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The Evaluation of Risk Factors and Results in Pregnant Women with Intrauterine Fetal Hydrocephalus: A Single Center Experience

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Introduction: Fetal hydrocephalus (FHC) occurs as a result of excessive production of cerebrospinal fluid (CSF) or CSF absorption or circulation disorders. Due to its rather complicated etiology, difficulties are experienced in follow-up and management. Our aim is to evaluate risk factors, management and analysis of results in pregnant women with FHC.

Materials and Methods: 117 pregnant women diagnosed with prenatal FHC in the perinatology center were included in the study with demographics and anomalies accompanying FHC. Frequency of fetal magnetic resonance imaging, amniocentesis and/or karyotype analysis, and termination frequency were evaluated in the perinatology council.

Results: Isolated FHC was observed in 32.5%, triventricular hydrocephalus in 6%, neural tube defects (NTD) in 35%, ventriculomegaly (VM) in 12%, cerebellar hypoplasia in 6.8% and Dandy-Walker Anomaly in 4.3%. Karyotype analysis was applied significantly less in case of NTD diagnosis ($p=0.001$). The gestational week was lower in the pregnant women who were terminated than in those whose delivery was decided (median pregnancy patient 20+3 vs 23+2) ($p=0.015$). In addition, termination rates in pregnant women with isolated FHC were found to be significantly lower than those with anomaly accompanying FHC ($p=0.018$).

Conclusion: Amniocentesis / genetic analysis is performed less frequently in case of prenatal diagnosis of NTD than in pregnant women with isolated FHC or other concomitant anomalies. Prenatal diagnosis and timing is an important factor affecting termination and live birth rates.

Keywords: Fetal hydrocephalus, prenatal diagnosis, pregnancy, neural tube defect, amniocentesis

Introduction

Fetal hydrocephalus (FHC) occurs as a result of excessive production of cerebrospinal fluid (CSF)/CSF absorption disorder or CSF circulation disorders (1). Fetal ventriculomegaly is defined as a lateral ventricular atrial diameter of ≥ 10 mm (normal range 6.1 ± 1.3 mm) (1, 2). Increasing the CSF concentration in the ventricular system

causes ventricular dilatation and increased intracranial pressure (1). In the literature, the incidence of FHC is reported to be between 0.3-2/1000 live births (3, 4). The most common finding of abnormal brain development in the second and third trimesters of pregnancy is FHC (1, 2).

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Chromosomal anomalies, genetic defects and intrauterine infections are generally reported for the etiology of FHC (5,6). In addition to the fact that its etiology is quite complicated, neurodevelopmental outcomes of the fetus also differ after birth. This situation causes many difficulties for clinical management, prenatal follow-up, delivery and postnatal management (1-3). After the diagnosis of FHC is made in pregnant women, scans are made in terms of accompanying anomalies [chromosomal anomaly and central nervous system anomaly (Chiari-II, Dandy-Walker malformation and corpus callosum agenesis, etc.)] and a decision is made with the parents in terms of the progression or termination of pregnancy. The easy use of ultrasonography (USG) makes it the most commonly used method in the diagnosis of FHC; depending on fetal position, cranial ossification, and technical reasons, diagnosis may be delayed or missed (1, 3, 5). In the literature, the rate of misdiagnosis of the first USG was reported to be approximately 12.8% (7). Magnetic resonance imaging (MRI), which is not affected by maternal and fetal factors, can be used to diagnose FHC and detect other abnormalities (8). Determining whether demographic characteristics have an effect on the development of FHC in pregnant can prevent FHC before and during pregnancy or take necessary precautions in early period.

Our primary is to evaluate the demographic datas and risk factors of pregnant who diagnosed with FHC in the perinatology. The investigations of management, amniocentesis rates, genetic etiologies and termination rates were second aim of the study.

Materials and Methods

Patients Selection

All pregnant diagnosed with FHC between January 2015 and December 2020 in the tertiary gynecology & obstetrics clinic and perinatology center were included in the present study. After giving written or verbal information about the

study, written consent was obtained from the patients who agreed to participate in the study. Ethics committee approval was given by the faculty scientific research ethics committee.

