

Fetal prenatal thickness and its correlated ratios between 16 and 23 weeks of gestation

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Abstract

Objective: The aim is to investigate the correlations and distributions of ratios of fetal prenatal thickness (PT), biparietal diameter/prenasal thickness (BPD/PT) and prenasal thickness/nasal bone length (PT/NBL) to the weeks of gestation (WG).

Methods: Women with healthy singleton pregnancies between 16 and 23 weeks of gestation were included in the study. With the biometric evaluations of fetuses, the fetal structures were examined in details. Prenasal thickness and nasal bone were measured and BPD/PT and PT/NBL ratios were calculated in each case. The correlation between PT and the week of gestation was evaluated by regression analysis. PT percentiles according to the weeks of gestation were calculated. The correlations between BPD/PT and PT/NBL ratios and the weeks of gestation were investigated and their percentile values were calculated.

Results: We included a total of 393 pregnant women in our study. It was found that PT increased significantly together with the week of gestation, and regression equation was calculated as $PT = WG \times 0.24 - 0.87$; $R=0.65$; $p<0.01$. Mean PT was 3.9 ± 0.7 mm and 95th percentile values were 4 mm at 16–18 weeks of gestation, 4.7 mm at 19 weeks of gestation, 5 mm at 20–21 weeks of gestation, and 6.0 mm at 22–23 weeks of gestation. When the correlation between PT and BPD was investigated, it was seen that there was a linear increase ($R=0.64$; $p<0.01$). However, there was no significant correlation between BPD/PT ratios and the week of gestation ($p=0.29$). Mean BPD/PT ratio was 12.3 ± 1.6 and 5th percentile value was 10. A significant correlation was found between PT and NBL ($R=0.63$; $p<0.01$). According to the regression analysis, there was a negative correlation between PT/NBL ratio and WG ($PT/NBL = -WG \times 0.016 + 1.02$; $R=0.25$; $p<0.01$). Mean PT/NBL ratio was 0.7 ± 0.1 and 95th percentile values were calculated as 1.1–0.9 between 16 and 23 weeks of gestation.

Conclusion: While PT and PT/NBL ratio changes together with the week of gestation between 16 and 23 weeks of gestation, BPD/PT ratio remains constant. Therefore, we think that using BPD/PT <10 (5th percentile) value in screenings could be more useful and practical.

Keywords: Biparietal diameter, nasal bone, prenasal thickness, week of gestation.

Özet: 16–23 gebelik haftaları arasında fetal prenasal kalınlık ve ilişkili oranları

Amaç: Fetüste prenasal kalınlık (PT), bipariyetal çap/prenasal kalınlık (BPD/PT) ve prenasal kalınlık/nazal kemik uzunluğu (PT/NBL) oranlarının gebelik haftası (GH) ile ilişkileri ve dağılımlarının araştırılması amaçlanmıştır.

Yöntem: Çalışmaya 16–23 gebelik haftaları arasında tekil sağlıklı gebelikler çalışmaya dahil edildi. Fetüsün biyometrik değerlendirilmesi ile birlikte fetal yapılar ayrıntılı olarak incelendi. Prenasal kalınlık ve burun kemiği ölçüldü ve her olguda BPD/PT ve PT/NBL oranları hesaplandı. PT'nin gebelik haftası ile ilişkisi regresyon analizi ile değerlendirildi. Gebelik haftalarına göre PT persentilleri hesaplandı. BPD/PT ve PT/NBL oranlarının gebelik haftası ile ilişkileri araştırıldı ve persentil değerleri bulundu.

