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RESEARCH ARTICLE

PERINATAL RESULTS OF ANTENATALLY DETECTED HYPOPLASTIC LEFT HEART SYNDROME IN A SINGLE TERTIARY CENTER: EXPERIENCE OF 5 YEARS TIME

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ABSTRACT

Aim: Our aim is to investigate Hypoplastic Left Heart Syndrome diagnosed pregnancies that were followed up in Tepecik Education and Research Hospital- Perinatology Unit, between 2015-2020, retrospectively.

Methods: The archieves were scanned retrospectively. Maternal features such as age, gravidy, parity, teratogen exposure, concominant disease existence, karyotyping rejection and decision for the pregnancies future and delivery type was noted. Also fetal features like gestational age at diagnosis, fetal growth, perinatal complications (eg: intrauterin growth retardation, additional anomaly, preterm delivery) and postnatal condition was noted.

Results: 9 of the 41 patients met the criteria. One of them had termination of the pregnancy. %37.5 of the rest had preterm delivery. 3 of the 8 patients (%37,5) had intrauterin growth retardation with estimated fetal weight below 10th percentile. There were no gender difference among infants. 75 percent of delivered infants, were operated postnatally. 2 of the infants were died before operation due to prematurity complications.

Conclusions: Hypoplastic Left Heart Syndrome is a very rare condition highly detectable in the antenatal period with high morbidity and mortality rates. These fetuses must be followed up in tertiary centers both because of antenatal problems' management and postnatal management.

Keywords: Hypoplastic Left Heart Syndrome, Fetal echocardiography

INTRODUCTION

Congenital heart defects (CHD) are one of the most common congenital anomalies and are responsible of meaningful part of neonatal deaths (1). Hypoplastic left heart syndrome (HLHS) is in the most severe part of the congenital heart defects spectrum. Without treatment it is responsible of nearly one third of all infant deaths due to CHD. It is comfortably seen at 2-3 percent among all congenital cardiac defects.

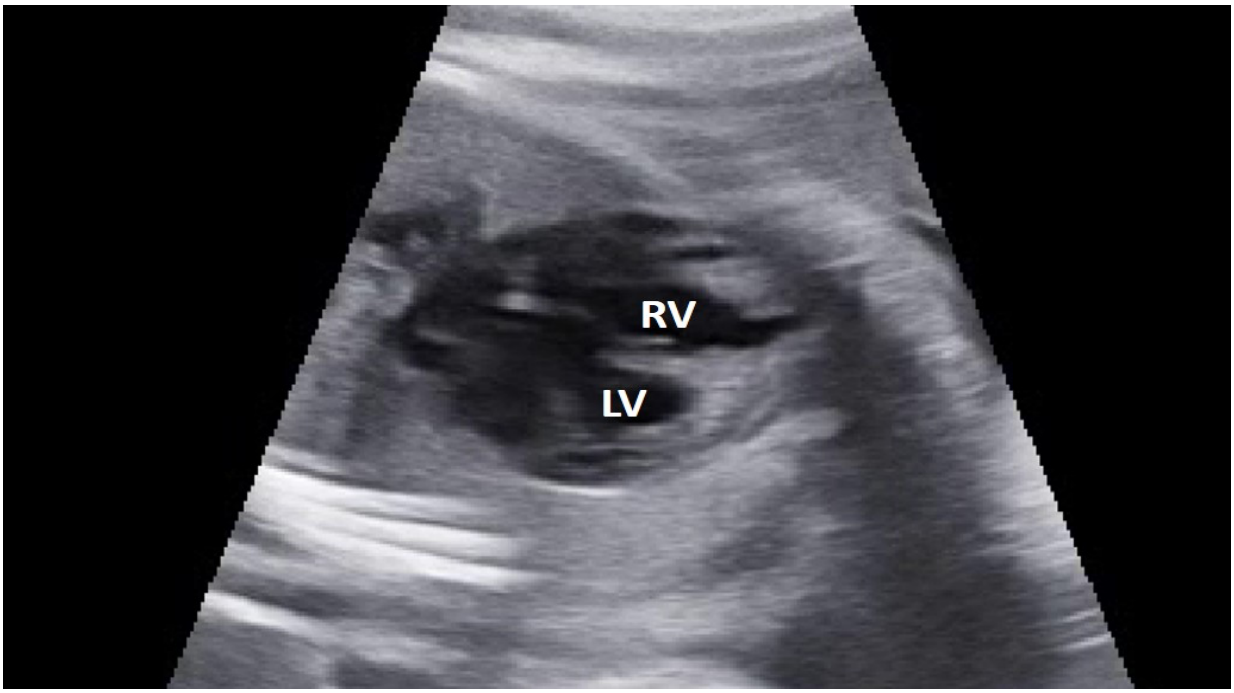

Figure 1. Abnormal four chamber view of Hypoplastic left heart syndrome. See the difference between right and left ventricules of the fetal heart.
Rv: right ventricle Lv: left ventricle

