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RESEARCH ARTICLE

# Prenatal diagnosis and postnatal outcomes of cavum septum pellucidum et vergae

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## Abstract

**Introductıon:** Evaluation of demographic characteristics and postnatal outcomes of fetuses with cavum septum pellucidum et vergae (CSPV) diagnosis followed in a tertiary center.

**Methods:** This retrospective study was conducted in Ankara Bilkent City Hospital perinatology clinic between 2020-2023. Cases with the prenatal diagnosis of CSPV were evaluated. Demographic features, prenatal ultrasound findings, noninvasive screening test results, invasive diagnostic test results, prenatal anomaly screening ultrasound findings, and postnatal outcomes were reported.

**Results:** There was a total of 24 prenatally diagnosed CSPV cases during the study period. The mean gestational week at diagnosis was 25.6 ± 3.2 weeks. Nineteen patients participated in noninvasive screening tests; five patients declined them. Noninvasive screening tests revealed low risk in 17 patients and high risk in 2. Amniocentesis was performed in 5 patients; 3 of them had a normal karyotype, 1 fetus was diagnosed with Smith-Lemli-Opitz syndrome, and 1 fetus had trisomy 21. Six patients with isolated CSPV were accepted and underwent fetal MRI, other eighteen patients refused MRI. MRI corrected the CSPV in all six patients, and they had no additional findings. Five (%21) fetuses were admitted to the intensive care unit because of recurrent absence convulsions (n=1), anal atresia (n=1), cleft lip palate (n=1), respiratory distress (n=1) and hypoplastic left heart syndrome (n=1).

**Conclusion:** CSPV is considered a normal variant of cavum septum pellucidum and can be diagnosed during ultrasound screening for fetal anomalies; in isolated cases perinatal outcomes are favorable.

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## Introduction

The cavum septum pellucidum, which is considered a normal anatomical variation in the brain, is a potential space containing fluid between the membranous leaves in the frontal region.[1] The CSP is a structure situated between the medial border of the frontal horns and the bodies of the lateral ventricles. It is closely associated with the corpus callosum, which defines its rostral and superior boundaries. The body of the fornix constitutes its posterior-inferior floor. At 10 to 12 weeks of gestation, this developmental process initiates and achieves its adult form at 17th gestatioanal week, which which aligns with the formation of the corpus callosum.

The corpus callosum is located close to the CSP and defines its superior and rostral borders. The posterior and inferior aspects of the fornix are formed by its own body. The CSP is not merely a membrane; it does not contain organised grey matter either. The CSP consists of two sheaths of white matter located close to each other along the midline containing fibres.[2,3] The prenatal observation of CSP is a key indicator of proper foetal brain development. The prenatal observation of CSP is a key indicator of proper foetal brain development. Developmental anomalies of this midline space are strongly associated with the development of neuropathological disorders.[4,5] Although the exact function of the CSP remains unclear, it is hypothesised to be an essential element of the limbic system and to influence behaviours such as anger and arousal.[6]

Cavum septum pellucidum et vergae (CSPV) is an anatomical variant that forms the continuation of the posterior wall of the CSP. This variant forms an extension that extends beyond the walls of the fornix and the Monro foramines. About 30% of newborns have this variant, but only less than 1% of adults have this structure. CSP and CSPV have been observed in nearly all premature infants with normal brain architecture.[7] The midline anatomical structures initiate the process of closure in a posterior direction. It has been demonstrated that the cavum vergae is the first to close. Furthermore, it has been established that the closure of the CSPV commences in the sixth month of gestation.[8,9]

The objective of this study was to undertake a comparative analysis of the prenatal and postnatal characteristics and demographic data of fetuses diagnosed with CSPV at a tertiary care center.

## Material and Methods

This is a retrospective observational study conducted between January 2021 and November 2023 in the perinatology clinic of a tertiary care hospital on cases with a diagnosis of CSPV. The study protocol received approval from the relevant institutional ethics committee (reference number E2-23-5191) and written informed consent was obtained from all participants prior to their involvement in the study. The following variables were recorded: demographic characteristics, antenatal ultrasound findings, results of non-invasive screening tests, results of invasive diagnostic tests, antenatal screening ultrasound findings regarding anomalies and postnatal outcomes. An ultrasound assessment was conducted by the same experienced perinatologist using a Voluson E10 with a 2-9 MHz abdominal convex probe. The assessment was initially conducted to screen for fetal anatomy at 20-24 weeks' gestation and subsequently repeated at two-week intervals until delivery to monitor the pregnancy.

