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How much can we evaluate fetal anatomy at 11–13+6 weeks of gestation?

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Abstract

Objective: The aim is to determine how much fetal anatomic structures can be displayed according to different CRL values in addition to the aneuploidy screening at 11–13 weeks which is a part of routine gestational examination.

Methods: In the study planned to be as retrospective descriptive case series, we analyzed the data of a total of 5238 single fetuses which had nuchal screening at 11–13 weeks of gestation between April 1, 2006 and September 30, 2017. We separated fetuses into 4 groups according to the CRL measurements (Group 1: CRL between 45 and 54 mm, Group 2: CRL between 55 and 64 mm, Group 3: CRL between 65 and 74 mm, and Group 4: CRL between 75 and 84 mm). For each group, we calculated imaging rates of organ and body parts of fetuses and carried out statistical analyses.

Results: The mean age of pregnant women was 30.1±4.65 (range: 17 to 46) years, and median CRL value of fetuses was 62 (range: 45 to 84) mm. In all groups, the organs and parts with the highest success of fetal anatomy imaging were upper extremity, lower extremity, cranium, nuchal translucency, nasal bone, vertebra and abdomen, respectively. The imaging rate for all of these structures was above 90%. A four-chambered heart could be identified in 52.6% of all groups, and cardiac outflow tracts were seen in 44.3% of all groups. It was found that kidneys were seen in 52.0% of all groups, and cardiac outflow tracts were seen in 44.3% of all groups. A four-chambered heart could be identified in 52.6% of all groups, and cardiac outflow tracts were seen in 44.3% of all groups. It was found that kidneys were seen in 52.0% of all groups, and cardiac outflow tracts were seen in 44.3% of all groups.

Conclusion: In our study, we found that basic fetal anatomic structures except heart and kidneys can be seen with a success rate over 90% during aneuploidy screening at 11–13+6 weeks of gestation, and as expected the imaging rates were increased parallel to the gestational week. Although the timing of the nuchal screening is favorable at 11th to 12th weeks classically, for the evaluation of fetal anatomy, 12th to 13th week are preferable.

Keywords: 11–13 weeks of gestation, fetal anatomy, ultrasonography, imaging success, first trimester, fetal heart.

Özet: 11–13+haftada fetal anatomiyi ne kadar değerlendirilebiliriz?

Amaç: Rutin gebelik muayenesinin bir parçası olan 11–13+ haftada anöploidi taramasına ilave olarak fetal anatomininkanlar farklı CRL değerlerine göre ne oranda görüntülenebileceği saptamak içinament.

Yöntem: Retrospektif tanımlayıcı olgu serisi olarak planlanan çalışmada, 1.4.2006–30.09.2017 tarihleri arasında, gebelikin 11–13+ haftalarında nukal tarama yapılan toplam 5238 tek fetiye ait veriler analiz edildi. Fetülere CRL ölçümüne göre 4 grub (CRL 45–54 mm arası Grup 1, CRL 55–64 mm arası Grup 2, CRL 65–74 mm arası Grup 3, CRL 75–84 mm arası Grup 4) ayrıldı. Her grup için fetişin organ ve vücut kısımlarının görüntülenebilme oranları hesaplandı ve istatistiksel analizleri yapıldı.

Bulgular: Gebelerin yaş ortalamaları 30.1±4.65 (aralık:17–46), fetülere ortanca CRL değeri 62 (aralık: 45–84) mm idi. Tüm gruplarda fetal anatomi görüntüleme başarısı en yüksek olan organ ve böülümler sırasıyla; üst ekstremite, alt ekstremite, kranyum, mide, mesane, ense kalınlıkları, burun kemiği, vertebra ve abdomen olarak belirlendi. Bu yapılanın hepsinde görüntülenebilme başarısı %90‘un üzerinde idi. Kalp dört odaklı tüm gruplarda %52.6 oranında, kalp büyük damar çıkışları tüm gruplarda %44.3 oranda izlendi. Böbreklerin tüm gruplarda %5.0 orunda gözlenmeli bir belirdi. CRL grupları arasında; kranyum, ense saydamlığı, abdomen duvarı, alt ve üst ekstremite her iki diğer anatominin ve aynı fetal kanalın görüntülenme oranları, istatistiksel anlamıyla farklılıkların en düşük görüntülenen olanları Grup 1’den iken en yüksek oranlar Grup 4’tedir.


Anahtar sözcükler: 11–13 hafta, fetal anatomi, ultrasonografi, görüntülenebilme başarısı, ilk trimester, fetal kalp.
Introduction
Fetal structural anomalies are seen in 2–3% of all pregnancies. Today, ultrasonography (USG) has become an inseparable part of routine prenatal care for the detection of these structural anomalies in developed countries. Although the mid-trimester anatomic USG evaluation performed between 18 and 22 weeks of gestation has been a standard approach to detect fetal structural anomalies for a few decades, the detection of fetal anomalies has increased and it has become possible to diagnose in the earlier weeks of gestation thanks to the continues improvements in the ultrasound resolution and increased experiences of specialists. First trimester detection of structural anomalies supports the early diagnosis of chromosomopathies as they may be concomitant with chromosomopathies while it also provides an early opportunity to get information and investigate the prognosis of isolated structural anomalies and prenatal or postnatal treatment options. It has become possible to detect fetal anomalies during the early weeks of gestation due to the use of transvaginal (TV) USG together with the first trimester USG screening of chromosomal anomalies and increase in the USG resolution in time.

The primary purpose of USG examination in the first trimester was to identify the fetal vitality, to determine fetus number and exact week of gestation. The measurement of nuchal translucency at 11–13+6 weeks of gestation included in the prenatal care beginning from the early 1990s paved the way for the assessment of early fetal anatomy. With the detailed examination of fetal anatomy during first trimester, 27.5–62% of all major structural anomalies can be detected. Sonography at first trimester has become an applicable option and even a routine practice in some institutions. First trimester structural anomaly examination may be more beneficial in populations with high risks such as anomaly history in previous pregnancies particularly for fetal anomalies, high values of nuchal translucency and increased biochemical risk or in populations where second trimester USG is technically difficult as in obese women. Since some fetal structures such as cerebellar vermis or corpus callosum are not completely developed in the first trimester, first trimester examination may detect at least half of the structural anomalies although it cannot rule out abnormalities in these structures. In mid-trimester examination, this rate is reported 60%.

We aimed to investigate the imaging rates of fetal anatomic structures according to different CRL values, and therefore to find out which CRL values would be more ideal for the examination of fetal structural anomalies together with chromosomopathy screening in this examination in addition to the aneuploidy screening at 11–13+6 weeks which is currently a part of the routine gestational examination.

Methods
In this study which was planned as retrospective descriptive case series, the data of 5,238 single fetuses which had nuchal screening at 11–13+6 weeks of gestation between April 1, 2006 and September 30, 2017 were collected retrospectively, and imaging success of various organs and anatomic structures were evaluated retrospectively.

The fetuses were assessed according to the guides of that period (Fetal Medicine Foundation - London - http://www.fetalmedicine.com), and USG examinations were performed transabdominally by two operators using HDI 4000 (Philips Healthcare, Andover, MA, USA) and Voluson 730 Pro, Voluson 730 Expert, Voluson E10 (General Electric Healthcare, Chicago, IL, USA). Transvaginal method was preferred only in cases where NT could not be seen (3%). Fifteen minutes at least and 20 minutes at most was allocated for each pregnant woman. When necessary, color Doppler blood flows were used for the presence and associations of vessels.

Cranial bones, midline falx cerebri, ventricles filled with choroid plexus, intracranial translucency, nuchal translucency, facial orbita, nasal bone, maxilla and mandible, vertebra and skin from cervical area to sacral area, symmetric lung tissues and pleural space in thorax, four-chamber view (the presence of two atriums, two ventricles and septum, space of atrioventricular valves), large vessel crossings, abdominal skin, integrity of anterior wall, stomach, kidneys, umbilical cord, umbilical arteries and bladder, long bones of lower and upper extremities, hands and feet, joint motions, and blood flows of ductus venosus and bilateral uterine artery were seen during fetal anatomic examination. The images were recorded to device memory, their photographs were taken, and they were reported also by recording in the computer system. When related internal structures and other parts could not be seen completely in especially the examinations of face, heart and extremities, no comment was added and the data field for related organ was left empty.
Fetuses were separated into 4 groups according to the CRL measurements (Group 1: CRL between 45 and 54 mm, Group 2: CRL between 55 and 64 mm, Group 3: CRL between 65 and 74 mm, and Group 4: CRL between 75 and 84 mm). For each group, the imaging rates of organ and body parts mentioned above were calculated and statistical analyses were carried out.

SPSS version 16 for Windows (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. For descriptive data, the descriptive statistical methods (mean, standard deviation) were used. Crosstabs were prepared for intergroup rates by descriptive analysis, and the presence or absence of difference among groups was calculated by chi-square test. The significance level was considered p<0.05.

**Results**

The mean age of pregnant women was 30.1±4.65 (range: 17 to 46) years, and median CRL value of fetuses was 62 (range: 45 to 84) mm. Basic recorded data of 5188 pregnant women were accessed, and 50 cases without basic data were excluded from the study. The distribution of pregnant women according to their CRL values is shown in Table 1.

In all groups, the organs and parts with the highest success of fetal anatomy imaging were upper extremity, lower extremity, cranium, stomach, bladder, nuchal translucency, nasal bone, vertebra and abdomen, respectively. The imaging rate for all of these structures was above 90%. The imaging rates of fetal anatomy according to CRL groups are shown in Tables 2 and 3.

The cranium was observed with a rate of 99.3% in all groups. There was no statistically significant difference among CRL groups in terms of observing the cranium (p=0.056).

It was found that the nuchal translucency could be measured in 97.4% of all groups. There was no statistically significant difference among CRL groups in terms of measuring NT (p=0.169).

The nasal bone was seen with a rate of 95.8% in all groups. There was statistically significant difference among CRL groups in terms of imaging the nasal bone (p<0.0001). Group 2 had the highest rate (96.7%) while Group 1 had the lowest rate (92.5%).

The vertebra was seen with a rate of 95.6% in all groups, and there was statistically significant difference among CRL groups in terms of observing the vertebra (p<0.001). While the lowest observation rate was 83.6% in Group 1, the highest rate was 99.0% in Group 4.

The visualization of four-chamber was achieved with a rate of 52.6% in all groups, and there was statistically significant difference among CRL groups in terms of observing the four-chamber (p<0.001). While the lowest rate for observing four cardiac quadrants was 40.1% in Group 1, the highest rate was 64.4% in Group 4.
Cardiac outflow tracts were examined in 4045 fetuses beginning from 2008 and it could be identified with a rate of 44.4% in all groups. There was a statistically significant difference among CRL groups in terms of observing the major cardiac outflow tracts (p<0.001). While the lowest observation rate was 34.3% in Group 1, the highest rate was 60.1% in Group 4. The imaging rates of four-chamber and cardiac outflow tracts are given in Table 4.

The thorax and associated structures were seen with a rate of 90.6% in all groups, and there was statistically significant difference among CRL groups in terms of observing the lungs (p<0.001). While the lowest observation rate was 82.1% in Group 1, the highest rate was 96.2% in Group 4.

The abdominal wall was seen with a rate of 93.4% in all groups, and there was no statistically significant difference among CRL groups in terms of observing the abdomen (p<0.315).

The stomach was seen with a rate of 99.0% in all groups, and there was statistically significant difference among CRL groups in terms of observing the stomach (p<0.001). While the lowest observation rate was 97.1% in Group 1, the highest rate was 99.8% in Groups 3 and 4.

The kidneys were seen with a rate of 52.0% in all groups, and there was statistically significant difference among CRL groups in terms of observing the kidneys (p<0.001). While the lowest observation rate was 33.5% in Group 1, the highest rate was 74.4% in Group 4.

The bladder was seen with a rate of 96.5% in all groups, and there was statistically significant difference among CRL groups in terms of observing the bladder (p<0.001). While the lowest observation rate was 90.0% in Group 1, the highest rate was 99.9% in Group 4.

The details of upper extremities were observed with a rate of 99.8% in all groups, and there was no statistically significant difference among CRL groups in terms of observing the upper extremities (p<0.201).

The lower extremities were observed with a rate of 99.5% in all groups, and there was no statistically significant difference among CRL groups in terms of observing the lower extremities (p<0.299). While the lowest observation rate was 99.1% in Group 1, the highest rate was 99.7% in Group 4.

Discussion

Our study has shown that structural examination of fetus during routine nuchal screening program at 11–13+6 weeks of gestation can be easily done in structures except four-chamber, outflow tracts and kidneys. General anatomical structures except heart, outflow tracts and kidneys had an imaging rate over 90% in proportion to CRL increase.

In a screening study performed for structural abnormalities by using TV USG, it was possible to image fetal anatomy in 94% of the cases except face and heart. Although we reached these rates in our study in time by the increase in the resolution of ultrasonography devices and operators’ experiences and TA USG, we found that certain rates could not be exceeded for imaging heart and kidneys. Successful imaging rates for heart chambers and kidneys were 44.6% and 52.0%, respectively.

In the echocardiography study of Hutchinson et al., the imaging rate for cardiac outflow tracts during 11–13+6 weeks of gestation was 79%. In fact, the authors could identify four-chamber even at 8 weeks of gestation at a rate over 50%. However, Souka et al. could achieve the same rate (79%) for cardiac outflow tracts only during detailed examination at 20–24 weeks of ges-

<table>
<thead>
<tr>
<th>CRL</th>
<th>Four-chamber (n)</th>
<th>Imaging rate for four-chamber (%)</th>
<th>Cardiac outflow tracts (n)</th>
<th>Imaging rate for vein outlets of heart (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–54 mm</td>
<td>799</td>
<td>40.1</td>
<td>637</td>
<td>34.1</td>
</tr>
<tr>
<td>55–64 mm</td>
<td>2373</td>
<td>51.6</td>
<td>1962</td>
<td>42.8</td>
</tr>
<tr>
<td>65–74 mm</td>
<td>1626</td>
<td>57.5</td>
<td>1232</td>
<td>49.4</td>
</tr>
<tr>
<td>75–84 mm</td>
<td>390</td>
<td>64.4</td>
<td>214</td>
<td>60.3</td>
</tr>
<tr>
<td>Total</td>
<td>5188</td>
<td>52.6</td>
<td>4045</td>
<td>44.4</td>
</tr>
</tbody>
</table>
tation. While Souka et al.\textsuperscript{[10]} reported 87.4\% as the imaging rate for four-chamber in the first period and 49.9\% as the imaging rate for cardiac outflow tracts, these rates were 52.6\% and 44.4\% in our study, respectively. In their presentation to detect cardiac anomalies in 519 cases, Dilek et al. from Turkey\textsuperscript{[11]} reported that they documented the images of four-chamber in all cases and the images of cardiac outflow tracts in 75\% of the cases. In our study, the rates of observing outflow tracts are lower than the rates reported by Hutchinson et al.\textsuperscript{[9]} and Dilek et al.\textsuperscript{[11]} and close to the rates reported by Souka et al.\textsuperscript{[10]}

We believe that this is the result of device quality in the first years, not performing special examination on heart and relatively short evaluation period.

Souka et al.\textsuperscript{[3]} combined TA and TV USG in their study in 2004, and reported the imaging rates at 11–14 weeks screening over 99\% in the structures except four-chamber (87.4\%) and kidneys (87.6\%). Ebrashy et al.\textsuperscript{[12]} compared the imaging rates of fetal anatomy at 13–14 weeks of gestation by TA and TV USG, and they reported that the anatomical structures could be observed at a rate over 90\% by TV USG except heart and kidneys. In our study where we evaluated 97\% of the fetuses by TA USG, we obtained rates similar to TA USG rates of that study. In the study of Ebrashy et al., imaging rates of the structures except abdominal wall were below 90\% by TA USG although the examination was performed at only 13 and 14 weeks of gestation. In our study, the rates we found for the same structures are higher.

