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Long-Term Mortality of Children with Congenital Heart Disease Admitted to the Departmental University Hospital of Borgou/Alibori from 2011 to 2022

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Abstract

Background: Congenital heart disease is a public health issue due to its incidence and mortality rate. The aim of this study was to investigate the long-term mortality of children with congenital heart disease admitted to the Departmental University Hospital of Borgou/Alibori (CHUD-B/A) from 2011 to 2022. **Methods:** This descriptive longitudinal study with analytical aims covered 11 years (April 1, 2011 to December 31, 2022). It consisted of a review of the records of children under 15 years of age with echocardiographically confirmed congenital heart disease. This was followed by an interview with the parents to assess the children's current condition. Data were entered using Kobocollect software and analyzed using R Studio 4.2.2. software. **Results:** A total of 143 complete files were retained. The median age at diagnosis was 14 months (IIQ: Q1 = 4; Q3 = 60) with a range of 2 days and 175 months, and the sex-ratio (M/F) was 0.96. Left-to-right shunts were the most frequent cardiopathy group (62.9%). Only 35 children (24.5%) benefited from restorative treatment. The mortality rate was 31.5%. Median survival under the maximum bias assumption was 114 months and 216 months under the assumption of minimum bias. Survival was significantly better in children with right-to-left shunts (p = 0.0049) under the assumption of minimum bias. The death risk factors were: age at diagnosis less than 12 months (aHR = 7.58;

95% CI = 3.36 - 17.24; p < 0.001), cyanogenic heart disease (aHR = 1.50; 95% CI = 3.36 - 17.24; p = 0.017), stopping medical follow-up (aHR = 3.80; 95% CI = 1.58 - 9.18; p = 0.003) and absence of restorative treatment (aHR = 2.04; 95% CI = 1.21 - 3.44; p = 0.007). **Conclusion:** The long-term mortality of congenital heart disease is high and favoured by the absence of restorative treatment. Local correction of congenital heart disease and medical follow-up will help to reduce this mortality.

Keywords

Congenital Heart Disease, Long-Term, Mortality, Parakou, Risk Factors

1. Introduction

Congenital heart disease is a public health issue. Indeed, they are among the most common congenital malformations, with a stable annual incidence of 17.9‰ live births worldwide from 1990 to 2017 [1]. They are the leading cause of mortality from non-communicable diseases in people under the age of twenty, with an estimated 217,000 deaths worldwide in 2019, including 150,000 deaths in children under one year of age [2] [3]. In Africa, 500,000 children are born each year with congenital heart disease [4]. Only 3% of those requiring cardiac surgery benefit from it [5]. In Benin, congenital heart disease accounted for 4‰ and 3.05‰ of admissions to paediatric department at the National University Hospital-Hubert Koutoucou Maga (CNUH-HKM) in Cotonou in 2014 and the CHUD-B/A in 2017, respectively [6] [7].

In addition to their high morbidity and mortality rates, these diseases entail considerable financial and social costs. In situations where treatment can be undertaken, it is limited by the impossibility of access to surgical treatment or interventional catheterisation, due to a lack of local technical possibilities. Transfer abroad is then the only recourse, but it is not easily conceivable because of the prohibitive cost. Non-governmental medical humanitarian aid organizations frequently play a crucial role in ensuring the successful implementation of therapeutic projects [8]. Apart from the beninese government, three philanthropic organisations (Mécénat chirurgie cardiaque, Terre des hommes and Chaîne de l'espoir) contributed financially to medical evacuations for children with congenital heart disease [9].

Poor access to surgery and lack of follow-up are leading to an increase in the number of children with uncorrected and/or complicated congenital heart disease [10] [11] [12]. The aim of this study was to investigate the impact of these diseases on the lives of children with congenital heart disease, and to identify mortality risk factors with a view to devising appropriate management strategies. This study aims to investigate the long-term mortality of children with congenital heart disease admitted to the Departmental University Hospital of Borgou/Alibori (CHUD-B/A) from 2011 to 2022.

2. Methods

This was a descriptive longitudinal study with analytical aims, covering admissions from April 1st, 2011 to December 31, 2022. The study population consisted of children under 15 years of age seen for consultation or hospitalisation in the Paediatrics Department of CHUD-B/A during the study period under consideration and presenting with signs leading to suspicion of congenital heart disease. All cases of congenital heart disease that occurred at CHUD-B/A during the study period and whose parents had given their free and informed consent were recruited exhaustively. Our study did not include children whose medical records were incomplete, with data missing, particularly therapeutic and evolutionary data. We did not include children aged between 15 and 18, as this is the transitional period to adulthood and is characterised by particular changes due to hormonal impregnation during this period, and a transfer of patients with congenital heart disease from paediatric to adult care.

The dependent variable was mortality. The independent variables were grouped into several categories: parents and children socio-demographic variables (age at diagnosis, sex, monthly family income, parents' education level), congenital heart disease characteristics (type and nature of the congenital heart disease), therapeutic aspect (treatment methods), regularity of medical follow-up.

All cases of congenital heart disease confirmed in the paediatric department of the CHUD-B/A were recorded using the consultation, hospitalisation and transfer registers of the philanthropic organisations (Terre des hommes and Mécénat chirurgie cardiaque). The parents of the children identified were then contacted to find out about their children's current condition. Children whose parents could not be contacted were declared lost to follow-up. This study was approved by the Local Ethics Committee for Biomedical Research of the University of Parakou (CLERB-UP048/2023). Data confidentiality was ensured. The free and informed consent of children over the age of majority and the parents of minors was obtained.

