Medical Science

pISSN 2321–7359; eISSN 2321–7367

Evaluation of the normal ratio of fetal brain choroidal plexus size to fetal head size at 11 to 13 weeks of gestation to obtain useful sonographic markers in spina bifida rule out

Tahereh Ghasemi[1], **Ayda Roostaee**[2], **Zeinab Safarpour Lima**[2], **Ladan Younesi Asl**[2*]

To Cite:
Ghasemi T, Roostaee A, Safarpour-Lima Z, Younesi-Asl L. Evaluation of the normal ratio of fetal brain choroidal plexus size to fetal head size at 11 to 13 weeks of gestation to obtain useful sonographic markers in spina bifida rule out. Medical Science 2022; 26:ms374e2351.
doi: https://doi.org/10.54905/disssi/v26i127/ms374e2351

Authors' Affiliation:
[1]Department of Radiology, School of Medicine, Shahid Akbar-Abadi Hospital, Iran University of Medical Sciences, Tehran, Iran
[2]Shahid Akbarabadi Clinical Development Unit (ShACRDU), Iran University of Medical Sciences, Tehran, Iran

[*]**Corresponding author**
Ladan Younesi Asl, Shahid Akbarabadi Clinical Development Unit (ShACRDU), Iran University of Medical Sciences,
Tehran, Iran
Email: ladanyoonesi@yahoo.com

Peer-Review History
Received: 11 June 2022
Reviewed & Revised: 14/June/2022 to 09/September/2022
Accepted: 18 September 2022
Published: 20 September 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Background: Early detection of open spina bifida (OSB) with ultrasound at 11 to 13 weeks of gestation is considered useful, but no information has been provided on the size and shape of the choroid plexus. Therefore, the aim of this study was to determine the normal ratio of the size of the choroid plexus of the fetal brain to the size of the fetal head at 11 to 13 weeks of gestation to rule out spina bifida. *Material and Methods:* Aimed to measure cervical transparency (NT: nuchal transparency) during the first trimester of pregnancy and at 11 to 13 weeks of gestation, the pregnant women who has only one fetus were screened and then were checked using E8 or E10 ultrasound machine. Our study was performed during April 2020 to December 2021. *Results:* The results of our study on 203 embryos are consisting of normal values of crown-rump length (CRL), biparietal diameter (BPD), the length of Choroid plexus (CPL), head area (HA), head circumference (HC), and choroid plexus area (CP-A). Evaluating the ratio of these indicators shows a significant positive correlation between CPA and other indexes include CRL, BPD, HC and HA ($p<0.001$). Additionally, significant positive correlations between CPL and others include BPD and HC, ($p<0.001$) and negative correlations between CRL and CPL/OFD and between CRL and CP-A/HA ($p<0.05$) was seen. *Conclusion:* With respect to these result it seems that these indicators can be used to distinguish healthy infants.

Keywords: Fetal brain choroidal plexus, Gestation, Sonographic markers, Spina bifida

1. INTRODUCTION

Spina bifida occulta (SBO) is a childhood spinal development disease and that last into adulthood if it doesn't heal on its own. This disorder, which affects 1

in 1000 newborns, is characterized by a defect in the formation of the posterior arch (Garne et al., 2005, Khoshnood et al., 2015). Although the diagnostic importance of this illness has been recorded in the first trimester, nearly 60% of cases were detected with open spina bifida (OSB) by ultrasound at this period, and in the second trimester generally newborns were at second for OSB (Syngelaki et al., 2019). As a result, current research has demonstrated the importance of ultrasound-derived indicators in the screening of OSB cases (Chen et al., 2017). The diagnostic signs include the non visualization of the fourth ventricular choroid plexus (CP) and intracranial translucency (IT) (Chen et al., 2017).

