Pregnancy Outcome of Fetuses With a Diagnosis of Hypoplastic Left Ventricle on Prenatal Sonography

Rebecca H. Allen, MD, MPH, Carol B. Benson, MD, Louise Wilkins Haug, MD, PhD

Objective. The goal of our study was to assess the pregnancy outcome of fetuses with a diagnosis of hypoplastic left heart syndrome (HLHS) on prenatal sonography to determine the frequency of intrauterine fetal demise (IUFD) and any factors associated with IUFD. Methods. We reviewed all cases with the diagnosis of HLHS on prenatal sonography at our institution from 1992 through 2003. Data collected included gestational age at diagnosis, sonographic findings, karyotype testing, and pregnancy outcome. Results. Our study included 176 fetuses with HLHS. One hundred thirty-four fetuses were liveborn; 32 pregnancies were terminated; 3 IUFDs occurred; and outcome was unknown in 7. Of the 134 liveborn fetuses, 2 had abnormal karyotypes and 30 had other anomalies. Two of the 3 fetuses with IUFD had abnormal karyotypes, 1 with trisomy 13 and 1 with trisomy 18, and both had other anomalies on sonography. The third fetus with IUFD had no other anomalies but was 1 of triplets, and the karyotype was unknown. Conclusions. Fetuses with HLHS diagnosed prenatally who have normal chromosomes are unlikely to die in utero. Key words: hypoplastic left ventricle; intrauterine fetal demise.

HLHS, hypoplastic left heart syndrome; IUFD, intrauterine fetal demise

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Address correspondence to Carol B. Benson, MD, Department of Radiology, Brigham and Women’s Hospital, 75 Francis St, Boston, MA 02115 USA.

E-mail: cbenson@partners.org

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HLHS diagnosed prenatally. The goal of our study was to assess the pregnancy outcome of fetuses with a diagnosis of hypoplastic left ventricle on prenatal sonography to determine the frequency of IUFD at our institution and any characteristics associated with IUFD.

Materials and Methods

We reviewed all cases with a diagnosis of hypoplastic left ventricle on prenatal sonography at our institution, a tertiary care referral center, from January 1992 through December 2003. All fetuses underwent a detailed ultrasound scan. Hypoplastic left heart syndrome was diagnosed sonographically when the left ventricle was substantially smaller than the right (Figure 1), when the left ventricle was poorly contractile and had echogenic walls (Figure 2), or when the left ventricle was so small that no chamber could be identified (Figure 3). Data collected from the electronic medical record included gestational age at diagnosis, sonographic findings, results of karyotype testing, if any, and pregnancy outcome. Excluded from our study were fetuses who underwent in utero cardiac interventions. All liveborn neonates were delivered at our institution, a tertiary care neonatal intensive care unit, with the exception of 1 neonate who was delivered at term at an outside hospital. The study was approved by our Institutional Review Board.

Results

Our retrospective review included 176 fetuses with HLHS over 12 years. Eleven fetuses who underwent in utero cardiac interventions were excluded. Gestational age at diagnosis ranged from 15.3 to 41.0 weeks (mean, 28.2 weeks). One hundred thirty-four fetuses were liveborn; 32 pregnancies were terminated; 3 IUFDs occurred; and outcome was unknown in 7. The 7 fetuses with unknown outcome were evaluated at an average gestational age of 23 weeks (range, 17–31 weeks). Ten fetuses in our study were fetuses in multiple gestations, including 8 dichorionic diamniotic twins and 1 monochorionic diamniotic twin pair who were all liveborn and 1 trichorionic triamniotic triplet gestation in which the second triplet had IUFD. Thirty-eight (22%) of 176 patients chose prenatal karyotyping. The overall frequency of abnormal karyotype was 16 (42%) of 38 cases. Table 1 lists the abnormal karyotypes and pregnancy outcome.

Among the entire study population, 54 (31%) of 176 fetuses had extracardiac structural anomalies. Table 2 lists the extracardiac anomalies associated with HLHS and pregnancy outcome. One hundred thirty-four fetuses were liveborn. Gestational age at birth of these liveborn fetuses ranged from 24.4 to 42.3 weeks (mean, 37.7 weeks).