The data collected was extracted from the KoboToolbox platform and analysed using R studio 4.2.2. software. For the descriptive analysis, the quantitative variables were described using mean ± standard deviation or median with the inter-quartile range after verification of normality using the Shapiro-Wilk test. Qualitative variables were described as proportions or frequencies. Survival was estimated according to Kaplan-Meier and the log rank test was used to compare survival curves according to sex and type of congenital heart disease. For the follow-up time, current age was considered for survivors, age at death for deceased children and age at diagnosis for those lost to follow-up. Survival was described according to the hypotheses of minimum bias (lost to follow-up = living) and maximum bias (lost to follow-up = deceased).

Univariate and multivariate analyses using the Cox proportional hazards regression model were performed to identify mortality risk factors, with the crude

and adjusted hazar ratios and their confidence intervals at the 5% threshold used as measures of association.

3. Results

3.1. Epidemiological Characteristics

During the period covered by our study, 57,100 children were admitted in the Paediatrics Department of CHUD-B/A. The diagnosis of congenital heart disease was confirmed in one hundred and seventy-two (172) children, meaning a hospital frequency of 3.0‰. Twenty-nine (29) children had incomplete records and were therefore excluded. The variables studied concerned only the remaining 143 children, meaning a participation rate of 83.1%.

The median age at diagnosis of the children was 14 months (IIQ:Q1 = 4; Q3 = 60) with a range of 2 days and 175 months. Of these, 49% were male, giving an M/F sex-ratio of 0.96. As for the parents, the average age of the fathers at diagnosis was 38.4 ± 9.4 years, with a range of 25 and 70 years. The mothers' ages ranged from 18 to 55 years, with an average of 31 ± 7.2 years. Table 1 shows the other sociodemographic characteristics of the children and parents.

3.2. Clinical, Paraclinical and Therapeutic Characteristics of Congenital Heart Disease

Left-to-right shunt predominated (62.9%). The most common congenital heart disease was isolated ventricular septal defect (32.9%), followed by Tetralogy of Fallot (19.6%), Atrial septal defect (8.4%) and Patent ductus arteriosus (7.7%). In addition, 67.1% of children had non-cyanogenic heart disease (Figure 1 and Table 2).

Of the cases registered, 108 (75.5%) received conservative medical treatment. Surgery was performed in 33 children (23.1%) and two children (1.4%) underwent interventional catheterisation.

Of the 143 children, 127 (88.9%) received medical treatment. The most commonly used drugs were diuretics (65.4%), anti-anaemics (48.8%) and beta-blockers (45.7%).

Thirty-one (31) of the 124 children with an indication for surgery were rejected, giving a rejection rate of 25.0%. The reasons given by non-governmental medical humanitarian aid organisations were: complex congenital heart disease (59.4%), comorbidities (22.5%) and Eisenmenger syndrome (18.1%).

Forty-five children (31.5%) were being followed.

A total of ninety-eight children (68.5%) discontinued their follow-up. The most common reasons given by parents for discontinuing medical follow-up were that the condition was fatal (16.3%), lack of financial resources (7.1%) and absence of symptoms (7.1%) (Table 3).

3.3. Long-Term Mortality in Children with Congenital Heart Disease

The mortality rate was 31.5%. Thirty-two children (22.4%) were lost to follow-up.

Table 1. Socio-demographic characteristics of parents and children with congenital heart disease admitted to the CHUD-B/A, 2011 to 2022 (N = 143).

	Frequency (N = 143)	Percentage (%)
Age at diagnosis (months)		
<1	3	2.1
[1 - 12]	67	46.9
]12 - 60]	38	26.5
>60	35	24.5
Gender		
Male	70	49.0
Female	73	51.0
Monthly household income (CFA francs)		
<52,000	40	28.0
52,000 - 100,000	79	55.2
101,000 - 200,000	15	10.5
201,000 - 300,000	5	3.5
>300,000	4	2.8
Place of residence		
Parakou	70	49.0
Outside Parakou	73	51.0
Father's level of education		
Primary studies	34	23.8
Secondary education	49	34.3
Higher education	33	23.1
Uneducated	27	18.8
Mother's level of education		
Primary studies	32	22.4
Secondary education	41	28.7
Higher education	12	8.4
Uneducated	58	40.5
Father's age in years		
≤50	123	86.0
>50	20	14.0
Mother's age in years		
≤35	99	69.2
>35	44	30.8

Table 2. Distribution of children with congenital heart disease admitted to the CHUD-B/A according to the nature of the congenital heart disease, 2011 to 2022 (N = 143).

	Frenquency (N = 143)	Percentage (%)
Left-to-right shunt		
Ventricular septal defect	47	32.9
Atrial septal defect	12	8.4
Patent ductus arteriosus	11	7.7
Truncus arteriosus	6	4.2
Complete atrioventricular septal defect	5	3.5
Ventricular septal defect + patent ductus arteriosus	4	2.8
Ventricular septal defect + atrial septal defect	2	1.4
Ventricular septal defect + atrial septal defect + patent ductus arteriosus	1	0.7
Ventricular septal defect + Patent ductus arteriosus + Aortic bicuspidity	1	0.7
Partial atrioventricular septal defect + Patent ductus arteriosus	1	0.7
Right-to-left shunt		
Tetralogy of Fallot	28	19.6
Complex congenital heart disease		
Transposition of the great vessels (2 associated with the double outlet right ventricle)	6	4.2
Pulmonary atresia with ventricular septal defect	5	3.5
Tricuspid atresia (1 associated with a total anomalous pulmonary connections)	4	2.8
Single ventricle	2	1.4
Double outlet right ventricle (1 associated with pulmonary stenosis)	2	1.4
Obstructive congenital heart disease		
Congenital mitral insufficiency	3	2.1
Coartaction of the aorta	1	0.7
Pulmonary valve stenosis	1	0.7
Supravalvular pulmonary stenosis	1	0.7

Sixty-six children (46.1%) were alive. Of the 45 deaths recorded, 4 occurred postoperatively, giving a postoperative mortality rate of 11.4%. The deaths occurred in one child before 1 month, two at 11 months and one at 99 months

Table 3. Distribution of children with congenital heart disease admitted to CHUD-B/A according to reasons for discontinuation of follow-up, 2011 to 2022 (N = 98).

