7)	4(50)	**0.2**

D TGA-Transposition of the Great Arteries, APVR- anomalous pulmonary venous return, DORV- Double outlet right ventricle

In addition, sub types of DORV

DORV was diagnosed in 104 children. DORV with sub pulmonic VSD, also called the Taussig Bing anomaly, occurred in 43 children (41%). DORV with sub aortic VSD (VSD physiology), 38 (37%), DORV/ pulmonary stenosis (Fallot type) 15 (14%), and DORV with doubly committed VSD found in 3 (3%). Two (2%) children had DORV with corrected TGA.

Table 3: Complex heart defects

Most children with complex heart defects were female.

Defect	Total number	Female Number (%)
Dextrocardia with left isomerism	14	10 (71.4)
Hypoplastic left heart syndrome (HLHS)	10	7 (70)
Ebstein's anomaly	7	4(57)
ALCAPA	3	1(33)
Univentricular heart	12	6 (50)

ALCAPA- Anomalous origin of the left coronary artery from the pulmonary artery

Less common CHDs

Some congenital defects were rare, namely: Aortopulmonary window, which was present in 6 (0.2%) of all CHD. Common atrium 13 (0.3%) with a female preponderance 10 (76%). Partial Anomalous Pulmonary venous connections (PAPVC) were present in 17 (0.5%). It commonly occurred with the sinus venous ASD. Median odiagnosis was 3 years (range 1 month-12 years). Bicuspid aortic valve occurred in 7(0.2%) of all congenital heart disease.

Total anomalous pulmonary venous connections (table 2) were reported in only 8 children (3%); 2 had the infracardiac type, 4 cardiac type and 2 the supra cardiac type.

Patients with dysmorphic features

One hundred eighty-five children had dysmorphic features. The majority 143 (76%), had a phenotypic diagnosis of Trisomy 21 (Down syndrome) with endocardial cushion defects as the most likely diagnosis. Sixty-one of the 186 children underwent genetic testing. Congenital Rubella Syndrome was present in 15 (8) % of cases from data extracted from the WHO-UHI-CRS Surveillance in 2014. Eighty-eight percent had CHD, 68% had ocular defects (cataracts) and 20% had hearing problems. PDA was the most common CHD (77%).

Table 4: Genetic abnormalities

Genetic disorder	N=61
Trisomy 21	24
22q11.2 deletion syndrome	10
Noonan syndrome	5
Turner syndrome	3
Kabuki	2
Holt Oram	1
CHARGE	1
Unrecognized dysmorphism	15

Of the children with 22q11.2 deletion syndrome, 7 had Tetralogy of Fallot, 2 Truncus Arteriosus and 1 had D-TGA. Noonan's syndrome was confirmed in 5 children; 4 had pulmonary stenosis.

Congenital heart defects and age at diagnosis

Most complex heart diseases such as univentricular heart defects, D-TGA, pulmonary atresia, tricuspid atresia, total anomalous pulmonary venous connections and Ebstein's anomaly were rarely diagnosed after the first year of life. Notably, no children with right isomerism/ heterotaxy were seen during the study period.

Table 5*: Congenital heart abnormalities and age at diagnosis*

Abnormality	Infancy	(> 1 < 5 years)	> 5 < 18Years
VSD	615	190	116
PDA	556	138	66
ASD	134	114	84
Pulmonary Stenosis	130	69	54
ECD	165	45	55
COA	6	2	6
TOF	83	98	66
Truncus Arteriosus	144*	20	1
DORV	72	18	8

*Diagnosed before 6 months of age

VSD, ASD, PDA, TOF, pulmonary stenosis and coarctation of the aorta continued to present in children older than 5 years. Defects not commonly diagnosed after 6 months included; Truncus arteriosus, DORV, Tricuspid atresia, TGA, anomalous pulmonary venous return and Hypoplastic left heart syndrome.

Discussion

This was a retrospective study with a large number of patients making it representative of the entire country.

Ventricular septal defects (VSD) were the most common congenital heart defects (26%) with the membranous type in high frequency. Our findings are similar to studies reported elsewhere[4,9-11]. Ekure and colleagues reported VSDs in 25% of Nigerian children[12] however, a higher prevalence stated in some studies notably Cameroon, included adults attesting to the fact that VSD patients survive into adulthood[6,13]. VSD is one of those defects that were diagnosed till 18 years.

Patent Ductus Arteriosus was the second most common defect. This may be due to increased number of premature deliveries, genetic syndromes, maternal rubella infection and peripartum hypoxia[12,13]. PDA is highly prevalent in extreme preterm babies with birth weight less than 1kg[14] Premature deliveries in Uganda directly eminent from multiple factors including; low and late antenatal attendance for the recommended visits hence mothers tend to miss drugs like Fansidar that are prophylactic for malaria. Premature deliveries have been linked to placental malaria in some studies, poor maternal preconception nutriton and adolescent pregnancies as well as child spacing less 24 months[15,16]. Anemia and gestational hypertension are the highest risk factors for preterm deliveries[15].

