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Ownership: On behalf of the Perinatal Medicine Foundation, Cihat Şen
Managing Editor: Murat Yayla
Administrative Office: Cumhuriyet Cad. 30/5 Elmadağ, Taksim
34367 Istanbul
Due the Press Law of Turkish Republic dated as June 26, 2004 and numbered as 5187, this publication is classified as a local periodical. Perinatal Journal is published by Deomed Publishing (Copyright © 2019, Perinatal Medicine Foundation).
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Phone: (0212) 225 52 15 • Fax: (0212) 225 23 22 e-mail: editor@perinataljournal.com
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6. Main text (subtitles)
7. References (listed according to the rules of ICME)
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The efficiency of emergency cerclage for the prevention of pregnancy losses and preterm labor

Necip Cihangir Yılanlioğlu, Altuğ Semiz, Resul Arısoy
Gynecology and Obstetrics Clinic, Memorial Şişli Hospital, Istanbul, Turkey

Abstract

Objective: To analyze the gestational outcomes of the cases who underwent emergency cerclage in our clinic.

Methods: The cases which underwent emergency cerclage in Memorial Şişli Hospital between 2005 and 2017 were analyzed retrospectively. Of the cases with singleton pregnancy, those without pain and uterine contraction, those with visible cervical dilation and amniotic membrane or those with prolapsed to vagina were included in the study. The cases without cervical dilation, multiple pregnancies, the cases which clinically have chorioamnionitis, preterm premature rupture of membrane, vaginal bleeding and ablatio placentae and the pregnant women with a chronic disease were excluded from the study. The clinical characteristics and gestational outcomes of the cases were analyzed.

Results: We included a total of 28 cases in our study. Mean week of gestation was 20.9±3.2 during the cerclage procedure, delivery week was 32.4±5.5, and mean period between cerclage and delivery was 81.1±42.5 days (11.6±6.08 weeks). Late pregnancy loss was seen in two (7.1%) cases. The rates of preterm labor (<37 weeks) and extremely early preterm labor (<28 weeks) were 76.9% and 14.3%, respectively. Mean birth weight was found 2268±984 g. It was reported that three cases died at the intensive care unit, and the neonatal mortality rate was 11.5%. The rate of bringing infants to home was 82.1% (23 infants).

Conclusion: In our study, we showed that the rates of pregnancy loss and preterm labor can be decreased by cerclage procedure in the cases with cervical insufficiency requiring emergency cerclage.

Keywords: Emergency cerclage, pregnancy loss, preterm labor, cervical insufficiency

Introduction

Cervical insufficiency is one of the most important reasons of second trimester pregnancy losses and preterm labor, and it is defined as the condition where cervix is unable to maintain pregnancy without uterine contraction. Typically, it is characterized by acute and painless cervical dilation and pregnancy loss at the second trimester. The incidence of cervical insufficiency is...
0.1–2% while it is 15% in pregnancies with the history of recurrent pregnancy loss between 16 and 28 weeks of gestation.\textsuperscript{[2]} The reason of cervical insufficiency is not known mostly, but it is considered to be a structural defect in cervicoisthmic junction. It has also been reported that decidual inflammation, intrauterine infection, hemorrhage, excessive uterine distension, acquired and structural functional defects (cervical conization, cervical laceration etc.), Mullerian anomalies, and Ehlers-Danlos syndrome may be associated with cervical insufficiency.\textsuperscript{[3–6]}

Today, surgical and non-surgical methods are recommended for the treatment of cervical insufficiency. Surgical approaches include transvaginal and transabdominal cervical cerclage. Standard transvaginal cerclage method used widely was first defined by Shirodkar in 1955,\textsuperscript{[7]} and it was modified by McDonald in 1957.\textsuperscript{[8]} McDonald procedure was defined as the purse string suture from non-resorbed material to cervicovaginal junction. Cerclage indications in the singleton pregnancies are painless pregnancy loss or cerclage history at the second trimester (cerclage - prophylactic cerclage with history indication), spontaneous preterm labor history (<34 weeks), cervical length being less than 25 mm before 24 weeks of gestation (cerclage with ultrasound indication) and painless cervical dilation at the second trimester (emergency or rescue cerclage).

In our study, we aimed to discuss the outcomes of the cases which underwent emergency cerclage.

**Methods**

The cases with 13–26 weeks of singleton pregnancy that were operated due to emergency cervical insufficiency at Memorial Şişli Hospital between 2005 and 2017 were analyzed retrospectively. Of the cases, those in need of emergency cerclage, those without pain and uterine contraction, those with 1–5 cm of cervical dilatation and visible amniotic membrane or those with prolapsed to vagina were included in the study. Cases with close cervix were excluded from the study. Also, multiple pregnancies and the cases which clinically have chorioamnionitis, preterm premature rupture of membrane, vaginal bleeding, ablatio placenta and chronic disease were excluded from the study

The patients were administered 1 dose of indomethacin (Endol) 100 mg suppository right after hospitalization and emergency cerclage was planned. The surgical procedure was performed under general anesthe-
Results

Twenty-eight cases whose full results obtained were included in our study. One case was excluded from the study as her results and family could not be reached. Mean age of the pregnant women was 33.5±4.4 and their mean gravida was 1.75±1.2. While 24 cases were primigravida (85.7%) and 4 cases were multigravida (14.3%), one case had the history of cerclage. Mean week of gestation when cerclage procedure was conducted was 20.9±3.2, mean cervical dilation before the procedure was 2.5±0.8 cm, and transvaginal cervical length was 5.4±4.5 mm. Transvaginal cervical length after the procedure was 30.8±5.3 mm. The clinical characteristics of the cases are shown in Table 1. No case had cervical injury or bleeding complication during or after the cerclage procedure.

In the follow-up of 28 cases, abortion was observed in 2 (7.1%) cases. Twenty-six cases had live birth (92.9%). Vaginal delivery was preferred in 4 cases (15.4%) and cesarean section was performed in the remaining cases. Mean delivery week was 32.4±5.5 and the mean period between cerclage and delivery was 81.1±42.5 days (11.6±6.08 weeks). Preterm labor was seen in 76.9% (20/26) of the cases (<37 weeks). Of these cases, 4 (4/26; 14.3%) cases had excessively preterm labor (<28 weeks), 6 (6/26; 23.1%) had premature preterm labor (28–32 weeks) and 10 (10/26; 38.5%) had preterm labor between 32 and 37 weeks. Mean birth weight was 2268±984 g. Twelve cases needed intensive care (7–50 days). Of these cases, when 3 died at the intensive care, neonatal mortality rate was found 11.5%. Twenty-three (82.1%) infants were discharged with full health and without any complication.