	Frenquency (N = 98)	Percentage (%)
Not specified	50	51.0
Fatality of the condition	16	16.3
Lack of financial resources	7	7.1
Healing the child	7	7.1
No symptoms	7	7.1
The mystical origin of the condition	4	4.1
Geographical accessibility	2	2.0
Medical evacuation fails	2	2.0
Tares	1	1.0
Contraindication to surgery	1	1.0
Benign conditions	1	1.0

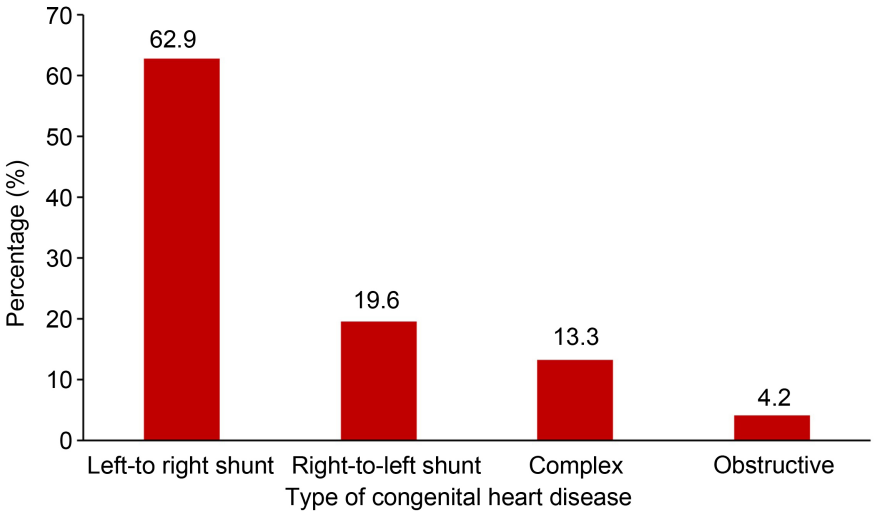

Figure 1. Distribution of children with congenital heart disease admitted to the CHUD-B/A according to the type of congenital heart disease, 2011 to 2022 (N = 143).

post-operatively. In the non-operated group, the case fatality rate was 38.0%. The main causes of death were heart failure (35.6%) and bronchopneumonia (20.0%) (**Table 4**).

3.4. Kaplan-Meier Estimation of the Survival Function of Children with Congenital Heart Disease

- Overall survival

Maximum bias assumption: Lost to follow-up = deceased.

The median survival time was 114 months. However, half (50%) of the children died before the age of 114 months (see **Figure 2**).

Minimum bias hypothesis: Lost to follow-up = living.

Table 4. Distribution of children with congenital heart disease admitted to CHUD-B/A according to cause of death, 2011 to 2022 (N = 45).

	Frequency (N = 45)	Percentage (%)
Not specified	18	40.0
Heart failure	16	35.6
Bronchopneumonia	9	20.0
Sepsis	6	13.3
Rhythm disorder	2	4.4
Endocarditis	2	4.4
Severe malnutrition	1	2.2
Severe anaemia	1	2.2

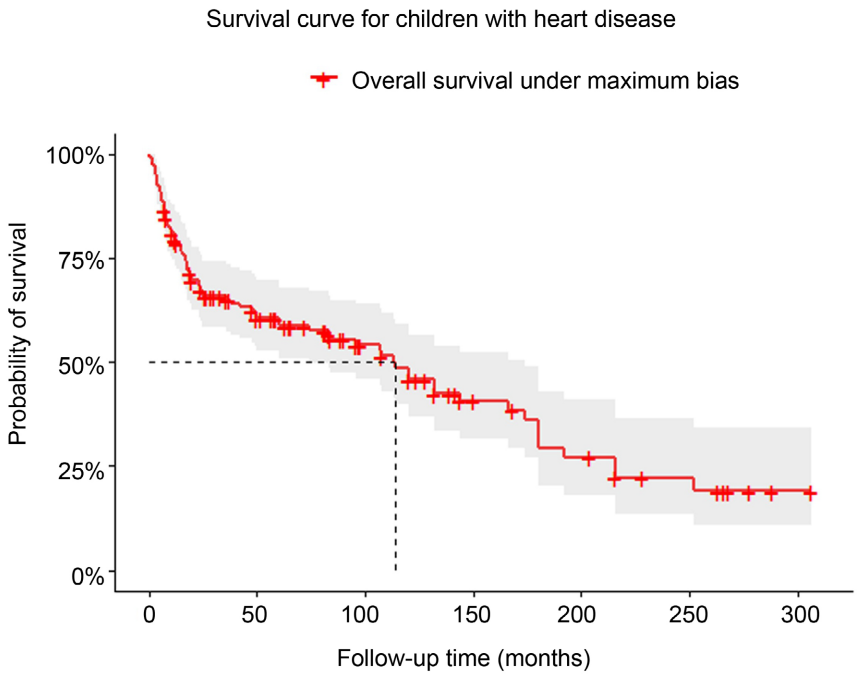

Figure 2. Survival curve assuming maximum bias for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

The median survival time was 216 months. However, half (50%) of the children died before the age of 216 months (See **Figure 3**).

- Survival by sex

Under the maximum bias hypothesis, the probability of survival was not statistically different according to sex (p = 0.79). However, survival was statistically better in women (median time not applicable) compared with men (median time = 174 months) with p = 0.045 under the minimum bias hypothesis. **Figure 4** and **Figure 5** summarise these results.

