

The Role of Fetal Transcerebellar Diameter in Determining Gestational Age in the Second Trimester

İkinci Trimesterde Gebelik Yaşının Belirlenmesinde Fetal Transserebellar Çapın Rolü

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Abstract

Objective: To evaluate the role of transcerebellar diameter (TCD) as an independent parameter for estimation of gestational age (GA) in the second-trimester and its diagnostic performance compared with other fetal biometric parameters (FBP) such as biparietal diameter (BPD), femur length (FL), abdominal circumference (AC), and head circumference (HC).

Materials and Methods: This retrospectively-designed cross-sectional study included recorded data of 120 healthy women between 19 and 24 weeks of gestation with normal singleton pregnancies who applied to our department for second-trimester anomaly scan between December 2020 and 2021. GA was calculated using nomograms on TCD and other FBP and compared with GA determined by last menstrual period (LMP). The relationship between GA based on LMP and FBP was evaluated. The correlation between parameters was evaluated with the Pearson correlation test.

Results: The mean BPD, HC, AC, FL, TCD weeks and TCD values (mm) were 21.39±0.99, 21.36±0.98, 21.28±0.95, 21.24±1, 20.11±0.73, 21.21±1.09, respectively. The highest correlation for GA estimation was shown with FL (r=0.858), followed by AC (r=0.843), TCD values (mm) (r=0.834), and the TCD (week) (r=0.822), respectively. All "r" values indicated a strong correlation and ranged from 0.794 to 0.858. All parameters used in the detection of GA in the second-trimester were statistically significant (p<0.001).

Conclusion: TCD provides successful results in the accurate estimation of GA in the second-trimester. Therefore, we recommend routine TCD measurements for anomaly screening

Öz

Amaç: Bu çalışmanın amacı transserebellar çapın (TSÇ) ikinci trimesterde gebelik yaşının (GY) tahmininde bağımsız bir parametre olarak rolünü ve biparietal çap (BPC), femur uzunluğu (FU), karın çevresi (KÇ) ve baş çevresi (BÇ) gibi diğer fetal biyometrik parametrelerle karşılaştırıldığında tanılal performansını değerlendirmektir.

Gereç ve Yöntemler: Retrospektif olarak tasarlanmış bu kesitsel çalışmaya Aralık 2020 ile 2021 arasında bölümümüze ikinci trimester anomali taraması için başvuran, normal tekil gebeliğe sahip 19-24 gebelik haftalar arasında 120 sağlıklı kadına ait veriler dahil edildi. GY, TSÇ ve diğer fetal biyometrik parametrelerin nomogramları

kullanılarak hesaplandı ve son adet tarihi (SAT) ile belirlenen GY ile karşılaştırıldı. SAT'a göre belirlenen GY ile fetal biyometrik parametreler arasındaki ilişki değerlendirildi. Parametreler arasındaki korelasyon için Pearson korelasyon testi kullanıldı.

Bulgular: Ortalama BPC, BÇ, KÇ, FU, TŞÇ haftaları ve TŞÇ ölçümleri (mm) sırasıyla $21,39\pm 0,99$, $21,36\pm 0,98$, $21,28\pm 0,95$, $21,24\pm 1,20$, $11\pm 0,73$ ve $21,21\pm 1,09$ idi. GY tahmini için en yüksek korelasyon FU ($r=0,858$), ardından KÇ ($r=0,843$), TŞÇ ölçümleri (mm) ($r=0,834$) ve ortalama TŞÇ haftası ($r=0,822$) ile bulundu. Tüm "r" değerleri güçlü korelasyona işaret etmekte ve 0,794 ile 0,858 arasında değişmekteydi. İkinci trimesterde GY tespitinde kullanılan tüm parametreler istatistiksel olarak anlamlıydı ($p<0,001$).

Sonuç: TŞÇ, ikinci trimesterde GY'nin doğru tahmininde başarılı sonuçlar vermektedir. Bu nedenle anomali taraması için rutin TŞÇ ölçümlerini öneriyoruz.