A statistical analysis was performed utilising the SPSS 22 software, produced by IBM Corp. in New York. The Kolmogorov-Smirnov test was employed in order to ascertain whether the data exhibited a normal distribution. For variables exhibiting a normal distribution, mean and standard deviation were employed as descriptive statistics. In the case of non-normally distributed continuous variables, the median and range were employed as the statistical measures. Categorical variables were expressed as frequencies and relative percentages.

## Results

The study period yielded a total of 24 identified cases of prenatal diagnosis of CSPV. A summary of the demographic characteristics and clinical presentation of all CSPV cases is provided in Table 1. On average, the gestational age at diagnosis was 25.6 ± 3.2 weeks. The mean age of the subjects included in the study was 28.4 ± 5.8 years. The median gravidity was 3 (range 1-8), and the median parity was 2 (range 0-7). The sex of 13 fetuses (54%) was male, and 11 (46%) were female.

Five patients refused prenatal screening. Prenatal screening tests were performed in nineteen patients. The non-invasive prenatal screening tests demonstrated that seventeen patients fell within the low-risk category for chromosomal abnormalities, while two patients were identified as being at a higher

risk. Amniocentesis was performed in five patients; three of them had a normal karyotype, 1 fetus was diagnosed with Smith-Lemli-Opitz syndrome and 1 fetus had trisomy 21. Although CSPV was an isolated finding on ultrasound in 18 (75%) of the foetuses, the remaining 6 (25%) foetuses exhibited additional anomalous findings on ultrasound. Additional fetal anomalies include a fetus with hypoplastic left heart syndrome (HSLS), a fetus with atrioventricular septal defect (AVSD), a fetus with anal atresia, a fetus with hemivertebra, ASD and single umbilical artery, a fetus with slight enlargement of the posterior lateral ventricle, and a fetus with cleft lip and palate.

Six patients with isolated CSPV were accepted and underwent fetal MRI, the other eighteen patients refused MRI. MRI confirmed CSPV in all six patients and they had no additional findings. Two pregnancies were terminated as a consequence of the presence of significant fetal anomalies or chromosomal abnormalities; one of the fetuses was terminated at 26 weeks' gestation because of Smith-Lemli-Opitz syndrome and the other at 24 weeks' gestation because of trisomy 21. Autopsies could not be performed due to lack of parental consent.

Table 1: Demographic features of Cavum Septum Pellucidum et vergae cases n=24

| | | |
|---|---|---|
| Maternal Age | | 28.4 ± 5.8 |
| Gravidity | | 3 (1-8) |
| Parity | | 2 (0-7) |
| Gestational age at diagnosis (week) | | 25.6 ± 3.2 |
| Noninvasive screening test | High risk | 2 |
| | Low risk | 17 |
| | Refused | 5 |
| Amniosynthesis | performed (n=5) | Normal (3)<br>Trisomy 21 (1)<br>Smith-Lemli-Opitz Syndrome (1) |
| Fetus gender | Male | 13 (%54) |
| | Female | 11 (%46) |
| MRI | Normal | 6 |
| | Abnormal | 0 |
| CSPV as an isolated finding | | 18 (%75) |
| CSPV with additional anomalies* | | 6 (%25) |

* Additional anomalies were: hypoplastic left heart syndrome, atrio-ventricular septal defect, anal atresia, hemivertebrae, ASD and single umbilical artery, dilatation of the right lateral ventricle (12 mm), cleft lip and palate

A summary of the short-term postnatal outcomes of CSPV live births is provided in Table 2. The mean gestational age of the remaining 22 fetuses was 37.2 ± 1.6 weeks. The mean birth weight was 2972 ± 586 grams. The mean Apgar scores for the fetuses were 7 (range 5-8) at one minute and 8 (range 6-9) at five minutes. A total of five fetuses (22.7%) were admitted to the neonatal intensive care unit (NICU). One for recurrent absence seizures (n=1), one for anal atresia (n=1), one for hypoplastic left heart syndrome (n=1), one for cleft lip palate (n=1) and one for respiratory distress (n=1). All infants born alive were followed up by a paediatrician and a developmental-behavioural paediatrician for a period of two years. At follow-up, isolated and chromosomally normal CSPV cases have normal neurological and physical development for their age.

Table 2: Postnatal outcomes of Cavum Septum Pellucidum et vergae cases (n=22)

| | |
|---|---|
| Birth week | 37.2 ± 1.6 |
| Birth weight (gram) | 2972 ± 586 |
| Apgar score 1st minute (range) | 7 (5-8) |
| Apgar score 5th minute (range) | 8 (6-9) |
| NICU admission* | 5(%27.7) |

NICU: neonatal intensive care unit
* Recurrent absance seizures (n=1), cleft lip palate (n=1), hypoplastic left heart syndrome(n=1), respiratory distress (n=1) and anal atresia (n=1).