- Survival by type of congenital heart disease

Survival was not statistically different under the assumption of maximum bias

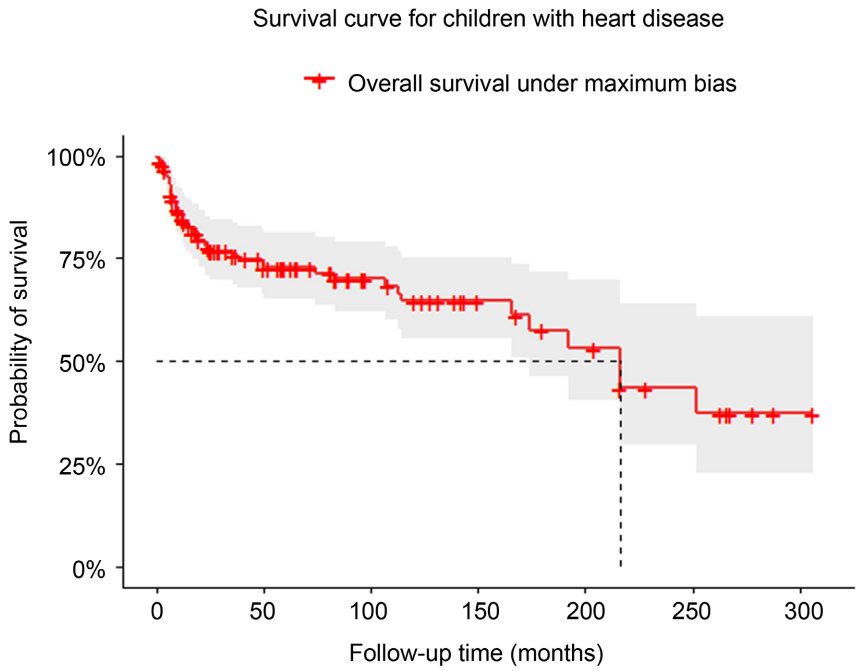

Figure 3. Minimum bias survival curve for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

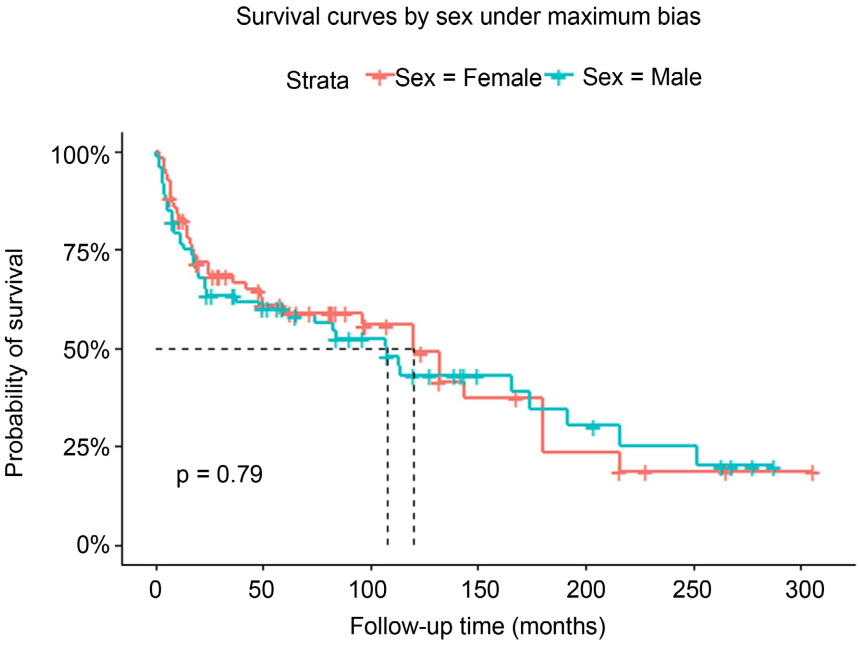

Figure 4. Kaplan-Meier estimate of the survival function as a function of sex under the assumption of maximum bias for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

($p = 0.053$). According to the minimum bias hypothesis, survival was statistically different according to the type of congenital heart disease ($p = 0.0049$). Right-to-left shunts had better survival (median time not applicable). Left-to-right shunts had

the second best survival with a median time of 216 months, followed by obstructive congenital heart disease with a median time of 166 months. Complex congenital heart disease had a median survival of 17 months less. Figure 6 and Figure 7 show these results.

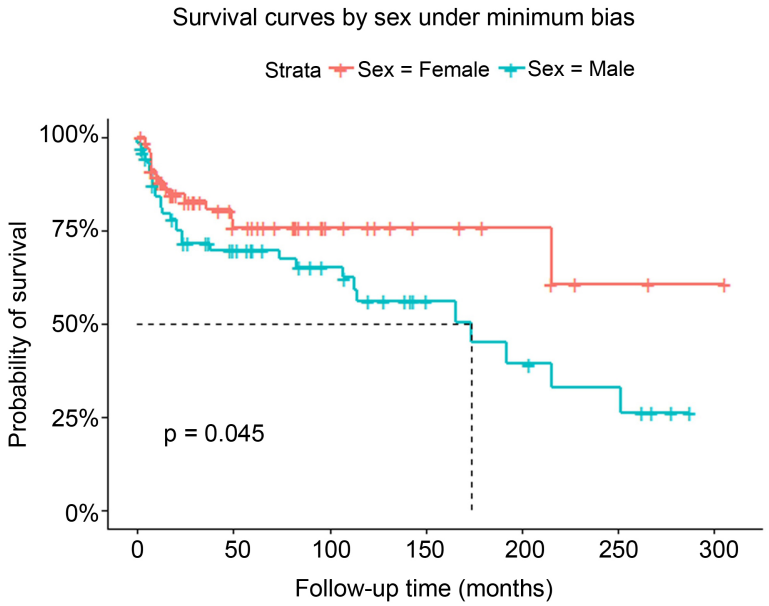

Figure 5. Kaplan-Meier estimate of the survival function as a function of sex under the assumption of minimum bias for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

