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ORIGINAL ARTICLE

Cyanotic Congenital Heart Disease in the Kingdom of Bahrain

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Abstract

Background and Objectives: Cyanotic congenital heart disease (CCHD) is a high-risk condition in infants with congenital heart disease (CHD) and often requires urgent management. It is important to have reliable information about the various cyanotic CHDs and their management. As there is no data on CCHD in the Kingdom of Bahrain, we conducted this study to analyze the different types of CCHD, their management, and outcomes.

Methods: This was a retrospective descriptive study conducted from 2000 to 2019 on 554 patients with confirmed diagnosis of CCHD.

Results: Mean age at presentation was 1.8 years (range 0 day to 56 years) and 108 (19.5%) were diagnosed within 24 hours of life. The mean duration of follow-up was 7.9 years. The most common CCHDs included Tetralogy of Fallot (TOF) (44.9%), univentricular heart defects (UVH) (11.4%), and D-transposition of great arteries (D-TGA) (10.5%).The least common CCHD was hypoplastic right heart syndrome (HRHS) (0.4%). The overall mortality was 15% (n=83). The mortality rate was highest in patients with hypoplastic left heart syndrome (HLHS), noted in 52% cases.

Conclusions: The most common CCHD was TOF, and the most common mode of presentation was cyanosis. The prognosis and outcomes were good in patients with biventricular repair but poor in patients with HLHS. Early diagnosis and timely intervention can reduce the morbidity and mortality associated with CCHD.

Keywords: Congenital; Cyanotic; Defect; Diseases; Heart

Introduction

Cyanotic congenital heart disease (CCHD) is a condition present at birth due to low blood oxygen level. It constitutes 25% of all congenital heart disease (CHD) cases.[1-3] Most CCHD patients present in the neonatal age with cyanosis, cardiovascular collapse, or congestive heart failure.[4] Echocardiography is the primary diagnostic tool to identify the various types of CCHD. There are no previous studies regarding the spectrum of CCHD

in the Kingdom of Bahrain. To fill this void, we conducted this study to assess the frequency of various types of CCHD, their management, and outcomes.

Material and Methods

This was a retrospective descriptive study conducted over 19 years, from January 2000 to December 2019, after obtaining approval from our institutional ethics committee. Data was collected from a pediatric cardiology database.

All patients with confirmed diagnosis of CCHD by echocardiography were included in the study. Patients with pulmonary arteriovenous fistula, primary or idiopathic pulmonary hypertension, and cyanosis due to Eisenmenger's syndrome were excluded. Data was recorded directly in a Microsoft Excel spreadsheet (Microsoft Inc., Redmond, Washington (USA). Statistical analysis was performed using IBM SPSS 25.0 software, and descriptive analyses were performed.

Results

There were a total of 554 patients with confirmed diagnosis of CCHD. The male to female ratio was 1.4:1. The mean age at presentation was 1.8 years (range 0 day to 56 years). The CCHD was classified into two major types: CCHD with decreased pulmonary blood flow (PBF) and CCHD with increased PBF. Of the 554 patients, 405 patients (73%) had CCHD with decreased PBF and 149 (27%) had CCHD with increased PBF (Figs 1 & 2).

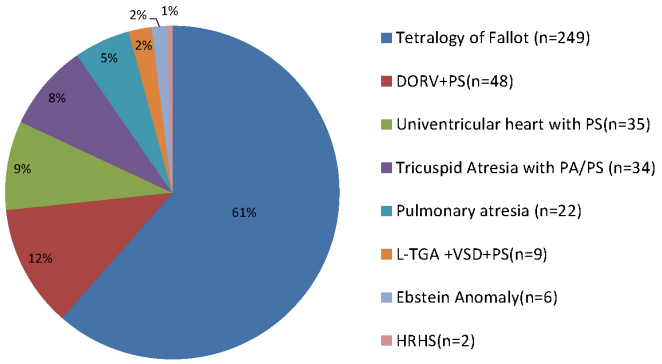

Figure 1: Cyanotic congenital heart disease with decreased pulmonary blood flow (n=405).