Introduction

Gestational age (GA) is the most used parameter as a standardization tool in the detection and evaluation of fetal development in pregnancy follow-up. Although the last menstrual period (LMP) is the most widely used modality for estimating GA, it can be a wrong guide (1-3). The reliability of LMP is low due to reasons such as inability to remember correctly, irregular menstrual cycle and differences in ovulation time, and first-trimester bleeding. It has been emphasized that only half of pregnant women can remember their LMPs correctly in the literature (1,2).

Fetal development is a dynamic process and no single biometric parameter exists completely accurate or reliable throughout pregnancy. Estimation of GA in the detailed ultrasonographic examination performed in the second-trimester is routinely made with fetal biometric parameters (FBP) such as femur length (FL), biparietal diameter (BPD), head circumference (HC), and abdomen circumference (AC) (4-8). These FBP can be affected by fetal development disorders and skeletal anomalies (9-11).

Transcerebellar diameter (TCD) is considered one of the new and reliable ultrasound parameters that attract the attention of researchers, especially for the estimation of GA in early pregnancy. This is due to the progressive growth of the cerebellum throughout the entire pregnancy period and to little effect from growth restrictions (4,5).

A considerable number of pregnant women who can't remember their LMPs are admitted to the hospital for the first time in the second-trimester. For this reason, accurately determining the GA of the fetus in this period is a challenge encountered in routine practice. Additively, ultrasonography is performed for anomaly scan between 18-24 weeks according to LMP in the second-trimester in Turkey.

In the light of all of these, we evaluated the role of TCD as an independent parameter for estimation of GA in the second-trimester and its diagnostic performance compared to routine FBP.

Materials and Methods

This cross-sectional retrospective study was conducted by the principles of the Declaration of Helsinki. Procedures were thoroughly explained to all participants and their informed consent was obtained. The ethics committee of Muğla Sıtkı Koçman University approved this study (protocol no: 210049, date: 18.01.2022).

In this study, we evaluated 120 healthy women between 19 to 24 weeks of gestation with normal singleton pregnancies without any risk factors who applied to our radiology department (Menteşe State Hospital) for the second-trimester anomaly scan during the one year between December 2020-2021. Only women aged 18-40 years, who were sure of their LMP, or who had a gestational dating scan up to 14 weeks, were included. We excluded women who have medical comorbidities such as heart disease, diabetes mellitus, chronic hypertension, gestational hypertension, and anti-phospholipid antibody syndrome, pregnancy-related pathologies such as oligohydramnios, polyhydramnios, congenital malformations and intrauterine growth restriction (IUGR). Also, pregnancies with a difference of more than 2 weeks between early pregnancy gestational dating screening and LMP (if performed) were excluded. All images and other information about the pregnancy were accessed from the hospital information system.

Ultrasound examinations were obtained using the Mindray DC-8 Expert (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China) ultrasound system with 3.2 MHz curvilinear probe (SC5-1E). After the pregnant women were placed on the examination table in the supine position, the second-trimester

anomaly scan was performed by one radiologist with 4 years of experience. Routine FBP were measured using the standard method (12).

From the plane of the BPD, the probe was moved slightly below the transventricular plane to show the septum pellucidum anteriorly, defining the thalamus centrally, while the cerebellum and cisterna magna were viewed posteriorly in the transcerebellar plane (13,14). This plane gives the widest TCD. The measurement of TCD was done by placing the on-screen caliper at the outer margins of the cerebellum (Figure 1) (15). GA was obtained within weeks for measured routine FBP, and TCD, as determined by the embedded software in the Mindray ultrasound scanner based on Hadlock et al.'s (16) and Snijders and Nicolaides et al.'s (17) nomograms. In addition, the measured TCD value (mm) was also noted.

