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The Effect of Prenatal Diagnosis of Critical Congenital Heart Disease on Postnatal Mortality and Morbidity: A Retrospective Cohort Study

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ABSTRACT: Background: Congenital heart disease (CHD) refers to malformations of the heart or great vessels that occur during the intrauterine period. Critical CHD refers to heart conditions that require medical intervention or surgical procedures in the early stages of life. **Methods:** In this retrospective cohort study, newborns aged 0 to 28 days who were admitted to the Neonatal Intensive Care Unit and the Pediatric Cardiovascular Surgery Clinic of our hospital with a diagnosis of critical CHD between January 2019 and September 2024 were evaluated. **Results:** Among 160 patients, 52 (32.5%) had a prenatal diagnosis. Overall mortality was significantly higher in the prenatally diagnosed group compared to the postnatally diagnosed group (51.9% vs. 19.5%, $p < 0.001$). However, in the subgroup of patients with hypoplastic left heart syndrome (HLHS), pulmonary atresia (PA), or aortic arch anomalies ($n = 67$), prenatal diagnosis was associated with significantly lower mortality (38.9% vs. 68.8%, $p = 0.018$). Multivariate logistic regression identified prenatal diagnosis (OR 3.11, 95% CI 1.37–7.06), presence of the above high-risk lesions (OR 3.29, 95% CI 1.25–8.67), and lower birth weight (per 1 kg, OR 2.09, 95% CI 1.13–3.88) as independent predictors of mortality. **Conclusions:** In this cohort, the overall higher mortality among prenatally diagnosed patients reflects a higher proportion of complex lesions (e.g., HLHS) in that group. Nevertheless, within the high-risk subgroup of HLHS, PA, and aortic arch anomalies, prenatal diagnosis was associated with a significant survival benefit. These findings suggest that the impact of prenatal diagnosis on mortality is lesion-specific and confounded by disease severity. Future multicenter prospective studies with larger, homogeneous populations are needed to clarify the true effect of prenatal diagnosis on outcomes.

KEYWORDS: Congenital heart disease; prenatal diagnosis; fetal echocardiography

1 Introduction

Congenital heart disease (CHD) refers to malformations of the heart or great vessels that occur during the intrauterine period [1,2]. CHDs represent the most common group of congenital anomalies, and they are observed in approximately 8 to 12 out of every 1000 live births [3,4]. Critical CHD refers to heart conditions that require medical intervention or surgical procedures in the early stages of life. These critical forms account for approximately 20–25% of all CHDs, corresponding to about one in every 500 births [1,5]. In recent years, advances in neonatal cardiac catheterizations, palliative and corrective surgeries, anesthesia techniques, and improvements in intensive care unit conditions have contributed to better outcomes for critical CHDs [6,7].

The increasing use of fetal echocardiography in clinical practice has enabled the prenatal diagnosis of many congenital heart diseases (CHDs), and this allows for the planning of delivery in cases where newborns are anticipated to require urgent medical intervention or treatment. Clinical guidelines on CHDs recommend performing fetal echocardiography between the 18th and 22nd weeks of gestation in pregnancies considered high-risk due to fetal, maternal, or familial factors [8]. Prenatal diagnosis provides valuable time for healthcare professionals and families, enabling a more informed management of the disease [9]. In particular, for patients with ductus-dependent critical CHDs, early detection through screening, before rapid clinical deterioration and the onset of symptoms, plays a vital role in initiating timely treatment [10]. This study aims to evaluate the independent effect of prenatal diagnosis on mortality and clinical outcomes after adjusting for disease severity.

2 Methods

2.1 Patients

In this retrospective cohort study, newborns aged 0 to 28 days who were admitted with a diagnosis of critical CHD to the Neonatal Intensive Care Unit and the Pediatric Cardiovascular Surgery Clinic of our hospital between January 2019 and September 2024 were retrospectively evaluated. Cases that did not result in live birth and those terminated *in utero* were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Clinical Research Ethics Committee of the University of Health Sciences, Gazi Yaşargil Training and Research Hospital (Decision No: 131, Date: 06 September 2024). Patient's guardian consent was waived due to the retrospective nature of the study and the use of de-identified data.

