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Evaluation of prenatal and postnatal outcomes of fetuses with intrauterine cardiac anomalies: Tertiary center experience

İntrauterin dönemde kardiyak anomali tanısı alan fetusların prenatal ve postnatal sonuçlarının değerlendirilmesi: Tersiyer merkez deneyimi

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Abstract

Objective: Fetal cardiac anomalies are among the leading causes of infant mortality due to congenital anomalies. The prenatal diagnosis of congenital heart diseases allows for the acquisition of prognostic information before birth and provides insights into treatment options either before or after delivery. This study aims to observe the correlation between the prenatal and postnatal diagnoses of fetuses with cardiac anomalies detected in our perinatology clinic. The goal, by tracking postnatal outcomes and identifying risk factors, is to assist in selecting the most appropriate approach, prioritizing maternal and fetal health.

Materials and Methods: The records of 188 fetuses diagnosed during the prenatal period by the Perinatology Department of Obstetrics and Gynecology at Çukurova University Faculty of Medicine, delivered and admitted to the Çukurova University Neonatal Intensive Care Unit, and undergoing fetal echocardiography by the Pediatric Cardiology Clinic between January 2016 and December 2021, were retrospectively evaluated. Postnatal transthoracic echocardiography results of the infants were also reviewed.

Results: Our study was conducted with 188 pregnant women. The most frequently detected cardiac anomalies in the fetuses were conotruncal anomalies, followed by right heart anomalies. The concordance between prenatal and postnatal findings was 88.8%, with a sensitivity of 96.55% and a specificity of 100%. Among the live-born infants with congenital heart disease, significant differences were observed between the group that survived the neonatal period and those who did not, in terms of parental consanguinity, gestational age at birth, birth weight, APGAR scores, and the rate of chromosomal anomaly assessment.

Conclusion: Our study emphasized several risk factors. A high concordance was found between our prenatal and postnatal echocardiography findings. In conclusion, we believe that increasing awareness and making screening a routine practice are essential to contributing to healthier future generations. This can be achieved by reducing perinatal mortality and morbidity through appropriate management and equipment, thereby optimizing the well-being of affected individuals in society.

Keywords: Congenital heart diseases, fetal anomaly, prenatal diagnosis

PRECIS: Fetal heart anomalies are the leading cause of infant mortality due to congenital anomalies. Prenatal diagnoses provide information about prognosis and help to determine treatment options. This study aims to evaluate the concordance between prenatal diagnoses and postnatal outcomes, to identify risk factors and to suggest the most appropriate management strategies.

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Öz

Amaç: Fetal kardiyak anomaliler, doğumsal anomalilere bağlı bebek ölümlerinin önde gelen nedenleri arasındadır. Konjenital kalp hastalıklarının prenatal tanısı, doğumdan önce prognostik bilgi edinilmesini sağlar ve doğumdan önce veya sonra tedavi seçenekleri hakkında fikir verir. Bu çalışmanın amacı, perinatoloji kliniğimizde tespit edilen kardiyak anomalili fetüslerin prenatal ve postnatal tanıları arasındaki korelasyonu gözlemlemektir. Amaç, doğum sonrası sonuçları izleyerek ve risk faktörlerini belirleyerek, anne ve fetüs sağlığına öncelik veren en uygun yaklaşımın seçilmesine yardımcı olmaktır.

Gereç ve Yöntemler: Ocak 2016-Aralık 2021 tarihleri arasında Çukurova Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Perinatoloji Bölümü tarafından prenatal dönemde tanı alan, doğum yapan ve Çukurova Üniversitesi Yenidoğan Yoğun Bakım Ünitesi'ne kabul edilen ve Çocuk Kardiyoloji Kliniği tarafından fetal ekokardiyografi yapılan 188 fetüsün kayıtları retrospektif olarak değerlendirildi. Bebeklerin doğum sonrası transtorasik ekokardiyografi sonuçları da gözden geçirildi.