The detection rate of fetal structural anomalies at 11–13\textsuperscript{+6} weeks was reported 27.5\% in the study of Hernandi and Töröcsik\textsuperscript{[9]} performed on 3991 cases, 53.8\% in the study of Economides et al.\textsuperscript{[14]} performed on 1632 cases, and 22.3\% in the study of Carvalho et al.\textsuperscript{[15]} performed on 2853 cases. Weiner et al.\textsuperscript{[16]} performed fetal anatomy screening at 11–14 weeks of gestation only when they suspected of structural anomaly when examining the fetus on sagittal plane, and they highlighted that approximately 50\% of fetuses with structural anomalies could be detected in this way. Hildebrand et al.\textsuperscript{[17]} reported fatal anomalies with a rate of 88\% at the first trimester and 92\% at the second trimester, the anomalies that may have adverse results in future with a rate of 35\% at the first trimester and 44\% at the second trimester, and all anomalies during routine screening with a rate of 13\% at the first trimester and 29\% at the second trimester. In Turkey, Dane et al.\textsuperscript{[18]} reported that they could detect major anomalies with a rate of 70\% at the first trimester.

In a study performed on 44,859 cases at an early period, the detection rate for structural anomalies was reported 43.6\%.\textsuperscript{[8]} All acrania, alobar holoprosencephaly, exomphalos, gastrochisis, megacystis and vertebra anomalies and 77\% of hand or foot agenesis, 50\% of diaphragmatic hernia cases, 50\% of fatal skeletal dysplasia cases, 60\% of polydactyly cases, 34\% of major cardiac defects, 5\% of cleft lips and palates, and 14\% of open spina bifida cases could be diagnosed.\textsuperscript{[9]}

Melekoğlu et al.\textsuperscript{[19]} from our country reported that 33.3\% of cases with ventriculomegaly, 25\% of cases with cleft lip-palate, 43.7\% of cardiac malformations, 33.3\% of cases with diaphragmatic hernia and 75\% of cases with lethal skeletal dysplasia were detected during first trimester screening program, but agenesis of corpus callosum, Dandy-Walker malformation, congenital pulmonary airway malformation and pulmonary sequestration anomalies could not be detected during first trimester screening. In our study, we did not perform detailed analysis and comparison for the anomalies we detected; however, we determined that the imaging rates for organs and structures with anomaly in the literature were consistent with the imaging rates we found in our study.

In a systematic analysis performed on 78,002 cases in Italy, structural anomaly detection rate at 11–13\textsuperscript{+6} weeks of gestation was 51\% by TA USG, 43\% by TV USG and 62\% by the combination of both techniques, and it was found that cardiac anomaly detection rate increased to 53\% if fetal echocardiography is conducted which was 43\% in routine screening.\textsuperscript{[20]} In another meta-analysis, 115,731 fetuses with low risk were evaluated, and detection rate for systemic major anomalies at 11–13\textsuperscript{+6} weeks of gestation was found 46.1\% and the rate to detect all anomalies was 32.4\%.\textsuperscript{[20]}

As the gestational week increases, the rates to detect structural anomalies also increase; the detection rate which is 45\% at 11 weeks of gestation increases to 76\% at 14 weeks of gestation.\textsuperscript{[21]} Similarly, imaging success for almost all structures in our study was the lowest in Group 1 and the highest in Group 4 (in those with statistically significant difference). The highest imaging rate for nasal bone was in Group 2; the rates of Groups 3 and 4 were also similar to the rates of Group 2. This is also consistent with the fact that imaging nasal bone is easier after 11 weeks of gestation.\textsuperscript{[22]}
In our study, while successful imaging rate for kidney is 33.5% when CRL is between 45 and 54 mm, it increases with the increase of CRL and reaches to 60.4% when CRL is between 65 and 74 mm, and 74.4% when CRL is between 75 and 84 mm. Souka et al.\textsuperscript{12} found median CRL 64.9 mm in their study and reported this rate 77.9 and 87.6% by TA and TV USG at 11–14 weeks of gestation, respectively. Ebrashy et al.\textsuperscript{13} included only 13–14 weeks old fetuses in their studies, and reported these rates 63% for TA USG and 85.6% for TV USG. Although the general rate in our study is 52%, our rates during these weeks are 60.4% and 74.4%, respectively. The fetuses in this study being only at 13 and 14 weeks old explain the high imaging success. In a prospective study performed on 2876 cases which also give anomaly incidence, no renal pathology was diagnosed at 13–14 weeks of gestation, respectively. In a prospective study performed on 21,189 cases that reported in their study performed on 2876 cases which also give anomaly incidence, no renal pathology was diagnosed at 13–14 weeks of gestation. Similarly, Hildebrand et al.\textsuperscript{17} reported in their study performed on 21,189 cases that they did not diagnose any renal pathology at 11–14 weeks of gestation.

Although approximately one out of two structural anomalies can be detected at first trimester screening, agenesis of corpus callosum, cerebellar or vermis hypoplasia, echogenic lung lesions, intestinal obstruction, renal defect or talipes cannot be diagnosed at first trimester examination.\textsuperscript{18} Harper et al.\textsuperscript{19} reported in their analysis that fetal anatomy screening at the first trimester may increase the detection of fetal anomalies, but considering the fetal anomaly prevalence below 5% in general and overweight populations, many screenings would be needed to detect a single additional anomaly, and therefore first trimester anatomy screenings can be suitable only for fetal anomalies in populations under high risk.

**Conclusion**

Thanks to the developing technology and extensive knowledge, imaging basic fetal organs and structures at 11–13\textsuperscript{th} weeks is now possible. The main purpose is to detect major anomalies early in particular. In our study, we found that basic fetal structures except heart and kidneys can be successfully observed with a rate over 90% at early period examinations. High imaging success can be possible by increasing device quality and the time allocated for examination, and also choosing transvaginal examination method.

**Conflicts of Interest:** No conflicts declared.


Nuchal translucency measurement: who is right, who is not?

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Abstract

Objective: Fetal nuchal translucency (NT) measurement at first trimester provides prediction for fetal aneuploidy and cardiac anomalies. Performance of NT as a screening marker has not been consistent in studies. Measurement of NT has high intra- and interobserver variability. Radiologists, obstetricians and perinatologists measure the NT. There is no consensus about who should perform the NT measurement. In this study we compared the correlation of NT measurement in three groups depend on mean thickness and distribution of NT.

Methods: A total of 929 participants were recruited for this study. 7 radiologists, 8 obstetricians and 1 perinatology expert measured NT. Crown-rump length (CRL), mean NT and NT distribution were calculated for each group.

Results: Perinatology expert’s mean NT measurement was significantly higher than that of radiologists and obstetricians (p<0.05). Measurements of the perinatal expert also had significantly different distribution than other groups (p<0.05). There was no significant difference between the groups in terms of CRL values. Interobserver reliability coefficients with 95% confidence intervals for CRL and NT were 0.967 (0.910–0.987, p<0.001) and 0.596 (0.455–0.845, p<0.001), respectively.

Conclusion: There are statistically significant differences for mean NT value and distribution in three groups. Measurements of the perinatal expert has higher mean thickness and distribution. It is obvious that there is a need for standardization in NT measurement and it is necessary to evaluate the perinatal outcomes of these three groups and to approximate the two groups with the most accurate result group.

Keywords: Nuchal translucency, perinatology, obstetrician, radiologist.

Özet: Ense kalınlığı ölçüüm: Kim doğru, kim yanlış?

Amaç: İlk trimesterde fetal ense kalınlığı (NT) ölçüümü, fetal anöploidi ve kardiyak anomaliler için kestirim olanağı sunmaktadır. Bir tarama belirteci olarak NT ölçüümünün yapılıması çalışmada tutarlı sonuçlar vermemektedir. NT ölçüümü, yüksek gözlemciler arasından ve gözlemciler içi değişkenliğe sahiptir. Radyologlar, doğum ve perinatoloji uzmanları NT’yi ölçmektedir. NT ölçüümü kimin yapması gerektiği konusunda fikir birliği bulunmamaktadır. Bu çalışmada, ortalamakalınlık ve NT’nin dağılımsına bağlı olarak üç grupa NT ölçüümünün korelasyonunu karşılaştırdık.

Yöntem: Çalışmaya toplam 929 katılmci dahil edildi. 7 radyolog, 8 doğum uzmanı ve 1 perinatoloji uzmanı NT’yi ölçtü. Her grup için tepe-makat uzunluğu (CRL), ortalamakalınlık ve NT dağılımı hesaplandı.

Bulgular: Perinatoloji uzmanının ortalama NT ölçüümü, radyologların ve doğum uzmanlarının ölçüümünden anlamlı şekilde daha yüksek (p<0.05). Ayrıca perinatoloji uzmanı ölçüümü diğer gruplardan anlamlı şekilde daha fazlakıl bir dağılıma sahipti (p<0.05). CRL değerleri bakımından gruplar arasında hiçbir anlamlı farklılık yoktu. CRL ve NT %95 güven aralığında göstericiler arası güvenilirlik katsayıları sırasıyla 0.967 (0.910–0.987, p<0.001) ve 0.596 (0.455–0.845, p<0.001) idi.

Sonuç: Çuş grupta ortalama NT değeri ve dağılımı bakımından istatistiksel olarak anlamlı farklılıklar bulunmamaktadır. Perinatoloji uzmanı ölçüümü daha yüksek ortalama kalınlık ve dağılıma sahiptir. NT ölçüümünde bir standart oluşturma ihtiyacı olduğu açıklık ve bu üç grubun perinatal sonuçları değerlendirilmesi ve iki grubun en doğru sonuç grubuna yaklaştırılması önemlidir.

Anahtar sözcükler: Ense kalınlığı, perinatoloji, doğum uzmanı, radyolog.
Nuchal translucency measurement: who is right, who is not?

Introduction
Nuchal translucency (NT) is a sonoluscent area behind the fetal neck in the first trimester and was first defined by Nicolaides et al.\(^1\) NT measurement at 11–13+6 weeks of gestation is one of the main points of Down syndrome screening. Increased NT is associated with 70% of Down syndrome alone.\(^2\) Risk calculation taking into account maternal age, fetal NT and maternal serum biochemistry at 11–14 weeks of gestation has a sensitivity of up to 85% for a false-positive rate of around 5%.\(^3\) Moreover, increased NT is associated with other chromosomal anomalies, genetic syndromes, and structural anomalies.\(^4\) Performance of NT varies from study to study. Besides the other factors, the difficulty of obtaining proper images changes the success of the test. Small differences in caliper placement not only have the potential to alter an individual patient’s calculated risk estimate significantly, but also may decrease the cumulative performance of the screening test by increasing rates of false-positive or false-negative results.\(^5\) The repeatability of NT measurement was found different in several studies.\(^6\)

The Fetal Medicine Foundation (FMF) and other foundations have published guidelines to promote a standardized measurement technique for obtaining a proper NT measurement. There is no consensus about who have to measure the NT. In our country radiologists, obstetricians and perinatology experts perform the first trimester aneuploidy scan. In our country, NT measurement is performed in private clinics, hospitals and university hospitals. Although NT measurement is taught in all three groups, it is not controlled in the following period. Aim of this study is to compare the NT measurement performance of these three groups at the same population.

Methods
This is a prospective study including 929 singleton pregnant women with first trimester aneuploidy scan. Inclusion criteria were having a singleton pregnancy and the agreement of the women to participate in this study. Measurements were carried out between June 2017 and September 2017. Each pregnancy was examined for number of fetuses, measurement of crown-rump length (CRL) and NT. Seven radiologists, 8 obstetricians and 1 perinatology expert measured the NT. Only the measurements of radiologists, obstetricians and perinatology experts who performed more than 100 measurements in a period of at least 3 months were included in the analysis. Only the perinatology expert had FMF certification for NT measurement. Radiologists and obstetricians were certified by Ministry of Health. All examiners examined and measured the fetal NT consecutively and independently without knowing the each other’s results. Additionally each examiner scanned the CRL.

Demographic characteristics, pregnancy week, CRL and NT values were recorded. NT scans were performed between 11 and 13+6 weeks of gestation with CRL between 45 and 84 mm. The ultrasound machine was GE Voluson S6 (General Electric Healthcare, Chicago, IL, USA) for all groups. Transabdominal ultrasonography was performed on all women using a convex 2–5 MHz probe (4C-RS; General Electric Healthcare, Chicago, IL, USA). CRL and NT were measured as described by Nicolaides et al. three times for each woman.\(^1\) The NT value was expressed in a decimal of a millimeter. When three images were not obtained within 30 min, transvaginal ultrasonography (using a 5–7.5 MHz probe) was performed and time was added to the previous scans. The average of the three measurements was accepted as the NT value. We compared the CRL, mean NT values, distribution width of NT values and standard deviation of NT values for three groups (radiologists, obstetricians, and perinatology expert).

We used the SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean±standard deviation. Differences between the values of NT and CRL in groups were tested by independent variables t test. The measurement results of the three examiners were analyzed for any significant differences and variations. Interobserver comparisons were done by reliability tests (Cronbach’s alpha correlation coefficients). Two-way mixed effects model was used in cases where people effects were random and measured effects were mixed (absolute agreement definition) statistical analysis was performed using the Friedman test, the chi-square test and a multivariate analysis for measurement variations. A probability value of <0.05 was considered statistically significant. Study approved by local ethics committee.

Results
Nine hundred and twenty-nine women with singleton pregnancies were included in the study. The mean maternal age was 28.3±5.5 (range: 16 to 47) years and
the mean gestational age at scan was 12 (range: 11 to 13+6) weeks. 14% of the pregnant women included in the study were over 35 years of age and all patients were Caucasian.

There was no significant difference between the groups in terms of CRL values. The mean of all group nonspecific median NT was 1.46±0.55. Interobserver reliability coefficients with 95% confidence intervals for CRL and NT were 0.967 (0.910–0.987, p<0.001) and 0.596 (0.455–0.845, p<0.001), respectively. For all groups median NT values, standard deviation and range are shown at Table 1.

Mean NT values for perinatology expert, radiologist and obstetrician were 1.66, 1.41 and 1.25, respectively. Standard deviation values for perinatology expert, radiologist and obstetrician were 0.75, 0.38 and 0.34, respectively. Mean NT values and distribution width were significantly higher in perinatology group (p<0.05) (Fig. 1). In the radiology group, the mean NT value and NT range was higher than the obstetrician group (Table 2).

**Discussion**

In this study we compared the inter-operator reliability of CRL and NT measurements by sonographers with different levels of experience. Our study is the largest study comparing three groups in the literature. The CRL and NT measurements are dominant parameters in prenatal screening for Down syndrome. Increased NT value has a major impact on the estimated risk for trisomy 21 and therefore on the patient’s decision for or against invasive testing. The difficulties encountered when examining the NT are mainly related to fetal position, an increased maternal body mass index, nuchal cord, maternal abdominal wall thickness, quality of ultrasound machine and the inability of inexperienced sonographers to perform the scan correctly and examine the NT. Variations in measurement decrease in comparison with experienced examiners.

