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ORIGINAL ARTICLE

Prenatal diagnosis and management of hypoplastic left heart syndrome: Single center results

Yunus Emre PURUT
Gürcan TÜRKYILMAZ

Department of Gynecology and Obstetrics, Van Training and Research Hospital, Van, Turkey

ORCID ID
YEP : 0000-0001-5779-3847
GT : 0000-0002-5514-0233

ABSTRACT

Objective: Hypoplastic left heart syndrome (HLHS) is the most common reason for neonatal deaths among congenital heart defects. Numerous studies showed that prenatal diagnosis improves prognosis. We aimed to review the prenatal assessment of associated extracardiac anomalies, postnatal outcomes, and surgical management in cases of HLHS that were detected in our center.

Material and Methods: The records of patients diagnosed with HLHS evaluated between March 2017 and April 2020. A detailed anatomy scan was performed, and karyotype analysis was recommended to all patients. Due to poor perinatal prognosis, termination of pregnancy (TOP) was offered an option to families. Serial ultrasonographic examinations every 2–4 weeks. Postnatal echocardiography was performed, and the prenatal diagnosis was confirmed in all offspring. Surgical outcomes were recorded.

Results: Sixteen patients were recruited in our study. The mean gestational age at diagnosis was 20.2±5.1 weeks. About 68.7% of cases were defined as classical type HLHS, and the remaining 31.3% were determined as variant type HLHS. TOP was performed in 9 (56.7%) patients. The mean follow-up interval was 16.4±4.7 months. Urge septostomy was performed in 2 (28.5%) cases after birth due to foramen ovale restriction. Three (42.8%) cases died before the first operation. Norwood procedure was performed in 4 (57.1%) cases. Two cases died after this operation. Glenn shunt and Fontan procedure were performed in the remaining two offspring. The total survival rate was 28.5%.

Conclusion: HLHS has high perinatal morbidity and mortality. Prenatal diagnosis allows the family for the fate of pregnancy and planned delivery in a tertiary center.

Keywords: Echocardiography, heart, mortality, prenatal.

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Correspondence: Gürcan TÜRKYILMAZ, MD. Van Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Van, Turkey.
Tel: +90 554 310 28 03 **e-mail:** gurcanturkyilmaz@gmail.com

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) is a complex cardiac anomaly that causes systemic perfusion failure by the left ventricle. Anatomically, various pathologies may lead to HLHS. Due to atresia of the mitral valve and aortic valve, the left ventricular cavity may completely absent, or the hypoplastic development of the aortic and mitral valve may allow the evolution of a small left ventricular cavity. Ascending aorta and aortic arch hypoplasia or aortic coarctation are associated with HLHS.[1]

HLHS has a frequency of 2–3/10,000 live births and constitutes 3–4% of all cardiac anomalies.[2,3] It is 50% more frequently in male babies than girls.[4] Although it is a rare cardiac anomaly, HLHS solely is responsible for 40–50% of cardiac deaths.[5] Non-cardiac anomalies are associated with 5–30% of cases, and the most common anomalies are the central nervous system, gastrointestinal system, and renal system malformations. Chromosomal anomalies are detected in 5–10% of cases, and trisomy 13–18 and monosomy X (Turner syndrome) are most common aneuploidies.[6] Rarely, it may be associated with microdeletion syndromes such as Williams-Beuren syndrome (7q11.23 deletion) and DiGeorge syndrome (22q11.1 deletion).

However, HLHS constitutes a small group of all cardiac anomalies; it is one of the most common cardiac anomalies in the prenatal period. Unlike conotruncal anomalies, an abnormal four-chamber view of the fetal heart seems to be the main factor facilitating the diagnosis. The most common finding in prenatal ultrasonography is the absence of the left ventricle in four-chamber view or the presence of a hypoplastic, hypocontractile, and hyperechogenic left ventricle. Numerous studies indicated that prenatal diagnosis had improved neonatal outcomes.[7]

In this study, we aimed to evaluate the prenatal findings and postnatal outcomes of the cases diagnosed prenatally with HLHS in our clinic.

