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Long-Term Follow-up of Congenital Cardiac Defects Diagnosed in Utero - A Longitudinal Study

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Abstract

Background: Congenital Heart Defects (CHD) is the leading cause of neonatal morbidity and mortality among birth defects with a prevalence of 6 per 1,000 live births. In utero diagnosis necessitates multidisciplinary prenatal counseling regarding the options and outcomes. Our aim was to examine the short-term outcomes during the prenatal period and following birth, as well as long-term morbidity and mortality.

Methods: This retrospective study included all fetuses diagnosed with CHD from January 2004 to January 2009. CHDs were categorized as simple or complex. Data regarding pregnancy characteristics and outcomes was retrieved from the department's patient database. Data regarding long-term follow-up and developmental characteristics was obtained by telephone questionnaire following parental consent. Simple and complex CHD were compared.

Results: Eighty-nine fetuses were diagnosed with CHD. Median follow-up was 12.3 ± 1.3 years. More pregnancies with complex CHD were terminated (p=0.001) or resulted in perinatal demise (p=0.001). More children with complex CHD underwent cardiac surgery (7.1% *vs*. 77.8%, P=0.001), and had longer cardiology follow-up (11.4 years ± 3.8 *vs*. 5.2 ± 4.7 years, P=0.02). In addition, higher rates of difficulties with physical activities such as school gym classes were reported among the group with complex CHD (33.3% *vs*. 0%, P=0.02). There were no significant differences in neurodevelopmental follow-up between groups.

Conclusion: Complex CHD is associated with short- and long-term clinical morbidity and mortality. These data could contribute to the prenatal counseling given to the parents following the diagnosis.

Keywords: Congenital heart defects; Fetus; Pregnancy; Ultrasound; Neurodevelopment

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Abbreviation

IUFD: Intrauterine Fetal Death; CHD: Congenital Heart Defects; NDD: Neurodevelopmental Disorders

Introduction

Congenital Heart Defects (CHD) are the most common fetal structural malformation and are the leading cause of neonatal morbidity and mortality due to birth defects. The estimated incidence of moderate and severe forms of CHD is 6/1000 live births [1]. Following sonographic prenatal diagnosis of CHD, fetal anatomy is usually evaluated thoroughly to rule out additional anomalies. Genetic analysis is usually performed as well. Parents of fetuses with complex CHD receive counseling from a multidisciplinary team, including cardiologists, cardiothoracic surgeons and pediatricians, regarding the time and place of delivery and immediate neonatal management [2]. Approximately 85% of babies born with CHD are expected to reach adulthood. While outcomes vary significantly depending on the type of heart defect, in general, long-term survival (20 years) rates are estimated to be 95% for simple CHD (e.g., atrial and ventricular septal defects, isolated semilunar valve disease) and 80% to 90% for severe CHD [3]. As survival has improved, there is increased recognition of the risk of neurodevelopmental delay in these children, particularly those with more severe defects. Several studies showed that these children are at-risk for deficits in visual-spatial and visual-motor skills, as well as impairment in speech, language, and executive functioning

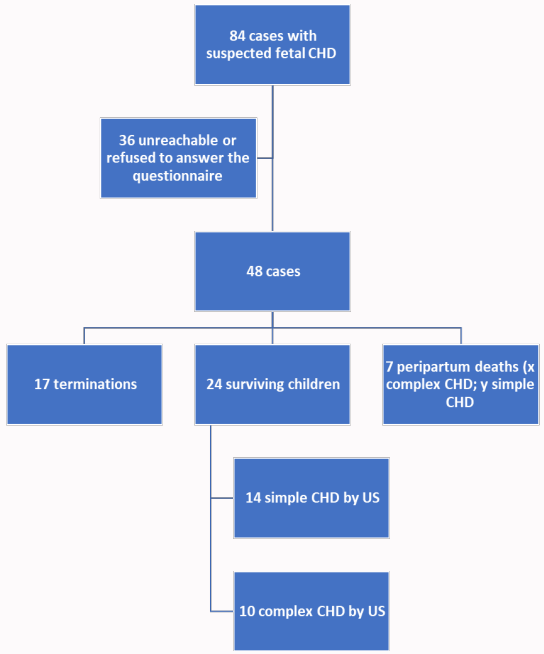

Figure 1: Flow diagram of patients included in the study.

[4-6].

Most current studies regarding the long-term sequelae of patients with CHD examined infants [7,8] and to lesser extent, fetuses [9]. The objective of the current study was to examine the outcomes of fetuses with CHD diagnosed prenatally or postpartum, and to investigate long-term morbidity and mortality, including neurodevelopmental abnormalities.

Materials and Methods

This retrospective study included all fetuses diagnosed with CHD from January 2004 to January 2009 at Meir Medical Center. Approval was granted by the local Institutional Review Board.

Simple CHD was defined as a single defect, such as ventral-septal defect or atrial-septal defect. Complex CHD was defined as more than one defect and/or cyanotic CHD and included hypoplastic left heart, tetralogy of Fallot, transposition of the great vessels, atrioventricular canal, single ventricle and truncus arteriosus [10,11].