Data Collection and Assessment of Patients

Demographic datas (gender, age, gestational week), gravida, parity, abortion and curettage numbers, and anomalies accompanying FHC were analyzed. The results of the pregnant in the perinatology council, the frequency of fetal MRI use, amniocentesis and/or karyotype analysis rates, and termination frequency were examined. In addition, the factors affecting the amniocentesis and termination/follow-up decision in pregnant who diagnosed with FHC in the prenatal period (gestational age, week, accompanying anomalies) were investigated.

Statistical Analysis

All data were analysed using the SPSS 25 (IBM, Armonk, NY: IBM Corp.) program. Continuous variables were expressed as mean±standard deviation, median (interquartile range, IQR), and categorical variables as numbers (n) and percentages (%). When the parametric test assumptions were met, t-test was used to compare differences between independent groups. When parametric test assumptions were not met, Mann-Whitney U test was used to compare differences between independent groups. The Fisher's exact probability or Chi-squared tests used to compare demographics. $p < 0.05$ was considered statistically significant.

Results

The medical records of 129 pregnant who diagnosed with intrauterine FHC were analyzed. Twelve pregnant were excluded from the study due to missing data. 117 pregnant who diagnosed with FHC were included in the study. The median age at the time of diagnosis was 25.5 (min: 16 – max: 41, IQR 22 - 30) years, while the median gestational week was 21⁺⁴ (min: 12⁺³ - max: 38, IQR 18⁺⁴ - 26) weeks. In addition, gravida, parity, abortion and curettage

are shown in Table-1. One third of pregnant [34.2% (n=40)] were primiparous. While 32.5% (n=38) of the pregnant had "isolated FHC" and 6.0% (n=7) had "triventricular hydrocephalus"; "ventriculomegaly (VM)" in 12% (n=14), "neural tube defects (NTD)" in 35% (n=41), "cerebellar hypoplasia" in 6.8% (n=8), and % 4.3 (n=5) had accompanying "Dandy-Walker Anomaly".

Table-1. Demographics of pregnant with FHC

Pregnancy age (year) [median (min-max, IQR)]	25.5 (16-41, 27-30)
Gestational week [median (min-max, IQR)]	21+4 (12+3-38, 18+4-26)
History (n) [median (min-max)] - Gravida - Parity - Abortion - Curettage	2 (1 – 9) 1 (0 – 9) 0 (0 – 9) 0 (0 – 2)
Anomalies/malformations accompanying FHC [n(%)] - Isolated hydrocephalus - NTD - VM - Cerebellar hypoplasia - Dandy-Walker	38 (32.5) 41 (35) 14 (12) 8 (6.8) 5 (4.3)

FHC: fetal hydrocephalus, IQR: interquartile range, NTD: neural tube defect, VM: ventriculomegaly

Gestational age and week and number of abortion and/or curettage did not have any effect on isolated FHC/accompanying anomaly /malformation ($p>0.05$). In our study, fetal USG was performed in all pregnant who diagnosed with FHC; fetal MRI was performed only in 3 (2.6%). In addition, while amniocentesis was performed in 17.1% (n=20), karyotype analysis was performed in 15.4% (n=18) (Table-2). No complications were observed in any of the pregnant who underwent amniocentesis. It was observed that the age and gestational week of the pregnant had no effect on the decision to perform amniocentesis (Table-3). While the presence of isolated FHC or accompanying anomalies has no effect on performing amniocentesis and karyotype analysis; karyotype analysis was applied significantly less in case of

NTD diagnosis ($p=0.001$) (Table-3). Live birth occurred in 75% (n=15) of the pregnant who underwent amniocentesis, termination was performed in 5 pregnant. Multipl anomalies with FHC were observed in 3 pregnant and isolated FHC was observed in 2 pregnant who underwent amniocentesis and were terminated. No any chromosomal anomalies were in any of the fetuses whose karyotype analysis was done.