Unsatisfactory quality of NT measurements can easily lead to overestimation or underestimation of the risk for Down syndrome. Small differences in measurement have the potential to significantly alter an individual’s risk estimate for aneuploidy and increase the chance for false-positive or false-negative diagnoses. When the karyotype is normal and the NT is enlarged, the fetus is still at risk for cardiac abnormalities and congenital fetal abnormalities.\(^7\) However, NT screening displays high-

**Table 1.** Demographic characteristics of the study group.

<table>
<thead>
<tr>
<th></th>
<th>n=929</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.3±6</td>
</tr>
<tr>
<td>Parity</td>
<td>0.7±1.1</td>
</tr>
<tr>
<td>Week</td>
<td>12.2±0.6</td>
</tr>
<tr>
<td>CRL</td>
<td>62.5±8.4</td>
</tr>
<tr>
<td>NT</td>
<td>1.46±0.55</td>
</tr>
</tbody>
</table>

**Table 2.** Nuchal translucency measurement results for each group (n=929).

<table>
<thead>
<tr>
<th></th>
<th>Obstetrician</th>
<th>Radiologist</th>
<th>Perinatology expert</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRL (mm)</td>
<td>62.5±8.4</td>
<td>61.7±9.7</td>
<td>62.1±8.7</td>
<td>NS</td>
</tr>
<tr>
<td>Mean NT (mm)</td>
<td>1.25</td>
<td>1.41</td>
<td>1.66</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Standard deviation (mm)</td>
<td>0.34</td>
<td>0.38</td>
<td>0.75</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NT range (mm)</td>
<td>0.7–6.1</td>
<td>0.7–5.7</td>
<td>0.8–7</td>
<td></td>
</tr>
</tbody>
</table>

NS: not significant, NT: nuchal translucency.
er variability and significant operator dependence. Kagan et al. showed that an underestimation and overestimation of the CRL has a major impact, resulting in substantial underestimation or overestimation of those risks. A study regarding the measurement of NT had established that the ability to obtain reproducible results improves with training and good results are achieved after 80 scans. In our study, only the measurements of the experts who had performed at least 100 NT measurements were included in the study to increase the quality and the repeatability of the test.

Several studies evaluated the performance of NT measurement by providers. The current cross-sectional study analyzes the performance of NT measurement in same population. Mean NT values were statistically different in three groups. Perinatology expert group had the highest mean NT value and standard deviation. If we accept the measurements of perinatology expert as the gold standard, the low mean NT measurement of the radiologist and obstetrician groups will result in a false low calculation of the first trimester aneuploidy risk. Aksoy et al. compared only obstetricians and radiologists in their study and found low interobserver reliability of NT measurement.

NT measurement performance depends on sonographer. Among our results who were previously trained for perinatology, median NT value and NT distribution were higher, suggesting that experience does matter. These variations in the NT measured by the inexperienced sonographer can be explained by the failure and inability to achieve the exact mid-sagittal view. There is no quality monitoring programme for NT measurement in our country. In our study, none of the obstetricians and radiologists had FMF certificate for NT measurement. In FASTER study Malone et al. showed that 7.4% of NT measurements were measured incorrectly. Dalton et al. also confirmed that data in their study. Interobserver reliability coefficients with 95% confidence intervals for CRL and NT were 0.967 (0.910–0.987, p<0.001) and 0.596 (0.455–0.845, p<0.001), respectively. This result shows us that the interobserver reliability and reproducibility were high in the CRL measurement. However, reliability and reproducibility for NT evaluation were relatively low.

In our study there was no statistically significant difference between the groups in terms of CRL measurement. Also in the known literature it is seen that the interobserver variability is low and the reliability is high in terms of CRL measurement. In the largest study on this subject Souka et al. showed that the reliability and reproducibility of CRL measurement was high. Salomon et al. performed a simulation study using a simulation model to evaluate the impact of error in CRL measurements in cases of sequential combined screening for Down syndrome. After more than 3200 simulated cases were analyzed, they reported that Down syndrome screening might be highly sensitive to errors in CRL measurements.

The fact that there was only one perinatologist in our study and that the perinatal outcomes were not assessed constitutes the weakness of our study. However, in literature our study is the first one in which a large population of 929 patients were evaluated on this subject.

**Conclusion**

Measuring fetal NT and CRL accurately is essential for optimal combined first-trimester screening performance and prenatal care. Our findings show that precision of NT measurements is still largely dependent on sonographer’s personal attitude in terms of endurance and accuracy. Interobserver reliability is high in CRL measurement. Although it was first defined 25 years ago, NT measurement still does not seem to be standardized. There is a need for a system that will standardize NT measurement and will make quality control over the years.

**Conflicts of Interest:** No conflicts declared.

**References**

Postpartum glucose tolerance test application rates and non-application causes in gestational diabetes mellitus cases

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Abstract

Objective: Gestational diabetes mellitus is a health problem with long-term consequences that concern the general population seen at increasing rates. This population should be followed up more closely and the reasons of those who do not apply should be investigated and these people should be included in follow-up protocols. In this study, we investigated the rates of application for postpartum glucose tolerance tests of women who had gestational diabetes mellitus diagnosis in a low socioeconomic population. We also examined the reasons for not applying to have a glucose tolerance test.

Methods: A total of 738 gestational diabetes patients with low socioeconomic status who were followed-up and treated at a tertiary care center were included in the study. These patients were reached after the 8th postpartum period to investigate the cases of having glucose tolerance testing and the reasons for not having it.

Results: 227 (30.7%) of the 738 patients who participated in the study, had applied for glucose tolerance testing in the postpartum period. Of the remaining 511 patients, 337 (65.9%) indicated that they did not apply because they were not informed about it, 98 (19.1%) of them indicated the financial impossibilities as the reason of not applying, 40 (7.8%) of them did not apply because their husbands did not take them the health center, 36 (7.2%) indicated that they did not attend because they did not consider it necessary.

Conclusion: In the postpartum period, glucose test admission rates are quite low in the low socioeconomic population. It is clear that there is a need for new health policies and follow-up systems following this population in terms of long-term outcomes.

Keywords: Gestational diabetes, glucose tolerance testing, postpartum, type 2 diabetes.

Özet: Gestasyonel diabetes mellitus olgularında postpartum glukoz tolerans testi uygulamasının oranları ve uygulanmamasının nedenleri


Yöntem: Çalışmaya, düşük sosyo-ekonomik düzeyde olan, üçüncü basamak bakım merkezinde takip edilen toplam 738 gestasyonel diyabet hastasının, postpartum dönemde glukoz tolerans testi için başvuran hastaların oranını araştırmak amacılı olarak, 8. postpartum dönemden sonra ulaştık.

Bulgular: Çalışmaya katılan 738 hastanın 227’si (%30.7) postpartum dönemde glukoz tolerans testi için başvurdu. Kalan 511 hastanın 337’si (%65.9) test uygulanmamıştı, 98’i (%19.1) nedeni bilgilendirilmeden, 40’ı (%7.8) finansal zorluklar nedeniyle, 36’ı (%7.2) hastaların sağlık merkezine getirilmesini engelledi, 36’ı (%7.2) ise testin gerekli olmadığını düşünmeli için geliştikleri belirtti.

Sonuç: Postpartum dönemde glukoz tolerans testi başvuru oranları düşük sosyo-ekonomik popülasyonda oldukça düşükktür. Uzun vadeli sonuçlar bakımından yeni sağlık politikalarında ve bu popülasyonu takip etmek için takip sistemlerine gereksinim olduğu açığtır.

Anahtar sözcükler: Gestasyonel diyabet, glukoz tolerans testi, postpartum, tip 2 diyabet.


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Introduction

Gestational diabetes mellitus (GDM) first recognized during pregnancy from those whose disease is a transient manifestation of pregnancy-related insulin resistance. GDM is a health problem seen at increasing rates. Although GDM usually recovers after pregnancy, it carries the risk for dyslipidemia, obesity, hypertension, cardiovascular diseases and other metabolic disorders, especially type 2 diabetes in long term. Because of long-term risks, postpartum glucose screening is recommended by all health systems. NICE state that up to 50% of women diagnosed with gestational diabetes develop type 2 diabetes within 5 years of the birth.

Women who are diagnosed as GDM are more motivated for treatment during pregnancy but do not show enough interest in the glucose test after pregnancy. Patients referred to the glucose tolerance testing (GTT) have a higher admission rate, especially in the high socioeconomic category, but remain lower in low socioeconomic group. Therefore, the objective of this study was to conduct an in-depth exploration of the experiences of, and perspectives on postpartum GTT screening with low socioeconomic status women diagnosed with GDM.

Methods

This is a cross-sectional study conducted between January 2015 and June 2016 at the Bursa Yüksek İhtisas Training and Research Hospital, which is a tertiary care center. In this period, 738 of 926 patients with low socioeconomic status and no previous diagnosis of diabetes or with no history of GDM in previous pregnancies that were reached by the hospital records and telephone numbers diagnosed with GDM were included in the study. Low socioeconomic status defined according to Turkish Statistical Institute January 2015 data. The study was approved by the local ethics committee (Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital, 613-2014).

A one-step approach was used in the diagnosis of patients. In 2010, International Association of Diabetes and Pregnancy Study Group (IADPSG) bring new criteria for the diagnosis of GDM. New IADPSG criteria were mainly prepared by focusing on the perinatal risk of parameters which are >90 percentile. For the diagnosis, the criteria endorsed by the American Diabetes Association (ADA) were used (one-step 75-g OGGT). According to ADA patient diagnosed GDM if one of three values (Fasting ≥ 92 mg/dL, first hour ≥ 180 mg/dL, second hour ≥ 153 mg/dL) are elevated. Patients receiving GDM diagnosis were followed up in the same diabetes clinic and informed by the diabetes nurse. Patients were informed about GDM when they were discharged from the hospital after the follow-up period of birth and they were called for the diabetes screening at postpartum 6th week.

All of the patients were called by telephone after the postpartum 12th week and a verbal questionnaire was applied after their verbal permission was obtained. Survey responses were recorded in the computer afterwards. At the end of the survey, the responses were confirmed by reading the participants again. All patients were asked the same questionnaire by the same researcher. During the telephone survey of all the participants were asked the total monthly income of the family and the participants whose income was below the poverty line were included in the study. Postpartum diabetes screening was defined as women who received an oral GTT at 6 to 12 weeks postpartum.

Basic demographic data and survey results were recorded in the SPSS v21 software (SPSS Inc., Chicago, IL, USA).

Results

The mean age of women with GDM was 30.8±5.1. The demographic characteristics of the patients are given in Table 1. 427 (57.8%) of the participants were high school graduates, 249 (33.7%) were primary school graduates and 62 (8.5%) were illiterate while none of them were university graduates.

Of the 738 patients who participated in the study, 227 (30.7%) reapplied for GTT in the postpartum peri-

| Table 1. Demographic characteristic of study population (n=738). |
|-----------------------|-------------|
| Age                   | 30.8±5.1    |
| Gravida               | 1.8±1.1     |
| Gestational week at birth | 38.9±1.7  |
| Pre-eclampsia         | 71 (9.6%)   |
| Cesarean              | 84 (11.3%)  |
od, while the remaining 511 (69.3%) did not reapply for GTT. As a result of the survey, the reasons for not having GTT were collected under 4 main headings. Of 511 patients stated that they did not go to the hospital because they were not informed enough and did not know about long-term risks, 98 (19.1%) said they did not go because of financial difficulties and health insurance problems, 40 (7.8%) of the participants stated that they could not apply because their husbands did not take them to hospital, and 36 (7.2%) of them claimed that they did not consider it necessary (Fig. 1).

**Discussion**

In our study, it is seen that the majority of patients with low socioeconomic status (69.3%) did not return to the health facility for GTT in the postpartum period. This creates a public health problem in terms of long-term complications. Women with GDM history are seven times more likely to develop type 2 diabetes during their lifetime compared with women without GDM history.[10] At the same time, it poses a risk for early diabetes in subsequent pregnancies. In the study by Ekelund et al. it was shown that 51% patients with GDM had impaired glucose tolerance and 30% developed diabetes mellitus over 5 years.[11] Gestational requirement for insulin and early gestational age at the time of diagnosis (ie, less than 24 weeks of gestation) are the major risk factors for the development of type 2 diabetes mellitus. In women who used insulin during pregnancy, relative measures of association range between 2.8 and 4.7.[12]

Studies have shown that the risk for type 2 diabetes is significantly reduced if high-risk individuals are identified early and lifestyle changes are made. Tuomilehto et al. showed that, lifestyle changes may reduce to type 2 diabetes rate up to 58%.[13] These patients need to be recognized early and referred to lifestyle changes and treatment if necessary.[14] It is not easy to make lifestyle changes in the populations with low socioeconomic status. When evaluated in terms of dietary changes, as the socioeconomic level decreases, the predominant eating habits of carbohydrates increase and the protein weighted diet decreases.

Postpartum GTT admission rates are high in developed countries. This ratio was found to be 85% in the study of Paez et al. Halle et al. found this rate as 97%. In our low socioeconomic status population, it was found to be 30.7%.[15,16]

The majority of patients (n=337, 65.9%) who did not apply for postpartum GTT said they were not adequately informed and they were not aware of the long-term complications. Women in this group indicated that they would make a postpartum GTT if they were aware of long-term risks. Disagreements among some health professionals regarding postpartum GTT make it difficult for patients to be referred to health care facilities.[17] Having different views of major health organizations, especially ADA, The American College of Obstetricians Gynecologists (ACOG) and World Health Organization (WHO), leads to confusion in this way. In addition, there are no precise criteria about who will (obstetrics, endocrinologists, family physicians) perform postpartum GTT screening in most countries. Turkish Ministry of Health recommend GTT screening between 24th and 28th gestational weeks in low risk population at pregnancy management guideline.[18] Turkish Perinatology Society recommends single-step 75-g diagnostic test for Turkish population. They stated that this approach seems more appropriate in terms of costs and patient compliance.[19]

98 (19.1%) of the patients who did not participate in the postpartum GTT screening indicated that they did not have sufficient financial means to reach and...
obtain this test. Some of the people at low socioeconomic status are not covered by health insurance, so they have difficulties at paying for these tests. At the same time this group also has difficulty about accessing the health facility. Normalization of blood glucose values in the early postpartum period leads the people not to have postpartum GTT. Especially women who do not see familial support excuse the absence of time and do not apply for postpartum GTT screening. The likelihood of long-term dieting and life-limiting measures also reduces the rate of patients applying to the postpartum GTT. In our population, 36 (7.2%) women did not apply because they did not consider postpartum GTT necessary.

Clark et al. showed that the rate of having postpartum GTT was higher in the population that was monitored and stimulated by the health system. Problems related to health insurance in the low socioeconomic populations as in our study also affect the rate of postpartum GTT admission. 98 (19.1%) of the patients in our population, showed health insurance problems as the cause for not applying. It is known that education level also affects the rates of postpartum GTT applications. In our population, 62 (8.5%) participants were illiterate while none of the participants were university graduates.

Forty (7.8%) of our patient population stated that they could not make the postpartum GTT because their partners did not take them to the health institution for screening tests. It seems that family members should also be educated about GDM. Bandyopadhyay et al. showed that the rate of postpartum GTT admission increased if family members participated in diabetes education.

One of the main limitations of this study is the lack of long-term follow-up results. It is not known if diabetes developed or not in the long-term follow-up of the population at risk. Also the results of subsequent pregnancies are not known for our study group.

All populations have different excuses not to apply for postpartum GTT. The most common cause in a study conducted in Canada was the lack of adequate time, while the most common cause in a study in the USA was long-term treatment needs. In our population, the most common cause is not to be informed sufficiently.

For the clinical practice, this study suggests that patients and their relatives should be adequately informed in the postpartum period before being discharged from the hospital. At the same time, this population should not be lost during the postpartum period due to health insurance problems. It is thought that sending mails or making reminder talks by telephone to the participants may increase the admission rate for postpartum GTT.

**Conclusion**

In our study it was found that patients with low socioeconomic status had a very low rate of admission to the GTT in the postpartum period. The follow-up of this group of patients and postpartum GTT applications should be considered as a public health problem and family physicians and obstetricians work in harmony to protect these patients from long-term complications.