Bulgular: Çalışmamız 188 gebe kadın ile gerçekleştirilmiştir. Fetüslerde en sık saptanan kardiyak anomaliler konotrunkal anomalilerdi, bunu sağ kalp anomalileri izledi. Prenatal ve postnatal bulgular arasındaki uyum %88,8, duyarlılık %96,55 ve özgüllük %100 idi. Konjenital kalp hastalığı olan canlı doğan bebekler arasında, yenidoğan dönemini atlatan ve atlatamayan grup arasında ebeveyn akrabalığı, doğumdaki gebelik yaşı, doğum ağırlığı, APGAR skorları ve kromozomal anomali değerlendirme oranı açısından anlamlı farklılıklar gözlenmiştir.

Sonuç: Çalışmamızda çeşitli risk faktörleri vurgulanmıştır. Prenatal ve postnatal ekokardiyografi bulgularımız arasında yüksek uyum saptandı. Sonuç olarak, farkındalığı artırmanın ve taramayı rutin bir uygulama haline getirmenin gelecek nesillerin daha sağlıklı olmasına katkıda bulunmak için gerekli olduğuna inanıyoruz. Bu, uygun yönetim ve ekipman yoluyla perinatal mortalite ve morbiditeyi azaltarak ve böylece toplumdaki etkilenen bireylerin refahını optimize ederek başarılabilir.

Anahtar Kelimeler: Konjenital kalp hastalıkları, fetal anomali, prenatal tanı

Introduction

Congenital heart diseases (CHD) refer to structural or functional abnormalities of the heart and large vessels associated with the heart that occur during the intrauterine period. CHD is the most common congenital anomaly[1], with an incidence of approximately 11 per 1,000 live births[2,3]. Approximately 40% of cardiac anomalies are diagnosed within the first year of life[4], suggesting that the actual prevalence of CHD may be higher. Recent studies have shown a high degree of heritability both independently and in association with other cardiovascular anomalies, especially left ventricular outflow tract obstructive disorders[5]. In 1 out of every 100 children with cardiac anomalies, there is an accompanying genetic or chromosomal anomaly, such as Down syndrome. Besides genetic factors, the risk of cardiac anomalies in the current pregnancy is increased by factors such as excessive alcohol consumption during pregnancy, maternal medication use, viral infections like rubella or measles, particularly during the organogenesis period, and a family history of cardiac anomalies in the mother or siblings[6]. In some complex or non-viable anomalies, termination may be considered based on the family's preference. Due to the risks of perinatal mortality and morbidity in patients with congenital cardiac anomalies, it is essential to properly manage these patients and identify high-risk groups for appropriate analysis. Prenatal evaluation plays a crucial role in this analysis and planning. CHD is the most lethal malformation in fetuses born with congenital anomalies. Therefore, early identification of the anomaly through prenatal diagnosis facilitates planned referral of the patient to the appropriate healthcare facility and reduces perinatal mortality and morbidity rates through proper management.

This study aims to contribute to the literature by examining the correlation between prenatal and postnatal diagnoses in fetuses with cardiac anomalies detected in our perinatology clinic during the prenatal period, identifying risk factors, and determining the most appropriate approaches through careful monitoring of high-risk groups.

Materials and Methods

In our study, we retrospectively reviewed the records of 188 fetuses diagnosed with cardiac anomalies during the prenatal period through detailed ultrasound examinations. These fetuses were delivered and monitored in the Neonatal Intensive Care Unit of Çukuorva University Faculty of Medicine, Department of Obstetrics and Gynecology and Perinatology, between January 2016 and December 2021. These records include cases where the fetuses were found to have cardiac anomalies and were delivered and survived.

Ethical approval was obtained from Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision no: 78, date: 05.11.2021). Data were collected on maternal age, parity, gestational age at the time of delivery or termination, presence of chromosomal abnormalities, and performance of an invasive procedure. The presence of consanguinity, extra cardiac anomalies in the fetus, and family history were assessed. History of cardiac anomalies, obstetric history, and maternal drug use during pregnancy were also questioned. Echocardiographic results in the prenatal and postnatal period were evaluated. Additionally, newborns' history of surgery during the neonatal period, postnatal morbidity, and mortality outcomes was thoroughly evaluated.

