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RESEARCH ARTICLE

Perinatal outcomes of choroid plexus cysts in a high-risk pregnant population: A tertiary center experience

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Abstract

Introductıon: The objective of this study was to present the results of fetuses followed up for choroid plexus cysts(CPC) in our clinic and to provide an additional benefit to the existing literature.

Methods: This is a retrospective cohort study conducted in Ankara Bilkent City Hospital perinatology clinic. All pregnant women who were followed up with a antenatally diagnosed choroid plexus cyst between 2021 and 2023 were included in the study. Demographic characteristics, prenatal ultrasound findings, non-invasive screening test results, invasive diagnostic test results, clinical management and postnatal outcomes were evaluated and compared between unilateral CPC group and bilateral CPC group.

Results: A comparison between unilateral and bilateral groups revealed no significant differences in maternal age, gravidity, parity, or number of abortions. However, the week of diagnosis was found to be smaller in the group with bilateral choroid plexus cysts (p=0.004). Patients undergoing invasive testing were higher in the bilateral CPC group, although these differences were not statistically significant. There was no statistically significant difference between the groups in terms of pregnancy termination rate, gestational week at delivery, neonatal weight, NICU admission, and APGAR scores. The group with additional anomalies exhibited a higher rate of high-risk screening tests, a higher rate of anomaly detection in invasive tests, and a higher rate of pregnancy termination. Nevertheless, these differences were not statistically significant

Conclusion: In conclusion, fetal choroid plexus cysts represent a risk factor for aneuploidy when associated anomalies are present.

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Introduction

The choroid plexus begins to develop at approximately six to seven weeks of gestation and fills approximately 75 percent of the lateral ventricular cavity by 9 weeks of gestation. Choroid plexus cysts (CPCs) are pseudocysts in the fetal choroid plexus.[1] They are diagnosed in approximately 1% of fetuses in the first and second trimesters of pregnancy during routine prenatal ultrasound scans.[2,3] The typical sonographic appearance is that of smoothly circumscribed, anechoic structures. Cysts may be unilateral, bilateral, bilobulated, or multiple.[4] Approximately 90% of cysts disappear after 28 weeks of gestation, and only a few show progressive enlargement.[5] In the absence of additional central nervous system abnormalities or other systemic abnormalities and risk factors for chromosomal aneuploidy, isolated choroid plexus cysts are considered a variant of normal. The shape, size, or laterality of the choroid plexus cyst is considered to be of no clinical significance. Fetuses with additional anomalies are at increased risk for chromosomal abnormalities, especially trisomy 18.

Several studies have demonstrated that patients with fetal isolated choroid plexus cysts exhibit favorable outcomes and no abnormalities in long-term follow-up after birth. A systematic review of several studies of children with a history of isolated choroid plexus cysts followed up until adolescence revealed no association with adverse health and neurodevelopmental outcomes.[6,7] However, due to the limited number of cases, the potential for selection bias, the lack of a clear definition, and the absence of a control group in these studies, the long-term prognosis remains uncertain. Furthermore, studies and case reports published in the last 20 years have indicated that CPCs may be associated with an increased risk of verbal learning difficulties and suboptimal neurodevelopment.[8,9]

The objective of this study was to present the results of fetuses followed up for choroid plexus cysts in our clinic and to provide an additional benefit to the existing literature.

Material and Methods

This retrospective cohort study was conducted on all consecutive prenatally detected choroid plexus cyst cases followed in Ankara Bilkent City Hospital's perinatology clinic between January 2021- August 2023. The study protocol was approved by the ethics committee with the reference number E2-23-5192 and all participants gave written consent. Non-invasive screening test results, invasive diagnostic test results, demographic features, prenatal ultrasound findings, and postnatal outcomes were reported.

All ultrasound assessments were made with Voluson E10 with a 2-9 Mhz abdominal convex probe by the same expert perinatologist (D.S.). The diagnostic criterion for choroid plexus cyst was the presence of a cyst with a diameter >5mm within the choroid plexus that could be detected by ultrasound. The first fetal ultrasound screening was performed at 14th-18th week of gestation and more ultrasound screenings were performed 2 weeks intervally until the time of delivery. Fetuses with major central nervous system anomalies were excluded.

The cases were initially stratified into two groups: fetuses with unilateral and bilateral choroid plexus cysts. A comparative analysis was conducted between these two groups, focusing on maternal characteristics, the presence of chromosomal abnormalities, and neonatal outcomes. Subsequently, the cases were divided into those with and without additional structural anomalies, and similar comparisons were made between these groups.

The statistical analysis was performed by SPSS 22 (IBM Corp., NY). Kolmogrov-Smirnov test was used to assess whether the data is normally distributed. Mean and standard deviation values were used for normally distributed continuous variables. Whereas, median and range values were used to present continuous variables without normal distribution. Categorical variables were presented as numbers and percentages.

