Volume Measurement of the Cavum Septi Pellucidi: Normative Values Between 20 and 40 Weeks of Gestation

Ruba Tuma MD[1,2*], Marwan Odeh MD[2,3*], Maya Wolf MD[2,3], Inshirah Sgayer MD[2,3], Nicola Luigi Bragazzi MD PhD[4], and Rola Khamisy-Farah MD[1]

[1]Department of Obstetrics and Gynecology, Clalit Health Service, Akko, Israel
[2]Department of Obstetrics and Gynecology, Galilee Medical Center, Nahariya, Israel
[3]Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel
[4]Laboratory for Industrial and Applied Mathematics (LIAM), Department of Mathematics and Statistics, York University, Toronto, Canada

ABSTRACT **Background:** The cavum septi pellucidi (CSP) is a brain-enclosed cavity located on the midline between the two leaflets of the septum pellucidum that separates the lateral ventricles. This structure develops in the fetus from week 18 and can be seen up to week 37 in almost all cases and then begins to disappear.

Objectives: To measure and determine the normative values of the CSP volume in fetuses between 20 to 40 weeks of gestation.

Methods: The study comprised 161 consecutive pregnant women between 20 to 40 weeks of gestation with single viable fetuses. All patients had normal, disease-free pregnancies. Transvaginal or transabdominal ultrasound was used according to the fetal presentation. The fetal head was assessed in mid-sagittal sections. Once the CSP was visualized, its volume was measured using three-dimensional ultrasound with Virtual Organ Computer-aided Analysis software. The width of the CSP was also measured at the biparietal diameter (BPD) plane.

Results: Of the 161 fetuses, the CSP volume was measured in 158. In three patients the CSP was not identified. The CSP volume correlated poorly with gestational age (r=0.229) and with the BPD (r=0.295). The mean CSP volume was 0.508 ± 0.372 ml (range: 0.03-1.78 ml). The simple measurement of the CSP width correlated better with gestational age (r=0.535) and the BPD (r=0.484).

Conclusions: The CSP volume had a poor correlation with gestational age; however, the volume did not exceed 2 ml regardless of gestational age. This information can be used to assess pathologies involving the CSP.

IMAJ 2024; 26: 236–239

KEY WORDS: biparietal diameter (BPD), cavum septi pellucidi (CSP), gestation, fetal head, reference (normative) values

*These authors contributed equally to this study.

Cavum septi pellucidi (CSP) is a brain-enclosed cavity located on the midline between the two leaflets of the septum pellucidum that separates the lateral ventricles [1]. It is a fluid-filled space less than 10 mm wide between the frontal horns of the lateral ventricles and below the anterior portion of the corpus callosum. It is not part of the ventricular system, does not communicate with it, and it does not contain the choroid plexus.

This structure develops in the fetus starting from week 18 and can be seen up to week 37 in almost all cases. After that, it begins to disappear, which is the reason why we do not see it in normal fetuses after birth [2].

Non-visualization of the CSP can be a normal finding in transabdominal ultrasounds before 18 weeks and after 37 weeks of gestation in 90% of fetuses [3]. Non-visualization of the CSP between 18 and 37 weeks may be an isolated abnormality; however, a thorough assessment of the fetal central nervous system is indicated, as it may be associated with midline malformations of the brain such as septo-optic dysplasia (de Morsier syndrome), alobar or semilobar holoprosencephaly, schizencephaly, hydranencephaly, Apert syndrome, Chiari type II malformation, rhombencephalosynapsis, or agenesis of the corpus callosum.

While absence or non-visualization of the CSP on prenatal imaging has been historically associated with a range of anomalies (e.g., agenesis of the corpus callosum, holoprosencephaly, aqueductal stenosis, ventriculomegaly, schizencephaly, or septo-optic dysplasia), sporadic cases of isolated agenesis of the CSP have been described. In these cases, the corpus callosum is present and no structural anomalies can be seen.

It is important to have reference (normative) values of the CSP volume. We conducted the present investigation because of contrasting findings reported in the existing scholarly literature.