Bulgular: Çalışmaya toplam 393 gebe dahil edildi. PT'nin gebelik haftası ile anlamlı olarak arttığı bulundu ve regresyon denklemi $PT = GH \times 0.24 - 0.87$; $R=0.65$; $p<0.01$ olarak hesaplandı. Ortalama PT 3.9 ± 0.7 mm ve 95. persentil değerleri 16–18 gebelik haftalarında 4 mm, 19. gebelik haftasında 4.7 mm, 20–21 gebelik haftalarında 5 mm ve 22–23 gebelik haftalarında 6.0 mm olarak saptandı. PT'nin BPD ile korelasyonu araştırıldığında lineer olarak arttığı ($R=0.64$; $p<0.01$) bulundu. Fakat BPD/PT oranları ile gebelik haftası arasında anlamlı korelasyon saptanmadı ($p=0.29$). Ortalama BPD/PT 12.3 ± 1.6 ve 5. persentil değeri de 10 bulundu. PT ile NBL arasında anlamlı korelasyon saptandı ($R=0.63$; $p<0.01$). Regresyon analizinde PT/NBL oranı ile GH arasında negatif korelasyon saptandı ($PT/NBL = -GH \times 0.016 + 1.02$; $R=0.25$; $p<0.01$). Ortalama PT/NBL oranı 0.7 ± 0.1 olup; 95. persentil değerleri 16–23 gebelik haftalarında 1.1–0.9 olarak saptandı.

Sonuç: 16–23 gebelik haftaları arasında PT ve PT/NBL oranı gebelik haftası ile değişmekte iken BPD/PT oranı sabit kalmaktadır. Bundan dolayı taramalarda BPD/PT <10 (5. persentil) değerinin kullanılmasının daha kullanışlı ve pratik olabileceği düşünülmektedir.

Anahtar sözcükler: Bipariyetal çap, nazal kemik, prenasal kalınlık, gebelik haftası.

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Introduction

Down syndrome is characterized with specific facial features such as flat face, hypoplastic midfacial structures and skin edema.^[1] While the most important markers for the screening for Down syndrome are increased nuchal translucency and lack of nasal bone in the first trimester,^[2,3] they are increased nuchal edema, lack of nasal bone or its hypoplasia, ventriculomegaly and the presence of aberrant right subclavian artery.^[4] Recently, it has been reported that prenasal thickness (PT) as well as nuchal thickness can also be used as a marker in skin edema evaluation and the screening for Down syndrome^[5] and that type IV collagen in basal membrane of prenasal skin tissues in cases with Down syndrome is significantly in high volume.^[6]

Persico et al.^[7] reported that PT increased significantly in fetuses with Down syndrome and that PT was >95th percentile in 73.1% of the cases. De Jong-Pleij et al.^[8] reported in their study that PT presented significant positive correlation with the week of gestation and prenasal thickness/nasal bone length (PT/NBL) ratio remained constant during the week of gestation, and emphasized that the PT/NBL ratio was >95th percentile in all of 30 fetuses with Down syndrome included in their study and PT/NBL ratio was a strong marker. Özcan et al.^[9] evaluated 242 cases with normal karyotype and 24 cases with Down syndrome, and reported PT at >95th percentile in 54.2% of the cases with Down syndrome; however, they stated that there was 80% chance to identify the syndrome with 5% false positivity ratio for PT/NBL >0.75 threshold value. Tournemire et al.^[10] showed in their study that PT/NBL ratio was a better marker than PT and NBL alone to identify Down syndrome (area under ROC curve: 0.99–0.82 and 0.91), and reported sensitivity as 88.5% and specificity as 100% for PT/NBL >0.98 to identify Down syndrome. Hagen et al.^[11] conducted their study on 130 cases with Down syndrome, and reported that PT/NBL ratio was >0.8 in 89.2% of the cases and it was the most identified marker. They found PT/NBL ratio >0.8 as a marker in 3 cases with Down syndrome but they found no other marker in these three cases; therefore, they emphasized that PT/NBL ratio is one of the most important markers in the screening of Down syndrome.

In this study, we investigated the correlations and distributions of PT measurements, and PT/NBL and biparietal diameter/prenasal thickness (BPD/PT) ratios to the weeks of gestation in fetuses without any anomaly between 16 and 23 weeks of gestation.

Methods

A total of 393 women with singleton pregnancy between 16 and 23 weeks of gestation selected through a cross-sectional method between January 3, 2013 and January 31, 2015 were included in the study. For the week of gestation, last menstrual period was taken into consideration; for those who did not know their last menstrual period, crown-rump length at first trimester or biparietal diameter measurements at second trimester were taken into consideration. Cases with structural and karyotype anomalies, multiple pregnancies, those with stillbirth history, cases who developed preterm rupture of membranes and intrauterine growth retardation and those with systemic disease were excluded from the study.