The termination rate was 47.9% (n=56) and live birth occurred in 51.3% (n=60) (Table-2). The gestational week was significantly lower in the pregnant who were terminated than in those who decided to live birth (median 20^{+3} vs 23^{+2}) ($p=0.015$) (Table-3). In addition, termination rates in pregnant with isolated FHC were lower than those with anomaly accompanying FHC ($p=0.018$). On the other hand, it was observed that the accompanying NTD or VM had no affect on the termination decision ($p=0.593$ and $p=0.865$, respectively)(Table-3).

Table-2. The results of pregnant who diagnosed with FHC

Variables	n	%
Fetal diagnosis - Fetal USG - Fetal MRG	117 3	100 2.6
Amniocentesis - Yes - No	20 97	17.1 82.9
Karyotype analysis - Yes - No	18 99	15.4 84.6
Results - Termination - Live birth - Stillbirth	56 60 1	47.9 51.3 0.8

FHC: Fetal Hydrocephalus, MRI: Magnetic Resonance Imaging, USG: Ultrasound Sonography Test

Discussion

Our study includes the characteristics, risk factors and management of pregnant who diagnosed with prenatal FHC, and anomalies accompanying the fetus with FHC. Although the incidence of FHC is reported as 0.3-2/1000 live births, the actual incidence is probably higher

Table-3. The factors affecting amniocentesis, karyotype analysis and termination decision and their comparison

Variables	Amniocentesis		Karyotype Analysis		Termination	
	+	-	+	-	+	-
Pregnancy age (y) [med (min-max)]	27 (20-37)	25 (16-41)	27 (16-41)	25 (16-37)	26 (16-40)	25 (17-41)
Gestational week [med (min-max)]	20 (14-30)	22 (12-38)	^δ 18 ⁺⁵ (15-37)	22 (12-38)	^φ 20 ⁺² (12-37)	23 ⁺¹ (14-38)
Isolated FHC [n (%)]	10 (26.3)	28 (73.7)	7 (18.4)	31 (81.6)	[§] 12 (31.6)	26 (68.4)
NTD [n (%)]	4 (9.8)	37 (90.2)	[*] 1 (2.4)	40 (97.6)	21 (51.2)	20 (48.8)
VM [n (%)]	3 (21.4)	11 (78.6)	7 (50.0)	7 (50)	4 (28.6)	10 (71.4)

FHC: fetal hydrocephalus, NTD: neural tube defect, VM: ventriculomegaly, med: median, min: minimum, max: maximum

^{*}The rate of karyotype analysis was lower in pregnant with NTD than others ($p=0.001$)

^δThe median gestational week of those who underwent karyotype analysis was significantly lower than those who did not ($p=0.036$)

^φGestational weeks were statistically significantly lower in pregnant who underwent termination than live birth ($p=0.015$)

[§]Termination rate was statistically significantly lower in those with isolated FHC than those had multipl anomalies ($p=0.018$)

since many fetal death cases are missed (3,4,10, 11). However, although it has been reported that FHC is seen mostly in primiparous women, this rate is controversial because the frequency of curettage is unknown (9-12). In our study, 34.2% of the pregnant who diagnosed with FHC were found to be primiparous. In addition, it was found that 13.7% of the pregnant had a curettage history at least once. Contrary to the literature, the number of primiparous was low in our study; however, this rate might actually be higher because the numbers of fetuses who underwent curettage were not knew.

Although prenatally detected FHC is seen as isolated, it is seen accompanied by triventricular (communicating HC, aqueductus stenosis, etc.), Dandy-Walker Anomaly and other anomalies (cerebellar, ventriculomegaly, corpus callosum agenesis). Approximately 60% of non-isolated FHC cases are accompanied by Dandy-Walker anomalies, NTDs and anomalies of the corpus callosum (13-15). In our study, similar to the literature, approximately one third of FHC cases were isolated, while NTD accompanied the other third. The primarily option for the diagnosis of FHC is fetal USG. Although it is easy to apply, fetal MRI is needed due to its nature, the inability to visualize some anomalies, and limiting factors such as technical reasons (16, 17). While Wang et al. found the accuracy of

USG to be 92.9% in the diagnosis of FHC in pregnant, Parazzini C et al. reported that USG could not diagnose in 27.4% of patients compared to MRI in 179 fetal ventriculomegaly cases(1,18). In our study, 97.4% of the pregnant with FHC were diagnosed with USG, while fetal MRI was performed in only 3 patients. Similar with literature, fetal MRI usage was lower in our study. The high experience of USG and technological developments of physicians in the perinatology center may explain this result.