The choroid plexus grows in tandem with the brain's ventricles, adapting and specializing to form a blood-brain barrier and aid to continual creation of cerebrospinal fluid (CSF). Between the weeks 11 and 13 of pregnancy, this structure comprises of two highly echogenic forms that fill the fetus' lateral ventricles (Sepulveda & Won, 2013). During the first trimester of pregnancy, changes in the choroid plexus display a "butterfly" sign which is the most sensitive marker for diagnosing structural brain problems such acrania and holoprosencephaly (Sepulveda & Won, 2013). Besides, its size is different from the lateral ventricles and has been linked to aneuploidy and has been used as a measure of ventriculomegaly in early pregnancy (Loureiro et al., 2012 and Manegold-Brauer et al., 2017). During the weeks 11 and 13 of gestation, OSB is associated with the increment of the CP length ratio to frontal occipital diameter (OFD) in fetuses. They revealed a reduction in lateral ventricular fluid volume and the choroid plexus (CP) occupied the whole headspace as a "dry brain" marker (Chaoui et al., 2020).

Other signs of this marker include the leakage of cerebrospinal fluid leaking and CP progression into the lateral ventricles. Based on their data, nearly 80% of fetuses with OSB had a CP-to-OFD ratio more than two standard deviations of predicted mean (Chaoui et al., 2020). In the study of Kalafat et al., (2021) through investigating the optimal mean ratio of chorionic plexus to occipito frontal diameter ratio, a positive predictive value of 90.9% was reported. Due to the availability of this method, further research should be considered to corroborate these and other markers.

Consequently, the present study was aimed to specify the normal ratio of fetal choroid plexus to head size between the weeks 11 to 13 of gestation to make appropriate sonographic markers to make precise decisions about spina bifida.

2. MATERIAL AND METHODS

Our study is a cross-sectional study in which the pregnant women with single fetuses who referred for their routine screening during the first trimester of pregnancy to measure the thickness of the nuchal translucency (NT: nuchal translucency) during April 2020 to December 2021. Embryos were examined using a high-resolution voluson E8 or E10 ultrasound machine with a transabdominal-vaginal ultrasound during the weeks 11 and 13 of gestation.

Crown-rump length (CRL), head circumference (HC), choroid plexus area (CP-A), choroid plexus length (CP-L), fetal head area (HA): head area and occipitofrontal diameter (OFD) were measured. The ellipse function of the ultrasound system was used to measure CP-A, HC, and HA in this investigation. For any of CP tissues, their longest length was considered and choroid plexus length was calculated as their mean.

Statistical analysis

The data was analyzed by SPSS and graph pad prism software. Descriptive statistics were expressed as mean and standard or median deviation (distance between quartiles) for quantitative variables and absolute and relative frequency for qualitative variables. Pearson or Spearman correlation test was used to examine the relationship between variables and linear regression was used to examine the effect of variables on the response.

Ethical consideration

All data were confidential and were only used for scientific research. The data was kept private, and only the researchers can access the information of participants. Moreover, participation in this research was voluntary, and prior to participation, each participant was provided written consent. The data analysis and publication process did not require any identifiable personal information. This research was approved by Iran University of medical science with code IR.IUMS.FMD.REC.1399.213.

3. RESULTS

Descriptive statistics obtained from a study of 203 infants at 11-13 weeks of gestation, were recorded. Accordingly, (table 1), Crown-rump length (CRL), was between 50 mm to 79 mm with a mean of 60.78 ± 5.61 mm. Head circumference (HC) and fetal head area (HA) were measured in fetuses aged 11 to 13 weeks and ranged from 55 to 91 mm with a mean of 70.96 mm and 226 to 672 mm with a mean of 383.43 mm, respectively.