The mode of delivery and the clinical findings of the patients in both the prenatal and postnatal periods were analyzed. Fetal hearts were evaluated during the prenatal period by high-risk pregnancy specialists in our clinic using a Voluson E6 ultrasound machine. In both the prenatal and postnatal periods, echocardiographic evaluations were performed using two-dimensional, pulsed-wave Doppler, and color Doppler

techniques with the Sonos 7500 (3-8 MHz convex probe) and Epiq 7 (2-9 MHz convex probe) machines. Two-dimensional and color Doppler imaging was used to assess the four-chamber view of the heart, the origins of the great vessels, the tracheal view, and views of the aortic and ductal arches. Examinations included the location of the heart and abdomen, systemic and pulmonary venous return, atrioventricular and ventriculoarterial connections, inter-atrial and inter-ventricular valves, heart chambers, and the ductal and aortic arches.

Statistical Analysis

Fetal echocardiography (ECHO) was performed by two pediatric cardiologists between 2016 and 2021. For patients with suspected pathological findings, repeated echocardiographic follow-ups were performed. Congenital cardiac anomalies were classified into seven subgroups, as presented in Table 1. Isolated hyperechogenic cardiac focus was not considered a cardiac anomaly.

Results

The maternal age range varied between 16 and 46 years, with a mean age of 29.46±6.3 years. Consanguinity was observed in 38 (20.2%) patients, and only 4 (2.1%) of the total number of patients, the parental consanguinity status was unknown. The gestational age at which mothers first presented and underwent fetal ECHO ranged from 12 and to 42 weeks, with a mean gestational age of 27.57±7.1 weeks. A history of multigravidity was present in 142 mothers, and 19 of these patients had previously given birth to a baby with a fetal cardiac anomaly. Among the 188 patients, 85.5% (n=159) led to live births. Of these, 59.7% were delivered by cesarean section, and 40.3% were delivered vaginally.

Termination was performed in 29 patients, of which 4 underwent feticide procedures prior to the procedure. In 2 patients, termination was performed due to intrauterine fetal death. A total of 38 patients accepted invasive procedures. Amniocentesis was the most commonly performed invasive procedure, applied to 22 patients. Genetic testing was conducted to further investigate and detail the genetic profiles of the samples obtained through invasive procedures. The most frequent result from chromosomal analysis was a normal genetic profile; however, Trisomy 21 and DiGeorge Syndrome with a 22q11 deletion, which presents with clinical findings, were observed among the associated anomalies (Table 2).

Maternal comorbidities and the potential role of certain medications in fetal development were also included in our analysis. No additional medical conditions were observed in 121 mothers within the study population. The most prominent factors observed were, due to a poor obstetric history, use of low molecular weight heparin, and the presence of diabetes mellitus in the mothers (Table 2).

Other system anomalies may accompany cardiac anomalies in these fetuses. In line with our study, anomalies of the genitourinary system and central nervous system are more prominently noted (Table 3).

The findings obtained from the ECHO performed by our perinatology team during the intrauterine period showed an agreement of 88.8% with the examinations conducted by our pediatric cardiologists in the neonatal intensive care unit, and a partial agreement of 11.3%. Among the 188 patients,

Table 1. Congenital cardiac anomalies

Code in statistics	Cardiac anomaly group	Subgroupings of CHD
0	CHD not observed	
1	Conotruncal malformations	Tetralogy of Fallot, TGA, truncus arteriosus, double outlet right ventricle
2	Malformations of the right heart	Ebstein anomaly tricuspid atresia/dysplasia Pulmonary atresia, stenosis
3	Malformations of the left heart	Hypoplastic left heart, coarctation of the aorta and interrupted aortic arch, aortic stenosis, double-entry left ventricle
4	Abnormal placement	Situs inversus, heterotaxy syndromes
5	Septal defects	ASD
		VSD
6	Myocardial and pericardial diseases	Hypertrophic CMP
		Dilated CMP
		Rhabdomyoma
		Pericardial teratoma
7	Abnormal cardiac Tachycardia/ bradiarrhythmia	Tachycardia/bradiarrhythmia

CHD: Congenital heart diseases, ASD: Atrial septal defect, VSD: Ventricular septal defect, CMP: Cardiomyopathy, TGA: Transposition of the great artery

12 exhibited discordance between antenatal and postnatal diagnosis, representing 6.5% of the total (Tables 4, 5).

The Kappa agreement values are interpreted with the following reference ranges, though the specific meanings are incomplete: <0 and 1. According to the analysis, a sensitivity of 96.55% and specificity of 100.0% were found in comparing the prenatal and postnatal diagnosis findings (p<0.001) (Figure 1).