2.2 Data Collection

A total of 160 patients who met the study criteria during the specified period were identified. For each case, data were recorded in a pre-designed case report form, including age at the time of diagnosis, body weight at the time of diagnosis, height at the time of diagnosis, vital signs at the time of diagnosis, blood gas analysis at the time of diagnosis, hemogram and biochemistry results at the time of diagnosis, sex, mode of delivery, gestational age, prenatal diagnosis, postnatal diagnosis, day of postnatal diagnosis, day of postnatal intervention, pre-intervention duration (time from diagnosis confirmation to intervention), mortality, surgical procedure performed, duration of mechanical ventilation, length of stay in the intensive care unit, total hospitalization time, and complications. Patients were divided into two groups: those with and without a prenatal diagnosis, and analyses were performed between these groups. The mean week of prenatal diagnosis for the group without prenatal diagnosis was calculated as 23.8 ± 3.9 (15~38) weeks. Mortality was calculated based on in-hospital mortality. For hospital mortality, all deaths occurring both preoperatively and postoperatively—from the time of admission to our unit until discharge—were included in both groups. The definition of morbidity now includes those with permanent organ damage. Patients requiring emergency septostomy or septotomy after delivery were considered to have a restrictive foramen ovale (RFO). The preoperative vasoactive inotropic score (VIS) was calculated according to the following formula: "VIS = $1 \times \text{dopamine } [\mu\text{cg/kg/min}] + 1 \times \text{dobutamine } [\mu\text{cg/kg/min}] + 100 \times \text{epinephrine } [\mu\text{cg/kg/min}] + 100 \times \text{norepinephrine } [\mu\text{cg/kg/min}] + 10 \times \text{milrinone } [\mu\text{cg/kg/min}] + 10,000 \times \text{vasopressin } [\text{U/kg/min}]$."

2.3 Statistical Analysis

Statistical analysis of the collected data was performed using SPSS version 24.0 for Windows (IBM Corp., Armonk, NY, USA). Normality was assessed by evaluating skewness and kurtosis values within the range

of -1.5 to $+1.5$ and by examining histograms. Descriptive statistics for continuous variables were presented as mean \pm standard deviation for parametric data and as median (minimum–maximum) for non-parametric data. In comparisons between two groups, the Chi-square test and Fisher's exact test (<5 samples) were used for categorical variables, and the independent samples t -test was applied for normally distributed continuous variables. For continuous variables not showing normal distribution, the Mann–Whitney U test was performed. Variables with clinical relevance (prenatal diagnosis, Aristotle score, presence of hypoplastic left heart syndrome (HLHS)/pulmonary atresia (PA)/aortic arch anomalies, shock symptoms, gestational age, and birth weight) were entered into the model simultaneously. A p -value of <0.05 was considered statistically significant.

3 Results

Among the 160 patients with critical CHD included in the study, 52 had a prenatal diagnosis, while 108 did not. When comparing the demographic and clinical characteristics of patients with and without a prenatal diagnosis, statistically significant differences were found between the groups in terms of sex, mean day of postnatal diagnosis, and clinical outcome ($p = 0.026$, $p = 0.004$, and $p < 0.001$, respectively) (Table 1). However, in the multivariate logistic regression analysis performed, it was seen that prenatal diagnosis, presence of any of the following: HLHS, PA, or aortic arch anomalies, and birth weight were found to have a significant effect on mortality rate; however, Aristotle score, gestational age, and the presence of shock symptoms at the time of initial diagnosis had no effect on mortality rate (Table 2).

Table 1: Comparison of the demographic and clinical characteristics of patients with and without a prenatal diagnosis.