Results

A total of 60 patients were included in the study. A total of 32 patients presented with a unilateral choroid plexus cyst (CPC), while 28 patients had bilateral CPC. In addition, 46 patients exhibited additional anomalies, while 14 patients presented with CPC as an isolated finding.

In the comparison between unilateral and bilateral groups, no significant difference was observed in terms of maternal age, gravidity, parity and number of abortions, whereas the week of diagnosis was found to be smaller in the group with bilateral choroid plexus cyst (p=0.004). The rate of high-risk in the first and second trimester aneuploidy screening test and the rate of aneuploidy detection in patients undergoing invasive testing were higher in the bilateral CPC group, although these differences were not statistically significant.

There was no statistically significant difference between the groups in terms of pregnancy termination rate, gestational week at delivery, neonatal weight, NICU admission, and APGAR scores. Table 1 presents a summary of the comparison of maternal characteristics, screening test and invasive test results, and obstetric outcomes in cases with unilateral and bilateral choroid plexus cysts.

Table 1. The comparison of maternal characteristics, screening test and invasive test results, and obstetric outcomes in cases with unilateral and bilateral choroid plexus cysts

	Unilateral (n=32) Mean ± SD	Bilateral (n=28) Mean ± SD	P
Age	30 ± 6.3	31.6 ±5.6	0.3
Gravidity	2.3 ± 1.2	2.1 ± 1.09	0.52
Parity	1.2 ±1.1	0.89±0.83	0.2
Abortus	0.5±0.9	0.6±0.9	0.45
Gestational age at diagnosis	20.2±5.3	16.9±3.2	**0.004**
Additional anomaly	67.9%	84.4%	0.13
High risk on first trimester aneuploidy scan	9.4%	21.4%	0.37
High risk on second trimester aneuploidy scan	0%	21.4%	0.019
Aneuploidy at invasive test result	18.8%	35.7%	0.29
TOP	3.6%	6.3%	0.45
NICU admission	23.3%	22.1%	0.92
Gestational age at birth	36.2±5.1	35.8±4.9	0.76
Newborn weight	2813±992	2636±804	0.45
APGAR 1	6.7±1.7	6.1±1.8	0.26
APGAR 5	8.2±1.3	7.6±1.8	0.16

$p<0.05$ accepted as statistically significant.
TOP: termination of pregnancy. NICU: neonatal intensive care unit.

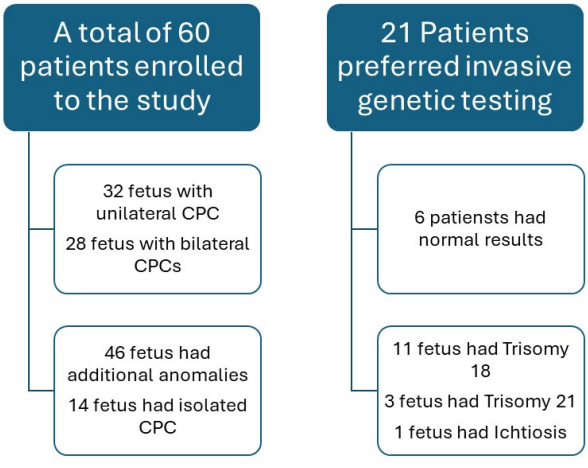
When the groups with and without additional anomalies were compared, no significant differences were observed between the groups in terms of maternal characteristics and neonatal outcomes. However, the group with additional anomalies exhibited a higher rate of high-risk screening tests, a higher rate of anomaly detection in invasive tests, and a higher rate of pregnancy termination. Nevertheless, these differences were not statistically significant. The results of the comparison between the groups with and without additional anomalies are presented in Table 2.

Table 2 The comparison of maternal characteristics, screening test and invasive test results, and obstetric outcomes between the groups with and without additional anomalies

	No additional anomaly (n=14) Mean ± SD	With additional anomaly (n=46) Mean ± SD	P
Age	29.2±4.9	31.2±6.3	0.29
Gravidity	2.4±1.2	2.2±1.1	0.6
Parity	1±0.9	1±1	0.98
Abortus	0.8±1.2	0.5±0.7	0.32
Gestational age at diagnosis	17±4	18±4	0.48
High risk on first trimester aneuploidy scan	7.1%	17.4%	0.26
High risk on second trimester aneuploidy scan	8.7%	14.3%	0.81
Aneuploidy at invasive test result	14.3%	30.4%	0.11
TOP	4.3%	7.1%	0.51
NICU admission	22.7%	23.1%	0.97
Gestational age at birth	34.5±5.8	36.5±4.7	0.19
Newborn weight	2509±938	2798±896	0.3
APGAR 1	6.7±1.6	6.3±1.8	0.51
APGAR 5	8.1±1	7.8±1.7	0.6

A total of 21 patients underwent invasive testing. Six patients exhibited a normal karyotype, 11 had trisomy 18, three had trisomy 21, and one had ichthyosis. One patient underwent cell-free DNA testing, which yielded a result of trisomy 21. However, the patient declined amniocentesis.