Table 1 Descriptive Statistics associated with sonographic marker for screening of open spina bifida

	Minimum	Maximum	
	Statistic	Statistic	Mean±SD
CRL	50.00	79.00	60.78±5.61
BPD	15.50	31.00	19.07±2.27
HC	55.00	91.00	70.96±7.06
Cp area Rt	39.00	111.00	62.75±12.51
CP area Lt	37.00	101.00	63.84±12.84
CPA total	78.00	208.00	126.39±24.05
HA	226.00	672.00	383.43±75.61
CP-A/HA	0.23	0.44	0.33±0.04
CP Length Rt	9.60	18.40	12.83±1.52
CP Length Lt	9.00	20.00	12.94±1.63
CPL mean	9.65	19.00	12.89±1.51
OFD	17.40	23.40	23.64±14.64
CP-L/OFD	0.45	0.73	0.57±0.06
Valid N (listwise)			

The size of the plexus choroid in these embryos was measured using two different indicators: choroid plexus area (CP-A) and choroid plexus length (CP-L). The choroid plexus area index (CP-A) was 78 to 208 mm, with an average of 126.39 mm, and the choroid plexus length (CP-L) was 9.65 to 19 mm, with an average of 12.89 mm. In 11 to 13 weeks of gastation, the occipitofrontal diameter (OFD) of the fetuses varied from 17.4 to 23.4, with an average of 23.64. CP-A/HA and CP-L/OFD, two of the most essential indices for diagnosing brain abnormalities, were evaluated, with CP-A/HA ranging from 0.23-0.44 and a mean of 0.33 and CP-L/OFD ranging from 0.45-0.73 and a mean of 0.57.

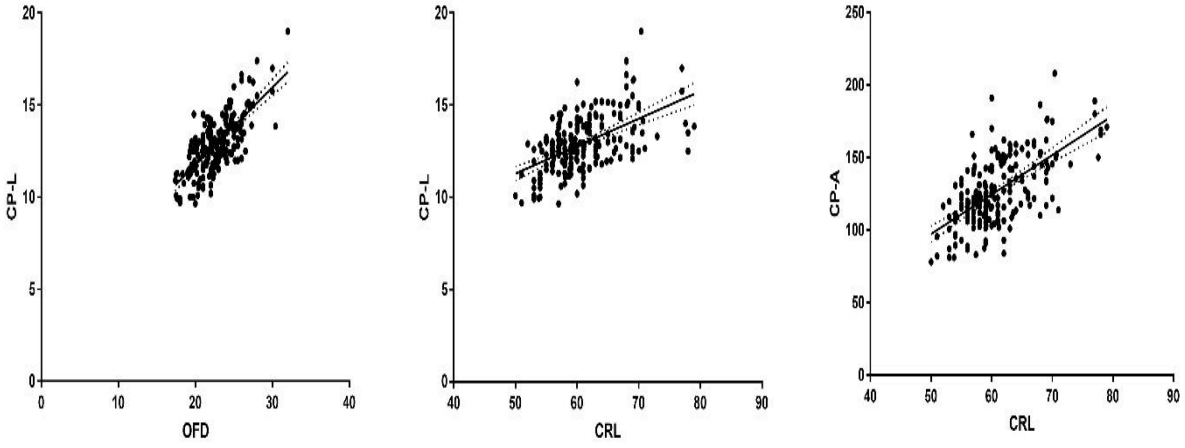

Figure 1 Scatter plots for specifying the correlations between crown-rump length (CRL), occipito frontal diameter (OFD), the length of Choroid plexus (CPL), head area, and choroid plexus area (CP-A).