Statistical Analyses

Data were analyzed using the SPSS (v.22 software for windows). Data normality was evaluated with the Kolmogorov-Smirnov test. While, Student t-test and One-Way ANOVA test were used for the parametric data, Kruskal-Wallis test was used for the non-parametric data. TCD, BPD, HC, AC, and FL values were compared according to GA using Pearson correlation. The coefficient of determination (R^2) was calculated. Univariate linear regression was used to identify significant predictors of GA and its relationship with TCD. $P < 0.05$ was considered statistically significant.

Results

The mean age of the women was found 28.35 ± 4.66 years (between 18-40). GAs of them were between 19-24 weeks according to their LMPs. The mean week of gestation was 21.04 ± 2.1 . Six groups were obtained according to gestational week. There was



Figure 1. TCD measurement method
TCD: Transcerebellar diameter

no significant relationship between GA and the age of the women.

The mean BPD, HC, AC, FL, and TCD weeks which were calculated with nomogram and TCD values (mm) were 21.39 ± 0.99 , 21.36 ± 0.98 , 21.28 ± 0.95 , 21.24 ± 1 , 20.11 ± 0.73 , 21.21 ± 1.09 , respectively. The mean values of BPD, HC, AC, FL, TCD value (mm) and the estimated TCD week divided into weeks according to GA calculated with LMP were given and Kruskal-Wallis analysis showed that all FBP increased with advancing GA as the fetus grows ($p < 0.05$) (Table 1).

The GA and all parameters showed a strong correlation. FL showed the strongest correlation with GA ($p < 0.05$) (Table 2). Strong correlations were detected between both TCD values (mm) and weeks with other FBP ($p < 0.05$). TCD value (mm) showed the strongest correlation with BPD (Table 3). Scatter diagrams were obtained to show the relationship between GA and other parameters (Figure 2). We found a formulation using linear regression analysis to estimate GA: $TCD(mm) \times (0.783 + 4.947)$.

Discussion

Accurate estimation of GA is a crucial point for clinicians for the management of pregnancies, and for planning a normal delivery or elective cesarean section. Since a significant number of pregnant women don't have any information about their LMPs and therefore the gestational week cannot be determined in the second-trimester, it becomes difficult to comment on conditions such as pregnancy progression, and fetal macrosomia or IUGR. Some inconsistencies may arise for each of the FBP in the determination of GA in the second-trimester. In the third-trimester, the differences may increase for more than 2-3 weeks (5,18). It is also known that routine FBP can be affected by fetal development disorders and skeletal anomalies (9-11). Therefore, a simple, reliable, independent parameter is needed for the accurate estimation of GA.

The cerebellum, consisting of a median part called the vermis and two hemispheres are surrounded by temporal and occipital bone in the posterior fossa. This anatomical position provides that it is less affected by external pressure (4,19,20). It is stated that the formation of the cerebellum, which can be seen ultrasonographically in the earliest 10-11th weeks

Table 1. Mean values and statistical analysis of BPD, HC, AC, FL, TCD (weeks) and TCD (mm) divided by weeks according to GA

GA*	n	BPD*			HC*			AC*			FL*			TCD (mm)			TCD*		
		Mean	SD	Mean-rank	Mean	SD	Mean-rank	Mean	SD	Mean-rank	Mean	SD	Mean-rank	Mean	SD	Mean-rank	Mean	SD	Mean-rank
19	5	19.66	0.54	8	19.57	0.53	6.9	19.71	0.49	9.4	19.6	0.34	8.1	19.4	0.44	7.6	18.89	0.33	8.1
20	26	20.54	0.87	29.4	20.48	0.82	28.42	20.42	0.81	28.4	20.30	0.80	27.96	20.23	0.73	28.44	19.47	0.52	28.73
21	46	21.37	0.56	58.98	21.31	0.57	56.12	21.16	0.50	53.98	21.17	0.53	55.41	21.10	0.50	55.41	20.04	0.35	55.74
22	33	21.92	0.62	81.55	21.98	0.51	86.77	21.92	0.47	88.59	21.87	0.49	87.86	21.87	0.71	86.56	20.52	0.48	85.68
23	7	22.67	0.75	103.21	22.76	0.75	105.14	22.65	0.59	108.64	22.51	0.70	103.21	22.73	0.99	103.5	21.14	0.67	104.14
24	3	23.14	1.08	109.67	22.67	0.97	101.83	22.91	1.33	102.5	23.33	1.41	107.17	23.9	0.79	117.5	21.81	0.46	117.33
Kruskal-Wallis Test		x ² :60.07		x ² :69.65		x ² :74.11		x ² :71.77		x ² :70.89		x ² :72.08							
		p<0.001		p<0.001		p<0.001		p<0.001		p<0.001		p<0.001		p<0.001		p<0.001			