In case of malformations, advanced maternal age, anomalies, genetic syndromes in fetal USG, or uncertain USG findings, further evaluation with genetic counseling, amniocentesis, and karyotype analysis methods is recommended (19, 20). Although amniocentesis is a reliable diagnostic method, complications may develop after the procedure. These complications are mostly inversely proportional to the experience of the person performing the procedure (21). In our study, the frequency of amniocentesis was found to be 17.1%, while our genetic analysis rate was 15.4%. The absence of complications in any pregnant after amniocentesis can be explained by the experienced physicians in the perinatology center. In addition, it has been reported that the incidence of chromosomal anomaly in genetic examinations performed after USG anomaly is seen is between 4-27%

(22-24). In our study, chromosomal anomaly was not detected in any of the samples. An insufficient number of patients who underwent amniocentesis. Therefore the genetic analysis performed in fewer patients may explain this. Inclusion of who were diagnosed with FHC (although some accompanying anomalies) and the absence of pregnant with suspected fetal chromosomal anomaly explains the result that anomaly was not observed in any fetus, contrary to the literature. In addition, it was observed that the age and gestational week of the pregnant did not have any effect on the decision to perform amniocentesis in our study. Also, the rate of amniocentesis/genetic analysis in pregnant who were diagnosed with NTD on fetal USG or MRI was lower than isolated FHC or other concomitant anomalies. The fact that the probability of chromosomal anomaly in pregnant diagnosed with fetal NTD is higher than the isolated FHC or other accompanying anomalies may explain this result.

In a study conducted by Garne E et al with the data of 4 countries in Europe, it was observed that the live birth rate was 47% in pregnant diagnosed with FHS, while the termination rate was 48% and the stillbirth rate was 5% (25). On the other hand, the same study reported that, in pregnant diagnosed with FHC in the prenatal period, live birth was reported as 35.7%, termination was 60% and stillbirth rate was 4.3% (25). In line with these results, it was suggested that prenatal diagnosis and timing are the main criteria that are effective in making the termination decision. The termination rate varies considerably due to the socioeconomic status of the countries, the role of women in social life, education levels, cultural factors and religious differences (26, 27). The termination is not allowed except in life- threatening situations for women and/or in 120 days of pregnancy in Muslim countries. For this reason, termination cannot be applied in pregnant who have fetal anomalies after 120 days and babies with anomalies are born (28). In our country,

education levels, socio-economic conditions, ethnic and religious differences also affect the termination rates (29). In our study, while the live birth rate was 51.3%, the termination frequency was 47.9%. Although all pregnant were diagnosed prenatally, the termination frequency was lower; it should be kept in mind that socio-economic conditions and religious differences in our country may also affect this decision. Similar to the literature, in our study, it was observed that the gestational week of the pregnant who underwent termination was lower than those who decided to live birth. This result supports that early prenatal diagnosis increases the frequency of termination.

Limitations of the study; (1) the single-center nature of our study constitutes an important limitation in the generalization; (2) Since it is retrospective, the follow-up of pregnant and the postpartum life expectancy are unknown.

Conclusion

FHC is one of the most common central nervous system anomalies in pregnant. The gestational week was significantly lower in the pregnant with FHC who were terminated than in those who decided to live birth. Termination rates in pregnant with isolated FHC were lower than those with anomaly accompanying FHC. Amniocentesis / genetic analysis is performed less frequently in case of NTD diagnosis.

Conflict of Interest

All authors declare no conflict of interest.

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