Incidence data vary among perinatal and pediatric studies (2, 3).

The etiology of HLHS is still unknown. Maternal race, maternal age, parity are ineffective on HLHS development (4). Although its association with chromosomal abnormalities has been shown such as trisomy 18 and 13, no specific gene is determined for the disease accept terminal 11q deletion, called Jacobsen syndrome (5, 6, 7). Blood flow changes during fetal heart's development may be responsible for the disease (8).

The main mechanism of HLHS is the single ventricular circulation dominated by the right ventricle. The left side of the heart (mitral valve, left ventricle, aortic valve, aort) is affected solely or together. Systemic circulation is supplied by right ventricle via ductus arteriosus. Thus HLHS is a ductus arteriosus dependent ciyanotic heart disease and must be intervened before ductal closure postnatally (8,9).

With the advances in technology and fetal cardiac examination guidelines, luckily it is diagnosable by 97 percent antenatally. Most of the cases can be detected easily by the 18-24 weeks of gestation with the appearance of abnormal cardiac four chamber view. In the first trimester scan, increased nuchal translucency is an important warning and nowadays latest studies are focusing on first trimester echocardiography (10,11).

HLHS can be seen with extracardiac anomalies therefore routine anatomical scan must be added after diagnosis (12,13).

HLHS is a highly mortal and morbid disease. It has utmost importance to give detailed information to parents about prenatal-postnatal prognosis and postnatal treatment options. During antenatal period some additional problems are determined, caused by HLHS in the literature. Although advances in surgical field its mortality is still high and long term adverse affects are noted including neurological ones and growth retardation in survivors (14, 15).

MATERIAL AND METHODS

Antenatally detected fetuses with hypoplastic left heart syndrome in Tepecik Education and Research Hospital Perinatology unit between 2015-2020 were analyzed retrospectively. The study is approved by Tepecik Education and Research Hospital ethics commitee. The patients who were diagnosed, followed-up, gave birth and operated in our hospital were included to this study. The patients who delivered and operated in another center postnatally were excluded.

Table 1. The maternal features of HLHS diagnosed fetuses

Cases	Age	Gravidy-Parity	Maternal disease	Drug use	Smoking	Consanguineous marriage	Karyotyping (antenatal)	Decision	Previous birth
1	25	g1p0	none	none	none	none	rejected	continuation	Vaginal delivery
2	38	g4p3	none	none	none	none	rejected	continuation	C/S
3	19	g1p0	none	none	none	none	rejected	continuation	Vaginal delivery
4	34	g1p0	none	none	none	none	rejected	continuation	Vaginal delivery
5	25	g2p1	none	none	none	none	rejected	continuation	Vaginal delivery
6	17	g1p0	none	none	none	none	rejected	continuation	C/S
7	21	g1p0	none	none	none	none	normal	termination	Vaginal delivery
8	18	g1p0	none	none	none	none	rejected	continuation	Vaginal delivery
9	23	g2p1	none	none	none	none	rejected	continuation	Vaginal delivery

The average maternal age, gestational age at diagnosis, time of delivery, birth weight, type of delivery, karyotyping information were noted. Postnatal operations were analysed and average survival was noted.

RESULTS

41 patients were detected, diagnosed with hypoplastic left heart syndrome in Tepecik Education and Research Hospital Perinatology unite antenatally between 2015-2020. Only 9 patients met the criteria. The average gestational time of diagnosis was 21 weeks of gestation. Two patients were detected at 29 and 30 weeks of gestation, respectively. These were patients who were not regularly followed up.

One of the pregnancies was dichorionic diamniotic twin pregnancy with only one fetus diagnosed with hypoplastic left heart sydrome.