The aim of this study was to determine normative values of the CSP volume between 20 and 40 weeks of gestation. The volume measurements will help to diagnose and understand some of the potential anomalies associated with the CSP. We also assumed as a working hypothesis that the CSP volume measurement would be more reliable than the classical sonographic bidimensional CSP measurements conducted by axial scans on the transventricular and transthalamic planes because the shape of the CSP is uneven. Due to the asymmetric nature of this structure, its width measurement would be inaccurate and would significantly vary among fetuses. Establishing normative values of a more reliable metric could significantly contribute to the knowledge of the anatomic integrity and biometry of the fetal brain as well as to the enhancement of the diagnostic accuracy for potential brain anomalies, thus leading to a better understanding and management of conditions associated with CSP abnormalities.

PATIENTS AND METHODS

The study was approved by the Helsinki Commission of the Western Galilee Medical Center. All pregnant women signed a consent form to participate in the study. Women between 20–40 weeks of gestation were examined abdominally or vaginally depending on the fetal head position.

Exclusion criteria included fetal chromosomal or structural malformations, intrauterine growth retardation, women with gestational diabetes, and women with hypertension or other systemic illnesses.

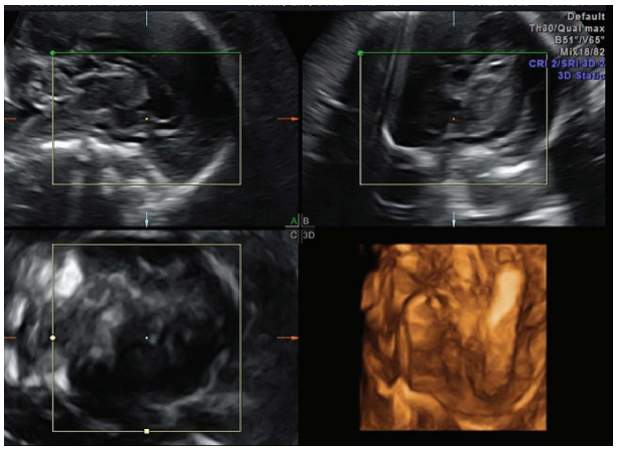
Measurement was performed using three-dimensional (3D) ultrasound. Patients were examined using transvaginal ultrasound (TVUS) with an endocavitary 5- to 9-MHz probe or trans-abdominal sonography (TAS) with 3–5 MHz transducers (Voluson E-8, GE Medical Systems, Milwaukee, WI, USA), depending on the fetal position. The fetal head was scanned at the mid-sagittal plan where both the corpus callosum and the CSP were visible [Figure 1A]. The Virtual Organ Computer-aided Analysis (VOCAL) software program (4D View® Version 10.x, GE Healthcare, USA) was applied using the maximal sweep angle to ensure that the entire CSP volume was included. Volume measurements were performed after patient discharge using 30° rotations of the volume of interest; thus, a sequence of six sections of the volume was measured. The CSP volume was measured manually by drawing the contour of the area of interest of each section [Figure 1B].

The results of these measurements were not disclosed to the women and were not used for clinical management purposes.

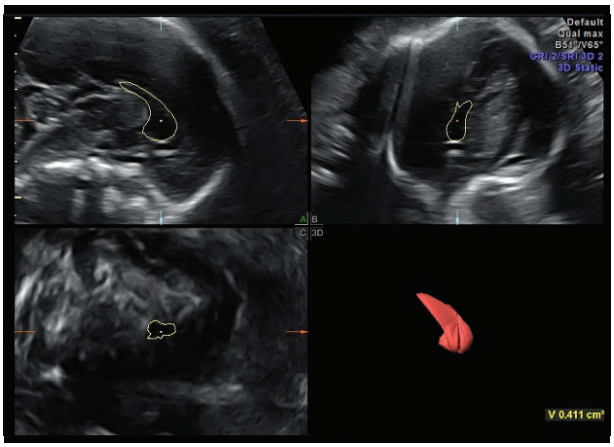
Figure 1: Sectional plans and volume rendering of the CSP area in a 22-week-old fetus

CSP = cavum septi pellucidi

[A]



[B] CSP volume measurement indicating 0.411 cc



RESULTS

The study included 161 women. We were able to measure CSP volume in 158 women (98.1%). All the children were born with a proper Apgar score, and their physical examination was normal. Table 1 shows the indications for testing. The most frequent reason for testing was ultrasound level 2, indicated in 56 cases (34.8% of all samples). Fetal growth was the second most common indication, with 25 cases (15.5%). Other notable indications included the evaluation of placental location in 16 cases (9.9%) and biophysical profiles in 19 cases (11.8%), both critical for assessing the well-being of the fetus and the placenta. Less common indications, each represented in only one or two cases, included specific conditions like fetal pyelectasis, targeted central nervous system (CNS) examination, and suspicion of cystic findings in the abdomen, among others.