Figure 1. Hypoplastic left heart syndrome. Sonogram of the fetal heart at the level of the 4-chamber view of the heart shows a very small left ventricle (LV, arrows) and an enlarged right ventricle (RV, arrows). LA indicates left atrium; and RA, right atrium.

Figure 2. Hypoplastic left heart syndrome. Sonogram of the 4-chamber (4C) view of the fetal heart shows a small left ventricle (LV, arrow) and a normal-size right ventricle (RV, arrow). As pregnancy progressed, the left ventricle failed to grow and became smaller and smaller relative to the right ventricle.
Two (1.5%) of the liveborn fetuses had abnormal karyotypes, and 30 (22%) had other anomalies. Other anomalies most commonly involved the central nervous system and thorax.

Overall, only 3 fetuses of the 137 fetuses not terminated died in utero (2.2%). Two of the 3 fetuses with IUFD had abnormal karyotypes, 1 with trisomy 13 and 1 with trisomy 18, and both had other anomalies on sonography. The third fetus with IUFD had no other anomalies but was 1 of triplets. Karyotype was not done on this fetus. All 3 IUFDs occurred in the third trimester at 28.9, 37.5, and 38.3 weeks' gestation, respectively.

**Discussion**

Hypoplastic left heart syndrome carries a poor prognosis with a reported 40% to 55% survival rate after prenatal diagnosis. Prenatal diagnosis has been shown to improve outcome when compared with neonates born with HLHS that was not diagnosed before birth. Antepartum identification affords parents the time to consider the options of termination of pregnancy, non-intervention after delivery of the affected neonate, or palliative surgery. If parents choose to continue the pregnancy, prenatal diagnosis allows for planning of perinatal management. The prenatal sonographic imaging of HLHS also allows for further prenatal testing, including evaluation for abnormal karyotype and extracardiac structural anomalies. This added information assists in counseling parents.

Karyotype evaluation is recommended in all fetuses with the diagnosis of HLHS. Studies have shown that findings of chromosomal abnormalities and extracardiac structural anomalies in fetuses with HLHS are associated with a worse prognosis. Only 22% of our patients chose prenatal karyotyping, with a 42% abnormal karyotype rate. This is much higher than that found in previous studies (4%–25%), but the number of patients who elected karyotype testing in our study was small. All the abnormal karyotypes in our study were associated with extracardiac structural anomalies. This is similar to other studies that showed that the rate of abnormal chromosomes in fetuses with isolated heart lesions on sonography was much lower than the rate when other anomalies were present. Thirty-one percent of fetuses in our study had associated extracardiac anomalies. This is similar to prior studies that reported that 23% of HLHS cases had associated genetic disorders, major extracardiac anomalies, or both.

Our study was limited by several factors. First, we did not include fetal echocardiographic data. Therefore, our pool of HLHS cases included not only classic HLHS but also variants of HLHS such as critical aortic stenosis with hypoplastic left ventricle. However, all prenatal ultrasound examinations were performed in a tertiary care center with experience in congenital heart anomalies. Second, in 7 of our cases, the outcome of the pregnancy was unknown. If these 7 cases underwent IUFD, then our IUFD rate would be an underestimate. Third, we conducted an institutional review rather than a population-based study. Therefore, data regarding the rate of IUFD may be underestimated because patients who may have had the diagnosis else-

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**Table 1. Outcome of Fetuses With HLHS and Abnormal Karyotype**

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>n</th>
<th>Liveborn</th>
<th>IUFD</th>
<th>TAB</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>45,X Turner Syndrome</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>46,XX deletion 22q11.2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

TAB indicates therapeutic abortion.
## Table 2. Associated Anomalies in Fetuses With HLHS and Outcome