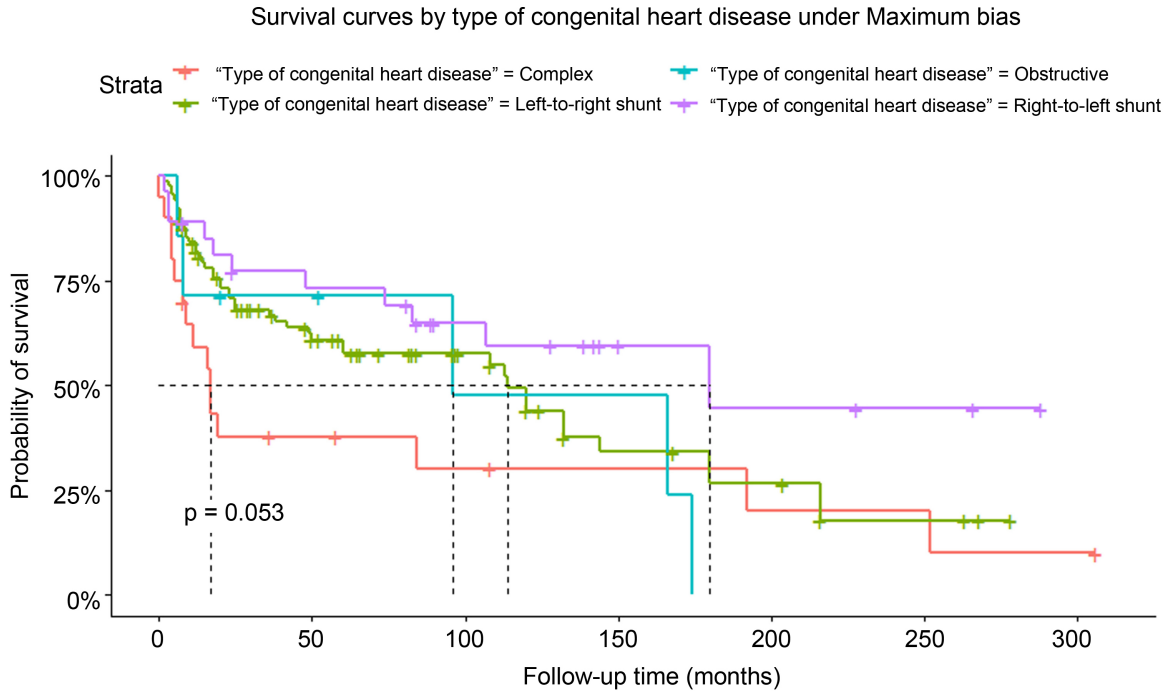

Figure 6. Survival curve according to type of heart disease under the maximum bias hypothesis for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

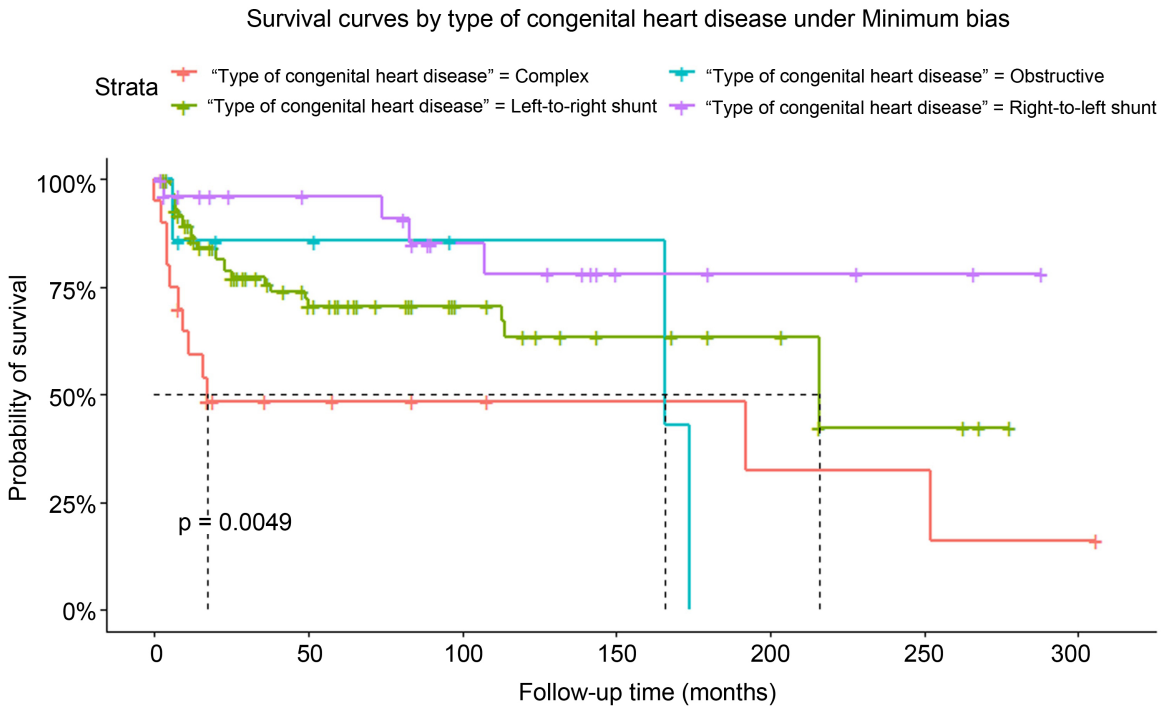

Figure 7. Survival curve according to type of heart disease, assuming minimum bias, for children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022.