## Discussion

According to this study, favourable outcomes were observed in the majority of CSPV cases. While prenatal diagnosis of fetal CSPV can prove challenging, detection rates have increased with the advent of more sophisticated imaging technologies and the accumulating experience in maternal-foetal medicine. Given our limited knowledge of the prognosis of prenatally detected cases, studies focusing on this specific topic may be useful to guide clinicians in providing accurate information to parents.

In a prospective study of 322 low-risk pregnancies, the frequency of CSPV and the morphological findings of CSP were investigated. In this study, the incidence of CSPV was found to be 7.2%. This study highlights the common morphological features of CSPV and the fact that CSPV is present in a significant proportion of clinically normal fetuses.[10]

In a prospective observational study conducted at a single centre involving 11,200 pregnant women, the frequency of CSPV was assessed through the utilisation of prenatal ultrasound, resulting in the detection of eight fetuses within this cohort. Anomalies were observed in five fetuses. Three of the five fetuses exhibited hydrocephalus, one displayed growth retardation, and one demonstrated a chromosomal abnormality (11/22 translocation). The pregnancy was terminated due to the presence of significant congenital anomalies and chromosomal anomalies in four fetuses. One neonate exhibited communication with the third ventricle of the CNS in accordance with the CSPV, while another demonstrated mild ventriculomegaly on postnatal ultrasound. The three surviving fetuses exhibited typical neurological development during the first months of life. The findings of this study indicate that isolated cases of CSPV may have normal neurological development, but it is crucial to consider the potential association with fetal malformations.[11]

In a retrospective single-center study evaluating 111 infants with confirmed 22q11.2 deletion (Di George Syndrome), magnetic resonance imaging (MRI) was performed on 24 infants who presented with neurological symptoms. MRI revealed that eight of the 24 infants exhibited persistent CSP and/or CSPV. The elevated prevalence of CSP and CSPV persistence indicates that the closure of these anatomical structures may be delayed or incomplete in chromosomal abnormalities. The findings revealed the types and frequencies of brain malformations observed in the case series, suggesting the prevalence of neuroanatomical anomalies in 22q11.2DS may be underestimated.[12] In contrast with the findings of recent studies, our investigation did not identify any patients with DiGeorge syndrome. It is hypothesised that this discrepancy can be attributed to the relatively limited patient population included in the study.

This retrospective case-control study involved the measurement of the length and width of the CSP in the axial plane of the fetal head, as defined by the CSP length/width ratio. The study included 323 normal fetuses and 20 fetuses with pACC between 20 and 34 weeks of gestation. In the general study population, the length and width of the CSP exhibited a positive correlation with increasing BPD, whereas the proportion of CSP demonstrated a negative correlation. In 85% (17/20) of foetuses with partial agenesis of the corpus callosum (pACC), the length of the CSP was below the 5th percentile, while in 65% (13/20) of cases, the width was below the 95th percentile. The CSP ratio was observed to be below the 5th percentile in 95% (19/20) of pACC foetuses, with 16/20 (80%) exhibiting a ratio that was below the empirically derived cut-off point of 1.5. A Z-score analysis demonstrated that foetuses with pACC exhibited a markedly diminished CSP rate in comparison to the control population ($p < 0.0001$).[13] As our study was retrospective and the CSP dimensions are not routinely recorded, we were unable to include the CSP ratio in our analysis.

## Conclusion

The principal strength of our study is that we evaluate cavum vergae, a subject that has not been extensively researched to date and has been regarded as a variant of normal until now, from a novel perspective. The current study is constrained by its monocentric design and comparatively small sample size, which is derived from a single ethnic group. The findings of our study concur with those of previous research in that cavum results have an excellent prognosis in isolated cases.

The advent of improved ultrasound technology has led to a significant advancement in the field of prenatal diagnosis of fetal anomalies over the past decade. Prenatal diagnosis is a crucial aspect in cases such as CSPV, as early detection allows for the possibility of anatomical and genetic screening for associated anomalies, preparation for neonatal care and interventions, and comprehensive patient information. The findings of our study indicate that isolated and chromosomally normal CSPV cases exhibited normal neurological and physical development during follow-ups. The findings of the recent study are largely in alignment with those of previous research. Further research into prenatal diagnosis and perinatal outcomes in this context may yield valuable insights for clinicians, enabling early diagnosis and management of patients with CSPV.

## *Statements & Declarations*

### *Informed consent*

The rights of all participants were protected and written informed consent was obtained prior to procedures in accordance with the Declaration of Helsinki.

*Conflicts of interest*

The authors have no competing interests to declare.

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