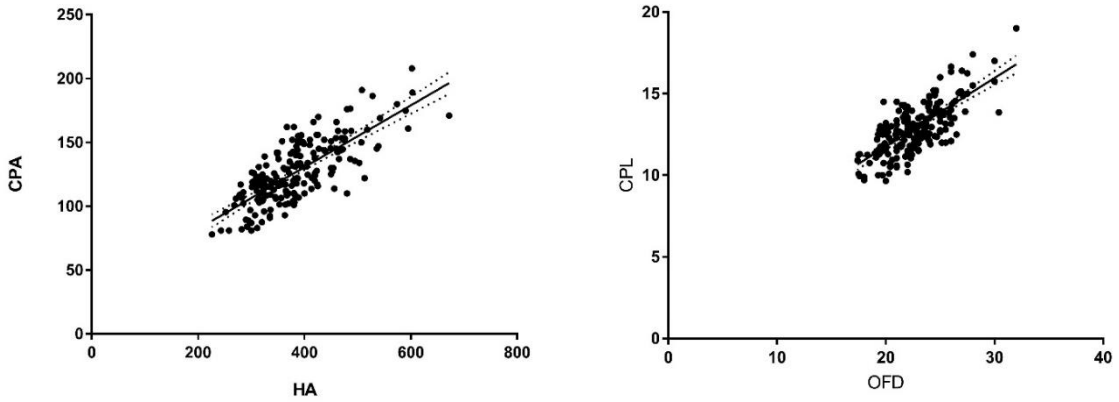

Figure 2 Scatter plots of correlations between the length of Choroid plexus (CPL), head area and occipitofrontal diameter (OFD), choroid plexus area (CP-A), and head area (HA).