The characteristics of five cases with poor outcomes (two cases of pregnancy loss, and three cases of neonatal death) are shown in Table 2. The clinical data of the cases with poor outcomes and the cases with successful outcomes were compared. However, no significant difference was found between two groups in terms of maternal age, week of gestation when the procedure was performed, cervical dilation before the procedure, cervical length and cervical length after the procedure (p>0.05) (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Clinical characteristics of the cases.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Operation day</td>
</tr>
<tr>
<td>Cervical dilation (cm)</td>
</tr>
<tr>
<td>Preoperative CL (mm)</td>
</tr>
<tr>
<td>Postoperative CL (mm)</td>
</tr>
<tr>
<td>Interval period (day)</td>
</tr>
<tr>
<td>Labor day</td>
</tr>
<tr>
<td>Birth weight (g)</td>
</tr>
</tbody>
</table>

BMI: body mass index; CL: cervical length.

<p>| Table 2. Clinical characteristics of the cases with poor outcomes. |
|--------------------|----------------|----------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Case</th>
<th>Procedure week</th>
<th>CD (cm)</th>
<th>Preoperative CL (mm)</th>
<th>Postoperative CL (mm)</th>
<th>IP (day)</th>
<th>DW</th>
<th>BW (g)</th>
<th>HDNICU (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abortion 1</td>
<td>14w 2d</td>
<td>2</td>
<td>7</td>
<td>30</td>
<td>16</td>
<td>16w 4d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abortion 2</td>
<td>21h</td>
<td>5</td>
<td>0</td>
<td>30</td>
<td>9</td>
<td>22w 2d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death 1</td>
<td>18w 1d</td>
<td>2</td>
<td>15</td>
<td>27</td>
<td>79</td>
<td>29w 3d</td>
<td>980</td>
<td>14</td>
</tr>
<tr>
<td>Death 2</td>
<td>23w 1d</td>
<td>2</td>
<td>0</td>
<td>24</td>
<td>32</td>
<td>27w 5d</td>
<td>890</td>
<td>14</td>
</tr>
<tr>
<td>Death 3</td>
<td>21w 4d</td>
<td>3</td>
<td>0</td>
<td>25</td>
<td>31</td>
<td>26w</td>
<td>850</td>
<td>3</td>
</tr>
</tbody>
</table>

BW: birth weight; CD: cervical dilation; CL: cervical length; DW: delivery week; HDNICU: hospitalization duration at newborn intensive care unit; IP: interval period up to delivery.
cerclage group and bed rest group, respectively. The rate of late pregnancy loss was 5.5% and 52.6% in the group which was on bed rest. They found that the interval period (16.8±7.9 weeks) up to delivery was significantly higher in the group which underwent emergency cerclage. They reported that the success rate of cerclage procedure in the presence of cervical dilation are controversial. However, in cases where the procedure is not or cannot be done, high rate of pregnancy loss has been reported. Ciavattini et al. compared the clinical characteristics of 19 cases that are on bed rest and 18 cases that underwent emergency cerclage, who all received diagnosis at similar weeks. They found that the interval period (16.8±7.9 weeks) up to delivery was significantly higher in the group which underwent emergency cerclage. They reported that the rate of term labor was 66.7% in this group while it was 10.5% in the group which was on bed rest. They found the rate of late pregnancy loss 3.5% and 52.6% in the cerclage group and bed rest group, respectively.

Stupin et al. retrospectively analyzed gestational outcomes of 182 cases with cervical insufficiency whose amniotic membrane prolapsed to vagina between 17 and 26 weeks of gestation, and they compared the gestational outcomes of 89 cases which underwent emergency cerclage with the gestational outcomes of 72 cases who underwent conservative procedure (bed rest, tocolysis and antibiotic treatment). They found that pregnancy was maintained significantly longer in cases which underwent cerclage (median period: 41 days vs. 3 days), and live birth rate was 72%. They found live birth rate 25% in the group which underwent conservative procedure, and they concluded that cerclage procedure improved gestational outcomes significantly. Similarly, Aoki et al. found in their study that cerclage procedure significantly improved gestational outcomes. In this study, the authors reported that median week of gestation when the procedure was performed was 22.6 (range: 15.9–26.1 weeks), the procedure extended the pregnancy period for 44 (range: 4–165) days, and mean delivery week was 32.4 (range: 19.4–41.6) weeks. In the same study, the authors found pregnancy loss in 2 (2/15; 13.3%) cases, preterm labor rate as 80% and excessively premature preterm labor rate as 20%. Prasad et al. analyzed 24 cases which underwent emergency cerclage in their study, and reported pregnancy loss 12.5%, and preterm labor rate 42%.

In our study, we also evaluated the cases which had cervical dilation and visible amnion membranes or prolapsed to vagina. The period extended by cerclage procedure was 81.1±42.5 days and mean delivery week was 32.4±5.5. We reported pregnancy loss in 2 (7.1%) cases. Similar to the literature, we found the rate of preterm labor 76.9% and the rate of excessively premature preterm labor 14.3%. With the loss of 3 cases out of 12 cases in need of intensive care, the neonatal mortality rate was 11.5% in our study. Twenty-three infants (82.1%) were discharged to their home. Zhu et al. reported the success rate of cerclage procedure 82.3% in their study. Mean number of extended days after the cerclage procedure was 52.2±26.6 and mean delivery week was 30.3±4.7. In their study, the authors reported labor rate 8.3% below 24 weeks of gestation and 12.7% at 24–28 weeks of gestation, and they found term labor rate 10.8%. Cok et al. published the results of 13 cases which underwent emergency cerclage (13–24 weeks) in their study and reported live birth in 11 (84.6%) cases, mean waiting period 9 weeks and 4 days and mean delivery week 28 weeks and 3 days. They reported that the labor was carried out before 34 weeks of gestation in 8 cases (72.7%).