A flowchart illustrating the ultrasound features and invasive findings of choroid plexus cysts in Figure 1.



In addition, the following anomalies were observed: ventriculomegaly in seven fetuses, renal pelviectasis in three fetuses, left heart hypoplasia in two fetuses, bilateral clubfoot in two fetuses, cleft lip and palate in two fetuses, single umbilical artery in two fetuses, corpus callosum dysgenesis in two fetuses, and nasal bone hypoplasia in two fetuses. One fetus exhibited an atrioventricular septal defect, one had a double outlet right ventricle, one had radial aplasia and hemivertebra, one had cataracts, one had megacystis, one had arrhythmia, one had a mega cisterna magna, and one had ambiguous genitalia.

Discussion

Fetal choroid plexus cysts are formed when cerebrospinal fluid is trapped in the choroid plexus and are typically identified during the second trimester ultrasound examination. Choroid plexus cysts are not considered to be a brain anomaly. However, various studies have demonstrated that they may be associated with aneuploidies.

When identified as a solitary finding, it is advised that choroid plexus cysts be regarded as a benign phenomenon. In a study in which 12,672 patients were screened and 336 choroid plexus cysts were detected, it was reported that the presence of additional structural abnormalities was observed in all cases with aneuploidy. It was determined that amniocentesis was not necessary in patients without additional anomalies.[6] In a separate study, in which ultrasound findings of fetuses with trisomy 18 were analyzed, choroid plexus cysts were detected in approximately half of the cases. However, in no case was this finding isolated.[10] A systematic review was conducted to examine the neurodevelopmental outcomes of children who were followed with isolated choroid plexus cysts and delivered at birth. The results demonstrated that there were no significant neurodevelopmental effects in these cases.[11] In a separate study examining the relationship between trisomy 18 and choroid plexus cysts, the analysis concluded that in order to identify one case of trisomy 18 in cases with isolated choroid plexus cysts, 477 fetuses with a normal karyotype would require amniocentesis. In consideration of the established risk of fetal loss associated with amniocentesis, it was estimated that two normal fetuses would be lost in order to diagnose one fetus with trisomy 18.[12]

In the present study, although the rate of aneuploidy detection by amniocentesis was higher in fetuses with additional anomalies compared to isolated CPC cases, this difference was not statistically significant. This result is partially consistent with the findings of previous studies in the literature. As the study was based on data from a perinatology clinic, the majority of patients were from the high-risk population. Consequently, the majority of cases exhibited associated anomalies. The lack of statistical significance may be attributed to the relatively small sample size and the fact that additional anomalies were not classified as major or minor structural anomalies.

Choroid plexus cysts may be single or multiple, unilateral or bilateral, septate or simple cysts, and typically measure less than 10 mm in diameter. These cysts, which have been demonstrated to be associated with aneuploidy in various studies, manifest in diverse forms, prompting the inquiry into the relationship between the characteristics of the cysts and aneuploidy.

A study of 435 CPC cases revealed that the aneuploidy rates of unilateral and bilateral CPC cases were comparable, although slightly higher in the bilateral group.[13] However, in a patient with no additional risk factors and only sonographic findings of bilateral large choroid plexus cysts, trisomy 18 was diagnosed by amniocentesis.[14] Similarly, a case report describes a patient with trisomy 21 and bilateral choroid plexus cysts as the only ultrasound finding.[15] Nevertheless, it is generally believed that choroid plexus cysts do not increase the risk of Down syndrome when detected as an isolated finding.[16,17] In a study of significant importance in this field, it was found that the presence of bilateral cysts had no effect on the risk of aneuploidy.[18] In the present study, the rate of aneuploidy detection by invasive testing was found to be higher in the bilateral CPC group than in the unilateral CPC group. However, this difference was not found to be statistically significant. The higher rate of aneuploidy detection in the bilateral CPC group may be attributed to the higher prevalence of concomitant anomalies and the higher rate of high-risk detection in screening tests. A comparison of isolated cases of CPC would have yielded more significant results in this regard. However, given that the patients in our study group were high-risk pregnant women, the majority of them exhibited associated anomalies.

In conclusion, fetal choroid plexus cysts represent a risk factor for aneuploidy when associated anomalies are present. Consequently, when such a cyst is

identified, a comprehensive anatomical examination and a meticulous evaluation of the patient's previous risk of aneuploidy should be conducted. In the event that genetic diagnosis is deemed necessary, patients should be referred for such testing. In instances where it is confirmed that the cyst is isolated, it is similarly crucial to avoid exacerbating the distress of the family.

The principal limitation of our study is its retrospective design and the relatively small number of patients included. However, the study also has notable strengths, including the evaluation of the relationship between bilaterality and the presence of concomitant anomalies in a single investigation.

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