**Conflicts of Interest:** No conflicts declared.

**References**


Maternal serum anti-Müllerian hormone levels in pregnant women with gestational diabetes

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Introduction
Anti-Müllerian hormone (AMH), also called as Müllerian inhibiting substance (MIS), is a glucoprotein which is a member of transforming growth factor beta (TGF-β) family.1 AMH is synthesized from preantral and antral follicles in the ovarian granulosa cells.1 In clinical practice, AMH is an essential marker to assess the ovarian reserve, and its level does not change dur-
Maternal serum anti-Müllerian hormone levels in pregnant women with gestational diabetes

By looking at different periods of menstrual cycle, it has been shown that serum AMH levels may be associated with metabolic conditions such as polycystic ovarian syndrome (PCOS) and obesity in addition to ovarian reserve.[1,4]

Although it has been reported in the literature that AMH levels decrease after 20 weeks of gestation, some studies did not consider this reduction significant. The reason is that AMH production is independent from gonadotropins. Menstrual cycle in pregnancy becomes inactive with the feedback effect and new follicle development is inhibited. The decrease of AMH levels in pregnancy is a result of the inhibition of follicles. AMH levels start to increase after a short time following the delivery.[5] Diabetes is a common complication seen during pregnancy, and insulin resistance at second trimester and concomitant hyperinsulinemia create a diabetogenic condition during pregnancy. Gestational diabetes mellitus (GDM) is the glucose intolerance seen during pregnancy and its incidence is between 2% and 5%.[6,7]

In the literature, an association was shown between serum AMH levels and HOMA-IR levels which is the parameter of insulin resistance.[1] Since insulin resistance also develops in gestational diabetes, the aim of our study is to reveal if there is any difference between pregnant women diagnosed with GDM and healthy pregnant women in terms of third trimester AMH levels or not.

Methods
Pregnant women with GDM who were newly diagnosed during between 24 and 28 weeks of gestation and healthy pregnant women with similar characteristics were included in this cross-sectional study. Our study was conducted between June 2014 and June 2015 at Şişli Etfal Training and Research Hospital after the approval of ethics committee was obtained. The consents of all patients included in the study were received. Pregnant women with GDM diagnosis over 32 weeks and healthy pregnant women who were known as the control group or who did not have any diagnosed gestational disease were included in the study. Pregnant women whose data could not be accessed completely, twin pregnancies, pregnancies under 32 weeks, patients with pregestational diabetes and those with preeclampsia diagnosis were excluded from the study. Also, the cases with the surgical history of endometrioma/endometriosis and polycystic ovarian syndrome history were excluded from the study.

Two-step oral glucose tolerance test (OGTT) was performed between 24 and 28 weeks of gestation for all pregnant women included in the study. After 50-g glucose challenge test, plasma glucose levels were measured from the peripheral blood sample at the first hour of the procedure. For the patients whose 1-hour plasma glucose levels were 140 mg/dl and above, 3-hour 100-g OGTT was applied on a different day in order to establish GDM diagnosis according to Carpenter-Coustan criteria. The plasma glucose value was 95 mg/dl for fasting blood glucose, 180 mg/dl for 1st hour, 155 mg/dl for 2nd hour and 140 mg/dl for 3rd hour. The cases whose at least two of these values were found to be higher were considered GDM.[8]

The demographic characteristics, weeks of gestation, delivery week and newborn weights of all patients included in the study were recorded. The age, gravida, parity, body mass index (BMI), smoking habit, clinical and laboratory parameters, gestational outcomes and serum AMH values of the patients were compared. After the samples were collected in lithium-heparin tubes, serum AMH level was measured by Cobas device (Roche Diagnostics, Risch-Rotkreuz, Switzerland) using Elecsys reagent kit (Elecsys Corporation, Lenexa, KS, USA) by ‘ECLIA’ method which is electrochemiluminescence immunologic test.

The data of the cases included in the study were analyzed by Statistical Package for the Social Sciences (SPSS 20.0) (SPSS Inc, Chicago, IL, USA). The data were presented as mean ± standard deviation. Independent t test was used for the numerical parameters with identified normal distribution in order to analyze the statistical difference between the study groups. Chi-square test was used for the categorical data. Spearman’s correlation analysis was carried out to find the correlation between the data. Multiple linear regression analysis was done for factors which may affect serum AMH levels. p<0.05 was considered statistically significant.

Results
Of 72 patients included in the study, 35 patients were in the GDM group and 37 patients were in the control group. No difference was found in terms of maternal age, gravida, parity, smoking habit and the week of ges-
tation when AMH was measured. Also, there was no difference between two groups in terms of week of gestation at delivery, and 1-minute and 5-minute Apgar scores (Table 1).

Maternal BMI, fasting blood glucose (FBG) and postprandial blood glucose (PBG) levels were significantly higher in the GDM group than the control group. Newborn weight was also found higher in the GDM group. A significantly positive correlation was found between newborn weight and FBG and PBG (r=0.03, p=0.76 for FBG; r=0.21, p=0.06 for PBG).

In terms of AMH values, there was no statistically significant difference. Serum AMH values were found 1.37±0.80 ng/ml in the GDM group and 1.52±0.99 ng/ml in the control group. There was no statistically significant correlation between serum AMH values and BMI (r=-0.04, p=0.72). Also, there was no significant correlation between serum AMH values and FBG and PBG checked at second trimester (r=-0.03, p=0.75 for FBG; r=-0.1, p=0.4 for PBG). No significant impact was observed in the multiple linear regression analysis including the parameters such as age, BMI and week of gestation which may affect AMH level. In the results of the multiple linear regression analysis where serum AMH level was dependent variable, the regression coefficient was 0.94 and 95% confidence interval was -0.06 – 0.13 (p=0.45) for BMI, the coefficient was -0.10 and 95% confidence interval was -0.06 – 0.02 (p=0.41) for maternal age, and the coefficient was 0.11 and 95% confidence interval was -0.09 – 0.26 (p=0.34) for week of gestation.

Discussion

In our study, we did not find any difference between pregnant women with GDM and healthy pregnant women in terms of serum AMH levels measured at third trimester. AMH is secreted from the granulose cells of prenatral and antral follicles from fetal life up to the period of menopause. In the studies performed in recent years, it has been shown that serum AMH levels may be associated with metabolic conditions such as PCOS and obesity in addition to ovarian reserve.

The studies performed for the AMH levels during pregnancy showed that AMH levels decrease at the third trimester; although this reduction was determined to be insignificant by some studies, other studies considered it significant. The reason for the decrease is the inhibition of menstrual cycle due to the lowered gonadotropin level and the suppression of follicular development. With the disappearance of follicular suppression after delivery, AMH levels increase. GDM is a clinical condition characterized by glucose intolerance, and metabolic and hormonal changes developing during pregnancy. The pregnancies complicated with diabetes have both maternal and fetal risks.

There are two studies in the literature investigating AMH levels in patients with GDM. In their study, Villarroel et al. compared healthy pregnant women with those with Type 2 DM and GDM diagnoses, and they found that there was no significant difference between two groups although AMH levels decreased in both groups at the third trimester. Gerli et al. showed in their study that AMH values were correlated with maternal age also during the pregnancy, but they were not affected by GDM, BMI, fetal birth weight and placental weight. In our study, we also found no correlation between AMH and fetal birth weight, FBG and PBG.

It was shown in the literature that serum AMH levels and HOMA-IR levels which is the parameter of insulin resistance are associated. Pregnancy is charac-

### Table 1. Comparison of demographic characteristics, laboratory data and delivery outcomes of GDM and control groups.

<table>
<thead>
<tr>
<th></th>
<th>GDM (n=35)</th>
<th>Control (n=37)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>29.4±5.59</td>
<td>27.2±4.06</td>
<td>0.061</td>
</tr>
<tr>
<td>Gravida</td>
<td>2.1±0.98</td>
<td>1.7±0.98</td>
<td>0.078</td>
</tr>
<tr>
<td>Parity</td>
<td>1.0±0.87</td>
<td>0.8±0.82</td>
<td>0.084</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.2±1.8</td>
<td>27.6±2.48</td>
<td>0.004*</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>6 (%17.1)</td>
<td>9 (%24.3)</td>
<td>0.453</td>
</tr>
<tr>
<td>Week of gestation</td>
<td>35.7±1.2</td>
<td>35.1±0.97</td>
<td>0.568</td>
</tr>
<tr>
<td>Delivery week</td>
<td>38.8±1.5</td>
<td>38.6±1.25</td>
<td>0.364</td>
</tr>
<tr>
<td>Delivery type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>24 (%68.6)</td>
<td>28 (%75.7)</td>
<td>0.501</td>
</tr>
<tr>
<td>Delivery by cesarean</td>
<td>11 (%31.4)</td>
<td>9 (%24.3)</td>
<td></td>
</tr>
<tr>
<td>Newborn weight (g)</td>
<td>3533.4±448.74</td>
<td>3337.8±330.10</td>
<td>0.038*</td>
</tr>
<tr>
<td>1-minute Apgar score</td>
<td>8.0±0.72</td>
<td>8.3±0.79</td>
<td>0.078</td>
</tr>
<tr>
<td>5-minute Apgar score</td>
<td>8.7±0.54</td>
<td>8.9±0.59</td>
<td>0.278</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dl)</td>
<td>86.9±8.67</td>
<td>80.9±5.17</td>
<td>0.001*</td>
</tr>
<tr>
<td>Postprandial blood glucose (mg/dl)</td>
<td>120.4±20.50</td>
<td>104.0±10.05</td>
<td>0.001*</td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>1.37±0.80</td>
<td>1.52±0.99</td>
<td>0.464</td>
</tr>
</tbody>
</table>

AMH: anti-Müllerian hormone; GDM: gestational diabetes mellitus; BMI: body mass index. *p<0.05 is statistically significant.
terized by a physiological insulin resistance. Nelson et al. carried out a study on AMH levels of pregnant women and they determined GDM as exclusion criteria in their study considering that insulin values and insulin resistance may affect AMH levels. Some authors suggested that the increase in insulin and androgen levels may affect serum AMH values; however, the studies showed that there is no correlation between insulin and AMH values. In our study, we found no significant different in terms of serum AMH levels although FBG, PBG and BMI were higher in the GDM group. This supports the result that AMH levels are not affected by insulin and glucose levels in pregnant women.

Lambert-Messerlian et al. reported in their study that AMH levels in pregnant women were not affected by glucose increase or food intake. Freeman et al. carried out their study on obese and non-obese women, and they found that AMH levels were lower in obese women than non-obese women. In our study, BMI was higher in the GDM group than the control group, but we found in the multiple linear regression analysis that BMI had no impact on serum AMH values.

Conclusion

In conclusion, we found no difference between the pregnant women with and without GDM diagnosis in terms of AMH levels at the third trimester. Although AMH values decrease at the third trimester, increases in serum insulin and glucose levels do not affect AMH levels. Since there are studies showing that AMH levels are higher in cases with insulin resistance, further studies are needed to reveal the GDM correlation.

Conflicts of Interest: No conflicts declared.

References

Postnatal maternal attachment: a retrospective study
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2Department of Nursing, Faculty of Health Sciences, Gümüşhane University, Gümüşhane, Turkey

Abstract

Objective: In this study, we aimed to determine the level of postnatal maternal attachment and the factors affecting the attachment.

Methods: A total of 300 women (of which 150 delivered vaginally and 150 delivered by cesarean section) who applied to family health centers in Gümüşhane city, delivered a live fetus at term vaginally or by cesarean section, did not develop any maternal or fetal health problem and complication during postpartum period, and had 0–60-month-old baby between April 20 and July 20, 2017 were included in this descriptive and cross-sectional study.

Results: In the study, no significant correlation was found among the factors such as women’s educational status, employment status, perceiving income status, family type, history of risky pregnancy, gravida, delivery week, delivery type, delivery duration, age of baby, having problem during pregnancy and delivery, postpartum depression, having support during delivery, the type of feeding baby, and attending pregnancy training classes. It was determined that the variables such as marital status, place of residence, marriage duration, number of delivery and child, whether the pregnancy is planned or not, first breastfeeding time after delivery affected the maternal attachment level of women. It was found that women whose age was between 27 and 35 years, who were housewife or civil servant, residing in a city, married for maximum 10 years, had single child and planned their pregnancies had higher maternal attachment levels.

Conclusion: In order to increase maternal attachment, women need to plan their pregnancies willingly, and families should be observed for attachment and supported for a safe attachment.

Keywords: Mother, delivery type, maternal attachment, postpartum.
Introduction

Kesebir et al. define the attachment as the child feeling an affinity to the caregiver in the relationship between them and as an emotional bond with consistency and continuity which becomes clear especially under stress.\textsuperscript{1,2} The attachment theory developed by Bowlby is based on the attachment of baby to mother during the early period as a result of biological trust, mother being available or not when baby needs her, and how reactions and behaviors of mother towards baby are perceived and interpreted by baby.\textsuperscript{1} Maternal attachment begins during pregnancy, continues after delivery and contributes to the development of maternity role in woman.\textsuperscript{3,5} In the attachment theory, it is highlighted that being attached to mother or any other relaxing object has a significant role for baby to maintain the life.\textsuperscript{6} When the bond between mother and baby is strong and based on love, it contributes to the development of child as a healthy individual socially, physically and mentally. When attachment, with foundations laid during infancy period, is determined once whether it is safe or not, it varies very slightly in the other periods of life.\textsuperscript{4} The level of attachment does not only ensure to have a healthy infancy period but also affects the health level during early childhood, late childhood, adolescence and adulthood periods. Bowlby stated that there is a link between insecure attachment and psychopathology. It is indicated that insufficient attachment is associated with propensity for violence, self-harm, substance abuse and drug addiction, negligence and abuse.\textsuperscript{7,8}

During postpartum period, mother is very willing to establish intimacy with her baby. Mother seeing, touching and communicating with baby affects the perception of baby positively. If this positive communication cannot be established between mother and baby, mother may neglect the care of baby, and the health of mother and baby may deteriorate. Meeting with baby right after the delivery in order to initiate the interaction between mother and baby is very important in terms of establishing maternal attachment rapidly.\textsuperscript{9} Factors such as protecting baby from harmful and dangerous situations, breastfeeding, caring and healthy attachment are effective in creating a positive environment for the healthy development of baby during postpartum period.\textsuperscript{10} It has been stated that early attachment and breastfeeding improve the mathematical and reading skills of children.\textsuperscript{11} While breast-fed babies are more compatible and cooperative, crying jags and anger are encountered less. According to the World Health Organization, depression seen in women disrupts the performance of fulfilling maternity roles, and also negatively affects the development and growth of baby.\textsuperscript{11}

Mothers may have knowledge deficiency or insufficient social supports about baby care during postpartum period. During this period, nurses should support and encourage parenting efforts of mothers and fathers.\textsuperscript{11} Nurses should assess the relationship of mother and baby during postpartum period by observation and record it. For example, mother calming baby, caressing it, holding it, talking to baby, feeding properly, breastfeeding baby, mother feeling comfortable when breastfeeding, making an eye contact and calling baby with its name or gender are the appropriate attachment behaviors expected from mothers. Also, during postpartum period, putting baby naked on prone position onto the naked breasts of mother (namely, direct skin contact) stimulates maternal oxytocin release and affects maternal attachment positively. For the healthy assessment of the approach of mothers for their babies, nurses play a significant role in the normal attachment process between mother and baby and in the development positive mother-baby attachment after delivery. Performing proper midwifery and nursing initiatives are significant for maintaining maternal and fetal health, and identifying risks early that may develop in the attachment relationship between mother and baby.\textsuperscript{10}

The purpose of this study is to determine the level of postnatal maternal attachment and the factors affecting the attachment.

Methods

The population and sample of the study

The population of this descriptive and cross-sectional study consisted of women living in a city of Eastern Black Sea region. The sample of the study consisted of women who delivered a live fetus at term vaginally or by cesarean section, did not develop any maternal or fetal health problem or complication at postpartum period and had a 0–60-month-old baby during the study period. A total of 300 mothers, of which 150...
delivered vaginally and 150 delivered by cesarean section, who were informed about the purpose of the study and voluntarily accepted to participate, were the sample of this study. The data of the study were collected between April 20 and July 20, 2017. Women who were the sample of the study were reached from the family health centers in Gümüşhane city.

Data collection tools

For the collection of study data, the information form developed according to the literature and maternal attachment scale were used.