CSP width ranged from 2.7 to 8.2 mm. CSP volume varied from 0.03 to 1.78 ml (mean CSP volume 0.508 ± 0.372 ml). To describe the relationship between gestational age and biparietal diameter (BPD) and CSP width and volume, the following formulas were adjusted:

- CSP (volume. ml) = -0.042 + 0.008 × BPD ($P < 0.001$)
- CSP (width, mm) = 1.730 + 0.052 × BPD ($P < 0.001$)
- CSP (volume, ml) = 0.058 + 0.016 × gestational age ($P = 0.003$)
- CSP (width, mm) = 1.859 + 0.123 × gestational age ($P < 0.001$)

Table 1. Indication for testing for each woman

Indication for testing	Number	Percentage
Fetal pyelectasis	1	0.6
Length of cervix	13	8.1
Targeted CNS examination	1	0.6
Amniocentesis	2	1.24
Suspicion of cystic finding in the abdomen	1	0.6
maternal tachycardia	1	0.6
Abdominal pain	5	3.1
Suspected placental abruption	6	3.7
Placental location	16	9.9
Fetal growth	25	15.5
Ultrasound level 2	56	34.8
Cesarean section scar thickness	13	8.1
Breech presentation	2	1.24
Biophysical profile	19	11.8

CNS = central nervous system

A significant, moderate relationship was found between BPD and CSP width (r=0.484), as well as between the width of the CSP and gestational age (r=0.535). However, the relationships between BPD (mm) and CSP (ml) volume and between the CSP volume and the gestational age yielded small, not significant values (r=0.295 and r=0.229, respectively) [Table 2].

DISCUSSION

In our study, we set norms related to 3D measurements of CSP. We assumed that CSP volume measurement using 3D ultrasound would be more accurate given the fact that the CSP is not a symmetrical structure; thus, using 3D ultrasound would be more accurate than just measuring diameters. The norms for measuring CSP width have been set in several studies and although the maximum CSP value was between 9–10 ± 2 mm, there were relatively significant differences between the different studies. This difference is probably due to measurements at different heights. This issue shows the need for measuring 3D volume in which the entire volume is measured no matter what the shape of the structure is.

A review of 111 prenatal magnetic resonance imaging scans and 90 prenatal ultrasound reports of absent fetal CSP noted both modalities had a high degree of accuracy and concordance with postnatal imaging, and a range of clinical outcomes was possible. For these reasons, long-term patient follow-up is necessary [3-7]. In the mid-trimester, non-visualization of the anechoic CSP in an axial section of the brain using transabdominal ultrasound does not always predict absence of the corpus callosum. In these situations, direct visualization of the corpus callosum and pericallosal arteries using the median plane of the brain should be the next step. On rare occasions, the CSP is obliterated or echogenic, but the corpus callosum is normal [8].

It is important to have reference values and for this purpose some investigators defined such values for the CSP. Its width was found to vary between 16 and 34 weeks, with mean normal values increasing from 3.0 to 6.3 mm as the biparietal diameter increased from 40 to 90 mm [9]. In addition, an increase in the length of the CSP has been observed in hypoplastic left heart syndrome, and both the length and the width increased in dextro-transposition of the great arteries [10-13].

Our findings indicated that CSP volume remained constant throughout pregnancy, as did width measure-

Table 2. CSP volume (ml) according to gestational age (in weeks)

Gestational age	N	Mean ± standard deviation	Median	95% confidence interval for mean	Minimum	Maximum
20–21	18	0.2583 ± 0.25559	0.1790	0.1312–0.3854	0.04	1.17
22–23	27	0.4403 ± 0.20869	0.4110	0.3577–0.5228	0.15	1.01
24–25	19	0.4285 ± 0.31233	0.2740	0.2780–0.5791	0.19	1.49
26–27	12	0.5353 ± 0.34849	0.4960	0.3139–0.7568	0.15	1.40
28–29	18	0.6634 ± 0.43144	0.5900	0.4488–0.8779	0.17	1.47
30–31	16	0.5769 ± 0.33774	0.5850	0.3969–0.7568	0.10	1.32
32–33	17	0.5082 ± 0.45645	0.3700	0.2736–0.7429	0.03	1.78
34–35	13	0.6404 ± 0.46935	0.5900	0.3568–0.9240	0.08	1.70
36–37	12	0.8005 ± 0.41762	0.7100	0.5352–10.0658	0.19	1.48
38–40	6	0.2450 ± 0.11996	0.2650	0.1191–0.3709	0.06	0.40
Total	158	0.5083 ± 0.37206	0.4000	0.4499–0.5668	0.03	1.78