It has been reported in the literature that some indicators can be used to predict the success of cerclage procedure. Amniotic membrane prolapse, presence of intraamniotic or systemic infection finding, presence of clinical symptom, and cervical dilation being ≥3 cm have been considered to be poor prognosis indicators. In our study, five cases had poor prognosis, there were two pregnancy loss cases, and three neonatal deaths due to prematurity-related problems. However, we did not find any significant difference between these cases and other successful cases in terms of cervical dilation, cervical length and cervical length after procedure. Insufficient number

### Table 3. Characteristics of the cases with successful and unsuccessful outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N=23)</th>
<th>Group 2 (N=5)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>32.9±4.2</td>
<td>34.2±1.9</td>
<td>0.489</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2±1.5</td>
<td>22.9±3.4</td>
<td>0.648</td>
</tr>
<tr>
<td>Operation day</td>
<td>147.1±21.7</td>
<td>137.4±24.4</td>
<td>0.589</td>
</tr>
<tr>
<td>Cervical dilation (cm)</td>
<td>2.4±0.7</td>
<td>2.8±1.3</td>
<td>0.671</td>
</tr>
<tr>
<td>Preoperative CL (mm)</td>
<td>5.9±4</td>
<td>4.4±6.7</td>
<td>0.411</td>
</tr>
<tr>
<td>Postoperative CL (mm)</td>
<td>31.6±5.4</td>
<td>27.2±2.8</td>
<td>0.071</td>
</tr>
<tr>
<td>Interval period (day)</td>
<td>91.5±38.2</td>
<td>33.4±27.3</td>
<td>0.006</td>
</tr>
<tr>
<td>Labor day</td>
<td>238.7±27.2</td>
<td>170.8±35.8</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Group 1: successful cases; Group 2: unsuccessful cases; CL: cervical length.

**Discussion**

Cervical insufficiency is among the significant reasons of second trimester pregnancy losses and preterm labor, and it is characterized by the dilation of cervix without uterine contraction. The success, reliability, and necessity of emergency cerclage procedure in the presence of cervical dilation are controversial. However, in cases where the procedure is not or cannot be done, high rate of pregnancy loss has been reported. Ciavattini et al. compared the clinical characteristics of 19 cases that are on bed rest and 18 cases that underwent emergency cerclage, who all received diagnosis at similar weeks. They found that the interval period (16.8±7.9 weeks) up to delivery was significantly higher in the group which underwent emergency cerclage. They reported that the rate of term labor was 66.7% in this group while it was 10.5% in the group which was on bed rest. They found the rate of late pregnancy loss 3.5% and 52.6% in the cerclage group and bed rest group, respectively.

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of cases or being the cases chosen from those in need of emergency cerclage (with cervical dilation and visible or prolapsed amniotic membrane) can be the reason. There are inconsistencies in the literature for the definitions of emergency cerclage and case selection. Therefore, this prevents proper evaluation of study results.

Wong et al. reported the complications that may develop due to cerclage procedure as bleeding, cervicovaginal fistula, perioperative membrane rupture, postoperative premature rupture of membrane, pulmonary edema (tocolysis-related), deep vein thrombosis, chorioamnionitis and ablatio placentae. Zhu et al. followed up 158 cases in their study and reported cervical laceration in 2 (1.25%) cases, pulmonary edema in 1 (0.61%) case and deep vein thrombosis in 2 (1.25%) cases. We found late pregnancy loss in two cases during the follow-up of our cases, but we did not observe any maternal complication.

**Conclusion**

In our study, we showed that the rates of pregnancy loss and preterm labor are decreased by cerclage procedure in the cases with cervical insufficiency requiring emergency cerclage.

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

**References**

The factors affecting amniocentesis decision by pregnant women in the risk group and the influence of consultant

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Abstract

Objective: The most frequent goal for prenatal diagnosis is to detect pregnancies with Down syndrome. Since karyotyping, which is the golden standard for the diagnosis, has not been replaced with a non-invasive method, pregnant women in the risk group should choose the method such as CVS and amniocentesis. Therefore, screening tests are performed by non-invasive method, and pregnant women under risk are provided genetic consultation and the family is expected to make a decision for invasive procedure.

Methods: One thousand pregnant women who were invited for second trimester, provided genetic consultation in a reference center offering Perinatology and Medical Genetics clinical services, who were candidate for chromosomal analysis, but only had increased risk in biochemical screening or due to advanced maternal age were included in the study. The requests of partners, who were accompanying during genetic consultation, of the pregnant women who approved the procedure, invasive procedure decision and the factors affecting this decision were listed.

Results: We observed that the pregnant women came for genetic consultation with an accompanying individual as the pregnant women felt that they were in a stressful environment when they came for genetic consultation. More than half of the pregnant women (52.1%) shared their decision right after genetic consultation. Almost two third of the pregnant women (63%) stated that they decided to undergo amniocentesis. The factors affecting this decision are the worthiness of pregnancy in terms of the family and potential risks of invasive procedure in general.

Conclusion: Genetic consultation is one of the most important tools of patient-doctor relationship. It is very effective thanks to its informative nature especially for making a decision for invasive procedure in pregnant women and deciding for the progression of pregnancy upon invasive test results. In this study, we aimed to emphasize the significance on genetic consultation of knowing demographic distribution according to geographical characteristics of our country, and being aware that a population, which is diverse in terms of sociocultural aspects in particular due to the cosmopolitan nature of metropolitan cities such as Istanbul, gets service.

Keywords: Genetic consultation, prenatal diagnosis, amniocentesis.

Özet: Risk grubundaki gebelerin amniyosentez kararı almasındaki faktörler ve genetik danışmanın etkisi


Yöntem: Perinataloji ve Tıbbi Genetik klinik hizmetine sahip bir referans merkezde genetik danışma verilen, kromozom analizi adayı; ancak sadece 1000 adet ikiçü üç ay gebesini çalıYNAMA dahil edildi. Onay veren gebelerin genetik danışma aldıkları sıradan; eşli bir birey isteği, invaziv girişim kararı, karar almasında etkili olan faktörler sıralanıyordu.

Bulgular: Gebelerin genetik danışma alması altya geldiklerinde bir stres ortamına girirgray hissine sahip olmaları nedeniyle, eşli bir birey genetik danışma alması tereci etkileri görülüyordu. Gebelerin yarışından fazlası (%52.1) genetik danışma aliektanda sonra kararını puastı. Gebelerin neredeyse üçte ikisi (%63) amniyosentez yapurma kararını aldığı bildirdi. Bu aracı etkileyen faktörlerin da genel olarak gebelikten aile açısından kıymeti ve invaziv girişim olası riskleri şeklinde sıralanabilirdi.