Ultrasonographic examinations were done by a single specialist through transabdominal (2–5 MHz) approach with General Electric Voluson E8 (Milwaukee, WI, USA) ultrasonography device. With the biometric evaluations of fetuses, the fetal structures were examined in details. Nasal bone was displayed on the plane where chin and lips of the fetus on midsagittal facial profile and through low brightness with 45 or 135 degree angle where maxilla and frontal bone are limited. The measurements were done as maximum length between the highest and lowest ends of nasal bone. In the same plane, PT measurement was carried out by measuring the length between fronto-nasal angle and the external surface of skin (**Fig. 1**). PT/NBL and BPD/PT ratios were calculated for each fetus.

The analysis of the patient data was done by SPSS 11.5 (SPSS Inc., Chicago, IL, USA). Pearson's correlation test, regression analysis and descriptive statistical

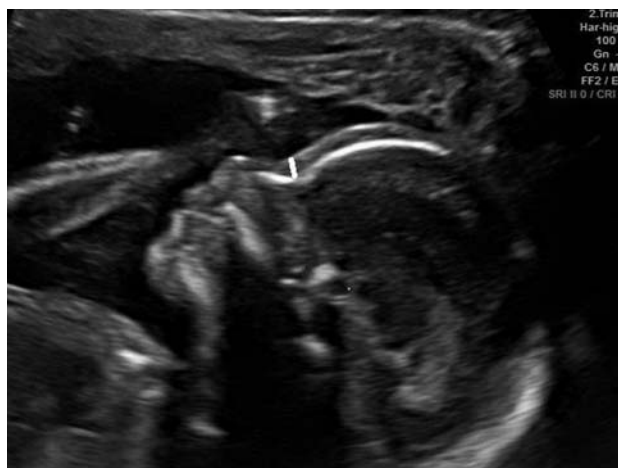


Fig. 1. Ultrasound image of prenasal thickness measurement.

Table 1. Prenasal thickness nomogram (mm) between 16 and 23 weeks of gestation.

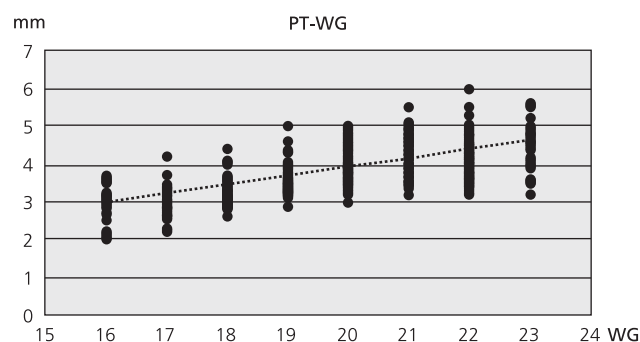
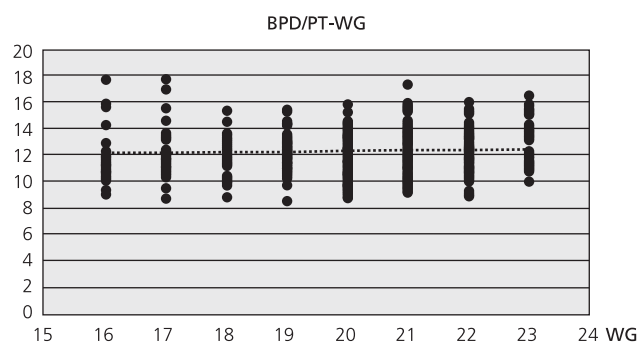
WG	Percentiles						
	5.	10.	25.	50.	75.	90.	95.
16	2.0	2.0	2.7	3.0	3.1	3.8	4.0
17	2.0	2.2	3.0	3.0	3.3	4.0	4.0
18	3.0	3.0	3.0	3.4	4.0	4.0	4.0
19	3.0	3.0	3.2	3.9	4.0	4.0	4.7
20	3.0	3.1	4.0	4.0	4.0	5.0	5.0
21	3.6	4.0	4.0	4.0	4.7	5.0	5.0
22	3.4	4.0	4.0	4.0	5.0	5.0	6.0
23	3.5	4.0	4.0	4.5	5.0	5.2	6.0

(mean, standard deviation, percentiles) analyses were carried out. Kolmogorov-Smirnov test was used for the presence of normal distribution, and Kruskal-Wallis and Mann-Whitney tests were used to compare groups. The results were evaluated within 95% confidence interval and according to $p < 0.05$ significance level.