SD: Standard deviation, GA: Gestational age, BPD: Biparietal diameter, HC: Head circumference, AC: Abdomen circumference, FL: Femur length, TCD: Transcerebellar diameter, *week

of pregnancy, is completed in the 15th week (4,21,22). However, some studies evaluating the closure of the vermis, have shown that the vermis is open at a rate of 13% at 16 weeks of gestation and even the posterior-inferior surface of the vermis can be found to be open until half of the 17th gestational week. For this reason, these studies suggest that cerebellum examinations should be performed after the 16th week (23). In the literature, sonographic examination of TCD reveals a linear relationship with GA in the second-trimester. Measurements in millimeters are approximately equal or close to GA in weeks. The cerebellar growth curve tends to flatten in the later stages of pregnancy (5,20).

In our study, the TCD values (mm) of 120 fetuses (between 19-24 weeks) ranged from 19.40 to 23.90 mm (mean 21.21±1.09 mm). Desdicoglu et al. (24) reported that the average TCD values according to the weeks ranged from 19.89 to 26.42 mm (1,124 pregnant cases between 19-24 weeks were evaluated). Göynümer et al. (22) found that TCD ranged between 18.86 and 25.29 mm in 586 pregnant women between 19-24 weeks of gestation. Although the TCD values in these two studies were almost similar to the current study, numerical differences are striking, especially towards the end of the second-trimester. Considering that only 8.3% of the cases in our study included pregnant women at 23rd and 24th weeks, this was thought to be the reason for the difference from other studies. When our three cases at 24 weeks of gestation were examined in detail, it is seen that TCD values were 23.0 mm, 24.2 mm, and 24.5 mm, respectively. We found that the mean TCD week was 20.11±0.73, and similar to other studies we showed that the mean TCD week increased in parallel with the increase in gestational weeks. In a study performed by Reddy et al. (4), with 50 pregnant women between 15 and 28 weeks, the mean TCD week in the second-trimester was found to be 21.12±4.45.

In our study, the highest correlation for GA estimation was shown with FL (r=0.858), followed by AC (r=0.843), TCD values (mm) (r=0.834), and TCD week (r=0.822), respectively. All “r” values indicated strong correlation and ranged from 0.794 to 0.858. All parameters used in the detection of GA in the second-trimester were statistically significant (p<0.001) and were compatible with the literature in this respect. Also, when the correlation of TCD values with routine FBP was evaluated, we found that the