Sonuç: Genetik danışma tıbbi genetiğini en önemli hasta hekim iliskisi araçlarından biridir. Özellikle gebelerde invaziv girişim karar almadan ve invaziv test sonuçlarıyla birlikte gebeliklerini ilerleme konusundaki karar vermede, bilgilendirici özelliği sayesinde çok etkili olmuştur. Bu çalıșmanda ülkemiz徵ini coğrafi özellikleri görece demografik dağılımları bulunmaktadır, İstanbul gibi büyük şehirlerde ise kozmopolit yapı nedeniyle, özellikle sosyokültürel açıdan çeşitli olarak arz eden bir nüfusun hizmet alacağına farkındayız, genetik danışmandaki önemi vurgulamaya çalıştır.

Anahtar sözcükleri: Genetik danışma, prenatal tanı, amniyosentez.

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Introduction

Non-invasive methods in prenatal diagnosis have the characteristics of a prediction test before deciding invasive methods. These methods are:

- First trimester combined test for Down syndrome
- Second trimester biochemical test for Down syndrome
- Maternal age-related screening only
- Perinatal ultrasonography screening
- Cell-free fetal DNA (cffDNA) screening in maternal blood

With the combination of all these methods with an effective genetic consultation, the families can make invasive procedure decision.

The methods above are mainly the screening procedures for the detection of Down syndrome and other chromosomal aneuploidies, and it is aimed to determine chromosome structure of infant by using an invasive method, amniocentesis in particular, and to rule out a potential aneuploidy. Among them, cffDNA screening seems to be the most sensitive and specific method; however, its cost-benefit ratio is arguable. On the other hand, even this method has restrictions.

The importance of genetic consultation is not only informing pregnant women about the options in a detailed and accurate way but also explaining the test results together with the restrictions accurately. The aim of the study is to compare and interpret the approaches and sociocultural characteristics of pregnant women that we provide genetic consultation in cases who call into doubt of the presence of aneuploidy fetus such as Down syndrome primarily but have biochemically increased risk of Down syndrome in first and second trimester screenings or due to advanced maternal age only. We conducted the study retrospectively by collecting the data of pregnant women who were provided genetic consultation in 2009.

Methods

A total of 1000 pregnant women who received genetic consultation in 2009 included in the study. All of these pregnant women were on the second trimester and candidate for amniocentesis. The distribution of these pregnant women according to referral reason is given in Fig. 1. The most common reasons were:

- Those found to have increased risk for Down syndrome in first and second trimester biochemical tests,
- Those not found to have any pathological ultrasound finding: Except those with nuchal translucency (NT) near the limits or soft marker
- Advanced age

In brief, not the cases who were considered to have chromosomal disorders most likely but the pregnant women who were referred due to low and medium level risk and were about the make a decision were included in the study. Amniocentesis decision of these pregnant women depended on the decision of the family more than the pregnant women who would be recommended to have most likely an invasive procedure such as ultrasound findings of major anomaly and/or the pregnant women who would more likely have termination, and the genetic consultant was more influential. Therefore, although more than 3000 pregnant women were provided genetic consultation, most of them were not included in this study. Some of them were the pregnant women whose data could not be obtained during the consultations. The cases with pathological ultrasound finding, those referred for molecular genetic analysis, those who were at a gestational period later than (the cases who were recommended cordocentesis) or earlier than (the cases who were recommended CVS) second trimester, and the pregnant women who had consanguineous marriage
but were also informed for different aspects were excluded from this study.

All pregnant women were provided genetic consultation routinely, and they were delivered signed forms documenting that all available options were offered.

The ethics committee approval (no. 2017-13/53) of this retrospective study was obtained from the Medical Research Ethics Committee of Acıbadem University.

For deciding / not deciding for amniocentesis, the first decisions of the pregnant women which they shared with us verbally were taken into consideration.

Results
Most of the pregnant women participated in the consultation either alone (519/1000) or with their husbands (191/1000) (Fig. 2). The pregnant women who came alone were said that they could participate in the consultation with their husbands; 71 pregnant women later re-admitted with their husbands, 71 pregnant women re-admitted alone and 14 pregnant women re-admitted with someone else and received genetic consultation. Of the pregnant women who were not alone or with their husbands, 166 came with a relative, 83 came with a relative of their husbands, and 41 came with an individual who was not a relative (Fig. 3). For the consultations, more than 2 people were not accepted due to physical conditions.

When the pregnant women who wanted to come with someone else other than their husbands were asked for the reason, they stated that:
- They were very stressed or excited,
- The person was someone they already share their secrets,
- They had to bring a family elder,
- They had difficulties to speak Turkish or express themselves.

After the consultation, most of the pregnant women made an instant decision and shared it with us (521/1000). While 191 of them said that they did not want to have amniocentesis (191/521), 330 of them said that they wanted to have amniocentesis (330/521) (Fig. 4).

When the clinical histories of the pregnant women (n=191) who did not want amniocentesis were reviewed, it was seen that almost half of them had a shared condition. Some of them were first pregnancy, and there were also the cases who got pregnant by using assisted reproductive technology and had the history of previous loss of pregnancy, and had miscarriage risk in this pregnancy (Fig. 5). Some of these pregnant women shared their opinions about why they did not want to undergo amniocentesis (Fig. 6). The most common reason was the fear of losing pregnancy due to amniocentesis including almost all of the pregnant women who had the history of a clinical condition (Fig. 5). Some pregnant women stated that they were motivated by the desire of delivering their babies under any circumstances according to their religious, cultural or personal beliefs. Some other pregnant women stated that they did not wonder the test results, and they preferred not to learn if their babies have any chromosomal anomaly or they did not have great expectations from the test results and they knew / now knew that chromosomal anomaly test could not eliminate congenital anomaly, mental retardation etc. alone. Some of them expressed that they understood that they were in the low risk group such as borderline age risk and therefore they were not afraid of pathological results.
The factors affecting amniocentesis decision by pregnant women in the risk group and the influence of consultant

The characteristics of the pregnant women who wanted to undergo amniocentesis were:

- Not desiring to deliver a disabled baby: Most of the pregnant women in this group had at least one healthy child. Some of them stated that the pregnancy was unwanted or unplanned pregnancy.
- Deciding its necessity: After genetic consultation, some of these pregnant women expressed that the consultation with us was the only factor for making a decision. A significant part of these pregnant women had soft marker in the ultrasound\(^7\) in addition to age or biochemical test risk.