**Participant Information Form:** The information form has 34 questions for demographic characteristics and details about delivery and postpartum period of woman. This form includes questions for demographic characteristics such as participant’s age, current marital status, educational level and spouse’s educational level, income information, marriage duration and family type as well as information such as pregnancy, miscarriage and delivery numbers, problems during pregnancy, delivery type, delivery duration, planning status of pregnancy, preparing for motherhood during pregnancy and breastfeeding time during postpartum period, having postpartum depression, feeding type, and social support perception during and after delivery.

**Maternal Attachment Scale:** The scale which evaluates the emotions and behaviors showing maternal love based on the self-statements of individual was developed by Mary E. Müller in 1994. The four-point Likert scale has a total of 26 items. Total score is obtained by adding all points given to scale items (min=26, max=104). The increase of the scale shows that maternal attachment has a good level. Cronbach’s alpha internal consistency reliability of the scale was 0.77 for mothers with 1-month-old baby and 0.82 for mothers with 4-month-old baby. In our study, Cronbach’s alpha internal consistency coefficient was 0.874.

Ethical aspect and practice of the study

The approval of Ethics Committee of Gümüşhane University was obtained to collect study data. The participants were informed that their personal information would be kept confidential and would be used only for the purposes of this study. Then, the mothers who agreed to participate and gave verbal consent were included in the sample of the study. After data collection forms were delivered, the participants were asked to complete the forms. The participants completed the data collection forms within 15–20 minutes.

The Analysis and Interpretation of the Data

The study data were analyzed in the SPSS 18.0 package program. Number and percentage distribution was used for the analysis of the data, and mean-standard deviation was used for continuous data. Since the data did not have normal distribution, Kruskal-Wallis H test, ANOVA, t test and Mann-Whitney U test were used to compare the mean values of two or more groups in the independent groups. The value p<0.05 was considered statistically significant.

The Limitations of the Study

The results obtained from this study are limited with the sample of this study. The results cannot be generalized to all mothers. Since the educational levels of women are different, it was observed that they had difficulties to complete the forms and they did not answer all questions in some forms. Also, as the questions are retrospective, some mothers had difficulties to remember some details, which was the greatest limitation of the study. Sample group being small, data being based on self-statement and the study being cross-sectional are other limitations.

Results

Some demographic characteristics of the participants are given in Table 1.

It was found that the ages of approximately half of the women (48.7%) were in the range of 27–35 (min: 19, max: 56, mean: 30.33±6.373) years, most of them (97.3%) were married, 3 out of every 10 women (34.7%) were high school graduate, approximately 7 out of every 10 women (68%) were housewife and did not work (68.3%) at the time of study. More than half of them (53%) were living in the city center, and 7 out of every 10 women (68.3%) perceived that their incomes were equal to their expenses. Most of the women (75.7%) had nuclear family, and the majority of them (71.3%) were married for 1–10 years.

Most of the women (69%) in this study were multi-gravida and approximately half of them (49%) had 2–3 children. A great majority of them (90%) did not end
their pregnancy by abortion previously, and most of them (73.3%) did not have involuntary miscarriage. Almost all of them stated that they had no health problem in their previous pregnancy, and the most common problem in the previous pregnancy was infection (n=8, %57.1).

The details of the last pregnancies of the participants are given in Table 2.

Most of the women (79%) included in the study planned their last pregnancies, and one of every 4 women (25%) had a risky pregnancy in their last pregnancies. The children of 67.3% of women were between 0 and 2 years old during the study period and 6 out every 10 women (59%) delivered at term. Almost all of them (97.3%) stated that their delivery took less than 3 hours. A great majority of women (81.3%) did not have postpartum depression. Of those who had postpartum depression, 42.9% stated that they received support mostly from their partners. Almost half of women (49.3%) said that they breast-fed their babies within the first half hour after delivery and most

**Table 1. Demographic characteristics of women.**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19–26</td>
<td>86</td>
<td>28.7</td>
</tr>
<tr>
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**Table 2. The details of the last pregnancies of women.**

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<td></td>
</tr>
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<td><strong>Treatment status of those with postpartum depression</strong></td>
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<tr>
<td>No</td>
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<td>75</td>
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<td><strong>Risky pregnancy history in last pregnancy</strong></td>
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<tr>
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<td>75.0</td>
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</tr>
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<td>More than 3 hours</td>
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<td><strong>Person supporting women during delivery</strong></td>
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<td></td>
</tr>
<tr>
<td>Spouse</td>
<td>94</td>
<td>31.3</td>
</tr>
<tr>
<td>Mother</td>
<td>73</td>
<td>24.3</td>
</tr>
<tr>
<td>Sibling</td>
<td>23</td>
<td>7.7</td>
</tr>
<tr>
<td>Family</td>
<td>97</td>
<td>32.3</td>
</tr>
<tr>
<td>Health professional</td>
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<td>2.0</td>
</tr>
<tr>
<td>No one</td>
<td>7</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>The first time when baby was breast-fed after delivery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No breastfeeding</td>
<td>29</td>
<td>9.7</td>
</tr>
<tr>
<td>0–30 min.</td>
<td>148</td>
<td>49.3</td>
</tr>
<tr>
<td>31–60 min.</td>
<td>72</td>
<td>24.0</td>
</tr>
<tr>
<td>61 minutes and more</td>
<td>51</td>
<td>17.0</td>
</tr>
</tbody>
</table>
of them (70%) said that they held their babies within the first hour. In their last deliveries, 31.3% of women said that they were accompanied by their partners, 24.3% of them were accompanied by their mothers and 32.3% of them were accompanied by someone else other than their mothers and sisters.

By the statistical analysis of the study, it was found that the factors such as women’s educational status, employment status, perceiving income status, family type, history of risky pregnancy, gravida, delivery week, delivery type, delivery duration, age of baby, having problem during last pregnancy and delivery, postpartum depression, having support during delivery, the type of feeding baby, and attending pregnancy training classes did not have a statistically significant impact on women’s maternal attachment scores.

The factors affecting the maternal attachment status of the participants are shown in Table 3. It was found that the mean scores women got from maternal attachment scale varied according to the age. Accordingly, the mean scores got from maternal attachment scale by women between 19 and 26 (97.92±6.199) years old and between 27 and 25 years old were higher than those of women who were 36 (97.03±5.395) years old and above (p=0.031).

It was determined that marital status of women was affecting the scores of maternal attachment scale. The mean scores got from maternal attachment scale by

<table>
<thead>
<tr>
<th>Table 3. Factors affecting maternal attachment scores of women.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>19–26 years old</td>
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<tr>
<td>27–35 years old</td>
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<tr>
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<tr>
<td>Civil servant</td>
</tr>
<tr>
<td>Worker</td>
</tr>
<tr>
<td>Craftsperson</td>
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<tr>
<td><strong>Residence</strong></td>
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<tr>
<td>Village</td>
</tr>
<tr>
<td>District</td>
</tr>
<tr>
<td>City</td>
</tr>
<tr>
<td><strong>Marriage duration</strong></td>
</tr>
<tr>
<td>1–10 years</td>
</tr>
<tr>
<td>11–20 years</td>
</tr>
<tr>
<td>21 years and above</td>
</tr>
<tr>
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<tr>
<td>Primiparous</td>
</tr>
<tr>
<td>Multiparous</td>
</tr>
<tr>
<td><strong>Number of children</strong></td>
</tr>
<tr>
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</tr>
<tr>
<td>2–3</td>
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<td>4 and more</td>
</tr>
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<td><strong>Willingly planned pregnancy</strong></td>
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<tr>
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<tr>
<td>No</td>
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<td><strong>The first time when baby was breast-fed after delivery</strong></td>
</tr>
<tr>
<td>No breastfeeding</td>
</tr>
<tr>
<td>Within first half hour</td>
</tr>
<tr>
<td>Between half hour and one hour</td>
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<td>After 1 hour</td>
</tr>
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The mean scores got from maternal attachment scale by

**Table 3. Factors affecting maternal attachment scores of women.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
<th>Test value</th>
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<td>100.00</td>
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</tr>
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<td>104</td>
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<td>72</td>
<td>104</td>
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<td>After 1 hour</td>
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<td>104</td>
<td>98.86</td>
<td>101.00</td>
<td>6.615</td>
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</tr>
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</table>
mothers who were single (92.88±9.538) during the study period were lower than those of women who were married (98.10±6.041) (p=0.018).

While there is no statistically significant correlation between employment status and maternal attachment scale scores of women, the mean scores of maternal attachment scale varied according to the professions of women. The statistical analysis showed that maternal attachment scores of women who are housewife and civil servant were higher than those of women who are worker or craftsman (p=0.025).

A statistically significant correlation was found between the place where women live and the scores of maternal attachment scale. Mean maternal attachment scores of women who continuously live in city were higher than those of women who live in districts or villages (p=0.050).

It was seen that the marriage duration of women was affecting their maternal attachment scores at a statistically significant level. The maternal attachment scores of women who are married for 11–20 years were lower (p=0.000).

It was found that the gravida of women was affecting their maternal attachment scores at a statistically significant level. Accordingly, there was statistically significant difference in terms of mean maternal attachment scores between primiparous women (98.70±6.377) and multiparous women (97.62±6.095) (p=0.032). The maternal attachment scores of primiparous women were higher. It was found in the study that the child number of women was affecting their mean maternal attachment scores at a statistically significant level. The mean maternal attachment scores of women who delivered their first child were higher than those of women who had more than one child (p=0.020).

There was a statistically significant correlation between planned pregnancy and mean maternal attachment scores of women (p=0.030). Accordingly, the mean maternal attachment scores of women who planned their pregnancies were higher.

In our study, maternal attachment scores of women who breast-fed their babies after the first 30 minutes following the delivery were higher than those of women who did not breast-feed their babies or breast-fed within 30 minutes after delivery (p=0.023). The factors associated with the maternal attachment scales are shown in Table 3.

In our study, there was a negative correlation between maternal attachment scores and marriage duration and numbers of pregnancy and delivery. As the marriage duration and numbers of pregnancy and delivery increased, maternal attachment scores decreased. Also, there was a positive correlation between maternal attachment scores and first breastfeeding time and the time when partner held the baby (Table 4).

### Discussion

In our study, we found that the mean scores women got from maternal attachment scale varied according to the age. The maternal attachment levels of women who are 36 years old and above are the lowest. While there is no statistically significant correlation between the ages and maternal attachment scores of women in some studies, there are also some studies showing that maternal attachment scores of women increase as their age increases. In our study, we believe that the correlation between the increase of age and decrease of attachment is associated with the increases of marriage duration and the numbers of children and delivery.

We found that the mean maternal attachment scores of women who were single during the study period were lower. We think that this may be related with the fact that women who are married spend more and high quality time with their children as they share domestic roles and house and child-care responsibilities with their spouses.

In our study, we found that there is no statistically significant correlation between employment status and

### Table 4. Factors associated with the scores of Maternal Attachment Scale.

<table>
<thead>
<tr>
<th>Associated factors</th>
<th>p value</th>
<th>Spearmen's correlation (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score - marriage duration</td>
<td>0.003</td>
<td>-0.168*</td>
</tr>
<tr>
<td>Score - number of children</td>
<td>0.014</td>
<td>-0.142†</td>
</tr>
<tr>
<td>Score - parity</td>
<td>0.009</td>
<td>-0.151*</td>
</tr>
<tr>
<td>Score - the time when spouse holds baby</td>
<td>0.009</td>
<td>0.150*</td>
</tr>
<tr>
<td>Score - the first breastfeeding time after delivery</td>
<td>0.011</td>
<td>0.146†</td>
</tr>
</tbody>
</table>

* p<0.01 level of significance; † p<0.05 level of significance.
maternal attachment scores of women while maternal attachment scores of women who are housewife and civil servant are higher. Some studies reported that maternal attachment scores were higher in working women.\textsuperscript{[16,17]} In another study, there was no statistically significant correlation between employment status and maternal attachment scores.\textsuperscript{[8]} The increase of maternal attachment scores may be explained with the facts that civil servants who have higher incomes compared to other profession groups and women who are considered to prefer to be a housewife as they do not have any financial difficulties spare more time for and take care of their children personally.

We found that women who were residing in the city had higher mean maternal attachment scores. Considering that the city where we conducted the study is an agricultural zone, we believe that the women who live in the city are more vigorous physically and mentally than women who live in the districts and villages due to the reasons such as having less work load and not dealing with physically tiresome works like agricultural labors as well as house works. Therefore, the women who live in the city spare more time for their babies than the women who live in districts and villages, and this extra time contributes to an active attachment.

In our study, women who were married for less than 10 years and more than 21 years had higher maternal attachment scores. Durualp et al. found in their studies that women who are married for 21 years and more had higher maternal attachment scores.\textsuperscript{[17]} Unlike the results, Mutlu et al. found no significant correlation between the marriage duration and maternal attachment.\textsuperscript{[15]} As the age of mother increases, the duration of marriage increases and attachment decreases. The care responsibilities for a growing child of couples who are married more than 21 years decrease, and they spare more time with newborn. It is also believed that being a mother after a long time is a long-awaited feeling and it may increase the attachment.

In our study where we investigated the impact of gravida on maternal attachment, we found that maternal attachment level was higher in primiparous women than multiparous women. While there many studies with similar results, there are also studies showing that maternal attachment increases with the increase of child number.\textsuperscript{[15,16,18,19]} The authors highlighted that the less number of children is important in terms of the safety of attachment.\textsuperscript{[18]} This result of the study shows that maternal attachment is affected positively by the facts that women who are going to be a mother for the first time are inexperienced in terms of motherhood, they approach more sensitively to their children as they are inexperienced for taking care of a baby, they make more communication and share more with baby and they care about their responsibilities regarding baby care.

In our study, we found that women who willingly planned their last pregnancies had significantly higher maternal attachment scores. Similarly, Durualp et al. reported that women with planned pregnancy had higher maternal attachment scores.\textsuperscript{[17]} In some studies, no significant correlation was found between planned pregnancies and maternal attachment scores.\textsuperscript{[4,15]} It is considered that the factors such as woman being ready to be a mother, desiring to be pregnant, deciding to be a parent together with their spouses and woman adapting pregnancy more easily in planned pregnancies increase the level of healthy maternal attachment.

According to our data, there was no statistically significant correlation between the delivery type and maternal attachment scores of women. Work is available in studies that show similarity, as well as studies showing that attachment to vaginal deliveries is higher.\textsuperscript{[7,15–17]} We believe that this finding may be the result of the facts that data were collected retrospectively and women who did not have postpartum complication were analyzed.

In our study, we did not find any statistically significant correlation between the delivery week / week of gestation and maternal attachment scores of women. Similarly, Mutlu et al. did not find any statistically significant correlation between maternal attachment scores and term or preterm labor.\textsuperscript{[15]} Some studies reported that the maternal attachment was deteriorated after delivery as preterm babies were lacking physical contact, maternal intimacy and care during hospitalization.\textsuperscript{[20,21]} This finding in our study is a result of the facts that pregnant women gave birth at term and there was less number of babies that needed intense care.

We found no statistically significant correlation between postpartum depression and maternal attachment. Some studies reported that postpartum depression negatively affected maternal attachment levels of
We think that our finding is caused by the fact that there are few women who were diagnosed with depression and on medication.

In our study, we found a negative correlation between maternal attachment scores and the increases of marriage duration and numbers of pregnancy and delivery of women. As the marriage duration and numbers of pregnancy and delivery increase, maternal attachment level decreases. There was also a positive correlation between the first breastfeeding time after delivery and maternal attachment score. The attachment increases as the breastfeeding time increases.

Durualp et al. reported that women who held their babies within first 30 minutes after delivery and breastfed had higher maternal attachment levels. Attachment begins immediately with early breastfeeding and it contributes to the psychological, physical and mental development of children in their future lives.

**Conclusion**

In this study, we retrospectively determined the factors affecting maternal attachment in women who delivered in the last five years. Women who are in young age group (27–35 years old), who are housewife or civil servant, live in the city, married for maximum ten years, have single child and planned their pregnancies have higher maternal attachment levels.