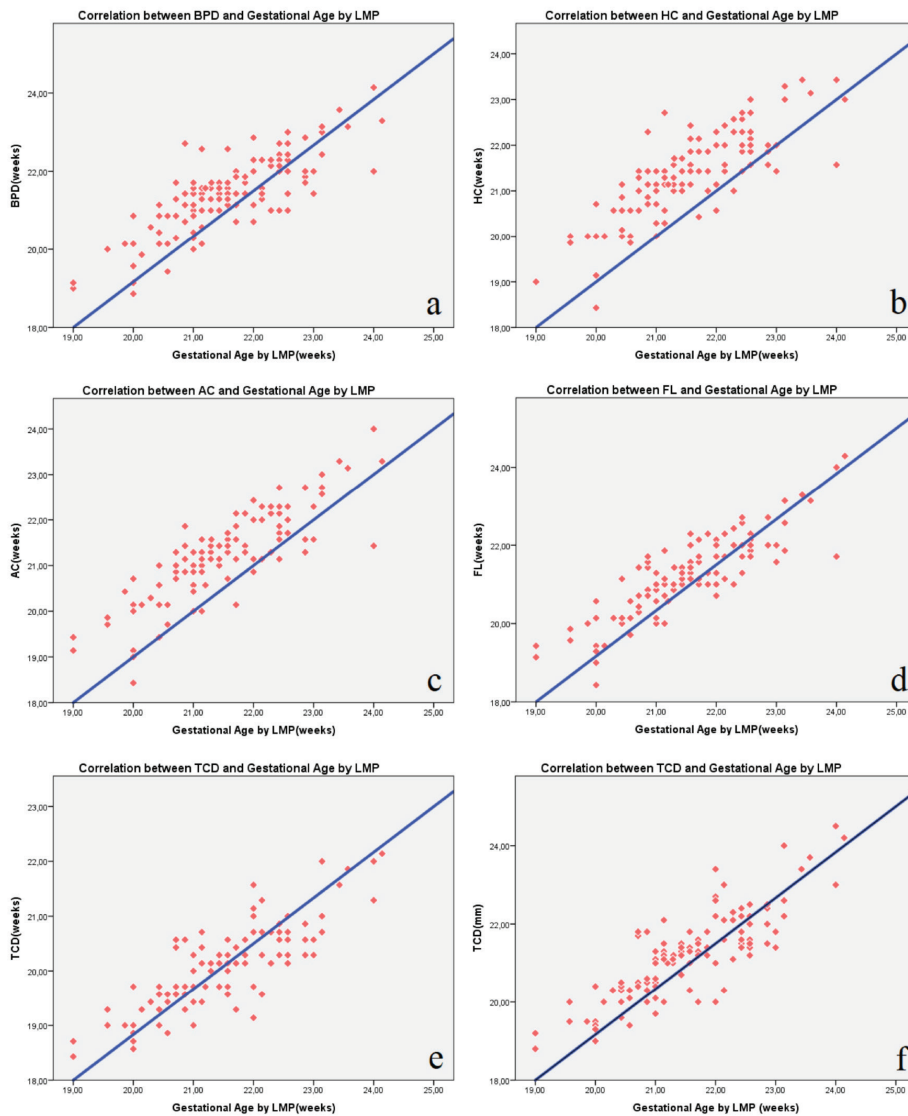


Figure 2. Scatter diagrams showing a linear correlation between the GA and the estimated GA by the BPD (a), HC (b), AC (c), FL (d), and TCD week (e). There is also a linear correlation between GA and measured TCD values (mm) (f)
 GA: Gestational age, BPD: Biparietal diameter, HC: Head circumference, AC: Abdomen circumference, FL: Femur length, TCD: Transcerebellar diameter

best correlation was with BPD ($r=0.884$; $p<0.001$). Göynümer et al. (22) defined that the TCD values high correlated with GA and HC, similar to ours. Desdicioglu et al. (24) found that the TCD values was strong correlated with FL ($r=0.881$; $p<0.01$) and GA ($r=0.802$; $p<0.01$). In the study of Reddy et al. (4), the highest correlation for GA prediction in the second-trimester (between 15-28 weeks) was shown with the TCD week ($r=0.998$), followed by FL ($r=0.997$) and HC ($r=0.997$), respectively. In many studies conducted in the third-trimester, it was found that the TCD week

and TCD values (mm) showed a higher correlation for GA prediction than other FBP (4-6,20). The highest correlation between GA and FL in current study may be explained by the lower rate of inconsistencies that occur in measurements made with routine FBP in the second-trimester compared to third-trimester. The fact that 91.6% of the pregnant women in our research population are in the early weeks of the second-trimester (weeks 19-22), supports this situation. Many second-trimester studies stated the correlation between GA and TCD were higher than our results

(4,22,24). We think that this was because other studies were nomogram studies, and their sample size was higher and more homogenous than the present study. Also, a strong correlation was found between TCD and other FBP [BPD had the highest correlation ($R^2=0.78$, $p<0,001$)].