The average maternal age was 24,4 (min:17, max:38). There were no use of teratogenics, alcohol abuse or cigarette smoking among mothers. There was no consanguineous marriages. None of the mothers had concominant disease.

All the patients were informed about karyotyping. Only one patient (%11) accepted antenatal invasive karyotyping which was documented as normal karyotype. 3 of the patients (%33) took karyotyping tests postnatally. Two of them were normal and one of them was diagnosed with *arr(1-22)x2* anomaly.

Detailed anatomic ultrasonographic examination was applied all the fetuses, accompanied by guidelines. Only one fetus had extracardiac anomaly and diagnosed with anal atresia.

All of the patients were discussed at Tepecik Perinatology counsil. All the patients were informed about postnatal prognosis and treatment options. One patient (%11) whom had antenatal invasive karyotyping also insisted on termination of pregnancy. After informed consent she had abortion of 525 gr male fetus. The other 8 patients chose the continuation of pregnancy.

3 of the 8 patients (%37,5) gave birth before 35 weeks of gestation with the indication of spontaneous early onset of labor. All of these patients were administrated two courses of corticosteroids and tocolysis theraphy. 2 of these 3 patients gave birth by vaginal delivery and one of them by cesarean section because of twin pregnancy and malpresentation of the fetuses. The average birth weight of these premature infants was 1863 gr.

5 of 8 patients (%62,5) average delivery time was 38 gestational weeks. 4 of the 5 term deliveries were by planned cesarean section and the last one was by vaginal delivery. The ceserean section were indicated only in two patients because of previous ceserean section. The other 2 of the cesarean sections were implemented because of timing concerns for

pediatrician and cardiovascular surgeon team accessibility.

3 of the 8 patients (%37,5) had intrauterin growth retardation with estimated fetal weight below 10th percentile.

prematurely and four patient (%44) was diagnosed with estimated birth weight below 10th percentile. Even %50 percent of these intrauterin growth retarded fetuses were below 3rd percentile.

All pregnancies, except for patients whose labor

Table 2. Main ultrasonographic findings of the fetuses

Cases	Type	Mitral stenosis	Aort stenosis	Left ventricle hypoplasia	Extracardiac anomaly	HLHS detection time	EFW percentile	Fetal gender
1	Twin(dichorionic-diamniotic)	yes	yes	yes	none	21w	< 2.5p	female
2	singleton	yes	yes	yes	none	19w	42 p	female
3	singleton	yes	yes	yes	none	21w	< 2.5p	female
4	singleton	yes	yes	yes	none	22w	94,7p	female
5	singleton	yes	yes	yes	Anal atresia	29w	18p	male
6	singleton	yes	yes	yes	none	24w	12p	male
7	singleton	yes	yes	yes	none	21w	43p	male
8	singleton	yes	yes	yes	none	30w	6.1p	female
9	singleton	yes	yes	yes	none	23w	9.5p	male

EFW: Estimated fetal weight

There were no gender difference among infants (5 female, 4 male,respectively.)

6 infants,75 percent of delivered 8 infants, were operated postnatally. They could only have the chance of getting Norwood stage 1 operation. All of the infants were died on the operation day. Two of the premature infants, 25 percent of all delivered infants, and %66 of delivered premature infants, died before the operation due to other prematurity complications.

DISCUSSION

In this study, our aim is to focus on prenatal problems and epidemiological features of HLHS fetuses and their mothers. In accordance with the literature, we found no link between maternal age, parity, teratogen exposure, alcohol use, cigarette smoking, consangineus marriage, maternal concominant disease and HLHS. Studies showed a slightly female dominance, our data showed %55,5 female dominance (4).

With the mechanism being discussed, decrease in systemic oxygenation, may lead to intrauterine growth restriction, lower brain volumes and preterm deliveries. This low oxygen supply is thought to lead to placental changes that cause the problems mentioned above (16,17,18,19). This problems were also detected in our study. 3 of our patients delivered started spontaneously, were followed up to term. In the literature fetal intrauterin demise is very rare due to ductus arteriosus and early delivery is not recommended (20,21,22). Because low birth weight and preterm delivery are poor prognostic factors for succesful operation (23).