Variable	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	Total (n = 160)	p -Value
Sex, n (%)				
Female	27 (51.9)	36 (33.3)	63 (39.3)	0.026 ^a
Male	25 (48.1)	72 (66.7)	97 (60.7)	
Birth weight (g)**	2760 (1700–4350)	2875 (1620–5000)	2820 (1620–5000)	0.997 ^b
Height (cm)**	48 (42–58)	48 (42–53)	48 (42–58)	0.105 ^b
Gestational age < 37 weeks, n (%)				
Yes	15 (28.9)	26 (24)	41 (25.6)	0.564 ^a
No	37 (71.1)	82 (76)	119 (74.4)	
Gestational age (weeks)**	37.5 (31–41)	38 (30–42)	38 (30–42)	0.278 ^b
Mode of delivery, n (%)				
NSVD	39 (75)	76 (70.4)	115 (71.9)	0.579 ^a
CS	13 (25)	32 (29.6)	45 (28.1)	
Need for CPR, n (%)				
Yes	13 (25)	40 (37)	53 (33.1)	0.153 ^a
No	39 (75)	68 (63)	107 (66.9)	
MV support, n (%)				
Yes	24 (46.1)	44 (40.7)	68 (42.5)	0.609 ^a
No	28 (53.9)	64 (59.3)	92 (57.5)	
Postoperative MV duration (days)**	0 (0–67)	0 (0–27)	0 (0–67)	0.380 ^b
Need for inotropes, n (%)				
Yes	21 (40)	38 (35)	59 (37)	0.254 ^a
No	31 (60)	70 (65)	101 (63)	

Table 1: Cont.

Variable	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	Total (n = 160)	p-Value
Day of postnatal diagnosis**	1 (1-1)	1 (1-28)	1 (1-28)	0.004 ^b
Preoperative hospitalization (days)**	8.5 (0-149)	11 (0-729)	10 (0-729)	0.443 ^b
Day of surgery**	9.5 (1-150)	12.5 (1-731)	11 (1-731)	0.117 ^b
Length of stay (days)**	25 (0-120)	20 (0-110)	22.5 (0-120)	0.092 ^b
NICU stay (days)**	20 (0-111)	18.5 (0-110)	19.5 (0-110)	0.087 ^b
Clinical outcome, n (%)				
Survived	25 (48.1)	87 (80.5)	112 (70)	<0.001 ^a
Deceased	27 (51.9)	21 (19.5)	48 (30)	

**Median (Min-Max), n (percentage %), a: Chi-square test, b: Mann-Whitney U test, CPR: Cardiopulmonary resuscitation, CS: Cesarean section, MV: Mechanical ventilation, NSVD: Normal spontaneous vaginal delivery, NICU: Neonatal intensive care unit.

Table 2: Evaluation of factors affecting mortality using multivariate logistic regression.

	B	Odds Ratio	Confidence Interval 95%	p-Value
Presence of prenatal diagnosis	1.13	3.11	1.37-7.06	0.007
Aristotle score	0.064	0.97	0.86-1.10	0.72
Presence of any of the following: HLHS, PA, or aortic arch anomalies	1.19	3.29	1.25-8.67	0.016
Having shock symptoms	0.316	1.37	0.18-2.25	0.49
Gestational age (weeks)	0.012	1.01	0.85-1.19	0.88
Birth weight (per 1 kg)	0.74	2.09	1.13-3.88	0.019

B: logistic regression coefficient.

In this study, an analysis of the prenatal diagnoses revealed that the most common conditions were HLHS in 18 patients (34.6%), pulmonary atresia in 13 patients (25.0%), and transposition of the great arteries (TGA) in 8 patients (15.4%) (Table 3).

Table 3: Distribution of prenatal and postnatal diagnoses among the patients included in the study.