DORV: Double outlet right ventricle, HRHS: Hypoplastic right heart syndrome, L-TGA: Levo-transposition of the great arteries, PA: Pulmonary atresia, PS: Pulmonary stenosis, VSD: Ventricular septal defect

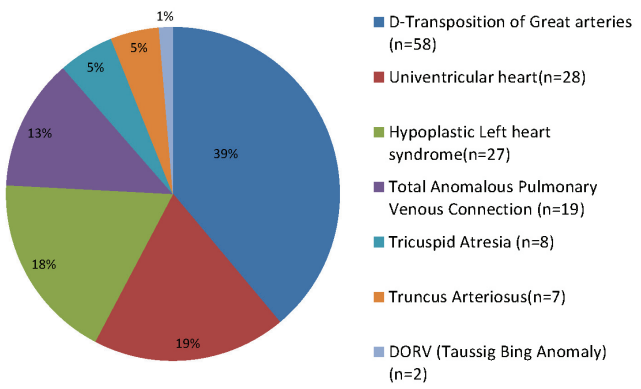

Figure 2: Cyanotic congenital heart disease with increased pulmonary blood flow (n=149).

D: Dextro, DORV: Double outlet right ventricle.

The various types of CCHD and their frequency distribution are illustrated in Table 1. The most common CCHD was Tetralogy of Fallot (TOF) with 249 (44.9%) cases followed by univentricular heart defects (UVH) with 63 (11.4%) cases and dextro-transposition of great arteries (D-TGA) with 58 (10.5%) cases. The least common CCHD was

Table 1: Types of cyanotic congenital heart disease

Type of CCHD	No of cases (n=554)	Percentage (%)
Tetralogy of Fallot	249	44.9
Univentricular heart (DILV, DIRV, Unbalanced AVSD)	63	11.4
D-Transposition of the great arteries	58	10.5
DORV	50	9.0
Tricuspid Atresia	42	7.6
Hypoplastic left heart syndrome	27	4.9
Pulmonary atresia	22	4.0
Total anomalous pulmonary venous connection	19	3.4
L-TGA+VSD+PS	9	1.6
Truncus arteriosus	7	1.3
Ebstein anomaly	6	1.0
Hypoplastic right heart syndrome	2	0.4

AVSD: Atrio-ventricular septal defect, CCHD: cyanotic congenital heart disease, D: Dextro, L: Levo, DILV: Double inlet left ventricle, DIRV: Double inlet right ventricle, DORV: Double outlet right ventricle, PS: Pulmonary stenosis, IVS: Interventricular septum, TGA: Transposition of the great arteries, VSD: Ventricular septal defect.

Table 2: Gender and age of patients at presentation

Variable	TOF	UVH	DTGA	DORV	TA	HLHS	PA	TAPVC	LTGA	Ebstein	Truncus	HRHS
Gender												
Male	149	35	32	27	24	18	17	9	5	3	4	1
Female	100	28	26	23	18	9	5	10	4	3	3	1
Ratio	1.5:1	1.2:1	1.2:1	1.2:1	1.3:1	2:1	3.4:1	0.9:1	1.2:1	1:1	1.3:1	1:1
Age at presentation												
0 - 7 D	47	27	20	16	20	16	13	6	4	4	1	1
8 D - 1 mo	46	10	12	12	8	9	5	3	3	2	1	0
2 mo - 1 y	83	14	15	13	5	2	2	10	2	0	5	1
2 - 5 y	28	6	4	1	2	0	0	0	0	0	0	0
6 - 10 y	8	4	4	2	1	0	1	0	0	0	0	0
11 - 13 y	9	2	0	1	2	0	0	0	0	0	0	0
>14 y	28	0	3	5	4	0	1	0	0	0	0	0
Mean age at presentation (months)	56	55	31.1	39.2	44.8	0.8	13.6	3.2	1.5	1.4	3.4	1.5

DORV: Double outlet right ventricle, D-TGA: Dextro-transposition of the great arteries, HLHS: Hypoplastic left heart syndrome, HRHS: Hypoplastic right heart syndrome, PA: Pulmonary atresia, TAPVC: Total anomalous pulmonary venous connection, TOF: Tetralogy of Fallot, UVH: Univentricular heart, TA: Tricuspid atresia.