Results

A total of 393 pregnant women complying with the inclusion criteria were included in the study, and the mean week of gestation was 20 ± 1.9 and BPD was 47.3 ± 6.3 mm during the evaluation. Mean PT was 3.9 ± 0.7 mm (2–6 mm). It was found that PT increased significantly together with the week of gestation (WG). The regression equation between PT and WG was found as $PT = WG \times 0.24 - 0.87$; $R = 0.65$; $p < 0.01$ (**Fig. 2**). PT nomogram displaying significant difference between 16 and 23 weeks of gestation is shown **Table 1**. Ninety-fifth percentile value of PT was 4 mm at 16–18 weeks of gestation, 4.7 mm at 19 weeks of gestation, 5 mm at 20–21 weeks of gestation, and 6.0 mm at 22–23 weeks of gestation.

When the correlation between prenasal thickness and BPD was investigated, it was seen that it increased linearly and the correlation was significant. The regression equation between PT and BPD was found $PT = BPD \times 0.071 + 0.573$; $R = 0.64$; $p < 0.01$ by the linear regression analysis. No significant correlation was found between the

**Fig. 2.** The correlation between prenasal thickness and week of gestation.**Fig. 3.** The correlation between the ratio of biparietal diameter to prenasal thickness and the week of gestation.**Table 2.** The nomogram of the ratio of biparietal diameter to prenasal thickness (BPD/PT).

WG	Percentiles						
	5.	10.	25.	50.	75.	90.	95.
16–23	10	10	11	12	13	14	15

week of gestation and BPD/PT ratios calculated for each case ($p=0.29$) (**Fig. 3**). Mean BPD/PT ratio was 12.3 ± 1.6 and 5th percentile value was 10 (**Table 2**).

A significant correlation was found between prenatal thickness and nasal bone, and the formula was determined as $PT = 0.393 \times NBL + 1.71$ ($R=0.63$; $p<0.01$). There was a good correlation between NBL and WG ($NBL = 0.451 \times WG - 3.42$; $R=0.79$; $p<0.01$). According to the regression analysis, there was a very weak negative correlation between PT/NBL ratio and WG ($PT/NBL = -WG \times 0.016 + 1.02$; $R=0.25$; $p<0.01$) (**Fig. 4**). Mean PT/NBL ratio was 0.7 ± 0.1 , and its nomogram between 16 and 23 weeks of gestation is shown in **Table 3**. Ninety-fifth percentile values of PT/NBL between 16 and 23 weeks of gestation was 1.1–0.9.

Discussion

The prenatal thickness measurement and its correlation with Down syndrome were first reported by Maymon et al. in 2005. The authors reported that PT increased together with the week of gestation and median values were between 2.8 and 4.1 during 16–23 weeks of gestation.^[5] Similarly, we found in our study that PT increased significantly between 16 and 23 weeks of gestation ($R=0.65$; $p<0.01$) and median values were 3–4.5 mm. Persico et al.^[7] also found a similar correlation between PT and the week of gestation ($R=0.781$; $p<0.01$), and they reported mean PT values between 2.4 and 4.6 mm in 135 cases during 16–24 weeks of gestation. De Jong-Pleij et al.^[8] reported median PT values 2.3–6.1 mm in 106 cases during 15–33 weeks of gestation and found that the correlation was better during these weeks of gestation ($R=0.85$; $p<0.001$). Yang et al.^[12]

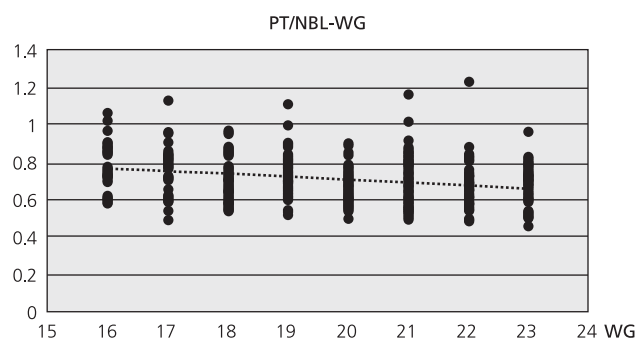


Fig. 4. The correlation between the ratio of prenatal thickness to nasal bone length and the week of gestation.