Prenatal Diagnoses n = 52	n (%)	Postnatal Diagnoses n = 108	n (%)
HLHS	14 (26.9)	HLHS	18 (16.6)
HLHS with RFO	4 (7.7)	HLHS with RFO	0 (0)
Total	18 (34.6)	Total	18 (16.6)
Pulmonary Atresia + IVS	9 (17.3)	Pulmonary Atresia + IVS	7 (6.5)
Pulmonary Atresia + VSD	4 (7.7)	Pulmonary Atresia + VSD	5 (4.6)
Total	13 (25)	Total	12 (11.1)
TGA (simple)	5 (9.6)	TGA (simple)	43 (39.8)
TGA with RFO	1 (1.9)	TGA with RFO	7 (6.5)
TGA with VSD	2 (3.9)	TGA with VSD	5 (4.6)
Total	8 (15.4)	Total	55 (50.9)
Hypoplastic Aortic Arch	5 (9.6)	Hypoplastic Aortic Arch	1 (0.9)
Single Ventricle	4 (7.7)	Single Ventricle	3 (2.8)
Tetralogy of Fallot	1 (1.9)	Tetralogy of Fallot	9 (8.3)
Truncus Arteriosus	1 (1.9)	Truncus Arteriosus	3 (2.8)

Table 3: Cont.

Prenatal Diagnoses n = 52	n (%)	Postnatal Diagnoses n = 108	n (%)
Ebstein's Anomaly	1 (1.9)	TAPVD	5 (4.6)
Double Outlet Right Ventricle	1 (2)	Double Outlet Right Ventricle	1 (0.9)
		Aortopulmonary Window	1 (0.9)

N (percentage %), HLHS: hypoplastic left heart syndrome, TGA: transposition of the great arteries, TAPVD: total anomalous pulmonary venous drainage, RFO: restrictive foramen ovale, IVS: intact ventricular septum, VSD: ventricular septal defect.

In this study, an analysis of postnatal diagnoses revealed that the three most common conditions were TGA in 55 patients (51.1%), HLHS in 18 patients (16.6%), and pulmonary atresia in 12 patients (11.1%) (Table 3).

When the treatments administered to patients with and without a prenatal diagnosis were compared, it was observed that arterial switch operation (ASO) and Tetralogy of Fallot repair were more frequently performed in the group without a prenatal diagnosis. A statistically significant difference was found between the groups in terms of ASO ($p < 0.001$), whereas no statistically significant difference was observed for Tetralogy of Fallot repair ($p = 0.169$). On the other hand, Norwood stage 1 operation, modified Blalock-Taussig shunt (MBT) shunt procedure, and aortic arch repair were more frequently performed in the group with a prenatal diagnosis, and statistically significant differences were found between the groups for these procedures ($p = 0.002$, $p < 0.001$, and $p = 0.001$, respectively) (Table 4).

No statistically significant differences were found between the groups with and without a prenatal diagnosis in terms of vital signs ($p > 0.05$) (Table 5).

In our study, both the VIS and Aristotle score were found to be higher in the group without a prenatal diagnosis; however, no statistically significant association was observed between these parameters and prenatal diagnosis (Table 5).

In this study, complications related to the treatments administered were examined, and it was found that 4 patients had arrhythmia (25%), 4 had sepsis (25%), 2 had atelectasis (12.5%), 2 had multiple organ failure (12.5%), 2 had gastrointestinal perforation (12.5%), 1 had acute renal failure (6.25%), and 1 had sternal dehiscence (6.25%).

When the biochemical parameters of patients with and without a prenatal diagnosis were compared, the mean aspartate transferase (AST) and lactate dehydrogenase (LDH) levels were found to be statistically higher in patients with a postnatal diagnosis, whereas the mean phosphorus level was statistically higher in those with a prenatal diagnosis (Table 6).

In our study, among the group of patients diagnosed with conditions associated with high complexity and mortality, namely HLHS, PA, and aortic arch anomalies, mortality was found to be significantly lower in those with a prenatal diagnosis ($p = 0.018$) (Table 7).

Table 4: Comparison of treatments administered to patients with and without a prenatal diagnosis.

Treatment Administered	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	Total (n = 160)	p-Value
ASO	12 (23.08)	58 (53.70)	70 (43.75)	<0.001 ^a
Norwood Stage 1 Operation	12 (23.08)	7 (6.48)	19 (11.87)	0.002 ^a
MBT Shunt Procedure	11 (21.15)	4 (3.70)	15 (9.37)	<0.001 ^b
Tetralogy of Fallot Repair	2 (3.84)	11 (10.18)	13 (8.12)	0.169 ^b
Aortic Arch Repair	9 (17.30)	3 (2.77)	12 (7.50)	0.001 ^b
TAPVD Repair	1 (1.92)	7 (6.48)	8 (5)	0.215 ^b
Truncus Arteriosus Repair	1 (1.92)	3 (2.77)	4 (2.5)	0.746 ^b

Table 4: Cont.