Table 3: Noncardiac associations and genetic syndromes

Noncardiac associations	Number of cases (n=76)
Down syndrome (Trisomy 21)	16
DiGeorge syndrome (Deletion 22q11)	16
Central nervous system disorders	11
Urogenital anomalies	8
Multiple congenital anomalies	7
Anorectal anomalies	6
Edward syndrome (Trisomy 18)	2
Noonan syndrome	2
Cayler syndrome	2
VACTERL association	2
Patau syndrome (Trisomy 13)	1
Goldenhar syndrome	1
Klippel-Feil syndrome	1
Kabuki syndrome	1

hypoplastic right heart syndrome (HRHS) with only 2 cases (0.4%).

Table 2 presents information on the demographic characteristics and Table 3 on the cardiac anomalies and genetic syndromes. The incidence of CCHD was noted to be more in males than females (324 males vs. 230 females with a ratio of 1.4:1). The mean age at presentation was 1.8 years (range 0 day to 56 y). The number of patients diagnosed on day 1 of life was 108 (19.5%) and within 1 month of life was 286 (51.6%). A total of 41 patients (2.5%) aged >14 years were seen for the first time in our clinic. These patients were followed up elsewhere and were referred to us for further long-term management.

A total of 76 patients (13.7%) had associated noncardiac anomalies. The most commonly associated genetic anomalies were Down syndrome (n=16) and DiGeorge syndrome (n=16).

Associated cardiac lesions

The associated cardiac lesions in CCHD patients were situs inversus with dextrocardia (n=13), isolated dextrocardia (n=9), isomerism (n=18), right aortic arch (n=22), and Pentalogy of Cantrell with exomphalos (n=1).

Management and outcome of various types of CCHD

The most common palliative surgery performed on CCHD patients was Blalock-Taussig shunt (BT shunt) in 223 patients (Table 4).

Table 4: Types of surgical procedures

Type of surgery	Number of patients
Palliative procedures	
Blalock-Taussig shunt	223
Bidirectional Glenn shunt	73
Fontan completion	58
Norwood stage 1	10
Damus-Kaye-Stansel procedure	2
Complete repair	
Tetralogy of Fallot - VSD closure+RVOT repair	202
Arterial switch operation	43
Rastelli (RV- PA conduit)	34
DORV Repair	16
TAPVC repair	10
Senning procedure	5
Truncus arteriosus repair	5
Ebstein anomaly repair	2
Mustard operation	2

DORV: Double outlet right ventricle, PA: Pulmonary artery, RV: Right ventricle, RVOT: right ventricular outflow tract, TAPVC: Total anomalous pulmonary venous connection, VSD: Ventricular septal defect.

1) Tetralogy of Fallot (TOF)

TOF was present in 249 patients, of whom 9 were with absent pulmonary valve and underwent VSD closure with homograft/conduit placement. Of the 202 (81%) patients who underwent complete repair, palliative BT shunt was required in 76 (30.5%) of them prior to the repair. A total of 25 (12.4%) patients required re-do procedures for residual lesions, of which 15 patients underwent re-do pulmonary valve replacement and 10 patients underwent percutaneous pulmonary valve implantation (PPVI). The mortality was 10.4% (n=26) out of which 4.4% (n=11) was in the immediate postoperative period.

2) Univentricular heart (UVH)

Sixty-three patients who had single ventricle physiology (unbalanced atrioventricular septal defects, double inlet left ventricle [DILV], or double inlet right ventricle [DIRV] were also included in this category) underwent multiple staged palliative surgeries – Stage 1: aortopulmonary shunt or BT shunt - 20 (34%), Stage 2: cavopulmonary shunt or bidirectional Glenn shunt (BDG) - 12 (20.3%), and Stage 3: Total cavopulmonary/Fontan connection (TCPC) - 19 (32.2%). The mortality rate was 14.3% (n=9) of which 7.9% (n=5) was in the immediate postoperative period.