Table 6 examines the differences between the parameters obtained from the 188 patients included in the study and the mortality outcomes. The rate of chromosomal anomalies was found to be significantly higher in patients who experienced mortality (p<0.001). The rate of maternal medication use was lower in patients who experienced mortality (p=0.039). Among the 38 patients who accepted invasive procedures, 12 underwent termination of pregnancy for the fetus. Chromosomal anomalies were detected in 2 of these 12 patients, one exhibiting trisomy 21 and the other triploidy. It was determined that 26.2% of the patients had their pregnancies terminated and subsequently experienced perinatal mortality (p<0.001). Additionally, the rate of cesarean deliveries was found to be higher in patients who experienced perinatal mortality (p=0.002). Cases of perinatal mortality had significantly lower values compared to live patients in terms of gestational age, 1-minute Apgar score, 5-minute Apgar score, duration of stay in the intensive care unit, and birth weight (p=0.009; p<0.001; p<0.001; p<0.001; p<0.001, respectively).

Table 2. Evaluation of the data of the cases

	Number (n)	Percent (%)
Invasive procedures	38	20.2
Chorionic villus sampling	11	28.9
Amniocentesis	22	57.9
Cordocentesis	1	2.6
Genetic analysis in the postnatal period	4	10.5
Chromosomal anomaly		
Not accepting the analysis	150	79.8
Accepting the analysis	38	20.2
Accepted chromosomal anomaly (n=38)		
Normal	28	73.7
DiGeorge syndrome	3	7.9
Triploidy	1	2.6
Jarcho-Levin syndrome	1	2.6
Trisomy 21	3	7.9
Trisomy 18	2	5.3
Maternal medication use	27	14.4
DM (insulin)	7	25.9
Thyroid (L-thyroxine or propylthiouracil)	7	25.9
Cardiovascular diseases (antihypertensives)	2	7.4
Epilepsy (antiepileptic medications)	4	14.8
Anticoagulants (low molecular weight heparins)	8	29.6
Others	2	7.4
Consanguinity		
No	146	77.7
Yes	42	22.3

Table 3. Associated anomalies

Associated anomalies	Number (n)	Percent (%)
	73	38.8
Gastrointestinal tract	7	9.6
Genitourinary system	10	13.7
Central nervous system	11	15.1
Skeletal system disorders	5	6.8
Craniopharyngeal anomalies	7	9.6
Other	33	45.2

Table 4. Evaluation of mortality, operation and medical treatment needs of the cases

	Number (n)	Percent (%)
Fetal mortalite		
Exitus	104	55.3
Alive	80	42.6
Feticide + medical termination	4	2.1
Need for emergency surgery		
No	129	68.6
Yes	59	31.4
Need for postnatal medical care		
yes	111	59.0
No	77	41.0
Termination	27	14.4
Termination	23	85.2
Feticide + medical termination	4	14.8

Table 5. Analysis of fit ratios

Compliance rates	Number (n)	Percent (%)
No	21	11.5
Yes	153	82.3
Partial compliance	12	6.5

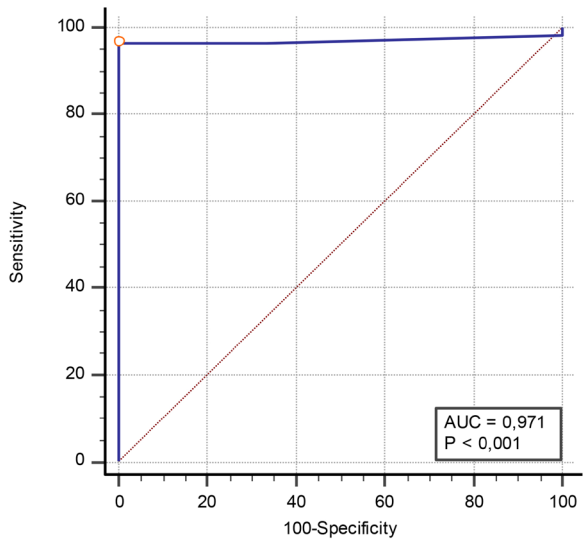

Figure 1. Diagnostic test performance between prenatal and postnatal diagnostic findings