Treatment Administered	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	Total (n = 160)	p-Value
Glenn Operation	2 (3.84)	2 (1.85)	4 (2.5)	0.449 ^b
Rastelli Operation	0 (0)	3 (2.77)	3 (1.87)	0.225 ^b
Comprehensive stage 2 Norwood	1 (1.92)	1 (0.92)	2 (1.25)	0.595 ^b
Pacemaker Implantation	0 (0)	1 (0.92)	1 (0.62)	0.486 ^b
Not surgery	1 (1.92)	9 (8.33)	10 (6.25)	0.152 ^b

N (percentage %), a: Chi-square test; b: Fisher's exact test, ASO: arterial switch operation; MBT: modified Blalock–Taussig shunt; TAPVD: total anomalous pulmonary venous drainage.

Table 5: Comparison of vital signs between patients with and without a prenatal diagnosis.

Vital Signs	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	Total (n = 160)	p-Value
Body temperature (°C)	36.13 ± 0.49	36.09 ± 0.49	36.11 ± 0.49	0.629 ^a
Heart rate (beats/min)	149.5 ± 19.7	148.3 ± 21.5	148.7 ± 20.8	0.742 ^a
Respiratory rate (breaths/min)	48.9 ± 8.7	49.2 ± 9.7	49.1 ± 9.4	0.867 ^a
Systolic blood pressure (mmHg)	66.9 ± 22.1	66.2 ± 18.6	66.5 ± 19.7	0.823 ^a
Diastolic blood pressure (mmHg)	42.2 ± 14.7	41.3 ± 11.9	41.6 ± 12.8	0.662 ^a
MAP (mmHg)	51.7 ± 17.5	49.1 ± 14.1	50.4 ± 15.8	0.311 ^a
Oxygen saturation (%)	80.9 ± 11.9	82.6 ± 8.6	81.8 ± 9.9	0.305 ^a
VIS**	0 (0–402), 25.71 ± 63.13	0 (0–440), 16.38 ± 60.21	0 (0–440)	0.368 ^b
Aristotle score*	12.73 ± 5.5	13.53 ± 4.6	13.13 ± 5.1	0.356 ^a

*Mean ± SD, **Median (Min–Max), Mean ± SD, a: Independent samples *t*-test; b: Mann–Whitney U test, MAP: mean arterial pressure, VIS: vasoactive-inotropic score.

Table 6: Comparison of biochemical parameters between patients with and without a prenatal diagnosis.

Biochemical Parameters	Prenatal Diagnosis (n = 52)	Postnatal Diagnosis (n = 108)	p-Value
Urea (mg/dL), median (min-max)	17 (5–73)	18.05 (3–93)	0.428 ^c
Creatinine (mg/dL), mean ± SD	0.61 ± 0.18	0.64 ± 0.31	0.602 ^b
Albumin (g/L), mean ± SD	30.40 ± 5.67	30.41 ± 5.47	0.995 ^b
AST (U/L), median (min-max)	51.15 (15–280)	98.1 (17–660)	0.004 ^c
ALT (U/L), median (min-max)	11.15 (5–98)	14.85 (4–426)	0.262 ^c
LDH (U/L), median (min-max)	409 (199–1320)	530 (261–2987)	0.024 ^c
Sodium (mmol/L), mean ± SD	141.6 ± 5.6	142.7 ± 5.9	0.284 ^b
Potassium (mmol/L), mean ± SD	4.1 ± 0.9	4.7 ± 1.01	0.625 ^b
Calcium (mmol/L), mean ± SD	9.22 ± 1.4	9.33 ± 1.51	0.656 ^b
Phosphorus (mmol/L), mean ± SD	6.0 ± 1.8	5.3 ± 1.3	0.016 ^b
Lactate (mmol/L)	3.95 (0–25)	4 (0.7–28.3)	0.320 ^c
Acidosis			
Present, n (%)	25 (48.1)	44 (40.7)	
Absent, n (%)	27 (51.9)	64 (59.3)	0.380 ^a