ments. No correlation was found between gestational age or BPD and CSP volume. The width measurement is a much simpler measurement and does not require significant experience in fetal ultrasound testing expensive and difficult instrumentation, or high skills to operate it. Therefore, it seems to us that, although CSP volume measurement is more accurate regarding the CSP's anatomical shape, it is sufficient to measure its width.

CONCLUSIONS

The measurement of CSP volume exhibited a poor correlation with gestational age; however, the volume did not exceed 2 ml regardless of gestational age. This information can be used in assessing pathologies involving the CSP. Further studies are needed to replicate our findings.

Correspondence

Dr. R. Khamisy-Farah
Dept. Obstetrics and Gynecology, Clalit Health Service, Akko 24664, Israel
Email: rkhamisy@yahoo.com

References

1. Jou HJ, Shyu MK, Wu SC, Chen SM, Su CH, Hsieh FJ. Ultrasound measurement of the fetal cavum septi pellucidi. *Ultrasound Obstet Gynecol* 1998; 12 (6): 419-21.
2. Hosseinzadeh K, Luo J, Borhani A, Hill L. Non-visualisation of cavum septi pellucidi: implication in prenatal diagnosis? *Insights Imaging* 2013; 4 (3): 357-67.
3. Barkovich AJ, Norman D. Absence of the septum pellucidum: a useful sign in the diagnosis of congenital brain malformations. *AJR Am J Roentgenol* 1989; 152 (2): 353-60.
4. Malinger G, Lev D, Kidron D, Heredia F, Hershkovitz R, Lerman-Sagie T. Differential diagnosis in fetuses with absent septum pellucidum. *Ultrasound Obstet Gynecol* 2005; 25 (1): 42-9.
5. Falco P, Gabrielli S, Visentin A, Perolo A, Pilu G, Bovicelli L. Transabdominal sonography of the cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. *Ultrasound Obstet Gynecol* 2000; 16 (6): 549-53.
6. Pilliod RA, Pettersson DR, Gibson T, et al. Diagnostic accuracy and clinical outcomes associated with prenatal diagnosis of fetal absent cavum septi pellucidi. *Prenat Diagn* 2018; 38 (6): 395-401.
7. Malinger G, Lev D, Oren M, Lerman-Sagie T. Non-visualization of the cavum septi pellucidi is not synonymous with agenesis of the corpus callosum. *Ultrasound Obstet Gynecol* 2012; 40 (2): 165-70.
8. Chaoui R, Heling KS, Zhao Y, Sinkovskaya E, Abuhamad A, Karl K. Dilated cavum septi pellucidi in fetuses with microdeletion 22q11. *Prenat Diagn* 2016; 36 (10): 911-15.
9. Saadeh M, Zhao Y, Galadima H, Chaoui R, Sinkovskaya E, Abuhamad A. Relationship between cavum septi pellucidi measurements and fetal hypoplastic left heart syndrome or dextro-transposition of the great arteries. *J Ultrasound Med* 2018; 37 (7): 1673-80.
10. Edwards TJ, Sherr EH, Barkovich AJ, Richards LJ. Clinical, genetic and imaging findings identify new causes for corpus callosum development syndromes. *Brain* 2014; 137 (Pt 6): 1579-613.
11. Cinar A, Sezik M, Yalcin SE, Yavuz A. Reference intervals and reliability of cavum septi pellucidi volume measurements by three-dimensional ultrasound between 19 and 24 weeks' gestation. *J Perinat Med* 2020; 49 (3): 333-39.
12. Lee JK, Wu J, Bullen J, et al. Association of cavum septum pellucidum and cavum vergae with cognition, mood, and brain volumes in professional fighters. *JAMA Neurol* 2020; 77 (1): 35-42.
13. Zhao D, Cai A, Wang B. An investigation of the standardization of fetal cavum septi pellucidi measurements using three-dimensional volumes of the fetal head. *J Clin Ultrasound* 2019; 47 (6): 331-8.