3.5. Mortality Risk Factors in Children with Congenital Heart Disease

In multivariate analysis, the risk factors for death were: age at diagnosis of less than 12 months, cyanogenic heart disease, absence of surgical or interventional treatment and discontinuation of medical follow-up.

Children diagnosed during their first year of life were 7.58 times (aHR 95% CI = 3.36 - 17.24, $p < 0.001$) more likely to die than those diagnosed after 12 months of life. Children with cyanogenic heart disease were 1.5 times (aHR 95% CI = 3.36 - 17.24, $p = 0.017$) more likely to die than those without cyanogenic heart disease. The risk of death for children who were not followed was 3.80 times higher than for those who were followed (aHR 95% CI = 1.58 - 9.18, $p = 0.003$). Children who did not receive restorative treatment had a 2.04 times greater risk of death (aHR 95% CI = 1.21 - 3.44, $p = 0.007$) than those who received surgery or interventional catheterisation (**Table 5**).

4. Discussion

4.1. Epidemiological Characteristics

The hospital frequency of congenital heart disease in our study was 3.0‰. Ba Ngouala *et al.* in Senegal in 2015 found a similar hospital frequency (4.3‰) [13]. Our frequency is higher than that reported by Diby *et al.* in Côte d'Ivoire in 2019 (2.3‰) [14]. Kinda *et al.* at the Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle de Ouagadougou in 2015 on the other hand had found a

Table 5. Results of the Cox regression model of risk factors for death in children with congenital heart disease admitted to CHUD-B/A from 2011 to 2022 (N = 111).

	Univariate		Multivariate	
	cHR [95% CI]	P	aHR [95% CI]	P
Age at diagnosis (months)		**<0.001**		**<0.001**
<12	5.43 [2.56 - 11.63]		7.58 [3.36 - 17.24]	
≥12	1		1	
Sex		0.237		
Male	1.46 [0.78 - 2.71]			
Female	1			
Monthly income (FCFA)		0.053		0.092
≤100.000	1.66 [0.99 - 2.78]		1.56 [0.93 - 2.62]	
>100.000	1		1	
Father's instruction		0.948		
Educated	1			
Uneducated	1.01 [0.72 - 1.43]			
Mother's instruction		0.456		
Educated	1			
Uneducated	1.12 [0.83 - 1.50]			
Type of congenital heart disease		0.870		**0.017**
Cyanogen	1.03 [0.75 - 1.40]		1.50 [1.08 - 2.10]	
Non-cyanogenic	1		1	
Follow-up		**0.001**		**0.003**
Yes	1		1	
No	2.12 [1.38 - 3.27]		3.80 [1.58 - 9.18]	
Surgery/catheterisation		**0.001**		**0.007**
Yes	1		1	
No	2.40 [1.43 - 4.02]		2.04 [1.21 - 3.44]	

higher hospital frequency at 9.8‰ [12]. The significant variation in the frequency of these malformations could be explained by the inclusion criteria and the age of the children at the time of diagnosis. Indeed, some small ventricular septal defects and atrial septal defects heal spontaneously during the first years of life. The means used for diagnosis, sample size and environment could also have an impact on frequency. Given that in Benin between 1700 and 2800 children are born each year with congenital heart disease, this hospital frequency is much lower than that expected in the Paediatrics Department of the CHUD-B/A, which is the reference centre for northern Benin [15].

The median age at diagnosis of the children in our study was 14 months (IIQ:

Q1 = 4; Q3 = 60). The median age of our population is similar to those of Aliku *et al.* in Uganda in 2021 and Tougouma *et al.* in Burkina Faso in 2016, who reported median ages of 12 months (IIQ: 4 - 48) and 20 months (IIQ: 6 - 60) respectively [16] [17]. Kamdem *et al.* in Cameroon in 2020 and Diby *et al.* in Côte d'Ivoire in 2019 reported "early" median ages of 90 days and 5.5 months respectively [14] [18].

These high ages at diagnosis in developing countries contrast with foetal and neonatal diagnosis in developed countries. Indeed, a study by Bakker *et al.* assessing the prevalence of antenatal diagnosis of critical congenital heart disease in 12 developed countries found an average antenatal detection rate of 24.7% in the UK/Gales, 87% in France-Rhône Alpes, 19.5% in Canada and 10.1% in Argentina from 2000 to 2014 [19]. An analysis of data provided by Belgium to the European Registration of Congenital Anomalies and Twins (EUROCAT) indicated that the rate of antenatal detection during the period 1997-2012 was 29.3% for all congenital heart diseases in general and 40.2% for critical ones [20].

This disparity only reveals the delay in diagnosis of these congenital conditions in sub-Saharan Africa. This could be explained by the absence of foetal echocardiography, despite a prenatal check-up often carried out during pregnancy. After birth, the delay in diagnosis may be due to the absence of a complete and systematic clinical examination of all newborns and, above all, screening for serious heart disease using saturometry, as recommended by the American Academy of Pediatrics (AAP) and the American Heart Association (AHA) [21] [22]. The reported deficiency in knowledge and utilization of saturometry for screening congenital heart disease was noted by Yakoubou *et al.* in Benin in 2019. Indeed, 12.73% of paediatricians were aware of the protocol for screening for severe congenital heart disease using saturometry, and only one centre had a screening programme [23].

The median age at diagnosis of the children was 14 months (IIQ: Q1 = 4; Q3 = 60) with a range of 2 days and 175 months. This wide-ranging study reports a number of elderly children with congenital heart defects who were diagnosed late, reflecting the unavailability of paediatric cardiologists and surgical facilities, among other factors. These patients most often had simple congenital heart defects that had not been diagnosed or complex cyanogenic defects that were naturally balanced and allowed an acceptable quality of life until late in life. Thus, although surgery for congenital heart disease should be available in developing countries, it must be linked to a strategy of early detection of congenital heart disease and the creation of a network enabling patients to be easily referred from primary care units to surgical centres. Paediatricians, obstetricians and cardiologists must interact in the design and implementation of protocols for the diagnosis, management and follow-up of patients with congenital heart disease, adapted to the conditions and environment of developing countries.