**Discussion**

Referring to screening tests in pregnancy follow-up and invasive method in cases suspected to have chromosomal anomaly is a routine approach. In all these conditions, genetic consultation is an important service and it should be provided to family in all stages. Genetic consultation which is tried to be improved technically all the time and be used more effectively\(^8\) is offered by the doctors who are medical genetic specialists in Turkey.

**Fig. 3.** Application with accompanying individuals.

**Fig. 4.** Pregnant women who made instant decision about undergoing amniocentesis after genetic consultation (n=521).
Educational level and social and cultural characteristics being spread to a wide spectrum in our country changes the feelings of families towards genetic consultation and the genetic consultant. There are also high numbers of pregnant women making a decision for invasive test with the influences such as religious beliefs and the views of family elders as well as the families who consider risk-benefit ratio according to the scientific data in our country. Another issue that should be taken into consideration in the conditions of our country is the geographical region. Both city and region differences and the distinction between city center and suburb in the same city affect such characteristics of patient population. These variables seem to be available in Asian populations, even in the members of families which immigrated to other countries. A physician offering genetic consultation should take all these characteristics in consideration. It is clear that this procedure, which is a kind of psychotherapy session, should be carried out in an unbiased and non-directive manner.

Since it is a multidisciplinary branch and it is understood today that almost all disease groups have a genetic background, patient groups from almost all medical discipline receive genetic consultation.

First trimester combined test has still been the preferred screening protocol in Turkey. In the last decade, it has been used more commonly for the screening of non-cell fetal DNA (cffDNA) in the maternal plasma, Down syndrome and other aneuploidies. Currently, cffDNA screening is far from being the first choice due to its high cost under today’s conditions of Turkey. However, screening test opportunities being broad can be the greatest support for decision-making process of families. Since the rates of false negative results in terms of Down syndrome in particular are low, it has a potential to decrease the necessity of invasive procedure considerably.

Sentimental values, beliefs, cultural characteristics and customs are also significant for the invasive procedure decision of families. This is a matter affecting all clinicians in modern medicine practices in the world. Furthermore, it is known that the patients tend towards spirituality not only during prenatal period but during terminal period in particular and it increases its importance in the relationship between patient and physician.

In Turkey, Simşek-Kiper et al. published an extensive study, which was planned as a questionnaire, about prenatal decision-making process. The study essentially aimed to discuss termination decision of pregnant women who had prenatal diagnosis. In the conclusion of the study which also provided statistical analysis as it is a systematized study, it was shown that the conditions such as referred geographical region and having a healthy child did not have a significant effect on decision-making process.
During up to the mid-periods of the first decade of 21st century where the efficiency of screening tests was lower, most of the pregnant women believed that invasive procedures for prenatal diagnosis was “a part of the routine”, so they questioned the procedure less and accepted it more easily.\textsuperscript{[15-17]}

In order for a genetic consultant to give healthy information, its standardization can be established. Introduction and meeting, informing about screening test, informing about diagnostic tests, and finally informing about the disease which is tested are generally accepted approaches for the procedure.\textsuperscript{[18]}

The choices of 1000 pregnant women included in this study are important. Since it was tried to highlight the importance and impact of genetic consultation on decision-making process, the pregnant women without high risk increase were preferred first. Pregnant women with only advanced maternal age or whose nuchal translucency measurement is not above the upper limit, those with increased risk in their first or second trimester screening, or those without any finding in the perinatal ultrasonography creating suspicion for a prominent aneuploidy seem ideal for this choice. These pregnant women are the candidates to be a mother requiring less invasive procedure thanks to the cell-free fetal DNA screening in the maternal blood which have become prevalent today. Since this opportunity was not available during the period where the service was included in the study, the pregnant women were being referred to the perinatology outpatient clinic by the center conducting the routine pregnancy follow-up. When it was understood that there was no other finding besides soft marker\textsuperscript{[7]} particularly in the perinatal ultrasonography, the patients were being referred to the Medical Genetics Clinic for genetic consultation in order to explain that invasive procedure is just an option rather than recommending it directly. As a result, 1000 pregnant women were included in this study although genetic consultation was recommended for more than 3000 pregnant women during the year. Failing to provide sufficient information was one of the reasons for excluding more than 2000 pregnant women from the study. It could be possible to guide those with pathological ultrasound finding in terms of the necessity of invasive procedure; as a matter of fact, some of these pregnant women directly subjected to invasive procedure without recommending them genetic consultation. The pregnant women referred for molecular genetic analysis were the cases to be checked for a mutation, which was already detected in the family, and for which the procedure was already decided. We tried to establish a similar group in terms of gestational period; it was important for them to have equal evaluation opportunities in the perinatal ultrasonography. The pregnant women, who were at a later period than second trimester, probably had ultrasound finding detected later and/or referred later; most of them underwent cordocentesis procedure. They were the pregnant women who were at an earlier gestational period, namely in the first trimester, and have findings usually including nuchal translucency, and were already planned for a molecular analysis due to the family history. Pregnant women who had consanguineous marriage but were also informed on different matters were excluded from this study.

After the consultation, more than 50% of the pregnant women (521/1000) made a decision and shared it with us. This shows that genetic consultant is successful to help about half of these pregnant women, who received this service, for making their decisions. In a matter that they probably did not have any information, and in such a condition which most likely causes anxiety where their unborn child “may be disabled”, it is shown that genetic consultation is an effective method in terms of informing patients and making them to make their own decision. Genetic consultation can be repeated. It is seen that 71 of the pregnant women who came alone re-admitted together with their husbands for genetic consultation. This can be related with the desire of making a shared decision. We also know that 71 pregnant women came alone and 14 pregnant women re-admitted together with another individual for genetic consultation. Reassuring the families sufficiently that they can re-admit to get information during decision-making process can be one of the most important goals of genetic consultation method.