AUC: Area under the curve

Table 7 discusses the striking differences in patients with perinatal mortality among the 188 patients included in the study are discussed. The rate of chromosomal anomaly was higher in patients who died (p<0.001). Maternal drug use rate was lower in patients who did not survive (p=0.039). Thirty-eight of our followed up pregnant women with fetuses with cardiac anomalies accepted the interventional procedure, and 12 of these pregnant women decided to terminate. In this group of 12 pregnant women with fetuses with cardiac anomalies whose pregnancies were terminated, chromosomal anomalies were detected in 2 fetuses. One of these patients had trisomy 21 and one had triploidy. In the group of patients with perinatal mortality, 26.2% of the pregnancies ended with termination (p<0.001). The rate of caesarean section was higher in cases with perinatal mortality (p=0.002). The time of delivery was earlier, and the 1st minute Apgar score, 5th minute Apgar score, duration of intensive care unit stay, and birth weight were lower in patients who developed perinatal mortality compared to living patients (p=0.009, p<0.001, p<0.001, p<0.001, and p<0.001, respectively).

Table 6. Differences between parameters and mortality findings for all patients (n=188)

	Perinatal mortality Yes (n=104)	Perinatal mortality No (n=84)	p†
	n (%)	n (%)	
Associated anomaly	43 (41.3)	30 (35.7)	0.431
Gastrointestinal system	4 (9.3)	3 (10)	0.921
Central nervous system anomalies	6 (14)	5 (16.7)	0.750
Genitourinary system anomalies	9 (20.9)	1 (3.3)	0.031*
Craniopharyngeal anomalies	5 (11.6)	2 (6.7)	0.479
Other anomalies	16 (37.2)	17 (56.7)	0.100
Skeletal system disorders	1 (2.3)	4 (13.3)	0.067
Invasive procedure	21 (20.2)	17 (20.2)	0.994
Chromosomal anomaly			
Not accepting the analysis	72 (69.2)	78 (92.9)	<0.001**
Accepting the analysis	32 (30.8)	6 (7.1)	
Accepted chromosomal anomaly analysis (n=38)			
Normal	28 (87.5)	-	<0.001**
DiGeorge syndrome	-	3 (50)	
Triploidy	1 (3.1)	-	
Jarcho-Levin syndrome	1 (3.1)	2 (33.3)	
Trisomy 21	2 (6.3)	-	
Trisomy 18	-	1 (16.7)	
Maternal medication use	10 (9.6)	17 (20.2)	0.039*
Termination	26 (25)	3 (3.6)	<0.001**

Table 6. Continued

	Perinatal mortality Yes (n=104)	Perinatal mortality No (n=84)	p†
	n (%)	n (%)	
Gravida			
Nullipar	30 (28.8)	17 (20.2)	0.175
Multipar	74 (71.2)	67 (79.8)	
Mode of delivery			
Vaginal	33 (30.8)	32 (38.1)	0.002**
Caesarean section	46 (43.0)	49 (58.3)	
Stillbirth	19 (17.8)	-	
Medical abortion	9 (8.4)	-	
Consanguinity	28 (26.9)	14 (16.7)	0.093
Maternal disease	19 (18.3)	25 (29.8)	0.064
Gender			
Male	64 (61.5)	55 (65.5)	0.578
Female	40 (38.5)	29 (34.5)	
Emergency surgery			
No	72 (69.2)	57 (67.9)	0.840
Yes	32 (30.8)	27 (32.1)	
Postnatal medical needs			
No	57 (54.8)	54 (64.3)	0.189
Yes	47 (45.2)	30 (35.7)	
	Mean ± SD	**Mean ± SD**	**p‡**
Diagnosis week	26.3±7.0	26.7±7.5	0.651
Birth week	34.4±7.1	37.3±4.9	**0.009****
1-minute APGAR score	4.51±3.1	6.79±2.0	**<0.001****
5-minute APGAR score	5.61±3.6	8.11±2.0	**<0.001****
Length of stay in the intensive care unit	11.0±18.2	18.6±19.9	**<0.001****
Weight (g)	2268.0±1145.2	2903.4±741.9	**<0.001****
Maternal age	28.6±6.3	30.2±6.3	0.053