Table 5: Summary of studies on the incidence of various CCHDs

Study	Country	Sample size	Results
Alabdulgader[7]	Saudi Arabia	2604 CHDs from 4 regions of Saudi	TOF is the most common CCHD – 3.5 -5.4 % of all CHDs followed by TGA – 2.1 %
Subramanyan et al[8]	Oman	992 CHDs	CCHD is 21.7 % of all CHDs. Incidence of TOF is 9.6 % of all CHDs. Diagnosis of CHDs under 1 month and 1 year of age 38 % & 40 % respectively
Zaqout et al[9]	Palestine	598 CHDs	Birth Prevalence of TOF is 6 % of CHDs followed by TGA of 5 %. Single ventricle lesions comprise only 0.5% and Ebstein anomaly with 0.33%
Al-Ammouri et al[10]	Jordon	383 CHDs	CCHDs accounts 11% of all CHDs of which most common type is TOF
Iman Ali B-Saddik et al[11]	Yemen	102 CHDs	TOF is the most common CCHD -10.7% followed by TGA – 4.9 % of all CHDs

CHD – Congenital heart disease, CCHD – Cyanotic congenital heart disease, TOF – Tetralogy of Fallot, TGA – Transposition of graet arteries.

3) D-Transposition of the great arteries (D-TGA)

Surgical correction was performed in 50 patients, of whom 43 (86%) underwent arterial switch surgery, 5 (10%) had Senning surgery, and 2 (4%) had Mustard surgery. The mortality was 6.8% (n=4) out of which, 3 babies died before any surgical correction could be performed due to associated persistent pulmonary hypertension.

4) Double outlet right ventricle (DORV)

DORV was noted in 50 patients, and all of them had other associated intracardiac lesions; 21 patients had TGA and coarctation of aorta was seen in 6 patients. DORV associated with TGA and subpulmonic VSD, known as Taussig-Bing anomaly was found in 2 patients. The common surgical procedure performed was biventricular repair. A total of 18 (36%) patients underwent primary repair and 12 (24%) patients who were not amenable to biventricular repair were treated similar to the cases with UVH. Mortality was seen in 7 cases, accounting for 14% of DORV patients.

5) Tricuspid atresia (TA)

There were 42 cases of TA, of which 34 patients had TA with decreased PBF and 8 patients had increased PBF. A total of 16 (38%) patients underwent univentricular pathway completion. The mortality rate was 21.4% (n=9) of TA cases: 8 patients died in the immediate postoperative period after the stage 1 palliative procedure (BT shunt - 6, PA band - 2) and 1 patient died due to plastic bronchitis – a late complication of Fontan procedure.

6) Hypoplastic left heart syndrome (HLHS)

Twenty-seven (4.7%) patients had HLHS: only 10 of them underwent Norwood procedure, 2 patients underwent Damus-Kaye-Stansel procedure, and 1 patient had hybrid procedure constituting pulmonary artery banding with stenting of patent ductus arteriosus (PDA). The mortality rate was the highest with 14 (51.8%) deaths, of which 7 neonates died prior to any surgical procedure and 3 died in the immediate postoperative period after Norwood stage 1.

7) Pulmonary atresia with intact interventricular septum (IVS)

There were total of 22 cases in this category. All patients required palliative BT shunt in the neonatal age. A total of 3 patients underwent biventricular repair and 9 patients underwent the univentricular pathway of Fontan completion. Mortality was 22.7% (n=5) and all 5 patients died in the immediate postoperative period of stage 1 palliative surgery.

8) Total anomalous pulmonary venous connection (TAPVC)

TAPVC was observed in 19 patients and the majority of them had the supracardiac type (n=11). Others included intracardiac TAPVC (n=3), infracardiac TAPVC (n=4), and mixed type of supracardiac and cardiac TAPVC (n=1). There were 3 mortalities (15.8%), all of them were with the infracardiac type and died in the neonatal age before surgical intervention.