<table>
<thead>
<tr>
<th>Extracardiac Structural Anomaly</th>
<th>Karyotype</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral right cleft lip</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Omphalocele</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Right clubfoot</td>
<td>46,XX deletion 22q11.2</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Hemivertebrae spine</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Bilateral cleft lip and palate, absent stomach</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Severe hydrocephalus, absent left kidney</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Duodenal obstruction, cystic hygroma</td>
<td>Trisomy 21</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>2-vessel cord</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Holoprosencephaly, left renal hydronephrosis, hydroureter, and ureterocele in bladder</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Cystic hygroma</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Meningomyelocele lumbar spine, hydrocephalus, Chiari II malformation</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Hemivertebrae spine, no stomach</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Esophageal atresia</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Unilateral left cleft lip</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Left clubfoot with polydactyly</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Echogenic bowel</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Absent left kidney</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Merocephaly</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Cystic hygroma, anencephaly versus acrania, clubfoot</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Unilateral facial cleft, small kidneys</td>
<td>Unknown</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Normal</td>
<td>Liveborn</td>
</tr>
<tr>
<td>Polydactyly, enlarged kidneys, small mandible</td>
<td>Trisomy 13</td>
<td>IUFD</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Trisomy 18</td>
<td>IUFD</td>
</tr>
<tr>
<td>Abdominal situs inversus</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Esophageal atresia</td>
<td>Normal</td>
<td>Unknown</td>
</tr>
<tr>
<td>Cystic hygroma with hydrops, echogenic bowel</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Left facial cleft, heterotaxy syndrome, hemmark syndrome on fetopsy</td>
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<td>TAB</td>
</tr>
<tr>
<td>Hydrocephalus, Dandy-Walker variant, hemivertebrae</td>
<td>Normal</td>
<td>TAB</td>
</tr>
<tr>
<td>Cystic hygroma with hydrops</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Bilateral choroid plexus cysts</td>
<td>Unknown</td>
<td>TAB</td>
</tr>
<tr>
<td>Cystic hygroma</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Dandy-Walker with hydrocephalus</td>
<td>Unknown</td>
<td>TAB</td>
</tr>
<tr>
<td>Dandy-Walker malformation</td>
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<td>TAB</td>
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<tr>
<td>Kyphoscoliosis, sacral agenesis, omphalocele</td>
<td>Normal</td>
<td>TAB</td>
</tr>
<tr>
<td>Gastrochisis, congenital diaphragmatic hernia, hypoplastic mandible, retrocerebellar cyst</td>
<td>Normal</td>
<td>TAB</td>
</tr>
<tr>
<td>Bilateral clubfeet, bilateral choroid plexus cysts</td>
<td>Trisomy 18</td>
<td>TAB</td>
</tr>
<tr>
<td>Right clubfoot</td>
<td>Unknown</td>
<td>TAB</td>
</tr>
<tr>
<td>Cystic hygroma with hydrops</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>Normal</td>
<td>TAB</td>
</tr>
<tr>
<td>Absent left hand</td>
<td>Normal</td>
<td>TAB</td>
</tr>
<tr>
<td>No forearms, normal chromosomes, Brachman de Lange syndrome on fetopsy</td>
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<tr>
<td>No stomach, hepatomegaly</td>
<td>Trisomy 18</td>
<td>TAB</td>
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<tr>
<td>Cystic hygroma</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Cystic hygroma</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Alobar holoprosencephaly</td>
<td>Trisomy 13</td>
<td>TAB</td>
</tr>
<tr>
<td>Abnormal hands, hypoplastic orbits, hydrops, cystic hygroma</td>
<td>Trisomy 18</td>
<td>TAB</td>
</tr>
<tr>
<td>Cystic hygroma, bilateral clubfeet</td>
<td>45,X</td>
<td>TAB</td>
</tr>
<tr>
<td>Alobar holoprosencephaly, hypotelorism</td>
<td>Normal</td>
<td>TAB</td>
</tr>
</tbody>
</table>

TAB indicates therapeutic abortion.
where and may have underwent IUFD were not counted. Conversely, as a tertiary care referral center, our rate of IUFD may be overestimated because we care for higher-risk patients with possibly more associated anomalies.

In summary, our findings emphasize that fetuses with isolated HLHS and normal chromosomes are unlikely to die in utero. In our study, the IUFD rate of all fetuses not terminated was 2.2%, but 2 of the 3 IUFDs occurred in fetuses with abnormal chromosomes.

References