The attachment is an emotional bond between the baby and the parents. It starts at the period between second and third trimester of pregnancy and reaches up to postpartum and newborn periods. It contributes to physical, psychological and emotional development. Safe attachment is essential for a healthy generation. Therefore, women need to plan their pregnancies willingly, and families should be observed for attachment and supported for a safe attachment.

**Conflicts of Interest:** No conflicts declared.

**References**


Three-year analysis to determine prognostic factors affecting success in single-dose methotrexate treatment: a single-center experience

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¹Gynecology and Obstetrics Clinic, Kırıkhan State Hospital, Hatay, Turkey
²Gynecology and Obstetrics Department, Kanuni Sultan Süleyman Training and Research Hospital, Health Sciences University, İstanbul, Turkey

Abstract

Objective: Our aim is to investigate the factors affecting treatment outcomes and treatment success in cases who received methotrexate for the diagnosis of ectopic pregnancy.

Methods: A total of 221 patients who admitted to Gynecology and Obstetrics Department of Kanuni Sultan Süleyman Training and Research Hospital at Health Sciences University between January 2015 and January 2018 and underwent single-dose methotrexate treatment were separated into two groups which were successful and unsuccessful. Potential demographic, clinical and laboratory results which may affect the success were compared retrospectively.

Results: The success rate after methotrexate treatment was found 76.9%. In the unsuccessful group, serum β-hCG values were significantly higher than the successful group (serum β-hCG values of successful group: 2301.61±385.9 mIU/ml, and serum β-hCG values of unsuccessful group: 5459.9±1255.3 mIU/ml; p<0.05).

Conclusion: In selected cases, single-dose methotrexate treatment is an effective alternative method for ectopic pregnancy treatment compared to surgery. β-hCG levels are significant criteria for treatment success.

Keywords: Ectopic pregnancy, single-dose methotrexate treatment, β-hCG.

Introduction

Ectopic pregnancy is defined as the condition where fertilized ovum implants mostly in Fallopian tubes, and anywhere except the uterine cavity. In recent years, the diagnosis of ectopic pregnancy can be established more early with the increased use of transvaginal ultrasonography and β-hCG in many centers. Early diagnosis contributes to the decrease in deaths related to ectopic pregnancy and cases can be diagnosed without being ruptured in this way. In ectopic pregnancy,
methotrexate was first used by Tanaka et al. in 1982.\textsuperscript{4} The success of methotrexate treatment can reach up to 92% when it is used in appropriate patients; however, since the tubal rupture risk continues despite the medical treatment and early diagnosis, it has been brought to the agenda to determine the success factors in medical treatment.\textsuperscript{5}

The purpose of our study is to investigate the factors affecting medical treatment in patients who received ectopic pregnancy diagnosis and underwent methotrexate treatment in a three-year period in our clinic.

**Methods**

A total of 471 patients who received ectopic pregnancy diagnosis and treated between January 2015 and January 2018 at the Gynecology and Obstetrics Department of Kanuni Sultan Süleyman Training and Research Hospital of Health Sciences University were reviewed retrospectively. Of the recorded patients, those underwent surgical procedure were excluded from the study. Two hundred and twenty-one patients who were suitable for single-dose methotrexate treatment were included in the study. Before the treatment, blood types, complete blood counts, liver function tests, and creatinine and blood urea nitrogen values of all patients were checked to determine conditions preventing methotrexate treatment. The patients were informed about methotrexate treatment and the informed consents of all patients were received. The cases who were stable hemodynamically, appropriate for follow-up after treatment, had ectopic focus sizes below 4 cm, were not ruptured and had no fetal cardiac activity were considered suitable for methotrexate treatment and they were administered 50 mg/m\textsuperscript{2} intramuscular single-dose methotrexate. After the administration, β-hCG values repeated on 4th and 7th day when MTX dose was administered. When there was a decrease for more than 15% between 4th and 7th days, all cases were followed up weekly until their β-hCG values decreased below 5 IU/ml, and these cases were considered successful for the methotrexate treatment. However, the cases who did not have a decrease more than 15% between 4th and 7th days, the cases with tubal rupture and hemodynamic instability, and the cases who received a second dose of methotrexate were considered to be unsuccessful cases.

In the beginning, 221 patients who underwent methotrexate treatment were separated into 2 groups, as the group with successful results for medical treatment and the group with unsuccessful results for medical treatment.

The patients in both groups were compared by reviewing retrospectively in terms of age, gravida, parity, abortion, curettage, risk factors for ectopic pregnancy, and β-hCG values in the beginning and during the medical treatment.

Statistical Package for Social Sciences 20.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis of the study. Data distribution was evaluated by Kolmogorov-Smirnov test. In addition to descriptive statistical methods (mean, standard deviation) for the analysis of the data with normal distribution, independent t-test was also used for pairwise comparison. The significance level of the results was considered p<0.05.

**Results**

The mean age of the patients was 32.33±5.5 years, week of gestation was 6.61±1.54, gravida was 2.9±1.6, parity was 1.2±1.1, curettage was 0.1±0.4, and abortion was 0.5±0.9 (Table 1). While single-dose methotrexate treatment was successful in 170 (76.9%) out of 221 patients, it was unsuccessful in 51 (23.07%) patients. Of 51 patients in the group with unsuccessful results for methotrexate treatment, laparoscopic salpingectomy was performed in 20 patients, salpingectomy by laparotomy in 10 patients and second-dose methotrexate was administered to 21 patients. Demographic, clinical and laboratory data of both groups are given in Table 2. No significant difference was found between two groups in terms of age, gravida, parity, hemoglobin and hematocrit levels. Serum β-hCG values on the day that methotrexate was administered (p<0.05), and

<table>
<thead>
<tr>
<th>Number of patients (n=221)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Gravida</strong></td>
</tr>
<tr>
<td><strong>Parity</strong></td>
</tr>
<tr>
<td><strong>Abortion</strong></td>
</tr>
<tr>
<td><strong>Curettage</strong></td>
</tr>
<tr>
<td><strong>Week of gestation at admission</strong></td>
</tr>
</tbody>
</table>
β-hCG values on 4th and 7th days was significantly higher in the group which was unsuccessful for single-dose methotrexate (p<0.001). First day methotrexate β-hCG value was 5459.9±1255.3 mIU/ml in the unsuccessful group while it was 2301.61±385.9 mIU/ml in the successful group.

When admission complaints were analyzed, there was no significant difference between two groups in terms of affecting the success of methotrexate treatment (p=0.498).

In Table 3, the groups which were successful and unsuccessful in methotrexate treatment were compared in terms of ectopic pregnancy risk factors, and the patients who had ectopic pregnancy previously and received methotrexate for risk factors and underwent surgical procedures were included. No difference was found in terms of parameters evaluated in both groups (p=0.207).

When the patients were analyzed according to the location of ectopic focus, no difference was found between two groups in terms of predicting the success of methotrexate treatment according to the location of ectopic focus (p=0.144) (Table 4).

### Discussion

Ectopic pregnancy is one of the most important reasons for maternal mortality and morbidity in the first trimester. With the increased use of ultrasonography and β-hCG values, the diagnoses can be established at an earlier period without any rupture development, and therefore medical treatment option can be offered. Since methotrexate use is effective and safe, the medical treatment decreased the frequency of surgical pro-

### Table 2. The comparison of two groups in terms of demographic, clinical and laboratory data.

<table>
<thead>
<tr>
<th></th>
<th>Successful (n=170)</th>
<th>Unsuccessful (n=51)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>32.4±5.79</td>
<td>32.0±4.67</td>
<td>0.645</td>
</tr>
<tr>
<td><strong>Gravida</strong></td>
<td>2.98±1.65</td>
<td>2.72±1.31</td>
<td>0.300</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td>1.18±1.08</td>
<td>1.17±1.05</td>
<td>0.973</td>
</tr>
<tr>
<td><strong>Abortion</strong></td>
<td>0.58±1.01</td>
<td>0.31±0.54</td>
<td>0.071</td>
</tr>
<tr>
<td><strong>Curettage</strong></td>
<td>0.11±0.47</td>
<td>0.09±0.43</td>
<td>0.780</td>
</tr>
<tr>
<td><strong>Week of gestation at admission</strong></td>
<td>6.49±1.56</td>
<td>7±1.41</td>
<td>0.040</td>
</tr>
<tr>
<td><strong>Hemoglobin value at admission (mg/dl)</strong></td>
<td>11.78±1.6</td>
<td>11.47±1.75</td>
<td>0.228</td>
</tr>
<tr>
<td><strong>Hemoglobin value at hospital discharge (mg/dl)</strong></td>
<td>11.88±1.12</td>
<td>10.41±1.22</td>
<td>0.358</td>
</tr>
<tr>
<td><strong>β-hCG value on the first day of methotrexate (mIU/ml)</strong></td>
<td>2301.61±385.9</td>
<td>5459.9±1255.3</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>β-hCG value on the 4th day of methotrexate (mIU/ml)</strong></td>
<td>1958.2±281.9</td>
<td>5844.1±1247.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>β-hCG value on the 7th day of methotrexate (mIU/ml)</strong></td>
<td>1226.1±200.3</td>
<td>5584.6±1253.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Admission complaints</strong></td>
<td></td>
<td></td>
<td>0.498</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>30 (13.6%)</td>
<td>8 (3.6%)</td>
<td></td>
</tr>
<tr>
<td>Stomachache</td>
<td>89 (40.3%)</td>
<td>23 (10.4%)</td>
<td></td>
</tr>
<tr>
<td>Inguinal pain</td>
<td>45 (20.4%)</td>
<td>19 (8.6%)</td>
<td></td>
</tr>
<tr>
<td>Menstrual delay</td>
<td>6 (2.7%)</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
</tbody>
</table>

p<0.05: statistically significant.

### Table 3. Risk factors for ectopic pregnancy in both groups.

<table>
<thead>
<tr>
<th></th>
<th>Successful (n=170)</th>
<th>Unsuccessful (n=51)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous ectopic pregnancy</td>
<td>10 (4.5%)</td>
<td>5 (2.2%)</td>
<td>0.207</td>
</tr>
<tr>
<td>Previous tubal surgery</td>
<td>6 (2.7%)</td>
<td>3 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>154 (69.6%)</td>
<td>43 (19.4%)</td>
<td></td>
</tr>
</tbody>
</table>

p<0.05: statistically significant.

### Table 4. Ectopic focus locations in both groups.

<table>
<thead>
<tr>
<th></th>
<th>Successful (n=170)</th>
<th>Unsuccessful (n=51)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubal</td>
<td>163 (73.8%)</td>
<td>46 (20.8%)</td>
<td>0.144</td>
</tr>
<tr>
<td>Cornual</td>
<td>6 (2.7%)</td>
<td>3 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Scar</td>
<td>1 (0.5%)</td>
<td>2 (0.9%)</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

p<0.05: statistically significant.
increases. However, ectopic pregnancies can also be observed in locations such as cervical area, cesarean scar line, ovary and abdomen. In our study, we did not observe any cervical and ovarian pregnancy in patients who received single-dose methotrexate; the ectopic focus was mostly in the ampulla which is consistent with the literature, and we observed in 207 (94.6%) patients that ectopic focus location was ampulla. However, the location of ectopic focus was not significant to predict methotrexate success.

In the ectopic pregnancies, different regimes are used for methotrexate treatment. They are single- or multiple-dose, local or systemic administrations. However, considering the ease of use and treatment cost, single-dose regime is preferred more frequently. In our study, we analyzed the patients who underwent single-dose methotrexate treatment.

Success rates of single-dose methotrexate administration for ectopic pregnancy reach up to 92%.[8] In our study, treatment success for the cases we administered single-dose methotrexate was 76.9%, which was consistent with the literature.

Some studies reported the presence of low β-hCG values in cases before the treatment (mostly <4000 IU/ml), absence of fetal cardiac activity and small ectopic pregnancy mass as the factors affecting the success of methotrexate treatment.[9,10] However, there are various studies reporting that high level of β-hCG in the beginning of treatment is the most important factor affecting treatment, which means that success rates significantly decreases as pre-treatment β-hCG level increases.[11,12] In our study, consistent with the literature, we found that β-hCG level was higher in unsuccessful group (5459.9±1255.3) compared to the successful group (2301.61±385.9).

In the study of Uğurlucan et al., where they reviewed 26 articles and 1327 cases, the authors found the success rate 89% for methotrexate treatment. In our study, we also found that high β-hCG value is one of the factors affecting the success rates negatively. However, we did not take ectopic focus size into consideration unlike the study of Uğurlucan et al.

Aka et al. retrospectively analyzed 65 patients who received single-dose methotrexate, and they found that 86.2% (n=56) of the patients were responsive to the methotrexate treatment while 13.8% (n=9) of them were unresponsive. While the mean hCG value of the responsive group was 1435.68±1186.1, it was 2960.11±1626.55 in the unresponsive group. There was no statistically significant difference between two groups in terms of β-hCG values. Similarly, Lispcomb et al. found that β-hCG levels were significantly high in the group which had unsuccessful results for single-dose methotrexate treatment, and they concluded that pre-treatment β-hCG values are the best prognostic data to predict the success of methotrexate treatment.[13]

Yıldırım et al. retrospectively analyzed 85 ectopic pregnancy cases who were treated with methotrexate, and found that the success rate was 88.2% after methotrexate treatment; unlike the literature, the authors found no significant difference between the cases responsive to the treatment and the cases unresponsive to the treatment in terms of pre-treatment β-hCG values, mass sizes and endometrial thickness. In our study, we considered that high β-hCG values were risk factors for the unsuccessful treatment, but we did not evaluate the endometrial thickness.

In the study of Yıldız et al., the authors retrospectively analyzed 351 patients who were established the diagnosis of ectopic pregnancy and received single-dose methotrexate, and they found that 240 (68.3%) of 351 patients were successfully treated with single-dose methotrexate while the treatments of 111 (31.7%) patients with single-dose methotrexate were unsuccessful. Mean β-hCG value was 1265 mIU/ml in the group which underwent successful single-dose methotrexate treatment while it was 5751 mIU/ml in the unsuccessful group.[14]

Kılıç et al. included 99 patients who underwent single-dose methotrexate treatment in the study, and the single-dose methotrexate treatment was successful in 67 (67.6%) patients. Serum β-hCG value was 3562 mIU/ml in the unsuccessful group and 819 mIU/ml in
the successful group, and the authors found that serum β-hCG values were significantly higher in the unsuccessful group than the successful group. [18]

Pulatoğlu et al. analyzed 101 cases with tubal ectopic pregnancy diagnosis who underwent single-dose methotrexate treatment, and they found the success rate of methotrexate treatment 77.2% (n=79). They concluded that the patients with β-hCG levels below 1362 mIU/mL are appropriate candidates for methotrexate treatment. [19]

**Conclusion**

Methotrexate treatment is safe and effective for ectopic pregnancy, and it is an effective alternative method for the treatment of ectopic pregnancy in selected cases compared to the surgical procedure. β-hCG levels are significant criteria for treatment success.

**Conflicts of Interest:** No conflicts declared.

**References**

The impact of serum anti-Müllerian hormone levels on preeclampsia prediction: a case control study

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Introduction

Preeclampsia is a gestational complication in a pregnant woman who is healthy previously but develops hypertension and proteinuria after 20 weeks of gestation.¹ It is seen in about 5–8% of all pregnancies.²,³ Preeclampsia has two types, which are early-onset and late-onset.⁴ Its physiopathology is still unclear. It has been suggested that placental hypoxia and reperfusion...
developing as a result of a problem in placental invasion are the reasons of early-onset preeclampsia. It is considered that late-onset preeclampsia is a maternal endothelial and vascular disease. Many molecules have been investigated for the prediction of preeclampsia. Anti-Müllerian hormone (AMH) is a glycoprotein hormone from the transforming growth factor family and it is also called Müllerian inhibiting substance (MIS). AMH is a hormone inhibiting the development of Müllerian ducts in male embryo. In women, it is secreted by granulose cells in small antral and preantral follicles of ovary. Serum AMH levels were found lower in women with the history of preeclampsia than normotensive women, and it has been suggested that vascular problems may have an impact on ovarian aging. The role of AMH in the cardiovascular system in addition to the endocrine system has been highlighted in the studies performed in recent years. The aim of our study is to investigate the activity of serum AMH levels in cases with late-onset preeclampsia.