9) Ebstein anomaly

There were 6 patients with Ebstein anomaly with decreased PBF: 2 patients underwent BT shunt in the neonatal age, 2 patients underwent Ebstein valve repair and pulmonary valve repair, and 1 patient underwent pulmonary valvotomy. The mortality rate was 33.3% (n=2). One infant died on day 7 of life due to sepsis and another died in the immediate postoperative period after Ebstein and pulmonary valve repair.

10) Truncus arteriosus (TA)

There were 7 patients with TA, of whom 5 patients underwent successful truncus repair and 2 patients (28.5%) died in the immediate postoperative period.

Mortality

In summary, the overall mortality rate was 15% (n=83) for all CCHDs. It was the highest in patients with HLHS (52%).

Followup and outcome

The mean duration of followup was 7.9 years (0-20 y). The Kaplan-Meier survival analysis (Fig. 3) revealed that patients who had corrective surgery

had an increased survival probability of 93% at 20 years whereas patients with palliative surgery alone had a survival probability of only 71% at 20 years.

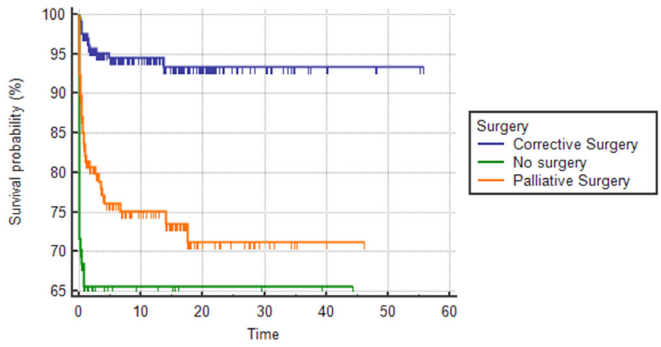

Figure 3: Kaplan-Meier survival curve (years).

Classification

We briefly discuss below the classification of CCHD and the current strategies for CCHD management. CCHD is classified into two major types:

1. CCHD with decreased PBF: Lesions with right ventricular outflow obstruction (RVOTO), e.g. TOF, TA with pulmonary stenosis, PA with intact IVS, UVH with pulmonary stenosis or atresia, severe Ebstein's anomaly with PS or functional pulmonary atresia, and HRHS.

2. CCHD with increased pulmonary blood flow: TGA, HLHS, TAPVC, TA, and UVH lesions without pulmonary stenosis,

In this study, majority of the CCHD cases were due to decreased PBF (73%) whereas CCHD resulting from increased PBF was only 27%. This finding is comparable to that reported in other similar studies.[5]

The age at diagnosis of CCHD depends on the type of heart lesion and other associated factors such as severity of the lesion and other comorbidities. Infants with PDA-dependent lesions such as HLHS, D-TGA, PA, TA, and UVH with decreased PBF were diagnosed earlier in the neonatal period compared to infants with simple TOF. Our diagnosis of CCHDs within 1 month of life was 51.7%, indicating high predictability. Vyas et al[5] recorded an overall predictability of CHD diagnosis for patients between 1 and 6 years of age to be 62.7%.

There are various studies regarding the incidence and prevalence of various CHDs in the Middle Eastern countries which are listed in Table 5. All the studies revealed TOF as the most common type of CCHD.

Management and outcomes comparison of various CCHDs

The management of children with CCHD often needs to be done in several stages. All babies with PDA-dependent circulation were started on prostaglandin E1 infusion to maintain the patency of the PDA until they underwent palliative or corrective surgery.

TOF was the most common CCHD identified in our study, comprising 44.9%, which is comparable to other studies.[5,12-16] TOF consists of four components – large malaligned VSD, overriding of aorta, RVOTO, and right ventricular hypertrophy. The extent and severity of RVOTO account for the variation in symptoms. Babies present early with cyanosis or cyanotic spells (due to infundibular spasm). The surgical policy in our center is to perform BT shunt if a baby presents with symptoms at less than 6 months of age and/or weighs less than 5 kg. BT shunt is a connection with an artificial conduit between the left subclavian artery of aorta and one of the pulmonary arteries. This is a palliative surgery. Complete repair consists of VSD closure and RVOT repair using a transannular patch and infundibular muscle resection. A transannular patch entails incising across the pulmonary valve annulus, resulting in free pulmonary regurgitation. This can cause right heart failure in the long term. Late pulmonary valve replacement is common in TOF repairs, 10-15 years postoperatively. Mortality after cardiac surgery has been reported to be <5%.[17] In this study, immediate postoperative mortality was 4.4% (n=11). TOF repair carries an excellent prognosis.