There are two options in follow-up of HLHS after diagnosis. These are termination of pregnancy or continuation of it. With the advances in surgical field and neonatal intensive care, choosing second option is increasing world wide which we also experienced in our study (24). Only one of our patient opted for termination of pregnancy. Although recent positive and promising advances in these areas, parents must be informed about low physchomotor index scores than normal population, feeding tube problems, reduced growth and exercise capacity, sensorineural deafness as a long term problems (14,15,25).

After birth the maintainance of ductus arteriosus is the first step (8). After the neonate is ready for operation, there is a three step operation determined in the literature. The first step is described as Norwood procedure, which enables right ventricle to provide systemic circulation and it is performed in the first weeks of life (26). When the infant is 5-6 months old, the second procedure (cavapulmonary shunt, Glenn procedure) is performed. At the age of 4-5 years the

Table 3. Postnatal features of HLHS neonates

Cases	Delivery time	Delivery type	Indication For C/S	Birth weight	0 minute APGAR	Postnatal karyotype	Operation	Exitus after operation
1	34w5d	C/S	Twin/malpresentaton	1760gr	7	arr(1-22)x2	Norwood stage 1	on the same day
2	38w6d	C/S	Previous C/S	3460gr	7	none	Norwood stage 1	on the same day
3	39w0d	C/S	Timing issues	2460gr	8	none	Norwood stage 1	on the same day
4	38w6d	C/S	Timing issues	4050gr	7	normal	Norwood stage 1	on the same day
5	38w3d	C/S	Previous C/S	2870gr	2	normal	Norwood stage 1	on the same day
6	34w5d	vaginal		2130gr	4	none	not operated	exitus before operation
7	21w abortion	abortion		525gr	0			
8	33w1d	vaginal		1700gr	1	none	not operated	exitus before operation
9	38w6d	vaginal		3060gr	5	none	Norwood stage 1	on the same day

last procedure (total cavopulmonary connection, Fontan circulation) is performed (27,28,29). Risk Adjustment for Congenital Heart Surgery (RACHS) gives highest risk score for Norwood procedure and some poor prognostic factors were noted for surgery like preterm birth, low birth weight, concomitant extra-cardiac anomalies (23,30). Our cases that have the chance for Norwood procedure were all died, 5 of the six on the operation day and 1 of the 6 before second stage. Two of the preterm infants died on the operation day and the last preterm infant could not be operated. One of the term infants were growth retarded and another one had rectal atresia. These poor prognostic factors can explain the high mortality levels in our study. Also because of karyotyping rejection, we don't know if any chromosomal anomaly was accompanied.

HLHS has a high diagnosis rates antenatally and it is generally significant with abnormal four chamber view of the heart. In this view left side of the heart is significantly smaller than right side and even sometimes only right ventricle can be seen as a univentriculer form. Aortic stenosis, mitral valve stenosis also may accompany. Because of the left ventricle is being out of order, systemic circulation is provided by right ventricle via ductus arteriosus (31,32). If mitral stenosis is severe and atrial septum is intact, the pulmonary venous return cannot be achieved and serious lung destruction occurs which is highly poor prognostic (33). It is important to use color Doppler for the degree of stenosis. In the literature it is stated that HLHS which are antenatally detected have worse prognosis than postnatally detected ones. It is considered that the more severe the disease, earlier diagnosis is done (34). Thus in the routine first trimester scan nuchal translucency and early cardiac examination must be done (11,35). In our study all the patients had mitral stenosis, aortic stenosis and hypoplasia of the left ventricle at the same time.

On the first days of life as a result of patent ductus arteriosus and patent foreman ovale, HLHS can be well tolerated (8). When we investigate infants 0 minute APGAR scores all term deliveries APGAR scores were greater or equal to 7, except the one whom has anal atresia. Preterm neonatal APGAR scores were low. These infants need medical treatment for ductal maintenance after birth until operation. This is the main reason why this fetuses must be delivered in a tertiary center.

Limitations of Study

It would be better to have large numbers for having an opinion about HLHS. Continuation of pregnancy option has being chosen increasingly, against termination of pregnancy in recent years. Also it is a very rare disease and only seen at about 6 out of

10.000 live births. Thus it will allow us to work with large HLHS groups.

CONCLUSION

Hypoplastic Left Heart Syndrome is a very rare condition highly detectable in the antenatal period with high morbidity and mortality rates. These fetuses must be followed up in tertiary centers both because of antenatal problems' management and postnatal management.

Conflict of interests: The authors declare that there is no conflict of interests.
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