Our study found a female predominance of 51.0% with an M/F sex ratio of 0.96. Namuyonga *et al.* in Uganda in 2020 also reported a female predominance

with a sex ratio of 0.82 [24]. The same is true for Diby *et al.* in Côte d'Ivoire in 2019 and Diop *et al.* in Senegal in 2020, who noted M/F sex ratios of 0.9 and 0.94 respectively [14] [25]. On the other hand, Adjagba *et al.* in Benin in 2018 reported a male predominance with an M/F sex ratio of 1.3 [9]. Studies carried out in Cameroon in 2022 and in Burkina-Faso in 2016 also noted a male predominance with sex ratios of 1.01 and 1.05 respectively [26] [27]. Sen *et al.* found a male predominance of 55.8% in 2017 in a study of children with operated congenital heart disease from 17 low- and middle-income countries [28]. This variation in the sex ratio could underline the absence of a relationship between sex and the occurrence of congenital heart disease.

85.0% of families had a monthly income of less than 100,000 CFA francs. This is in agreement with studies by Brousse *et al.* in Senegal in 2011 who noted that 95% of families had incomes below 230 Euros per month or 150,856 CFA Francs [8]. Adjagba *et al.* in Benin in 2018 reported a modest average monthly income of 107,477 ± 120,721 CFA Francs in the families of children with congenital heart disease who were rejected for surgery and interventional catheterisation [9]. Similarly, Kologo *et al.* in Burkina-Faso in 2017 noted an average income of 50,000 CFA francs among the families of children with congenital heart disease who benefited from medical evacuations [29]. All these studies highlight the low socio-economic level of the sub-Saharan African population, making it difficult to access care in a healthcare system that has no health insurance. A low monthly family income could delay the diagnosis of congenital heart disease and reduce access to care for children with congenital heart disease, leading to complications and even death.

4.2. Clinical, Paraclinical and Therapeutic Characteristics

In our study, left-to-right shunts were predominant at 62.9%, with Isolated Ventricular septal defect leading the way at 32.9%. This predominance of left-to-right shunts has been reported by Kamdem *et al.* in Cameroon and Diby *et al.* in Côte d'Ivoire with frequencies of 62.1% and 72.6% respectively [14] [18].

In Cotonou, Eyisse Kpossou *et al.* in 2014 reported that Ventricular septal defect, whether isolated or associated with other cardiac lesions, was the most frequent congenital heart disease (70.3%) [30]. This predominance of Ventricular septal defect was also reported by Abdulkadir and Abdulkadir in Nigeria in 2016 with a frequency of 40.6% [31]. The same is true of Namuyonga *et al.* in Uganda in 2020 and Ndongo-Amougou *et al.* in Cameroon in 2022, who noted Ventricular septal defect frequencies of 27.2% and 42.9% respectively [24] [27]. Meberg in Norway and Mohammad *et al.* in Pakistan reported a predominance of Ventricular septal defect with frequencies of 57.0% and 29.9% respectively [32] [33].

Despite differences in frequency from one country to another, Ventricular septal defect generally remains the most frequent congenital heart disease and the most common type of left-to-right shunt in the world.

In terms of cyanogenic congenital heart disease, Tetralogy of Fallot topped the

list in 19.6% of cases, confirming the data in the literature which place this anomaly at the top of the list of cyanogenic congenital heart diseases [13] [16] [26] [30] [34].

Surgical treatment was indicated in 86.7% of children. This finding was reported by Tougouma *et al.* and Aliku *et al.* with respective frequencies of 86.0% and 76.0% [16] [17]. The rate reported by Kamdem *et al.* in Cameroon in 2018 is lower (46.2%) [35]. These high rates of surgical indication only confirm the enormous need for advanced care in paediatric cardiac surgery in sub-Saharan Africa.

Surgery was performed in 33 children (23.1%) and two children (1.4%) underwent interventional catheterisation. This is in line with the studies by Tougouma *et al.* and Aliku *et al.* who reported surgical intervention frequencies of 21% and 14% respectively [16] [17]. Ndongo-Amougou *et al.* reported a higher frequency (41.9%) in Cameroon in 2022 [27]. These proportions are much lower than those reported by Amedro *et al.* in France, where surgery was the most frequently requested therapeutic modality (64.5%), followed by cardiac catheterisation at 28.0% [36]. Amodeo *et al.* in 2017 found a proportion of 83.5% of surgical and medico-surgical management in Italy [37]. These differences in results could be explained by the difference in socio-economic and technical levels between northern and southern countries. In most of the African series, interventional and surgical treatments were carried out by means of medical evacuations abroad, which is a factor limiting restorative management. This observation underlines the indisputable interest in developing cardiac surgery locally.

Only 35 children (24.4%) received restorative treatment. This observation indicates the limited access to these restorative treatments for children due to the limited financial accessibility of parents, the relatively long time for the study of the file by humanitarian organizations and the slowness in compiling the administrative file with children who die in the process. The delay in diagnosis favors the appearance of progressive complications which contraindicate surgical interventions. In addition, complex heart diseases remain inaccessible to surgical treatment with little hope of optimal results even in developed countries. Thus these children with complex heart diseases are unlikely to benefit from medical evacuation. Comorbidities, particularly syndromic heart diseases, constitute a prohibitive criterion for medical evacuation despite the improvement in the prognosis induced by surgery. As the number of medical evacuations is limited, preference would be given to those without comorbidities in order to maximize the chances of success of the intervention.