The variables assessed included maternal age, medical background, gravidity, parity, nuchal translucency, biochemical screening tests during pregnancy, karyotype exam, sonographic evaluation, fetal echocardiography, pregnancy outcomes, gestational age at delivery, gender, birth weight, Apgar scores, hospitalization in neonatal intensive care unit, and clinical evaluation of the newborn and neonatal echocardiography. Cardiac surgeries, need for physiotherapy, special assistance in school, neurodevelopmental clinic visits, and diagnosis of attention deficit disorder were also evaluated.

Data were retrieved from the department's electronic patient database. Antenatal follow-up test results along with pregnancy and neonatal outcomes were routinely entered into the database during prenatal follow-up visits, at admission for delivery and postpartum. Data regarding long-term follow-up and developmental characteristics were obtained by telephone questionnaire after parental consent was obtained.

Statistical analysis

Data are described as mean and standard deviation for continuous variables and as numbers and percentage for nominal variables. Chi-square was used to find differences between two groups for qualitative variables. Distribution of continuous variables was checked for normality (Shapiro-Wilk test) and t-test or Mann-Whitney non-parametric tests were used, each when appropriate. $P<0.05$ was considered statistically significant. All data were analyzed using SPSS-25 (IBM, Armonk, NY, USA).

Results

During the study period, 89 fetuses at 14 to 24 weeks of gestation were diagnosed with CHD, in our hospital. Among the parents, 36 either could not be reached (n=33) or refused to answer the questionnaire (n=3). Among the 53 remaining cases, 17 had undergone termination of pregnancy (TOP) (32.0%). The heart malformations among the terminated pregnancies were mostly due to atrioventricular canal, situs inversus and hypoplastic left heart. There was one case of intrauterine fetal death after 20 weeks of gestation and 6 cases of neonatal-infant death from 8 hours up to 12 months of age. Among the 29 living children (54.7%) who were diagnosed with CHD, 14 were defined as simple CHD and 10 as complex based on sonographic findings. Five were considered as misdiagnosis after birth (Figure 1).

The pregnancy outcomes of 48 fetuses with complex as compared to simple CHD are presented in Table 1 and Figure 2. Significantly more pregnancies with complex CHD were terminated (p=0.001) or experienced infant death (p=0.001).

The average age of the surviving children was 12.3 ± 1.3 years. There was no difference in age between children with simple (11.4 ± 16.5 years or complex CHD (12.4 ± 9.4, P=0.86).

Table 2 presents the long term clinical and neurodevelopmental characteristics of the study population, including comparison of simple and complex CHD. Significantly more children with complex CHD underwent cardiac surgery (77.8% *vs.* 7.1%, P=0.001). One child, who was diagnosed with hypoplastic left heart, had 3 surgeries. In addition, higher rates of difficulties in physical activities, such as gym classes as school were reported among the group of complex CHDs (33.3% *vs.* 0%, P=0.02). The duration of cardiology follow-up was longer among the complex CHD group (11.4 ± 3.8 years) *vs.* the simple CHD group (5.2 ± 4.7 years, P=0.02). There were no significant differences in neurodevelopmental follow-up between the two groups.

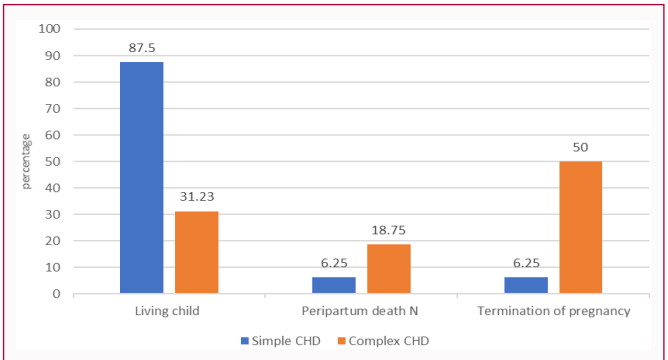

Figure 2: Pregnancy outcomes of fetuses with heart defects diagnosed by ultrasound (*P=0.001).

Table 1: Obstetric and perinatal outcomes of newborns in who congenital heart defect (CHD) was detected during pregnancy.

Parameter	Simple CHD (N=14)	Complex CHD (N=10)	Total	P-value
Spontaneous vaginal delivery, n (%)	5 (35.7)	6 (60)	11 (45.8)	0.4
Operative vaginal delivery, n (%)	2 (14.3)	1 (10)	3 (12.5)	1
Cesarean section, n (%)	7 (50)	3 (30)	10 (41.7)	0.42
Neonatal Intensive Care Unit admission, n (%)	6 (42.9)	6 (66.7)	12 (50)	0.4
Additional system malformation, n (%)	0 (0)	3 (30)	3 (12.5)	0.06
Duration of hospitalization after birth (days), mean ± SD	11.4 ± 16.5	12.4 ± 9.4	11.8 ± 13.9	0.86

Table 2: Clinical and neurodevelopmental characteristics of 10 to 14 years-old children in whom fetal heart defect was detected during pregnancy.