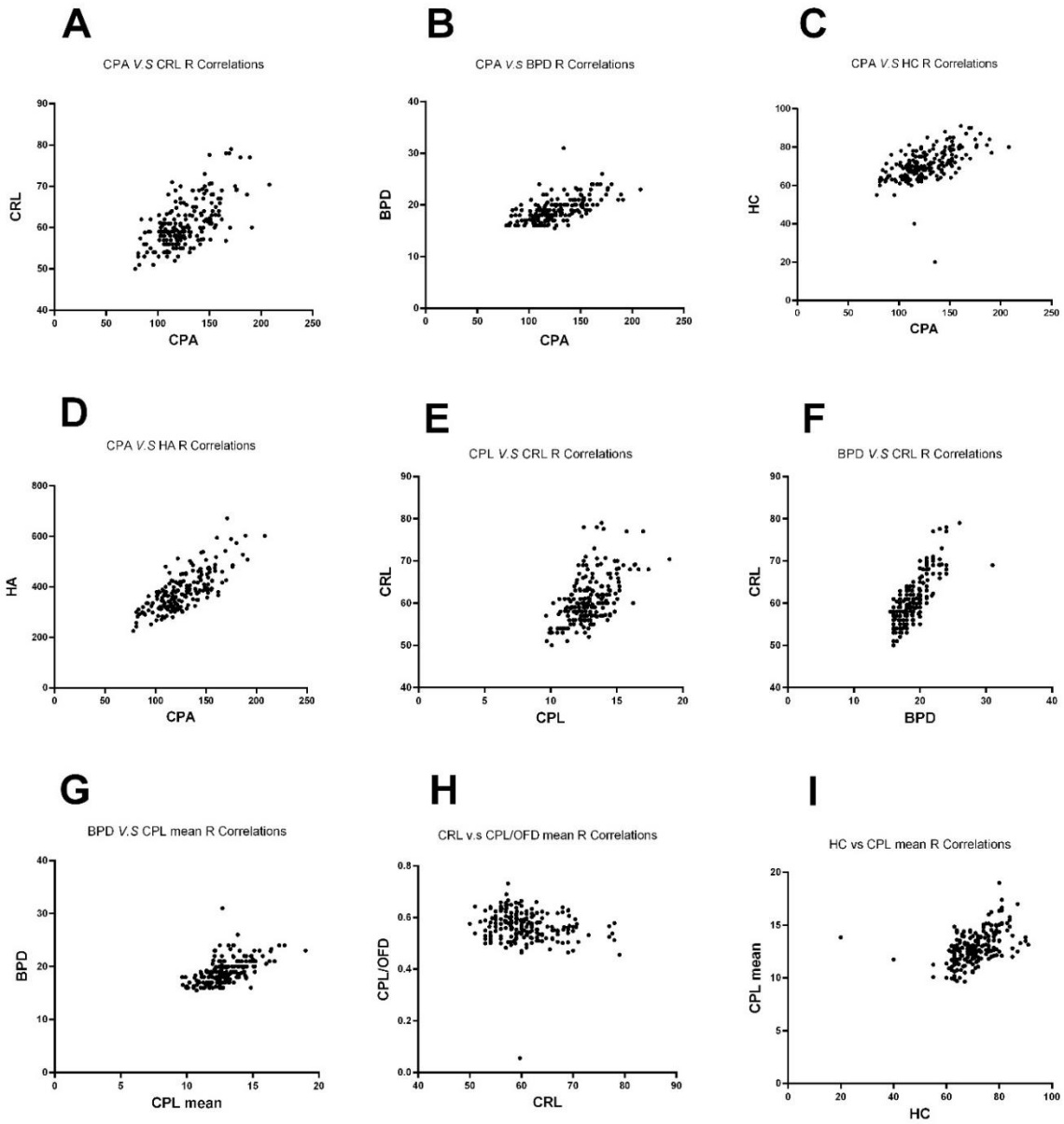

Figure 3 Scatter plots of correlations between crown-rump length (CRL), choroid plexus area (CP-A), the length of Choroid plexus (CPL), head area and occipito frontal diameter (OFD), head circumference (HC) and head area (HA).

As observed in figure 1, by examining the correlation between CPL and OFD, CPL and CRL and between CP-A and CRL, the significant positive correlation was observed. Therefore, increasing OFD and CRL has led to a significant increase in CPL. Similarly, higher CP-A levels were observed in healthy infants with larger CRLs. According to figure 2, increase in HA and OFD led to a significant increase in choroid plexus indices such as CPA and CPL and a significant positive correlation was observed between them. By examining the correlation between fetal size indices, BPD, CRL and HC with CP-A/HA and CP-L/OFD indices, a significant negative correlation was observed between them ($p<0.05$) (Figure 3).

4. DISCUSSION

Compared to healthy embryos, open Spina bifida embryos have a smaller OFD and BPD, as well as a longer mean CP length and a higher mean CP length to OFD or BPD ratio (Kalafat et al., 2021). In this study, 203 healthy fetuses between the ages of 11-13 weeks who underwent first trimester screening including nuchal translucency and nasal bone ultrasound were studied. Comparing the data from our study with other related reports demonstrated that fetuses between the weeks 11 and 13 had approximately the same CRLs, OFD, BPD and CPL. In our investigation, a rise in CRL was related with a large increase in CP-A and a significant drop in CP-L/OFD and CP-A/HA, similar to another study (Chaoui et al., 2020). In our study, HC and BPD indices, likewise directly associated to CRL, were found to be adversely correlated with CP-L/OFD and CP-A/HA, similar to CRL.

The size of the CP-A, CP-A/HA, and CP-L/OFD ratios in OSB fetuses faced a dramatical increase compared to the normal population. At 11-13 weeks of pregnancy, the choroid plexus (CP) nearly entirely fills the fetus' lateral ventricles as a pair of enormous hypercogenic structures. Previous research has focused on CPs and their natural form during early pregnancy, called as the "butterfly sign," which aids in the diagnosis of alobar holoprosencephaly (Sepulveda and Wong, 2013). Availability of asymmetry in CP tissues between the left and right sides has been described explained as a normal variety (Abu-Rustum et al., 2013). This index was not explored in our research, but it appears to be beneficial by evaluating it and identifying its standard limit in normal fetuses' vs OSB cases. In addition, comparing CP size to lateral ventricular size has revealed aneuploidy and ventriculomegaly (Loureiro et al., 2012; Manegold-Brauer et al., 2016). However, because normal fetuses were screened and the gestational age was 11-13 weeks, these markers were not explored in our study. Studying this index, on the other hand, looks to be a useful technique to figure out OSB.