Mean ± SD, Median (Min–Max). Given the exploratory nature of these comparisons, *p*-values were not adjusted for multiple testing; results should be interpreted cautiously. a: Chi-square b: Independent samples *t*-test; c: Mann–Whitney U test, AST: aspartate transferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase.

Table 7: Comparison of clinical outcomes based on prenatal diagnosis status in patients with HLHS, PA, and aortic arch anomalies.

Properties	Survived (n: 32)	Deceased (n: 35)	Total (n: 67)	p-Value*
Prenatal diagnosis	22 (61.1)	14 (38.9)	36	
Postnatal diagnosis	10 (31.2)	21 (68.8)	31	0.018

*Chi-square test; HLHS: Hypoplastic Left Heart Syndrome; PA: Pulmonary Atresia.

4 Discussion

CHD represents the most common group of congenital anomalies in the neonatal period, encompassing a wide spectrum ranging from mild cardiac defects to critical CHD that require rapid diagnosis and intervention for the newborn's survival [10,11]. Prenatal diagnosis of CHD is considered beneficial as it enables the identification of critical cardiac defects before birth. This, in turn, allows for parental counseling and the planning of delivery at a specialized cardiac center where immediate postnatal treatment can be initiated [12]. In our study, it was observed that the diagnosis of critical CHD that was not diagnosed prenatally was delayed until the late neonatal period.

Some studies have reported that more adverse outcomes are observed in prenatally diagnosed CHDs [13,14]. This finding may be explained by the fact that more critical types of CHD are more easily detected during ultrasound screening. These findings suggest that survival may no longer be the most important outcome, or prenatal diagnosis may not be the most appropriate criterion for measuring the impact on CHD, particularly in settings with easy access to specialized healthcare. In our study, we consider that the higher mortality rate in the prenatally diagnosed group, in the evaluation where all cases were included, is due to the presence of more critical diseases in this group, the exclusion of patients who died without postnatal diagnosis, the ease and speed of access to health care, and the heterogeneity of the distribution of diagnoses and procedures among the groups. In fact, in our study, it was determined that surgical interventions such as the Norwood operation, aortic arch repair, and Blalock-Taussig shunt, which have high mortality rates, were performed more often in the prenatally diagnosed group.

TGA is one of the most common critical CHD in the neonatal period, and the rate of prenatal diagnosis is increasing. TGA is currently one of the most commonly misdiagnosed CHD *in utero*. Due to the lack of prenatal diagnosis, patients are often born outside tertiary cardiac centers and cannot be adequately monitored after birth to ensure timely surgical treatment; this may lead to potentially preventable mortality or multi-organ damage [15]. UK national cardiac surgery surveillance data show that prenatal detection for infants with TGA undergoing ASO has increased from 50% before 2016 to over 80% in recent years [16]. Particularly in recent years, survival rates after ASO applied in TGA patients have been reported to be above 97% [17]. In our study, TGA, which has a low postnatal mortality rate, constituted more than half of the patients diagnosed postnatally. In contrast, while the TGA rate was low in patients diagnosed prenatally, HLHS, which has high postnatal mortality, was the most common cardiac pathology. This situation may be related to the high overall mortality rate in patients diagnosed prenatally.