MATERIAL AND METHODS

Our study was carried out in the Perinatology Department of Van Training and Research Hospital between March 2017 and April 2020. Diagnosis of HLHS was achieved in those findings: (1) In the apical four-chamber view of the heart, the left ventricle is absent, or there was a small and hyperechogenic left ventricle with reduced contractility. (2) The apex of the heart was formed by the right ventricle. (3) No transition from the mitral valve to the left ventricle in color Doppler evaluation. (4) The foramen ovale flap was placed by opening from right to left instead of from left to right (Fig. 1). Furthermore, the absence of the aorta in the three-vessel trachea plan and the aortic arch filling with a reverse flow from the ductal arch in the color Doppler examination confirmed the diagnosis (Fig. 2). Cases with no visible left ventricle in the apical four-chamber examination were defined as classical type HLHS. In contrast, cases with a hyperechogenic and hypocontractile left ventricle were determined as variant type HLHS due to stenosis of the aortic and mitral valve. In all cases, prenatal diagnosis was confirmed with a consensus of perinatologist and pediatric cardiology specialist. After the diagnosis, a detailed fetal anatomic evaluation was performed in all cases to rule out extracardiac anomalies, and karyotype analysis was recommended. Due to poor neonatal prognosis, the option of termination of pregnancy (TOP) was offered to families in all cases. Serial follow-up was performed every 2–4 weeks in cases wishing to continue the pregnancy. All women were delivered in tertiary care centers. Echocardiography was performed in all cases after birth, and the diagnosis of HLHS was confirmed. Long-term surgical procedures and survival rates of the cases were recorded. Statistical analysis was performed using SPSS version 24 (Statistical Package for the Social Sciences, IL, USA). Results were expressed as mean and standard deviation.

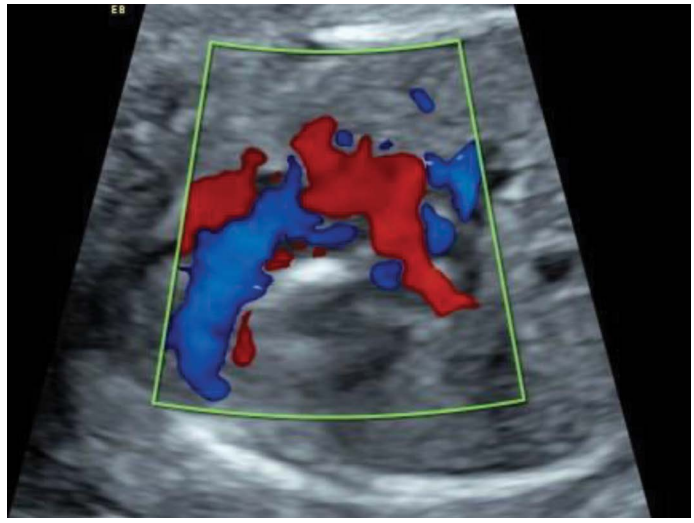

Figure 1: There is no filling of the left ventricle in color Doppler examination and left ventricle hypoplasia is observed in 26 weeks of gestation.

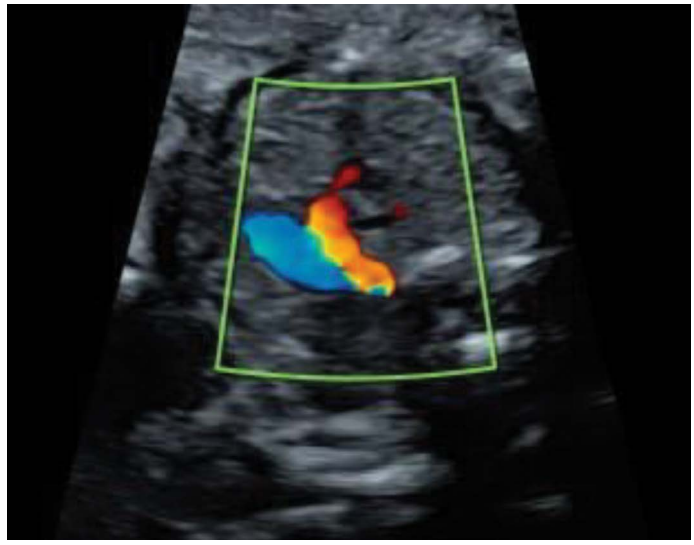

Figure 2: Reverse flow in the aortic arch in three-vessel trachea view in a 19-week fetus.