**Methods**

After the approval of ethics committee was obtained, our study was conducted as a prospective case control study in the Şişli Hamidiye Etfal Training and Research Hospital of Health Sciences University between January 2015 and January 2016.

The patients who were diagnosed with preeclampsia after 34 weeks of gestation were included in the study. Healthy pregnant women at the same weeks of gestation were included in the control group. The pregnancies below 34 weeks of gestation, the patients with body mass index (BMI) over 35 and the patients whose data could not be accessed completely were excluded from the study.

Preeclampsia is defined as the condition where systolic blood pressure measured twice with 4-hour interval is >140 mmHg and diastolic blood pressure is >90 mmHg in pregnant women who were previously normotensive, and protein level in 24-hour urine is >300 mg/dL or protein/creatinine level in spot urine is >0.3 mg/dL. In the absence of proteinuria, there are also thrombocytopenia (platelet count <100,000/μL) accompanying the hypertension, impaired liver function tests (increased serum transaminase level at least two times higher than normal levels), newly-developed renal failure (serum creatinine levels >1.1 mg/dL or two times higher than the previous levels), pulmonary edema or new-onset cerebral or visual disorders. The demographic characteristics, clinical and laboratory parameters, gestational outcomes and serum AMH values of the patients measured at the third trimester were compared. Serum AMH levels of the patients were measured at the time of admission. After the samples were collected in lithium-heparin tubes, serum AMH level was measured by Cobas device (Roche Diagnostics, Risch-Rotkreuz, Switzerland) using Elecsys reagent kit (Elecsys Corporation, Lenexa, KS, USA) by ‘ECLI’ method which is electrochemiluminescence immunologic test.

**Statistical analysis**

When analyzing the data of the study, SPSS (Statistical Package for Social Sciences; SPSS Inc, Chicago, IL, USA) for Windows 20.0 was used for statistical analysis. Normal distribution was evaluated by Kolmogorov-Smirnov test. Independent t test was used for parametrically distributed numeric data, and Mann-Whitney U test was used for non-parametrically distributed numeric data. For the categorical data, chi-square test was used for parametric data and Fisher’s exact test for non-parametric data. For the correlations between serum AMH levels and other factors, Pearson’s or Spearman’s correlation analysis was used according to the distribution of data. The results were presented as mean ± standard deviation. p< 0.05 was considered statistically significant.

**Results**

A total of 62 pregnant women (32 preeclamptic and 30 control cases) were included in our study. There was no difference between two groups in terms of the demographic data. Systolic blood pressure, diastolic blood pressure, uric acid value and Esbach value were found to be significantly higher in the preeclampsia group. Fetal birth weight and week of gestation at the time of delivery were significantly lower in the preeclampsia group (Table 1).

Serum AMH values were 0.79±0.40 ng/ml in the preeclampsia group and 1.45±0.93 ng/ml in the control group (p=0.01). Serum AMH levels were significantly lower in the preeclampsia group (Table 1).

The correlation between serum AMH values and other factors was analyzed. In the correlation analysis,
negative correlation was found between the systolic blood pressure and serum AMH values ($r=-0.292$, $p=0.02$) (Table 2). No correlation was found between serum AMH levels and age, gravida, BMI, week of gestation and uric acid values (Table 2).

Discussion

In our study, we found that serum AMH values measured at the third trimester was lower in the preeclamptic pregnant women compared to the healthy pregnant women. Also, we found negative correlation between serum AMH levels and systolic blood pressure.

Preeclampsia is a complication seen frequently during the pregnancy and it is still one of the leading reasons in the world for fetal morbidity and mortality. The physiopathology of preeclampsia is still unclear. Some theories claim that genetic predisposition and the imbalance between thromboxane and prostacyclin are effective factors for the development of preeclampsia. This indicates that the maternal immune system has a significant role in the preeclampsia. In the preeclampsia, placental disorders develop between 10 and 20 weeks of gestation, and biochemical and clinical findings can only be revealed weeks, even months after these changes.

AMH is a glycoprotein hormone from the transforming growth factor family and it is also called MIS. Being a reliable indicator of ovarian reserve in particular, it is a significant marker used in ovary stimulating treatments, dose selection, prediction of poor response and ovarian hyperstimulation syndrome (OHSS), and diagnosis of polycystic ovary syndrome (PCOS). After the role of AMH in the endocrine system, its levels and physiology during pregnancy have been investigated. Köninger et al. showed that AMH levels decreased during pregnancy and they reported that the reason of this decrease is the suppression of ovary. After delivery, maternal AMH levels recover rapidly.

AMH levels in pregnant women were first investigated by La Marca et al. In their study, the authors analyzed

<table>
<thead>
<tr>
<th>Table 1. Comparison of preeclampsia and control groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preeclampsia (n=32)</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Gravida</td>
</tr>
<tr>
<td>Parity</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>AST (U/l)</td>
</tr>
<tr>
<td>ALT (U/l)</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
</tr>
<tr>
<td>Week of gestation when AMH level was measured</td>
</tr>
<tr>
<td>Week of gestation at the time of delivery</td>
</tr>
<tr>
<td>Birth weight (g)</td>
</tr>
<tr>
<td>Esbach (mg/day)</td>
</tr>
<tr>
<td>Serum AMH (ng/ml)</td>
</tr>
</tbody>
</table>

AMH: anti-Müllerian hormone; BMI: body mass index. *p<0.05 is statistically significant.

<table>
<thead>
<tr>
<th>Table 2. Correlation analysis according to serum AMH level.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Correlation coefficient</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Gravida</td>
</tr>
<tr>
<td>Parity</td>
</tr>
<tr>
<td>BMI</td>
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<td>Week of gestation</td>
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<td>Systolic blood pressure</td>
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<td>Diastolic blood pressure</td>
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<tr>
<td>Uric acid</td>
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<tr>
<td>Birth weight</td>
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<tr>
<td>1-minute Apgar</td>
</tr>
</tbody>
</table>

BMI: body mass index. *p<0.05 is statistically significant.
AMH levels during pregnancy and in the periods right after the delivery. In this study, it has been showed that there were no significant changes in AMH levels during pregnancy. It was seen that there was a decrease in the AMH levels at the third trimester which was not statistically significant. Although it is controversial if there is any placental AMH production or not, AMH levels decrease after the delivery. On the other hand, the impact of high estrogen levels on AMH gene decreases after the delivery. High level of progesteron during delivery may cause a decrease in follicles. It has been shown in other studies that there is a correlation between AMH and estradiol. AMH affects FSH sensitivity in ovaries and regulates estradiol levels.

Preeclampsia is the result of an impaired vascular condition and it has been shown that impaired vascular condition may cause the early aging of ovary. When the serum AMH levels of women with preeclampsia history and normotensive women are compared, it was found lower in women with preeclampsia (2.00±1.87 μg/L vs. 2.26±2.56 μg/L).

There are limited numbers of studies in the literature about the serum AMH levels in patients who were diagnosed with preeclampsia during pregnancy. Shand et al. found that AMH levels at the first trimester were lower in preeclamptic pregnant women compared to normotensive pregnant women. Tokmak et al. found lower levels of third trimester AMH levels in preeclamptic pregnant women compared to normotensive pregnant women, but they found no correlation between poor gestational outcomes and AMH levels. In the study, third trimester AMH value was 0.62±0.51 ng/ml in the preeclampsia group while it was 0.93±0.83 ng/ml in the control groups. In our study, we found that AMH levels were lower in the pregnant women diagnosed with preeclampsia at the third trimester compared to the healthy pregnant women (0.79±0.40 ng/ml vs. 1.45±0.93 ng/ml). Also, we found reverse correlation between serum AMH values and systolic blood pressure in our study. Our finding supports our hypothesis that the vascular factors in preeclamptic patients may suppress serum AMH level.

We believe that the low AMH levels in preeclamptic pregnant women are the result of the inhibition ovarian AMH production by vascular factors. Showing the correlation between premenopausal cardiovascular risk factors and early menopause and finding lower AMH levels in women with preeclampsia history support the hypothesis that vascular factors accelerate ovarian aging. When a correlation was found between low serum AMH levels and cardiovascular risk in the recent studies, other studies have started to investigate the functions of AMH on systems in addition to reproductive system. Although the receptor of AMH in placenta has been shown regarding to the pregnancy, there is still not sufficient information about the placental production of AMH in the literature. Also, further studies are needed to investigate the role of serum AMH levels at the first trimester in the prediction of early-onset preeclampsia and late-onset preeclampsia.

**Conclusion**

Consequently, serum AMH values are lower in the preeclamptic pregnant women at the third trimester compared to normotensive pregnant women. There is a negative correlation between serum AMH levels and systolic blood pressure.

**Conflicts of Interest:** No conflicts declared.

**References**


Intrauterine fetal transfusion in cases with immune hydrops fetalis: when and how effective it is?

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Abstract

Objective: We aimed to assess perinatal and neonatal outcomes in cases who underwent intrauterine fetal transfusion due to immune fetal hydrops, and to determine the factors associated with intrauterine fetal loss.

Methods: The cases who underwent intrauterine fetal transfusion due to the diagnosis of immune fetal hydrops within 13 months at Şanlıurfa Training and Research Hospital were retrospectively included in the study. The cases were classified according to the severity of hydrops findings. The cases with intrauterine fetal loss after intrauterine fetal transfusion were examined in terms of hydrops severity, total transfusion number, the week of gestation when transfusion was initiated and other potential associated factors compared to the cases with live fetuses. Other procedure-related complications were evaluated.

Results: A total of 11 cases with immune fetal hydrops were found, and 8 cases underwent 19 intrauterine fetal transfusion procedures. Four of 8 cases had intrauterine fetal loss after the procedure, and 4 cases gave live birth. The week of gestation that hydrops developed was determined as the primary factor associated with intrauterine fetal loss. After the procedure, it was seen that one case had spontaneous preterm labor at 31 weeks of gestation.

Conclusion: While the primary factor for the success of intrauterine fetal transfusion in cases with immune-related fetal hydrops is the severity of fetal anemia, the success rate of fetal transfusion decreases in fetal hydrops cases with early-onset anemia. The first intrauterine fetal transfusion being successful is a significant prognostic factor in order to achieve live birth.

Keywords: Fetal therapy, intrauterine transfusion, hydrops fetalis, erythrocyte alloimmunization.
Introduction
The primary indication for intrauterine fetal transfusion is the erythrocyte alloimmunization-induced fetal anemia. It is also carried out due to rarer reasons such as Parvovirus B19 infection, fetomaternal hemorrhage, twin-to-twin transfusion syndrome, and fetal/placental tumors. With the addition of Rhesus D (RhD) screening and immunoprophylaxis into the routine practice and being used more frequently, perinatal Rhesus hemolytic disease decreased prominently. Yet, it is still a significant problem due to the reasons such as insufficient practice, unidentified fetomaternal hemorrhage and timing delays. Also, with the decrease of RhD-associated alloimmunization, fetal erythrocyte alloimmunization associated with non-RhD antigens comes into prominence.

Hydrops fetalis is defined as the abnormal fluid accumulation in fetal soft tissues and serous cavities. Non-immune hydrops fetalis defines the group not associated with erythrocyte alloimmunization, and it may develop due to multiple fetal anatomic and functional reasons, and genetic and metabolic disorders. Fluid accumulation in serous cavities is defined as fetal acid, fetal pericardial effusion and fetal pleural effusion. Skin edema is also a definitive finding which develops late in hydrops cases. The most important matter in the approach towards the cases with hydrops fetalis is to define whether there is a condition that can be treated by intrauterine procedure or not. The most important part of treatable cases is the cases with fetal anemia-induced hydrops. Transfusing erythrocytes into fetus is the most successful practice among intrauterine procedures. As shown in many observational studies, intrauterine fetal transfusion prominently increases the survival rate in severe anemic fetuses. More successful results are obtained with the transfusions performed at an early stage before anemia reaches to a severe level. Therefore, transfusion can be planned in risky patients when hemoglobin level decreases below 30%.

Since the time when fetal anemia was first reported to be identifiable as non-invasive in 2000, middle cerebral artery peak systolic velocity (MCA-PSV) Doppler measurement has been used in the follow-up of the fetuses under risk. The preferred method today is to collect cord blood sample when MCA-PSV is 1.50 MOM and higher in the follow-up of the patient group under risk and to initiate first transfusion when fetal hemoglobin is below two standard deviations.

Intrauterine fetal transfusion is the standard management method in the treatment of fetal hemolytic disease, and it may be required to repeat many times during the pregnancy. Preterm labor, early rupture of membrane, chorioamnionitis, emergency cesarean section, and fetal and neonatal deaths are among the major complications associated with the procedure. Procedure-related fetal loss risk is 1–3%, and complication risk per procedure is 9%.

Methods
This retrospective study was conducted at the Perinatology Clinic of Şanlıurfa Training and Research Hospital, and the cases with fetal hydrops developed due to erythrocyte alloimmunization between June 2017 and July 2018 were included in the study group. As a tertiary center in the southeastern region of Turkey, our clinic is a busy center which accepts patients referred from nearby cities and carries out 35,000–40,000 deliveries annually. The approval of ethics committee was not obtained since the retrospective method of the study and patient management did not make any change, and the approvals for the use of patient data were taken when collecting the informed consents. The approval for using medical data in scientific studies was obtained from the hospital management. Fetal hydrops was defined according to the ultrasonographic findings. The presence of at least two findings among the following findings was defined as hydrops: Fetal acid, fetal pericardial effusion, fetal pleural effusion and fetal skin edema.

The severity of the hydrops was defined according to the ultrasonographic fetal findings. When free fluid accumulation was observed in only two cavities, it was defined as mild hydrops; with or without subcutaneous edema, fluid accumulation in more than two cavities was defined as severe hydrops. For the definition of erythrocyte alloimmunization as the etiology of hydrops, the presence of increased velocity in MCA and maternal indirect Coombs test positivity were sought. Direct Coombs test was performed on fetal cord blood sample collected before the additional first fetal transfusion, and alloimmunization was confirmed with the positive test result. Fetal karyotypes were examined on cord blood sample of all fetuses included in the study, and the aneu-
ploidies were ruled out. All transfusions were carried out as intravascular transfusion as previously defined in the literature, and transfused erythrocyte volume was calculated by the related formula (http://perinatology.com/protocols/rhc.htm). All intrauterine transfusion procedures were conducted by a single physician (EE). During the repeating transfusions, second transfusion was done ten days later, third and fourth transfusions were done two weeks later, and it was waited for three weeks for the fifth transfusion. Before the repeating transfusions, MCA-PSV being 1.32 MOM and more was considered as a criteria. When it was below that value, the transfusion was not performed. If the pregnancy was not terminated for another reason, it was followed up until 36 weeks and electively terminated at 36 weeks of gestation.

The data of the patients included in the study such as age, gravida, parity, week of gestation when diagnosis was established, initial fetal hemoglobin levels before transfusion, total transfusion numbers and weeks of gestation when transfusions were performed, transfused erythrocyte volumes, RhD or non-RhD alloimmunization data, labor indications and gestational weeks when delivery was carried out were recorded. Neonatal exchange transfusion need was reported.