*: p<0,05, **: p<0,001, †: Ki-kare, ‡: Mann-Whitney U, SD: Standard deviation

Discussion

Among congenital anomalies, congenital heart anomalies (CHA) account for the highest proportion of cases. These anomalies can either be life-threatening or impair the quality of life. Interventions may be necessary during the intrauterine or neonatal periods, and these affected fetuses may require emergency intervention[7]. Therefore, minimizing the loss of time provides us with a strategic approach and enables us to achieve success in reducing mortality and perinatal morbidity. The rapid advancement of technology, which has recently been reflected in our daily lives, has had positive contributions to the field of health. With these positive reflections of technology, especially in the last two decades, progress is being made in the field of perinatology to understand the intrauterine fetal period. Anatomical screening is recommended in pregnancy follow-up, examining the heart's anatomy, its position with the surrounding organs and large vessels, and the orientation and connections of the large vessels themselves. In general, a large number of patients are detected in routine screening.

Table 7. Differences between neonatal period parameters and mortality groups in pregnancies resulting in live birth (n=159)

	Perinatal mortality Yes (n=78)	Perinatal mortality No (n=81)	p†
	n (%)	n (%)	
Associated anomaly	33 (42.3)	28 (34.6)	0.316
Central nervous system anomalies	6 (18.2)	5 (17.9)	0.974
Genitourinary system anomalies	5 (15.2)	1 (3.6)	0.130
Craniopharyngeal anomalies	4 (12.1)	2 (7.1)	0.515
Other anomalies	12 (36.4)	16 (57.1)	0.105
Skeletal system disorders	1 (3.0)	4 (14.3)	0.110
Invasive procedure	12 (15.4)	15 (18.5)	0.599
Chromosomal anomaly			
Not accepting the analysis	51 (65.4)	77 (95.1)	<0.001**
Accepting the analysis	27 (34.6)	4 (4.9)	
Accepted chromosomal anomaly analysis (n=38)			
Normal	23 (85.2)	-	<0.001**
DiGeorge syndrome	-	3 (75)	
Triploidy	-	-	
Jarcho-Levin syndrome	1 (3.7)	-	
Trisomy 21	1 (3.7)	1 (25)	
Trisomy 18	2 (7.4)	-	
Maternal medication use	9 (11.5)	16 (19.8)	0.155
Termination	4 (5.1)	9 (11.1)	0.169
History of a child with cardiac anomaly			
Gravida	19 (24.4)	16 (19.8)	0.483
Nullipar	59 (75.6)	65 (80.2)	
Mode of delivery			
Vaginal	29 (37.2)	32 (39.5)	0.118
Caesarean section	44 (56.4)	49 (60.5)	
Stillbirth	5 (6.4)	-	
Consanguinity	24 (30.8)	13 (16)	0.028*
Maternal disease	16 (20.5)	24 (29.6)	0.185
Gender			
Male	49 (62.8)	53 (65.4)	0.731
Female	29 (37.2)	28 (34.6)	
Emergency surgery			
No	49 (62.8)	54 (66.7)	0.612
Yes	29 (37.2)	27 (33.3)	
Postnatal medical needs			
No	34 (43.6)	51 (63)	0.014*
Yes	44 (56.4)	30 (37)	

Table 7. Continued

	Perinatal mortality Yes (n=78)	Perinatal mortality No (n=81)	p†
	n (%)	n (%)	
Diagnosis week	28.0±7.1	27.1±7.3	0.469
Birth week	37.5±3.5	38.1±2.8	0.325
1-minute APGAR score	5.70±2.3	7.04±1.6	**<0.001****
5-minute APGAR score	7.09±2.4	8.41±1.3	**<0.001****
Length of stay in the intensive care unit	13.8±19.2	19.2±19.9	**0.005****
Weight (g)	2730.7±777.2	2963.6±638.3	0.085
Maternal age	28.8±6.4	30.2±6.4	0.148

*: p<0,05, **: p<0,001, †: Ki-kare, ‡: Mann-Whitney U, SD: Standard deviation

The proportion of live births with life-compatible CHD is approximately 0.8%[8]. If we consider the percentage of all pregnancies, this proportion becomes broader due to the inclusion of various pregnancy outcomes. This difference arises because some CHDs have severe clinical courses and can lead to fetal loss during the intrauterine period. Additionally, screenings conducted in perinatology often reveal that certain anomalies are incompatible with life before delivery and that the clinical presentation of the existing condition is aggressive. In such cases, families may be presented with the option of termination or they may seek care at our clinic due to intrauterine fetal death.