RESULTS

We recruited 16 cases during the study period. Mean maternal age was 25.6±5.2 years, and mean gestational age at diagnosis was 20.2±5.1 weeks. About 68.7% of fetuses were defined as classi-

Table 1: Prenatal features of 16 cases

Variable	n=16 (%)
Maternal age (years)	25.6±5.2
Gestational age at diagnosis (weeks)	20.2±5.1
HLHS type	
Classical	11 (68.7)
Variant type	5 (31.3)
Nuchal translucency (mm)	3.2±1.1
Karyotype analysis	8 (50)
Extracardiac anomaly	2 (12.5)
Foramen ovale restriction	2 (12.5)
TOP	9 (56.2)

TOP: Termination of pregnancy.

Table 2: Outcome of seven cases who survived in neonatal period

Variable	n=17 (%)
Gestational age at birth (weeks)	37.4±2.1
Birth weight (grams)	2530±355
Route of delivery	
Vaginal	2 (28.5)
Cesarean	5 (71.4)
Sex	
Male	4 (57.1)
Female	3 (42.9)
Foramen ovale restriction	2 (28.5)
Follow-up period (months)	16.4±4.7
NICU stay (day)	86±23
Neonatal death	3 (42.8)
Norwood procedure	4 (57.1)
Glenn shunt	2 (28.5)
Fontan procedure	2 (28.5)
Overall survival	2 (28.5)

NICU: Neonatal intensive care unit.

cal type HLHS and 31.3% as variant type HLHS. The mean nuchal translucency measurement of cases was 3.2±1.1 mm in the first trimester. Karyotype analysis was performed in 8 (50%) cases, and normal karyotype was found in all patients. An extracardiac anomaly was observed in 2 cases (12.5%), including 1 case with unilateral renal agenesis and 1 case with unilateral pes equinovarus. Foramen ovale restriction was revealed in the prenatal period in (31.3%) of the fetuses. TOP was performed in 9 (56.7%) cases. The mean gestational age at birth was 37.4±2.1. The mean birth weight was 2530±355 g of 7 (43.7%) cases born alive. Two (28.5%) cases were delivered vaginally, and 5 (71.5%) cases were delivered by cesarean section. Four (57.1%) cases were female, and 3 (42.9%) cases were male. The mean follow-up period was 16.4±4.7 months, and the mean length of stay in the neonatal intensive care unit was 86±23 days. Foramen ovale restriction was detected in 2 (28.5%) cases after birth, and emergency septostomy was performed in those babies. Three (42.8%) cases died before the first operation. Two of these three cases required emergency septostomy after delivery due to prenatal foramen ovale restriction. Norwood procedure was performed in four babies. Two cases died after this operation. One of those two patients died on the 1st post-operative day, and the other died 5 days after the Norwood procedure. Glenn shunt and Fontan procedure were performed in the remaining two cases. Overall survival calculated as 28.5%. Prenatal features and outcome of cases were demonstrated in Table 1 and Table 2.

DISCUSSION

Recently, progressions on ultrasonography technology and amelioration in physicians skills and experience have improved prenatal diagnosis of fetal anomalies. While cardiac anomalies are detected in 5–8/1000 of all fetuses, some cardiac anomalies remain undiagnosed in the prenatal period. Morris et al.[8] studied 3.4 million birth records in Texas between 1997 and 2007 years and had found the prenatal diagnosis rate 39% for in 558 isolated HLHS babies. Between 2002 and 2012 years, van Velzen et al.[9] had investigated the results of the standard anomaly scanning program in the Netherlands and found the rate 59.6% in prenatal diagnosis for cardiac anomalies. HLHS is the most diagnosed anomaly, and 94% of all fetuses with HLHS were diagnosed correctly.

Getting a prenatal diagnosis of HLHS helps provide the family with detailed counseling regarding postnatal results and treatment methods. Because HLHS treatment can comprise multiple operations and mortality rates are high, some families choose TOP. In their study, Liu et al.,[10] including 381 patients diagnosed with a single ventricle, showed that percentage of 16 families selected TOP. The most crucial factor that affects the TOP decision is being diagnosed before 20 pregnancy weeks. Beroukhim et al.[11] showed 32% TOP rate for the study, including 312 fetuses with a single ventricle. In our study, 9 of 16 cases selected TOP (56.2%). High TOP rates in our study can be explained by the fact that HLHS operation carries out only in limited centers in our country, and mortality rates are still high compared to developed countries.