The impact of prenatal diagnosis on survival varies depending on the type of cardiac defect. It is suggested that prenatal diagnosis may allow for the prompt initiation of treatment in order to maintain ductal patency in the newborn, thereby preventing metabolic acidosis, hypoxemia, and organ damage, and ultimately reducing mortality and morbidity. Several case series have reported that this approach has lowered mortality rates in patients diagnosed with HLHS, TGA, and aortic coarctation [18,19]. In conditions such as TGA or HLHS, early intervention is essential to prevent cardiac or neurological damage resulting from hypoxia and adverse hemodynamics. Although these patients often present with more severe lesions compared to those diagnosed postnatally, prenatal diagnosis has been associated with a reduced need for mechanical ventilation, antibiotic therapy, and emergency surgical intervention [20]. In support of this, although overall mortality was found to be higher among patients with a prenatal diagnosis in our study, a significantly lower mortality rate was observed in the subgroup of patients diagnosed with HLHS, PA, and aortic arch anomalies, conditions associated with high complexity and mortality. This finding suggests that prenatal diagnosis in these three critical CHD groups may significantly reduce postnatal mortality.

Studies have reported that the need for cardiopulmonary resuscitation (CPR) at birth is associated with increased mortality [21,22]. In our study, although the difference was not statistically significant ($p = 0.153$), the need for CPR was higher in the group without a prenatal diagnosis (37%) compared to those with a prenatal diagnosis (25%). Additionally, the significantly higher AST and LDH levels and the significantly later timing of diagnosis in patients without a prenatal diagnosis suggest that these patients may have been diagnosed under poorer clinical conditions. This indicates that patients without a prenatal diagnosis may be more prone to conditions such as acidosis and multiple organ failure, which are known to increase mortality and morbidity.

VIS is a tool used to evaluate cardiovascular pharmacological support. It is calculated as the weighted sum of all administered vasoactive and inotropic agents [23]. Studies have identified the maximum VIS value reached within the first 24 h after surgery as an independent predictor of postoperative mortality and morbidity [23,24]. The Aristotle scoring system, on the other hand, was developed in 1999 under the leadership of Lacour-Gayet with the participation of 50 cardiac surgeons from 23 countries. Its first version, the Aristotle Basic Complexity Score (ABS), is based on three main factors: risk of death, potential for complications, and anticipated technical difficulty. Accordingly, cases are scored between 1.5 and 15 in the ABS system [25]. In our study, no statistically significant difference was found between patients with and without a prenatal diagnosis in terms of VIS and ABS.

5 Limitations

The primary limitations of this study include its retrospective design, which is inherently subject to bias. Prenatal follow-up was conducted at centers with varying standards of care, and limited accessibility to prenatal data precluded its inclusion in the analysis. The distribution of diagnoses was not homogeneous between groups, which may affect comparability. Patients who died before a diagnosis could be established or prior to referral to our unit were excluded. The exclusion of patients who terminated their pregnancies and those who died intrauterine may also affect mortality statistics. The higher proportion of males in the prenatally diagnosed group may reflect known sex differences in CHD presentation, but its effect on mortality is likely minimal, as sex was not an independent predictor in regression. Confounding by disease severity cannot be ruled out. As a single-center study, the generalizability of our findings is limited. Small subgroup sizes reduced statistical power, and the regression model has inherent constraints. Finally, long-term outcomes were not available.

6 Conclusions

In this retrospective cohort, overall mortality was significantly higher among patients with a prenatal diagnosis of critical CHD. This finding is largely explained by the overrepresentation of high-complexity lesions (e.g., HLHS, PA, and aortic arch anomalies) in the prenatally diagnosed group. However, within that specific high-risk subgroup, prenatal diagnosis was associated with a significantly lower mortality rate, suggesting a genuine survival benefit. Prenatal diagnosis may improve outcomes in selected high-risk CHD subgroups, but its overall impact on mortality is confounded by disease severity, case mix, and exclusion of deaths before diagnosis. Therefore, multicenter, prospective studies with longer follow-up and larger, more homogeneous patient populations are needed.

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Availability of Data and Materials: The data supporting the findings of this study are available from the first author, Aygül Kaya Akıllı, upon reasonable request.

Ethics Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Clinical Research Ethics Committee of the University of Health Sciences, Gazi Yaşargil Training and Research Hospital (Decision No.: 131, Date: 06 September 2024). Patient's guardian consent was waived due to the retrospective nature of the study and the use of de-identified data.

Conflicts of Interest: The authors declare no conflicts of interest.

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