The proportion of children whose medical follow-up was stopped was 68.5%. The main reasons given were that the condition was fatal (16.3%) and that there were insufficient financial resources (7.1%). Adjagba *et al.* in 2018 reported a similar frequency of 72.7% [9]. This finding underscores the importance of effective communication between physicians and parents or guardians, as well as with children, to enhance understanding of the condition and the significance of

continued follow-up. Additionally, these results emphasize the necessity of implementing universal health insurance.

4.3. Long-Term Mortality

Mortality rate in our study was 31.5%. This rate is higher than that reported by Kinda *et al.* in Burkina Faso (26.7%) [12]. Abid *et al.* in Tunisia reported a lower case fatality rate (23.0%) in 255 children with congenital heart disease followed for one year [38]. This difference could be explained by the high number of children who stopped medical follow-up in our series.

The causes of death reported in our study were dominated by heart failure (35.5%) and bronchopneumonia (20%). Abid *et al.* in Tunisia also reported the predominance of heart failure and bronchopneumonia [38]. The same finding was reported by Xiang *et al.* in China (heart failure, sudden death, bronchopneumonia) [39].

Thirty-two children (22.4%) were lost to follow-up. This frequency is close to that of Kinda *et al.* in 2016 in Burkina-Faso, which was 21.8% [12]. Ba Ngouala *et al.* in Senegal and Diby *et al.* in Côte d'Ivoire found lower frequencies of 18.3% and 19.5% respectively [13] [14]. These figures contrast with those of the Mécénat Chirurgie cardiaque en 2021 study, which reported a rate of 8.8% [40]. Xiang *et al.* in China in 2018 also reported a lower rate of 8.0% [39]. These high rates in Sub-Saharan Africa could be explained by the asymptomatic nature of certain congenital heart diseases and the clinical improvement of children who undergo surgery.

4.4. Mortality Risk Factors

The risk of mortality decreased significantly with age at diagnosis ($p < 0.001$). In fact, the risk of mortality was 7.58 (aHR 95% CI: 3.36 - 17.24) times greater in children diagnosed during their first year of life compared with those diagnosed after one year of life. Oster *et al.* in the United States reached the same conclusion in their study evaluating the one-year survival of children with congenital heart disease. They reported that one-year survival was 71.7% in children diagnosed no later than the first day of life compared with 82.5% in those diagnosed after the first day of life ($p < 0.001$) [41]. Knowles *et al.* in the UK, on the other hand, reported that a weekly increase in age at diagnosis increased the risk of mortality (RR 95% CI: 0.94 - 0.97 $p < 0.001$) [42]. This could be explained by the fact that severe congenital heart disease manifests itself earlier than benign congenital heart disease, which can remain asymptomatic for a long time. Severe congenital heart disease also requires surgery at a younger age, which is inaccessible in our context.

In addition, our study found that cyanogenic heart disease had a 1.50-fold higher risk of death (aHR 95% CI = 1.08 - 2.10) than non-cyanogenic heart disease ($p = 0.017$). Diby *et al.* in Côte d'Ivoire also found a significant association between death and type of heart disease. In their study, death was 6.58

times higher in children with cyanogenic heart disease than in those with non-cyanogenic heart disease (OR 95% CI = 2.09 - 21.12; p < 0.0001) [14]. The same observation was made by Mandalenakis *et al.* in Sweden who reported that patients with cyanogenic heart disease had the highest risk of death (HR = 64.07; 95% CI = 53.39 - 76.89) [43]. Given that cyanotic heart disease stems from a disruption in cardiac architecture, leading to the contamination of systemic circulation with deoxygenated blood, the numerous complications associated with cyanosis are likely to contribute to increased mortality.

Children who stopped medical follow-up had a risk of death 3.80 times greater than those who continued follow-up (aHR 95% CI = 1.58 - 9.18, p = 0.003). Adjagba *et al.* in Benin, on the other hand, reported no significant difference between the group of children who stopped medical follow-up after recusal and those who continued medical follow-up (p = 0.24) [9]. Medical follow-up would enable complications to be detected early and treated.

The risk of death for children who did not undergo restorative treatment was 2.04 times higher than for those who underwent surgery or interventional catheterisation (aHR 95% CI = 1.21 - 3.44, p = 0.007). This would indicate the importance of surgery and interventional catheterisation in the treatment of congenital heart disease. Surgery and interventional catheterisation are the real treatments for congenital heart disease.

4.5. Limitations of the Study

Our study nevertheless has a number of limitations to highlight. The large number of children lost to follow-up whose vital status is not known constitutes a limitation to this study, preventing us from knowing a very precise long-term mortality of children with congenital heart diseases.

The rate of lost to follow-up was not negligible in our study. For this reason, instantaneous survivals were estimated according to the maximum and minimum bias hypotheses. However, the multivariate analysis excluded those lost to follow-up. This choice could affect the estimation of the hazard ratio as well as the generalisation of the results. More effective analysis techniques, in particular imputation of missing data, could make it possible to better investigate the type of missing data in order to judge whether the observed data used for the analysis are representative of the unobserved data. Similarly, a sensitivity analysis of two different loss-to-follow-up scenarios could provide a better assessment of the impact of these scenarios on the results. All of this is a limitation of our study and should be taken into account when interpreting and using the results.

5. Conclusion

Congenital heart disease is a rare and serious disease. In Parakou, the delay in diagnosing these congenital diseases is obvious. Repairing these malformations remains a challenge in the absence of suitable infrastructure. As a result, the mortality rate remains high. This mortality is strongly influenced by the type of

congenital heart disease, the type of treatment and therapeutic non-compliance. Improved diagnosis, local correction of heart disease and medical follow-up will help to reduce this high mortality rate.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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