In terms of incidence, CHD occurs in about 8 per 1,000 live births, with its rate among stillbirths being 3-4%, and ranging from 10-25% in spontaneous abortions. Among premature neonates, the incidence is approximately 2%[4,9,10]. Our study does not reflect the prevalence of CHD in the population. This is because our study focuses on prenatal and neonatal periods, thus only considering anomalies detectable during the fetal stage.

The generally accepted ideal time for diagnosis is between 18 and 22 weeks of gestation. Fetal cardiac evaluation can even be performed during the first trimester using transvaginal or transabdominal ultrasound. In our study, the earliest diagnosis was made at 13 weeks-gestation, with the average gestational age for fetal transthoracic echocardiograms being 28±7.13 weeks. The earliest CHA we diagnosed was hypoplastic left heart syndrome, identified at 13 weeks of gestation. Our center's approach is to perform ECHO at 18-22 weeks gestation for assessing the risk of CHAs.

In our clinic's research, the most prominent anomalies observed were conotruncal anomalies, followed by right heart anomalies. A study indicated that septal defects were the most frequently observed; and among cyanotic heart diseases, the most common were conotruncal anomalies such as tetralogy of Fallot (TOF)[11]. Another study reported that septal anomalies were predominant[12]. In the study by Burger et al.[13], septal defects were also the most commonly observed isolated cardiac anomalies. In the work presented by Best et al.[14], among a total of 5070 patients with CHAs, the anomalies identified included ventricular septal defect (n=2182, percentage=43%), pulmonary stenosis (n=428, percentage=8.4%), atrial septal defect (n=422, percentage=8.3%), TOF (n=271, percentage=5.3%), atrioventricular septal defect (n=264, percentage=5.2%), and coarctation of the aorta (n=258, percentage=5%).

In our research, the sample size for definitive diagnosis was limited due to the low prevalence of pregnancies in our community. Invasive procedures were performed on 4% of patients. Among the samples we collected, amniocentesis was predominantly observed with 22q11 deletion microdeletion leading to the identification of DiGeorge syndrome.

In our study group, 37 patients accepted invasive procedures for a definitive diagnosis, with chromosomal anomalies detected in 9 patients (24%). In a study by Ko[15] in Korea, isolated CHAs and patients with extracardiac anomalies were examined in a cohort of 791 individuals, with amniocentesis performed on 182 patients. Chromosomal anomalies were identified in 21 patients (11.5%). Among this cohort of 791 patients, 627 (79.3%) had isolated CHAs, and live births were reported for 299 patients.

In the study conducted by Elshazali et al.[16], a total of 141 infants were evaluated. It was found that CHAs were more common in male fetuses. A total of 11.3% were dysmorphic (n=16) (including Down syndrome, Noonan syndrome, and others). Additionally, 9% (n=9) had previously mentioned exclusion criteria, that positively contributed to birth weight. A very small percentage of families had a positive history of CHAs (0.7%). The average birth weight of the samples was 2.59 kg, with 31.9% having low or very low birth weight. All cases had low birth weight; 50% were reported to have very low birth

weight. In the study by Levin et al.[17], among 37 infants with CHD, 21 were of appropriate weight for gestational age, while 16 were small for gestational age.

In a study conducted by Lopes et al.[18] in Brazil involving 52 infants with CHD, the mortality risk among newborns with CHD was found to be twofold higher than that among low-birth-weight premature infants, particularly for newborns with CHD who have an Apgar score of less than 7 during the first minute of life. The presence of certain comorbidities, in addition to CHD, was associated with mortality outcomes, increasing the risk nearly threefold. The average length of stay in the neonatal unit was observed to be 75 days, with 25% of patients failing to reach this duration. In our study, the weights of the newborns varied. There was a subgroup of patients with cardiac anomalies who did not reach term, with the highest weight recorded at 3885 g and the lowest at 685 g, resulting in an average weight of 2985 g. In cases where mortality occurred, the gestational age, 1-minute Apgar score, 5-minute Apgar score, duration of stay in the intensive care unit, and birth weight of the patients were all found to be significantly lower than those who survived ($p=0.009$; $p<0.001$; $p<0.001$; $p<0.001$; $p<0.001$, respectively). The presence of a low Apgar score at one minute suggests that certain cardiac defects may be active during the intrauterine period, potentially compromising blood flow and thereby affecting perinatal morbidity and mortality by preventing adequate nutrient and oxygen supply to the fetus. This underscores the importance of adequate prenatal diagnosis and monitoring.