Delivery of HLHS diagnosed fetuses must be done in tertiary centers experienced in this field. Morris et al.[8] have found 21% perinatal mortality. The baby delivery center was <10 min distance to the cardiac surgery center, 25.1% perinatal mortality with distance 10–90 min, and 39.6% with distance more than 90 min, respectively. Thakur et al.[12] published a meta-analysis that included 228 prenatal, 381 postnatal diagnosed patients and showed that neonatal death rates among babies were 11% and 17% for prenatally and postnatally diagnosed babies. Otherwise, pre-operative acidosis, inotropic agent need, and mortality rate after Stage-1 surgery were found significantly to be lower in the prenatally diagnosed group. Our study delivery

of all cases prenatally diagnosed has been ensured to carry out in tertiary centers under elective conditions.

About 30% of babies with HLHS are accompanied by genetic or/and extracardiac anomalies. Genetic disorders such as Trisomy 18, Turner syndrome, and DiGeorge (22q11.21-2 deletion) and Jacobson syndrome (11 q deletion) are related to HLHS. Hinton et al.[13,14] showed an association between chromosomal mutations 10q22 and 6q23 with HLHS, and they have found that HLHS risk for subsequent pregnancy was 8.1%. We also suggested karyotype analyze in all cases, and results were found normal for all eight patients.

Newborns diagnosed with HLHS are asymptomatic if there is no restriction of foramen ovale during the prenatal period, but 24–48 h after delivery, ductus arteriosus shuts down, and systemic hypoperfusion, hypotension, and metabolic acidosis occur. If urgent medical care cannot be given, death will be inevitable. HLHS has the most complicated surgery treatment among all cardiac anomalies, and incompatible with life if it remains untreated. However, in recent years, survival rates have increased in parallel with amelioration in surgical techniques and improved intensive care units. HLHS treatment includes the stepwise surgical procedure. The first operation is the Norwood procedure that is done 2 or 3 weeks after birth. The two-way Glenn shunt is made after 2–6 months after delivery. The last stage is the Fontan operation and is held when the patient is between 2 and 5 years old. After HLHS surgical treatment, survival rates between 3 and 6 years old are 60–70%.[15,16] High mortality surgical intervention is Norwood operation, and if this operation is successful, the long-term survival rate can reach 90%.[17] A study investigating 26-year birth statistics in Atlanta between 1979 and 1984 has found 0% neonatal survival rate of HLHS patients. However, between 1999 and 2005 years, this rate was 45%.[18] In our study, the long-term survival rate was 28.5%. This ratio is below the rates of developed countries.

Among the patients operated because of single ventricle physiology, long-term studies revealed a high risk of neurodevelopmental retardation. In the single ventricle reconstruction trial study, where 321 children underwent the stepwise surgical treatment in the case of HLHS, the primary surveillance time was 14.3±1.1 months. Mean Bayley score and psychomotor development score in operated patients were found significantly low than the same in the healthy control group.[19] Mahle et al.[20] revealed considerably lower neurodevelopmental test scores in over 8-year-old children who underwent HLHS operation than in the control group.

In parallel with the improvements in fetal surgical techniques, prenatal treatment methods have been tried invariant type HLHS cases. In a few specialized centers, eligible cases with critical aortic stenosis and sufficient left ventricle volume undergo fetal treatment procedures. In their 100 case series between 2000 and 2013 years in fetuses who underwent fetal surgery, Freud et al.[21] showed fetal aortic valvuloplasty bettering the newborn long-term consequences.

CONCLUSION

HSKS is rare, but the most common cause of death due to cardiac anomalies in the neonatal period. Diagnosis in the prenatal period enables delivery to be performed at a tertiary center and improves long-term results.

Statement

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – GT, YEP; Design – GT, YEP; Supervision – GT, YEP; Resource – GT, YEP; Materials – GT, YEP; Data Collection and/or Processing – GT, YEP; Analysis and/or Interpretation – GT, YEP; Literature Search – GT, YEP; Writing – GT, YEP; Critical Reviews – GT, YEP.

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