The correlation between the TCD value (mm) and the TCD week was found to be very strong ($R^2=0.98$, $p<0.001$). The TCD values correlated more strongly with GA than with the TCD week ($r=0.834$ vs. $r=0.822$, $p<0.001$). Göynümer et al. (22) showed that TCD values have different percentile values over 22 weeks compared to other parameters in the Turkish population, and the variation increased when compared with other nomograms in the literature. We think that the correlation differences between the device-dependent algorithm in calculating the GA depending on TCD week and TCD values, may be related to this in our study. This finding suggests that nomograms may need to be updated based on

countries' populations. In a nomogram analysis study by Chavez et al. (25), the agreement between the TCD values and the TCD week calculated with the nomograms was found to be quite high ($R^2=0.94$; $p<0.001$). It has been shown that this correlation is superior in the second-trimester compared to the third trimester. This shows TCD values (mm) have a high success rate at the second-trimester level in estimating the gestational week directly. In the light of the literature and our data, we can say that TCD values measured in millimeters are almost equal to the week of gestation in the second-trimester.

Our study had some limitations. Firstly, the heterogeneity of the case distribution and the presence of a small sample size, especially at weeks over 23th. Therefore, further studies with large samples may be needed to support our findings. Secondly, since fetuses with normal development without gender discrimination were included in our study, no comparison was made regarding gender. The inclusion of only normal pregnancies in the study should be kept in mind as another limitation. Finally, a small proportion of pregnant women had not an age-confirming ultrasound during the first-trimester.

Table 2. Correlations of different ultrasonographic FBP with GA in the second-trimester

FBP	Compared with GA*		
	r	R ²	p-value
BPD*	0.794	0.630	<0.001
HC*	0.822	0.676	<0.001
AC*	0.843	0.711	<0.001
FL*	0.858	0.736	<0.001
TCD*	0.822	0.676	<0.001
TCD (mm)	0.834	0.696	<0.001

GA: Gestational age, BPD: Biparietal diameter, HC: Head circumference, AC: Abdomen circumference, FL: Femur length, TCD: Transcerebellar diameter, FBP:Fetal biometric parameters, *week

Table 3. Correlations of different ultrasonographic FBP with TCD values (mm) in the second-trimester

FBP (week)	Compared with TCD (mm)		
	r	R ²	p-value
BPD	0.884	0.781	<0.001
HC	0.881	0.776	<0.001
AC	0.876	0.767	<0.001
FL	0.869	0.755	<0.001
TCD	0.993	0.986	<0.001

TCD: Transcerebellar diameter, BPD: Biparietal diameter, HC: Head circumference, AC: Abdomen circumference, FL: Femur length, FBP: Fetal biometric parameters

Conclusion

TCD provides useful and consistent results in the detection of GA, especially in the second-trimester. Therefore, TCD measurements in anomaly screening will increase the success in estimating GA. Large-scale data obtained by multicenter evaluation of more fetuses and comparing sex, ethnic group, normal and abnormal fetuses will provide more precise results.

Ethics

Ethics Committee Approval: The ethics committee of Muğla Sıtkı Koçman University approved this study (protocol no: 210049, date: 18.01.2022).

Informed Consent: Procedures were thoroughly explained to all participants and their informed consent was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.E.O., Concept: Y.E.O., Design: Y.E.O., Data Collection or Processing: Y.E.O., V.S.Ö., Analysis or Interpretation: Y.E.O., V.S.Ö., Literature Search: Y.E.O., V.S.Ö., Writing: Y.E.O., V.S.Ö.

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