We see that about 20% of the pregnant women who were evaluated in our center in this regard were referred due to advanced maternal age. This can be related with the distribution of socioeconomic level in the admissions made in related center. We conducted our study in the state training and research hospital which is a reference center. Most of the cases admitted to private centers may have higher education, a good career, married at an older age and/or decided to have child at an older age. In this case, the results of the study may change with center data where pregnancies at advanced ages are predominant rather than bio-
chemical risks. Also, in admissions with accompanying individuals, some of the pregnant women expressed that it is compulsory to come with a family elder, and this statement is remarkable in terms of the sociocultural structure of our society. It is possible that these pregnant women are influenced by someone else when deciding for or declining amniocentesis procedure. The reason of having genetic consultation for some pregnant women with an accompanying individual is the communication difficulty in terms of language. Also, admitting reference center by the cases that come from different regions due to demographic characteristics is important in this respect. It should be kept in mind that the communication is carried out not with the accompanying individual but pregnant woman during genetic consultation. Non-verbal communication and eye contact should be maintained in order to provide a beneficial genetic consultation environment. Today, with the prevalent use of mass media, communication problem in Turkish has become a rare case among the admissions of young pregnant women; this issue is seen due to health tourism. Trying to provide a medical service such as genetic consultation, which is primarily based on communication, to a foreign individual through a translator may cause different issues. It is necessary to document genetic consultation notes and keep a written copy in medical records.

Our study has some limitations. Since proper records cannot be obtained in order to have statistical distribution of these opinions, we classified only qualitative data. It is important to understand that cfDNA test was not a routine practice in Turkey during the years when the study was conducted and the data were collected; because it is the screening test with highest sensitivity and specificity levels today. The availability of this test will possibly affect the quality and the results of genetic consultation. With the advancement of the technique, enrichment of the literature and publication of updated good practice guidelines, prenatal screening criteria such as the definition of soft marker have been changing over time. For example, soft marker identification and screening criteria are updated every 5 years in Australia.\(^\text{[19]}\) In our study, we questioned the decisions of pregnant women made after the clinic service but we did not follow up them, and therefore we could not calculate certain rates of those who actually underwent an invasive procedure; however, the documentation of the decision made by families after genetic consultation is important. Re-designing the study and repeating it by up-to-date screening methods and determining the rate of those who actually underwent invasive procedure, and adding genetic consultation details after the test and the attitude of families about maintaining or terminating pregnancy would create beneficial data for our country. Genetic consultation in prenatal diagnosis has gradually become significant as new technologies have been implemented and genetic analyses have become more inclusive. There are similar reports about this topic, even a small number of them;\(^\text{[20]}\) however, up-to-date reviews,\(^\text{[21]}\) and even good clinical practice guidelines are needed.

**Conclusion**

In general, there are three important factors affecting genetic test decision of pregnant women who receive genetic consultation before the test. These are the information obtained from genetic consultation, risk-benefit ratio, opinion about termination, and cultural factors. Therefore, it is very important for medical genetic expert to provide unbiased and non-directive genetic consultation and establish communication in order to enable the family to make their own decisions.

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

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7. Van den Hof MC, Wilson RD; Diagnostic Imaging Committee, Society of Obstetricians and Gynecologists of Canada; Genetics Committee, Society of Obstetricians and

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**Perinatal Journal**

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The analysis of the termination of pregnancies at and after ten weeks of gestation – a monocenter study

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Abstract

Objective: We aimed to manage the termination of pregnancies, which were performed at and after 10 weeks of gestation in our clinic, better and to develop appropriate approaches for them by investigating the indications and obstetric characteristics of these cases.

Methods: The maternal data, obstetric characteristics and indications of 379 cases whose termination procedures were performed in our clinic between January 2012 and January 2019 were evaluated. The indications were grouped as maternal reasons, amniotic fluid anomalies, and isolated structural, multiple congenital and genetic disorders. The groups were classified according to their characteristics and they were compared among each other.

Results: The mean age was 30.2±6, the mean week of gestation was 17.4±3.5, and mean termination duration was 16.4±14.5 hours. The most common reason for termination was amniotic fluid anomalies (n=126, 33.2%). Among fetal reasons, the most common one was isolated structural anomalies (n=114, 30.1%). The anomalies of central nervous system were the most common isolated structural anomalies (n=60, 15.8%). Of 379 termination cases, 25 (6.6%) were caused by maternal reasons. The rates of requesting invasive examination for genetic disorders and of performing the examination were 49.6% (n=197) and 31.7% (n=120), respectively. Chromosomal anomalies were found in 69 (18.2%) cases, with trisomy 21 being the most common anomaly (n=39, 55.7%). It was found out that chromosomal anomalies were identified in more advanced maternal ages and at earlier weeks of gestation. On the other hand, isolated structural and multiple congenital anomalies (cardiac and urogenital anomalies in particular) were identified at younger ages and further weeks of gestation (maternal age, p=0.002; week of gestation, p<0.001).

Conclusion: The analysis of fetal and maternal reasons and termination complications in the management of termination cases will serve as an example for the management of diagnosis and termination processes of following pregnancies. We believe that considering the ethical, psychological and legal aspects of the terminations of pregnancies will be beneficial in developing standard approaches for this matter with the help of collaboration between families and physicians.

Keywords: Termination of pregnancy, prenatal screening, fetal anomaly.

Özet: On hafta ve üzeri gebelik terminasyonların analizi – Tek merkezli çalışma

Amaç: Kliniğimize yapılmış olan 10 hafta ve üzeri gebelik terminasyonlarının endikasyonlarını ve obstetrik özelliklerini inceleyerek, bu oлогları daha iyi yönetebilimiz ve doğru yaklaşımları geliştirebilmeyi amaçladık.


Bulgular: Ortalama yaş 30.2±6, ortalama terminasyon haftası 17.4±3.5, ortalama terminasyon süresi 16.4±14.5 saati. En sık amniyotik sıvı anomalileri nedeniyle terminasyon yapıldığı izlandı (n=126, %33.2). Fetal nedenler içerisinde en sık izole yapılıs anomalileri (n=114, %30.1) tespit edildi. Santral sinir sistemi anomalileri en çok görülen izole yapılıs anomaliler iddi (n=60, %15.8). Terminasyonların 25/379’u (%6.6) maternal nedenli idi. Genetik bozukluklar için invaziv tetkik istenme oranı %49.6 (n=197), yapılması oranı %31.7 (n=120) idi. En sık trizomi 21 (n=39, %55.7) olmak üzere kromosomal anomaliler 69 (%18.2) olduğu tespit edildi. Kromosomal anomalilerin daha ileri maternal yaş ve daha erken gebelik hafıltalarında tespit edildiği izlandı. İzole yapılıs ve çok konjenital anomalilerin ise daha genç yaşta ve daha ileri gebelik hafıltalarında saptandığı görüldü (özellikle kardiyak ve urogenital anomaliler) (maternal yaş, p=0.002; gebelik haftası, p<0.001).