Parameter	Simple CHD N (%)	Complex CHD N (%)	Total, N (%)	P-value
Cardiac surgery during childhood, n (%)	1 (7.1)	7 (77.8)	8 (33.3)	0.001
Physiotherapy during childhood, n (%)	4 (28.6)	4 (44.4)	8 (33.3)	0.66
Neurodevelopmental follow-up during childhood, n (%)	11 (78.6)	9 (100)	20 (83.3)	0.25
Current cardiologist follow-up, n (%)	7 (50)	7 (77.8)	14 (58.3)	0.23
Special education attendance, n (%)	1 (7.1)	1 (11.1)	2 (8.3)	1
Currently has individual supervision by extra staff member at school, n (%)	4 (28.6)	3 (30.0)	7 (29.2)	1
Attention Deficit Hyperactivity Disorder, n (%)	2 (22.2)	2 (14.3)	4 (16.7)	0.63
Difficulty with physical activities, n (%)	3 (33.3)	0 (0)	3 (12.5)	0.02
Current BMI percentile, mean ± SD	43.6 ± 29.5	41.0 ± 29.6	42.5 ± 29.6	0.9
Duration of cardiologic follow up (years), mean ± SD	5.2 ± 4.7	11.4 ± 3.8	8.2 ± 5.1	0.02

Discussion

Results of the current study demonstrate that fetuses with CHD, especially when complex, undergo long-term cardiology follow-up, including surgery and have higher rates of difficulties in physical activities, such as gym classes at school. There were no significant differences in the neurodevelopmental follow-up between the children with simple or complex CHD.

Significantly more pregnancies with complex CHD underwent termination of pregnancy (p=0.001). Complex CHD resulted in significantly more perinatal deaths (p=0.001). Previous studies reported that Intrauterine Fetal Death (IUFD) rate among fetuses with CHD was a little higher than found in our study, and was approximately 4.5%. The risk factors associated with IUFD were cardiomegaly, hydrops, pericardial effusion and extra-cardiac abnormalities [12,13]. A nationwide cohort study in Norway found an infant death rate of 17.4% for complex CHD and 3% for simple CHD, with 8.8% late TOP or IUFD. These reported rates of perinatal deaths are higher than those in our study. On the other hand, the reported higher rate of TOP in our study resulted in fewer ongoing pregnancies with severe and complex CHD and thus, fewer cases of intrauterine or infant death. Indeed, pregnancies with anatomical abnormalities that may cause severe morbidity and mortality may be offered termination following multidisciplinary consultation [14]. The high rate of perinatal deaths among patients with CHD, especially complex, should be included in the prenatal counseling given to couples after the diagnosis of CHD.

An additional finding in our study was the high rate of cardiac surgeries (77.8%) and longer cardiologist follow-up (11.4 years ± 3.8) among children who were diagnosed with complex CHD. Advances in congenital heart surgery have considerably improved the survival rates for children with CHD, beginning in the neonatal period. A prenatal diagnosis of CHD requires special follow-up, including in some cases delivery in tertiary medical centers with of the availability cardiac surgeons, for example [15,16].

The present study found high rates (33%) of difficulties in physical activities during school among those with a diagnosis of complex CHD. Data from previous studies conflict. Some reported limitations related to specific heart defects [17], while others that evaluated the limitation with objective tools found no limitations among children with any type of CHD [18].

In recognizing the need to optimize healthy development and long-term cardiovascular health in children with CHD, consensus statements have recommended that patients with CHD (with few exceptions) should aim to meet general population guidelines for regular physical activity [19,20]. There were no significant differences in the neurodevelopmental follow-up between the two groups.

A large study examining the prevalence of Neurodevelopmental Disorders (NDD) in a general population of 119,367 children in the USA [21], found a rate of 13.87% of any NDD among children. In our study, 7.1% of the children with simple CHD (P=0.46) and 11.1% of those with complex CHD (P=0.79) attend special education due to NDDs. Although this is statistically the same the more severe type of NDDs are included. Specifically, the prevalence of ADHD among children ages 11 to 17 years was 8.93%. In our study population, the rates of ADHD among children with simple CHD or complex CHD were 22.2% (P=0.08) and 14.3% (P=0.47), respectively.

The current study was limited in that the follow-up data were obtained from telephone questionnaires from parents, which are subjective and may be subject to bias. However, the questions were objective and were based on data and not on assumptions or impressions. The cohort was smaller than that reported previous studies and there may be a selection bias because three parents refused to participate. Among them, two of the children were diagnosed with tetralogy of Fallot and one with ventral-septal defect.

The main strength of this study is the long-term follow-up after prenatal diagnosis of CHD in which counseling and surveillance began during pregnancy. This type of information is still lacking in the literature and might provide additional aspects to the counseling given during pregnancy, regarding short and long-term expectations of morbidity and mortality.

Conclusion

Complex CHD is associated with short- and long-term clinical morbidity and mortality. These data could contribute to the prenatal counseling given to the parents following the diagnosis. A larger study with longer follow-up is currently underway.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the Helsinki national guidelines on human experimentation, and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (0115-18-MMC).

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