PDA is one of the cardiac manifestations of Congenital Rubella syndrome reported in infants whose mothers suffered Rubella infection during pregnancy[17]. Other abnormalities include; VSD, peripheral pulmonary branch stenosis, ocular complications and central nervous system problems[18]. A recently concluded World Health Organization Congenital Rubella Surveillance in Uganda showed a high percentage (77%) of PDAs in those infants with serologically confirmed Congenital Rubella Syndrome[19].

At present, Uganda lacks a National rubella vaccination program, developed countries vaccinate children with the MMR (Mumps Measles Rubella vaccine which drastically dropped CRS incidence[20].

Atrial septal defects ranked third. As reported in other studies there was a female preponderance at 56%, with 88% secundum type. ASDs tend to be well tolerated through infancy and childhood and are still diagnosed into adulthood.

We postulate that very few children of neonatal coarctation were seen because they are not referred early to our center and could have been missed by the primary health care provider. Critical neonatal coarctation often presents as an emergency with a new born in shock and fatal without immediate intervention[21-23]. Similarly, aortic coarctation among older children was rare. This may imply a low prevalence of this condition or show that man of these patients are not detected because blood pressure measurements are not routinely carried out in children[22]. The few cases in our study presented after 5 years of age. It has also reported in the Nigerian Congenital Heart Disease registry that coarctation of the aorta was one of the rare CHD[12].

Tetralogy of Fallot remains the most common cyanotic heart defect as has been reported elsewhere[2,24,25]. There is a relatively large population of unrepaired patients alive which implies greater survival in less severe cases. This trend has improved with more patients accessing corrective surgery that is now available at the Uganda Heart Institute. By 2014, 80% of the open heart surgeries were performed by our local team and only 20% were referred abroad who mainly included complex congenital heart defects[23].

Five percent of the patients had Truncus arteriosus which is higher than what is reported in other settings that give an overall prevalence of 2.4%[26,27]. This was reflected consistently in the number of cases detected on a yearly basis over the study period. Most cases were diagnosed early (before 6 months) owing to an early presentation with heart failure. No new cases were seen in children above 5 years. Truncus arteriosus is associated with a high prevalence of genetic disorders. Thirty-nine percent of the children who underwent genetic testing had truncus arteriosus. This strongly suggests a genetic etiology in our population.

Cases of D-TGA were rare in the study. Transposition of the great arteries has been associated with a high mortality as reported in some studies[9]. The advent of palliative atrial septostomy at the Uganda Heart Institute that acts as a bridge to surgery, offers hope to these critically ill infants who may present with TGA with restrictive interatrial shunts.

Other complex defects were most prevalent in the first year of life. These were not diagnosed after the first birthday. They have been associated with a high mor-

tality, two thirds of children with complex heart defects such as Hypoplastic left/right heart syndrome do not cerebrate their first birth day5. Unfortunately, limited treatment options are available in the country for such children.

We noted that some CHDs were rare in our study population, a case in point TAPVC (3%) prevalence was comparable to that reported in the Nigerian Congenital Heart Registry (12). Others; Aortopulmonary window, Ebstein's anomaly and bicuspid aortic valve.

Genetic studies though limited, had a high likely hood of a positive result indicating a need for routine genetic screening in children with congenital heart disease. Deletion 22q11.2 which is associated with immunodeficiency, hypocalcaemia and learning difficulties was also been diagnosed by our team based on clinical findings. Prior knowledge of a genetic syndrome improves surgical outcomes for patients, given the fact that the surgical teams plan for any related complications for such abnormalities. Doell and friends in Switzerland reported no difference between children with genetic syndromes versus those without who underwent open heart surgery for CHD, a genetic syndrome was an independent risk factor for re intubation, and kidney injury[28].

Digital archiving enabled cases to be discussed with colleagues from other centers and there was an opportunity for re-evaluation of cases at follow up which improved diagnostic accuracy.

Our major limitation was having a retrospective study at a single site whose results may not be fully representative of the nation. However, two other sites have been established in the northern and western parts of the country.

Conclusion

Congenital heart disease is common among children. VSD, PDA and ASD were the commonest acyanotic heart defects while Tetralogy of Fallot and Truncus arteriosus topped the cyanotic defects. Genetic studies are called for in our population to further understand this high prevalence of Truncus arteriosus.

Acknowledgments

We would like to thank all children and families that contributed to this work. Ms Allen Nakiboneka who assisted with the analysis of this data and the entire department of paediatric cardiology.

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