Sonuç: Terminasyon olgularının yönetiminde fetal ve maternal nedenlerin ve terminasyonu komplikasyonlarının analizi, takip eden gebeliklerin tani ve terminasyon süreçlerinin yönetiminde örnek olacaktır. Gebelik terminasyonlarının etkisi, psikolojik, ekonomik ve yasal boyutlarının dikkate alınması, aile ile hekim ilişkili çerçevesinde bu konuda standart yaklaşımlar oluşturulmasına etkili olacağını görüyoruz.

Anahtar sözcükler: Gebelik terminasyonu, prenatal tarama, fetal anomalisi.

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Introduction
Today, the improvements in ultrasonography and genetic field increase the prenatal diagnosis rates of fetal malformation. Therefore, the termination of pregnancy is offered to patients more frequently as an option. This approach may also introduce some medical, ethical and legal issues.[1,2] In Turkey, termination of pregnancy can be performed upon the request of families in pregnancies which are below ten weeks of gestation in accordance with the law no. 2827.[3] At ten weeks of gestation and above, without any upper limit, termination procedure can be carried out by reasoned reports including objective results in maternal factors which may risk the maternal life or in chromosomal or congenital anomalies which may cause serious fetal outcomes.[4]

Our aim in this study is to manage the termination of pregnancies, which were performed at and after 10 weeks of gestation in our clinic, better and to develop appropriate approaches for them by investigating the indications and obstetric characteristics of these cases.

Methods
A total of 379 termination cases, which underwent their termination procedures in the Perinatology Clinic of Adana Application and Research Center at Başkent University between January 2012 and January 2019, were analyzed by years retrospectively. By using the computer system records of our hospital (Nucleus version 9.3.39; Monad Yazılım ve Danışmanlık, Ankara, Turkey), the pregnancies terminated at 10 or higher weeks of gestation due to maternal or fetal indications were evaluated. Age, gravida and parity, weeks of gestation, delivery method (spontaneous/assisted reproductive technologies), number of pregnancy (singleton/twin) and, if any, karyotype assessments of the pregnant women who underwent termination were recorded. The period up to termination, hospitalization duration, presence and number of previous uterine surgery, balloon procedure for cervical dilatation, hysterectomy frequency, hemorrhage complications after curettage, and the frequency of intracavitary balloon procedure were found.

Termination indications were separated into two groups as maternal and fetal reasons. Fetal reasons were classified as multiple congenital anomalies, isolated structural anomalies, amniotic fluid anomalies and genetic disorders. The genetic disorders were separated into 2 sub-groups as chromosomal anomalies and hereditary gene disorders (sickle cell anemia, thalassemia). The terminations before 14 weeks of gestation were determined as first trimester and at and after 14 weeks of gestation as second trimester. In addition, early and late terminations were determined as before and after 23 weeks of gestation, respectively.

Amniotic fluid anomalies were primarily separated into two groups as cases developing anhydramnios associated with preterm premature rupture of membranes (PPROM) and clinical chorioamnionitis cases. Clinical chorioamnionitis diagnosis is established by at least one of the following findings in addition to maternal fever (38°C): malodorous / purulent cervical drainage during speculum examination, uterine sensitivity during abdominal examination, maternal tachycardia (>120 bpm), persistent fetal tachycardia (>160 bpm), leucytosis (>15,000/mm³), and C-reactive protein > 5 mg/L.[5]

In our clinic, pathological assessment of placental material is performed routinely in the cases which undergo termination due to amniotic fluid anomaly. The cases diagnosed with chorioamnionitis were identified histologically. In accordance with these assessments, amniotic fluid anomalies were categorized under three groups which are PPROM-anhydramnios, clinical chorioamnionitis and clinical-histological chorioamnionitis.

Fetal deaths and pregnancies before 10 weeks of gestation were excluded from the study. Chorionic villus sampling or karyotype assay by amniocentesis were recommended for the cases considered necessary. Microarray and whole exome sequencing were recommended beginning from 2017 for all patients whose karyotype analysis results were normal. Microarray was performed only in one patient due to its cost; however, no result was obtained in that patient. The cases whose karyotype analysis results were normal, whose karyotype analysis did not yield any result or those whose families did not want karyotyping were evaluated apart from the chromosomal anomaly group.

The distribution of fetal anomalies according to maternal age, week of gestation, gravida and parity was analyzed by Kruskal-Wallis test while the distribution of fetal anomalies according to delivery type and fetus number was analyzed by chi-square test. SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) 21.0 was used. In all tests, the statistical significance level was considered 0.05.
Termination indication was decided by the committee in our clinic which included three specialists and some physicians from other branches in necessary cases. As termination protocol, 400 μg vaginal misoprostol (Cytotec; Ali Raif, İstanbul, Turkey) was administered with 3-hour intervals. Misoprostol administration doses and intervals were arranged individually in accordance with the clinical guidelines by considering obstetric and clinical characteristics such as week of gestation and history of uterine surgery.[6,7]

In cases which are at and above 23 weeks of gestation (late termination cases), termination procedure was initiated after performing intrauterine feticide. Intrauterine feticide procedure was performed by administering 2 cc 7.5% potassium chloride (KCl) after reaching fetal cardiac cavity via 22 Gauge 120 mm spinal needle with the help of transabdominal ultrasonography.

In cases which were non-responsive to misoprostol, dilation was performed by intracervical Foley catheter. Aspiration curettage was performed in cases which were found to have rest material after abortion. Hysterectomy was performed in cases which were non-responsive to induction or had uterine rupture complication.

Post-termination hemorrhages were taken under control by inflating intracavitary Foley catheter with physiological saline solution (about 80 cc). In cases with higher weeks of gestation and uterine volumes, post-partum hemorrhage could only be taken under control by Bakri balloon (Cook Women’s Health Spencer, Bloomington, IN, USA).

The consents of all patients related with the procedures to be performed were obtained.

This study was approved by the Medicine and Health Sciences Research Committee of Baflkent University (project no. KA18/329).