Tricuspid atresia is the absence of the tricuspid valve, and atrial septal defect (ASD) is mandatory for survival. Such cases can present either with decreased or increased PBF. These patients require univentricular repair/palliation. In neonates with increased PBF, the first operation is pulmonary artery banding to prevent the development of pulmonary hypertension. If the neonate presents with decreased PBF, the first palliative surgery is BT shunt. All these patients have to undergo

second-stage BDG shunt consisting of dividing the superior vena cava and anastomosing it with the pulmonary artery at around 6 months of age. This reduces the load on the single ventricle. The third-stage surgery is Fontan/TCPC operation in which a conduit is placed between the inferior vena cava and the right pulmonary artery. The single ventricle is thus relieved of the load of pulmonary circulation and can now pump blood into two circulations in a series instead of two ventricles pumping blood into two circulations in parallel.

For all lesions with univentricular physiology, the treatment protocol is similar to the one followed for tricuspid atresia. The common variant of this is HLHS. It consists of hypoplastic left ventricle and hypoplastic or atretic aorta with aortic arch interruption or coarctation. These babies need the Norwood procedure as stage 1 palliation, wherein the main pulmonary artery is disconnected and reconnected to the systemic circulation to enhance the arch. The pulmonary circulation is provided by a BT shunt. The patient subsequently undergoes BDG and Fontan/TCPC procedures. HLHS carries a guarded prognosis.

TGA is the prototype of CCHD with increased PBF. The aorta arises from the right ventricle (RV) and the pulmonary artery from the left ventricle. About 50% of patients are born with intact ventricular septum and 25% with VSD. ASD and PDA repairs are mandatory for the survival of the baby before an arterial switch operation (ASO), which is the transfer of aorta and pulmonary artery along with coronary arteries. These babies ideally should be operated within 2 to 3 weeks of life as the left ventricle loses its ability to sustain the systemic circulation beyond this period as it adapts to the lower pulmonary artery pressures. When these patients present late, the options are to proceed with atrial switch operations (Senning and Mustard procedures) which have a lower mortality rate. The right atrium is directed to drain into the left ventricle and the left atrium is directed to empty into the RV. The disadvantage of this procedure is that the RV, which is not designed to sustain the systemic circulation for long periods, is placed in the systemic circulation. This results in many of these patients developing heart failure later and requiring heart transplant. Therefore, ASO is the operation of choice for TGA as the long-term results are excellent. Most of our infants underwent ASO (n=43) and only 7 patients underwent atrial switch operation.

Mortality rates after surgery differ markedly depending on the complexity and severity of the cases, comorbidities, quality of surgery, and postoperative care.

Conclusions

The overall incidence of CCHD is more in males. Cyanosis is the most common presentation. TOF was the most common CCHD diagnosed. In this study, the predictability rates of CCHD within day 1 of life and 1 month of life were about 20% and 52%, respectively. This was due to early identification and referral of neonates. The advancement in health sciences has helped in early diagnosis, and awareness among general pediatricians and early referral to pediatric cardiologists have resulted in an increase in the reported prevalence of CHD.[18,19] We found an association of noncardiac factors and genetic syndromes with CCHD in 13.7% of the patients. Genetic syndromes are a major risk factor for the development of CHDs.[20] Early diagnosis and timely intervention can help reduce the morbidity and mortality associated with these heart conditions.

Limitations

As our center is the only interventional tertiary care center in the country, we get all CCHD cases needing immediate intervention. This study included only those patients who attended our institution. As it was a single-center study, the findings may not reflect the true incidence or prevalence of various types of CCHD in the community.

Recommendations

Early referral of infants with CCHD is mandatory. There is a need of a national registry for all CHDs to ascertain the true incidence rate of the lesions and the burden of the disease in the country.

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