reported similar correlation between PT and WG during 12–33 weeks of gestation in 143 cases ($R=0.83$; $p=0.004$). It is clear that PT increases together with the week of gestation, and it is understood that the differences in the correlation coefficient is caused by the differences in case number and distribution according to the week of gestation. In our study, there were acceptable case number and range for week of gestation, and we have shown that there is a medium-level correlation. Also, we have found similar correlation between PT and BPD ($R=0.64$; $p<0.01$).

Unlike other studies, we investigated the correlation between PT and BPD and reported the results. We found a positive correlation between PT and BPD ($R=0.64$; $p<0.01$), and also unlike the other studies, we found that BPD/PT ratio we calculated did not change together with the week of gestation ($p=0.29$). We found 5th percentile value of BPD/PT ratio between 16 and 23 weeks of gestation as 10. Since PT ratio changed signif-

Table 3. The nomogram of PT/NBL ratio between 16 and 23 weeks of gestation.

WG	Percentiles						
	5.	10.	25.	50.	75.	90.	95.
16	0.6	0.6	0.7	0.8	0.9	1.0	1.1
17	0.5	0.6	0.7	0.8	0.8	1.0	1.1
18	0.6	0.6	0.6	0.7	0.8	0.9	1.0
19	0.6	0.6	0.7	0.7	0.8	0.9	1.0
20	0.6	0.6	0.6	0.7	0.8	0.8	0.9
21	0.6	0.6	0.6	0.7	0.8	0.9	0.9
22	0.5	0.6	0.6	0.7	0.7	0.8	0.9
23	0.5	0.5	0.6	0.7	0.8	0.8	0.9

icantly together with the week of gestation, we believe that BPD/PT ratio is more practical and easy to use for the screening of Down syndrome. However further studies are needed to determine the sensitivity of BPD/PT ratio to identify Down syndrome.

It is seen in the literature that PT/NBL ratio gets more attention and studied more than PT. The reason was reported that the use of PT/NBL ratio seen as a single and constant ratio was easier and more applicable method since PT increases together with the week of gestation and therefore a separate threshold value is required for each week of gestation.^[5-10] Yang et al.^[12] also reported that PT/NBL ratio remained constant during 12–33 weeks of gestation ($R=0.12$; $p>0.10$) and 95th percentile value was 0.93. However, we found in our study that PT/NBL ratio displayed a weak but significant correlation with the week of gestation ($R=0.25$; $p<0.01$) and we calculated 95th percentile values of PT/NBL 1.1–0.9 during 16–23 weeks of gestation. We believe that this difference results from the case number and distribution according to the week of gestation. There was a medium-level correlation between PT and the week of gestation ($R=0.65$), and the presence of good correlation between NBL and WG confirms the decrease of PT/NBL together with the week of gestation. Yang et al.^[12] also found that the correlation between NBL and WG ($R^2=0.73$) was better than the correlation between PT and WG ($R^2=0.67$). De Jong-Pleij et al.^[8] also reported similar correlation ratios. However, both studies reported a constant correlation between PT/NBL and WG.^[8,9] In our study, we determined that PT/NBL ratio was not constant and considering this as a constant ratio would lead to incorrect evaluation. We believe that it would be better to use this ratio as 1.1 during 16–17 weeks of gestation, 1 during 18–19 weeks of gestation, and 0.9 during 20–23 weeks of gestation.

Conclusion

In conclusion, BPD/PT ratio remains constant while PT and PT/NBL ratio significantly change together with the week of gestation, and therefore we believe that the use of BPD/PT <10 (5th percentile) value would be more convenient and easy. However, more potent studies are needed to determine the sensitivities of PT and BPD/PT ratio in the screening of Down syndrome.

Conflicts of Interest: No conflicts declared.

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