### Results

During this period, a total of 11 cases with fetal hydrops associated with erythrocyte alloimmunization were identified, and 3 of them were excluded from the follow-up as they refused intrauterine fetal transfusion procedure. One case had twin pregnancy and 10 cases had singleton pregnancy. The mean maternal age was 34±4.2 (range: 24–43) years. A total of 20 intrauterine fetal transfusion procedures were performed for eight cases with singleton pregnancy. Mean week of gestation was 25±2 weeks at the time of diagnosis. While the hydrops was severe in six out of eight cases, fetal free fluid was only limited to abdominal and pericardial areas. Alloimmunization was associated with anti-RhD antibodies in 2 out of 8 patients while it was associated with non-RhD antibodies in 2 cases. Except one case with non-RhD alloimmunization, all cases had the history of fetal hydrops. Fetal loss occurred within the first 24 hours after the procedure in four of eight cases who underwent transfusion. In 3 of 4 ongoing pregnancies, the pregnancy was terminated electively at 36 weeks of gestation. In one case, the pregnancy was terminated due to spontaneous preterm labor at 31 weeks of gestation. Transfused erythrocyte suspension volumes, timings and follow-ups during repeated transfusions of the cases included in the study are given in Table 1. Except one pregnancy case terminated at 31 weeks of gestation, other three cases did not have neonatal exchange transfusion need. No neurological morbidity was found in the postnatal examination of the newborns.

### Discussion

Intrauterine fetal transfusion performed in company with ultrasonography is a golden standard treatment method for the intrauterine management of fetal anemia associated with erythrocyte alloimmunization. Although the proper approach is to initiate transfusion before hydrops develops, it is also effective when it is performed after hydrops develops.

In a wide meta-analysis, fetal survival rates were reported 80.5–93.5% for the fetal intrauterine transfusion performed due to erythrocyte alloimmunization. In a review analyzing 19 studies on intrauterine transfusion due to fetal hydrops, mean fetal survival rate was 68% (range: 50–91%). In our study, four of eight cases who underwent intrauterine transfusion due to immune fetal hydrops had fetal loss within first 24 hours after the procedure, and we found fetal survival rate 50%. Although the number of the cases in our study was less than other studies, we found similar survival rates.

All pregnancies continuing after the first transfusion achieved live births. This indicates that the continuation of the live pregnancy after the first intrauterine transfusion is significant in terms of the prognosis of hydropic fetuses. While mean week of gestation is 26.2±2.2 weeks in the ongoing pregnancies, it was 23.75±0.5 weeks in cases with fetal loss after the transfusion. Also, mean initial fetal hemoglobin level was 1.83±0.43 g/dl before the transfusion in cases with fetal loss while it was 5.7±2.5 g/dl in pregnancies which achieved live birth. Many studies reported a negative correlation between the severity of fetal anemia and fetal survival after transfusion.

Considering the severity of fetal hydrops, hydrops was severe in all of the cases with intrauterine fetal loss while it was severe in two of four fetuses which were born alive and mild in two of them. Initial fetal hemo-
globin level was more than 5 g/dl in mild hydrops cases. Van Kamp et al. evaluated the cases, who underwent intrauterine fetal transfusion due to immune fetal hydrops, according to the severity of hydrops. They reported survival rate 55% in severe hydrops cases and 98% in mild hydrops cases. Although there were insufficient data to reach this conclusion in our study, the early-onset of hydrops causes it to be severe and it seems to affect survival rate negatively.

Despite a few reported cases supporting the hypotheses that improving severe anemia and fetal hydrops by intrauterine transfusion may result with neurological sequelae of newborn, this could not be confirmed by further studies. The condition observed in these cases was rather associated with prematurity. Weisz et al. did not observe any neurological morbidity in newborns after the intrauterine transfusion treatment of 40 cases with hydrops. In our four cases, the results of newborn neurological examination were normal.

Spontaneous preterm labor started after the fourth procedure in one of four cases in which fetus was alive after the intrauterine transfusion. Except this case, there was no further complication associated with the procedure in the ongoing pregnancies. In a study where 740 cases underwent intrauterine transfusion, severe fetal bradycardia, fetal death and preterm labor, rupture of membrane and intrauterine infection were reported as the major complications associated with the procedure.

The retrospective design of our study and insufficient number of patients are the major limitations of our study.

### Conclusion

It seems that the week of gestation when hydrops develops is the most significant factor for the success of procedure in cases undergoing intrauterine fetal transfusion due to immune fetal hydrops. Fetal anemia is
more severe in cases with hydrops developing in the early second trimester, and the fetal loss risk after intrauterine fetal transfusion is higher. The first transfusion being successful is considered to be the most important prognostic factor in terms of achieving live birth.

Conflicts of Interest: No conflicts declared.

References
Evaluation of the fourth ventricle and nomogram of intracranial translucency at 11–13 weeks of gestation

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¹Department of Obstetrics and Gynecology, Haseki Training and Research Hospital, Health Science University, Istanbul, Turkey
²Perinatology Clinic, International Hospital, Istanbul, Turkey

Abstract

Objective: The aim of this study was to evaluate normal reference ranges of intracranial translucency (IT) diameter, and to obtain its nomogram in normal fetuses, during 11–13 weeks of gestation.

Methods: This was a retrospective data evaluation of first trimester ultrasound scans. A total of 2417 singleton pregnancies were included in the study. IT was measured in the nuchal translucency plane. Nomogram and formula of IT diameter were defined according to crown-rump length (CRL).

Results: The IT diameters were measured successfully in 2250 fetuses (93.1%). The mean maternal age was 31.8±4.0 years. The mean CRL was 62.0±6.9 mm. The mean IT diameter was 1.83±0.29 mm. The linear tendency was determined according to the following formula: IT (mm)= 0.54 + 0.02 × CRL (mm); r²=0.24.

Conclusion: We presented the feasibility and a nomogram of IT diameter at 11 to 13⁶ weeks of gestation in our population to be used for early prediction of neural tube defects.

Keywords: Fourth ventricle, intracranial translucency, nomogram.

Introduction

Central nervous system (CNS) malformations are the second most common category of congenital anomalies after congenital heart disease. Prenatal diagnosis of spina bifida and other neural tube defects (NTDs) is a relevant issue in modern antenatal care. Most of them are detectable by maternal serum alpha-fetoprotein or anomaly screening after first trimester.¹ [Fetal head’s sonographic findings such as “lemon-shaped” head and a “banana-shaped” cerebellum and “hydrocephalus” have been well-established in the second trimester. However, these signs may be subtle or even absent in the first trimester.²] Only a few cases of spina bifida can be detected before 12 weeks of gestation by noting irregularities of the bony spine or a bulging within the posterior contour of the fetal back³ or by the measurements of biparietal diameter.⁴

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Screening at 11 to 13\textsuperscript{th} weeks of gestation is now performed not only for the measurement of nuchal translucency (NT), but also for detecting severe malformations including open NTDs. The fourth ventricle, which presents as an intracranial translucency (IT), is easily demonstrated in the mid-sagittal view of the fetal face used for measurement of NT.\cite{6} After the IT measurement was defined, it became a part of the sonographic evaluation at 11–13\textsuperscript{th} weeks of gestation.\cite{7–12}

Since June 2011, we have introduced the measurement of IT diameter during first trimester scanning into our routine practice. Consequently, in this study, we aimed to visualize and obtain the reference ranges of IT diameter according to fetal crown-rump length (CRL) in our population and to obtain a local IT nomogram.

Methods

This study was a retrospective descriptive case series of first trimester ultrasound scans of 2531 fetuses of singleton pregnancies. All chromosomal abnormalities (n=53), cardiac anomalies (n=20), CNS anomalies (n=19), lung abnormalities (n=13), extremity anomalies (n=5) and other system anomalies (n=4) were excluded from the study which were determined by either first or second trimester screening, and 2417 fetuses were included in this study. All evaluations and measurements were performed by a single operator (MY) during 11–13-week NT scan without prolonging the scanning time. The posterior brain was examined in the mid-sagittal view as defined by Chaoui et al.\cite{6} at the first trimester screening of consecutive single pregnant women between July 2011 and December 2017. The scans were performed transabdominally using Voluson 730 Expert, E8 and E10 (General Electric, Chicago, IL, USA). When the nuchal translucency was not visualized transabdominally, a transvaginal scan was performed. In the same mid-sagittal view of the fetal face as used for measurement of NT and nasal bone, fourth cerebral ventricle (IT) was visible and measured (Fig. 1). A total of 2250 cases of which IT diameters could be measured were analyzed for this study. Postnatal outcomes were available. Biometric evaluation of all fetuses was performed by CRL and other routine parameters. According to CRL, the fetuses were divided into four groups as CRL 45–54 mm was Group 1, CRL 55–64 mm was Group 2, CRL 65–74 mm was Group 3, and CRL 75–84 mm was Group 4. The mean and standard deviation were calculated for IT diameter according to CRL groups. Nomograms and formula of IT diameter were obtained according to CRL.

Statistical method

Statistical analyses were performed using SPSS (Version 16; SPSS Inc., Chicago, IL, USA). Descriptive statistics were performed for all variables as appropriate. Mean and standard deviations of IT diameter were calculated according to groups. Linear regression analyses were used to determine the association between IT diameter and other biometric parameters.

Results

The mean maternal age was 31.8±4.0 years, and the mean CRL was 62.0±6.9 mm. The IT diameters were measured successfully in 2250 fetuses (93.1%). Maternal obesity, lack of available plane for IT visualization, early weeks of gestation and inadequate time for expanding examination were the main causes of the lacking measures. The mean IT diameter for the 11–13\textsuperscript{th} weeks of gestation was 1.83±0.29 mm, the mean values of IT diameters according to CRL ranges are shown in Table 1 and the mean

<table>
<thead>
<tr>
<th>CRL (mm)</th>
<th>Mean±SD (mm)</th>
<th>n</th>
<th>% of total n</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–54</td>
<td>1.60±0.24</td>
<td>305</td>
<td>13.6</td>
</tr>
<tr>
<td>55–64</td>
<td>1.79±0.25</td>
<td>1145</td>
<td>50.9</td>
</tr>
<tr>
<td>65–74</td>
<td>1.96±0.27</td>
<td>711</td>
<td>31.6</td>
</tr>
<tr>
<td>75–84</td>
<td>2.12±0.29</td>
<td>89</td>
<td>4.0</td>
</tr>
<tr>
<td>Total</td>
<td>1.83±0.29</td>
<td>2250</td>
<td>100.0</td>
</tr>
</tbody>
</table>

CRL: crown-rump length; IT: intracranial translucency.
values of IT diameters according to percentiles are shown in Table 2.

Minimum and maximum IT measurements were ranged between 1.2 mm and 2.6 mm (5th and 95th percentiles) during 11–13 +6 weeks. IT diameter increased linearly with CRL from a mean of 1.6 mm at CRL 45–54 mm to 2.1 mm at CRL 75–84 mm (p<0.0001). There was a significant increase in IT diameter with increasing CRL (p<0.001). A weak positive correlation was determined between IT and CRL according to the following formula: IT (mm) = 0.54 + 0.02 × CRL (mm); r²=0.24 (Fig. 2).

Discussion

Spinal dysraphism or spina bifida refers to protrusion of the spinal contents through a bone defect in the spine. Most of the spinal dysraphic defects (80–85%) are open defects and are detectable by maternal serum alpha-fetoprotein screening or by ultrasonography after first trimester. The remaining 10 to 15 percent of them are closed by normal skin covering the bone defect. Approximately 80 percent of lesions are in the lumbar, thoracolumbar, or lumbosacral areas of the spine, and the remaining lesions are in the cervical and sacral areas.[1]

Since the banana and lemon signs cannot be relied upon at first trimester, the fourth ventricle, which presents as an IT between the brain stem and choroid plexus, was first suggested in 2009 and its compression was defined as a possible marker for the detection of open spina bifida.[6] Non-visualization of the cisterna magna and posterior shift of the brain stem towards the occipital bone have also been described as early signs of open spina bifida.[7,8] In open NTD, IT is not measurable in 18%, and is under the 1st percentile in 45% of the cases.[7] Paradoxically, IT is enlarged in Blake’s pouch cyst.[8,9]

In our study, we show that IT diameter can be reliably measured in 93.1% of all normal fetuses in the standard mid-sagittal view of the face at 11–13 +6 weeks of gestation. The varying rates were reported in the literature between 87.2% and 100%.[6,7,11–15] Fetal position, obesity, gestational age and whether sonographers were obstetricians or maternal-fetal medicine specialists with a particular interest in sonography or not were significantly associated with the success of IT visualization.[7,12,14,15]

Different mean IT diameters have been reported by different clinics.[6,16,17] In a prospective multicenter trial from Germany, a total of 16,164 fetuses were examined, and 11 open spina bifida cases were identified at the first trimester screening and mean IT diameter was reported 2.1 mm.[7] In our study, we reported mean IT diameter 1.83±0.29 mm. Mean IT diameter increased from 1.6 mm at 45 mm CRL to 2.1 mm with 84 mm CRL. A prospective study with 1479 cases from our country reported mean IT diameter 1.99±2.6 mm.[14] Another study from our country reported mean IT diameter 1.77±0.4 mm.[15] This study had lower sample size compared to our data and some CNS abnormalities were not excluded from the normal cases. Peixoto et al.[16] assessed 199 fetuses at 11–13 +6 weeks of gestation in a Brazilian population. Mean fetal IT ranged from 1.6 mm at 45 mm CRL to 2.0 mm at 84 mm CRL with a mean of 64 mm CRL. A prospective study with 111 cases from China reported that IT diameter increases from 1.35 to 2.6 mm at the same gestation with a mean of 65 mm CRL.[11]
In our study, we showed that the IT diameter increased linearly with increasing CRL, which was consistent with the previous reports. A weak positive correlation was found between increasing CRL and IT in some studies like our study, but high correlation was noted in other studies. The main difference in our report was the higher sample size than previous reports.

Conclusion

We evaluated the measurability of the IT during routine first trimester NT and anatomy scanning and presented a nomogram of IT diameter at 11–13+6 weeks of gestation in our population. This marker can potentially be used for early prediction of cerebral abnormalities and other NTDs.

Conflicts of Interest: No conflicts declared.

References

Recent Advances in Ob&Gyn
3-4 November 2018
MEMORIAL ANKARA HOSPITAL
Recent Advances in Ob&Gyn

Course Directors Cihat Şen, Sertaç Esin

3 November / Kasım 2018 Saturday/Cumartesi

08.30  Registration / Kayıt

09.00  Welcome / Açılış

ULTRASOUND CARE
09.30  3D-Ultrasound in the evaluation of the fetal behavior
10.00  Preeclampsia: from prevention to prediction

10.30-11.00  Coffee time / Ara

FIRST TRIMESTER
11.00  The vanishing twin syndrome in fetal-maternal medicine
11.20  Implementation of the sFlt-1/PIGF ratio in the clinical practice
11.40  Importance of counseling in fetal screening, NIPS and CVS-AS
12.00  Aklıci ilaç kullanımı

12.15-13.30  Lunch time / Öğle

FETAL HEART
13.30  Management of fetal arrhythmias
14.00  Right aortic arch: How difficult the diagnosis is?
14.30  Fetal cardiac interventions: current results

15.00-15.30  Coffee time / Ara

FETAL INTERVENTION
15.30  Interventions for TOPS, TAPS, sUGR Management
16.00  Interventions for LUTO
16.30  Interventions for fetal lung

4 November / Kasım 2018 Sunday/Pazar

09.30-10.30

FETAL ANOMALIES
09.30  First trimester combined test vs. cfDNA: omitting NT?
09.50  How severe is hypoplasia of corpus callosum?
10.10  Posterior fossa or vermis?

10.30-11.00  Coffee time / Ara

GYNECOLOGY
11.00  Ultrasound in the evaluation of gynecological tumors
11.20  Ultrasound guided embryo transfer
11.40  Endometrial receptivity and Doppler
12.00  Uterine anomalies and perinatal outcomes

HANDS-ON SESSION
12.30-14.00  First trimester anatomy, second trimester anatomy, fetal heart, fetal brain

Chair: Cihat Şen, Murat Yayla - Oluş Api

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Editor-in-Chief does not allow any conflicts of interest between the authors, editors and reviewers. Only he has the full authority to assign a reviewer and is responsible for final decision for publication of the manuscripts in Perinatal Journal.
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