The most probable reason for changes in CP-head size in fetuses with OSB is a temporary decrease in cerebrospinal fluid in the brain ventricular system of affected fetuses between the weeks 11-13. As a result of the spinal deformity's leak, the head is relatively tiny (Karl et al., 2012; Khalil et al., 2013; Bernard et al., 2012). We showed changes in lateral ventricular CP levels in this study and then we advised to measure them for a precise objective assessment. If so, various indicators in this study include CRL, BPD, HC, CP area right, CP area left, CPA total, HA, CPA/HA, CP length right, CP length left, CPL mean, OFD, CPL/OFD was analyzed. We verified the predictive utility of mean CP length relative to OFD in a quite large set of pregnancies. In addition, other indicators investigated in this study can also be taken into account.

5. CONCLUSION

Examining the indicators of this study along with other similar studies, and the changes in these indicators that occur in fetuses with OSB, it seems that these indicators can be used to distinguish healthy infants from infants with OSB. Furthermore, numerous signs must be evaluated at the same time and referenced.

Acknowledgement

We thank the participants who were all contributed samples to the study.

Author Contributions

All authors contributed to the design of the study, as well as data collection and analysis, and the writing of the manuscript. All authors read and approved the final manuscript

Ethical approval

The study was approved by the Medical Ethics Committee of Iran. (Ethical approval code: IR.IUMS.FMD.REC.1399.213).

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Bernard Jp, Cuckle Hs, Stirnemann Jj, Salomon Lj. Screening for fetal spina bifida by ultrasound examination in the first trimester of pregnancy using fetal biparietal diameter. Am J Obstet Gynecol 2012; 20(7): 306. e1-306. e5.
2. Chaoui R, Benoit B, Entezami M, Frenzel W, Heling KS, Ladendorf B, Pietzsch V, Sarut Lopez, A. Ratio of fetal choroid plexus to head size: simple sonographic marker of open spina bifida at 11–13 weeks' gestation. Ultrasound Obstet Gynecol 2020; 55: 81-86.
3. Chen FC, Gerhardt J, Entezami M, Chaoui R. Detection of Spina Bifida by First Trimester Screening - Results of the Prospective Multicenter Berlin IT-Study. Ultraschall Med 2017; 38: 151-157.
4. Garne E, Loane M, Dolk H, De Vigan C, Scarano G, Tucker D, Stoll C, Gener B, et al. Prenatal diagnosis of severe structural congenital malformations in Europe. Ultrasound Obstet Gynecol 2005; 25: 6-11.
5. Kalafat E, Ting L, Thilaganathan B, Papageorghiou AT. Diagnostic accuracy of fetal choroid plexus length to head biometry ratio at 11 to 13 weeks for open spina bifida. Am J Obstet Gynecol 2021; 224: 294.e1-294.e14.
6. Karl K, Benoit B, Entezami M, Heling K. Small biparietal diameter in fetuses with spina bifida on 11–13-week and mid-gestation ultrasound. Ultrasound Obstet Gynecol 2012; 40: 140-144.
7. Khalil A, Coates A, Papageorghiou A, Bhide A. Biparietal diameter at 11–13 weeks' gestation in fetuses with open spina bifida. Ultrasound Obstet Gynecol 2013; 42: 409-415.
8. Khoshnood B, Loane M, De Walle H, Arriola L, Addor MC, Barisic I, et al. Long term trends in prevalence of neural tube defects in Europe: population based study. Bmj 2015; 351: h5949.
9. Loureiro T, Ushakov F, Maiz N, Montenegro N. Lateral ventricles in fetuses with aneuploidies at 11-13 weeks' gestation. Ultrasound Obstet Gynecol 2012; 40: 282-7.
10. Manegold-Brauer G, Oseledchyk A, Floeck A, Berg C, Gembruch U. Approach to the sonographic evaluation of fetal ventriculomegaly at 11 to 14 weeks gestation. BMC Pregnancy Childbirth 2016; 16: 3.
11. Sepulveda W, Wong AE. First trimester screening for holoprosencephaly with choroid plexus morphology ('butterfly'sign) and biparietal diameter. Prenat Diagn 2013; 33: 1233-1237.