In studies where the subject did not have CHD, the risk of having a sibling with CHD was observed to be between 2% and 6%. The likelihood of detecting CHD in a fetus increases with the number of affected siblings[19]. In our study, the proportion of patients with a family history of CHD was 10.1%. We believe another reason for the elevated rate and increase in incidence may be that the institution is a tertiary center, and therefore the patient population consists of high-risk cases in our country compared to Western societies.

Women with diabetes prior to pregnancy have been observed to have approximately four times the likelihood of experiencing a pregnancy affected by CHD compared to those without diabetes[20]. Researchers indicate that about 8% of the CHDs occurring each year may arise from poorly controlled diabetes before and in the early stages of pregnancy[21]. In our study, there was no observed increase in fetal CHD risk among pregnancies with gestational diabetes, included in the maternal diabetes group. The lack of increased fetal CHD rates in infants of mothers with pre-existing diabetes may be attributed to the inclusion of gestational diabetes in the same group, and the small sample size as a limitation.

Our study demonstrated an agreement rate of 88.8%, with 11.2% discordance. The sensitivity of prenatal and postnatal diagnoses was found to be 96.55%, with 100% specificity. In a study conducted by Ozkutlu et al.[22] in 2022, the sensitivity for comparing prenatal and postnatal diagnoses of cardiac anomalies was reported to be 93%, with 100% specificity. Another study conducted by Özbarlas et al.[23] at our center calculated the sensitivity of ECHO examinations to be 96%, with 99% specificity. Considering the classification used by Silva et al.[24], 77.6% of cases showed congruence between prenatal and postnatal CHD diagnoses. In the study by Chakraborty et al.[25], the agreement rate for complex CHDs between prenatal and postnatal diagnoses was reported to be over 80%. The results of our study align with the literature and highlight the importance of prenatal ECHO.

Study Limitations

The primary limitation of our study is its retrospective design, which has led to difficulties in accessing certain data. The patients who underwent fetal echocardiographic examination were not consistently monitored, and there were gaps in the prenatal follow-up schedules at our hospital after the optimal diagnosis week during the third trimester. Additionally, a significant portion of patients was referred from external centers outside the city. Furthermore, socioeconomic factors and religious beliefs resulted in the inability to perform invasive procedures for definitive diagnosis in many cases, which constitutes a limitation of our study.

Conclusion

The prevalence of fetal heart anomalies is significantly higher among live births, and their distribution varies. The correlation observed in a substantial proportion of fetuses diagnosed with CHD, approached with a preliminary diagnosis of heart anomaly during the neonatal period, underscores the importance of managing patient stratification accurately. This must be done within the healthcare system by ensuring appropriate conditions before birth. This is crucial for effectively managing higher-level care and necessary preparations during deliveries. By implementing suitable management and facilities, we can reduce perinatal mortality and perinatal morbidity, thereby contributing to the optimal well-being of individuals in our society and promoting healthy generations. Therefore, it is essential to integrate screenings into routine practice and enhance awareness to educate the community.

Ethics

Ethics Committee Approval: Ethical approval was obtained from Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision no: 78, date: 05.11.2021).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.M.Y., S.C.D., S.A., İ.C.E., M.S., Concept: G.M.Y., S.C.D., S.A., İ.C.E., M.S., Design: G.M.Y., S.C.D., S.A., İ.C.E., M.S., Data Collection or Processing:

G.M.Y., S.C.D., S.A., İ.C.E., M.S., Analysis or Interpretation: G.M.Y., S.C.D., S.A., İ.C.E., M.S., Literature Search: G.M.Y., S.C.D., S.A., İ.C.E., M.S., Writing: G.M.Y., S.C.D., S.A., İ.C.E., M.S.

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