Results
It was seen that 507 termination cases occurred and the reason for 128 cases was fetal death during a seven-year period. In our study, mean age was 30.2±6 (range: 15–52), median gravida was 2 (range: 1–7), median parity was 1 (range: 1–5), and mean week of gestation was 17.4±3.5 (range: 10–27.6) weeks. Mean termination duration was 16.4±14.5 (range: 1–120) hours and mean hospitalization was 2 (range: 1–13) days. In terms of termination durations, there was no difference between the groups (p=0.114). Of the pregnancies, 356 (93.9%) were singleton and 23 (6.1%) were twin. The number of pregnancies conceived by assisted reproductive technologies was 45 (11.9%). One hundred pregnancies (26.4%) had previous history of uterine surgery. Mean termination duration was 16.6±14.4 hours in the cases which did not undergo uterine surgery while it was 15.8±15.2 hours in the cases which underwent uterine surgery (p=0.67). In addition, the termination procedure was completed in 24 hours in 162 (80%) cases with unscarred uterus and in 78 (81.3%) cases with scarred uterus (p=0.50).

The termination procedure was performed after 23 weeks of gestation (late termination) in 24 (6.3%) patients. In these cases, termination procedure was carried out after performing feticide by intracardiac potassium with the help of ultrasonography.

The dilatation was carried out by intracervical Foley catheter in 25 (6.6%) patients who were non-responsive to misoprostol and the termination was performed. The terminations were completed in 44.7 hours by intracervical Foley procedure. It was found that hysterotomy was performed in 1 (0.26%) patient due to uterine rupture associated with misoprostol and in 2 (0.79%) patients due to induction failure. Hemorrhage was taken under control by Foley catheter due to uterine atony in 3 patients who underwent abortion. It was found that the vaginal hemorrhage which developed in 9 (3.2%) patients who had higher weeks of gestation and uterine volume was taken under control by applying Bakri tamponade in uterine. It was found that all pregnancies which underwent Bakri balloon and hysterotomy were at second trimester (>15 weeks of gestation).

Mean termination periods and durations according to the termination indications are given in Table 1. Of 379 termination cases, 25 (6.6%) were caused by maternal reasons (Table 2). The distribution of terminations is given in Fig. 1. Amniotic fluid anomalies were the most common fetal reasons (n=126, 33.2%). They were grouped as PPROM-anhydramnios (without detecting any additional anomaly in the ultrasound screening) (n=57, 45.6%), clinical chorioamnionitis (n=10, 8%) and clinical-histological chorioamnionitis (n=58, 46.4%). Of the cases with amniotic fluid anoma-
Isolated fetal structural anomalies were detected in 114 (30.1%) cases. Among the isolated fetal anomalies, central nervous system (CNS) anomalies were the most common ones (n=60, 15.8%). Of 397 cases, invasive examination was requested for 197 (49.6%) cases and it was performed in 138 (34.8%) cases. Chromosomal anomaly was found in 69 (53.9%) out of 128 cases which underwent karyotype analysis. The distribution of genetic disorders found in the cases which underwent invasive prenatal assay is shown in Table 3.

The distribution of terminations in seven years beginning from 2012 is given in Table 4. It was observed that terminations associated with genetic disorders were the most common during the first trimester. It was seen that isolated anomalies could be diagnosed mostly during the second trimester. It was found that there was an increase in the rates of terminations associated with maternal indications in the last year, and that the rates of amniotic fluid anomalies tended to decrease over the years (p=0.001).

While chromosomal anomalies were observed in more advanced maternal ages, multiple congenital anomalies and isolated CNS anomalies were more common in younger maternal ages (p<0.001). Chromosomal anomalies and hydrops were identified at early weeks of gestation while cardiac and urogenital anomalies were identified at further weeks of gestation (p<0.001). In pregnancies with multiple congenital anomaly, median gravida and parity were lower than the other groups (p<0.001).
The rates of amniotic fluid anomalies were higher in multiple pregnancies and the pregnancies conceived by assisted reproductive technologies (independent from being multiple pregnancy) \( (p<0.05) \). The incidence of cardiac anomalies (27.3%) and amniotic fluid anomalies (16%) was statistically higher in pregnancies conceived by assisted reproductive technologies \( (p=0.04) \).

**Discussion**

The most common reason for termination was amniotic fluid anomalies (33.2%) in our clinic. Amniotic fluid anomalies frequently develop in association with underlying PPROM. Histological chorioamnionitis is identified almost 70% of PPROM cases. In the presence of clinical or suspected chorioamnionitis, delay in the decision for termination may increase maternal morbidity.\(^7,9\) In our series, we found histological chorioamnionitis in 46.4% of PPROM cases.

Excluding amniotic fluid anomalies, isolated structural anomalies \( (n=114, \ 30.1\%) \) and CNS anomalies among them were the most common ones in line with the literature.\(^1,4,10–14\) Also, Down syndrome is the leading indication in the terminations with chromosomal anomaly indication, which is consistent with the literature.\(^1,12,14,15\) This can be explained with the higher rate of diagnosing trisomy 21 in the countries carrying out national screening program during first trimester as in Turkey.\(^12,14\) Vaknin et al. performed karyotype assay in 71.4% of their cases in their study while this rate was 29.6% in our study group. Lower rate of diagnosing chromosomal anomalies in our study may be associated with the low rate of performing karyotype analysis.\(^11\)

The rate of late terminations is 13.2–34.6% in the literature.\(^17,18\) We found that the rates of late terminations (>23 weeks of gestation) were quite low (6.6%) in our study group. In addition, all of 3 hysterotomy and 12 intrauterine balloon procedures in our series were in second trimester. One of our cases with recurrent cesarean (3 CS) which was at 21 weeks of gestation

<table>
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<td>-</td>
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<td>-</td>
<td>2</td>
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</table>

Total
63 (16.6%) | 65 (17.2%) | 43 (11.4%) | 60 (15.8%) | 59 (15.5%) | 43 (11.4%) | 46 (12.1%) | 379

CNS: central nervous system; tri: trimester (1st trimester: <14 weeks, 2nd trimester: ≥14 weeks).
underwent hysterotomy associated with uterine rupture at 12th hour. Additionally, two cases, one of which was at 22 weeks of gestation and had recurrent CS and the other one at 23 weeks of gestation with previous history of CS, underwent hysterotomy due to non-responsive ness to induction (dilatation by misoprostol + intracervi cal Foley catheter balloon) at 50th and 120th hours of induction, respectively (0.79%). In another study investigating 263 cases in our region reported 6 hysterotomy procedures (caused by induction failure in 4 cases, HELLP syndrome in 1 case and uterine rupture in 1 case) (2.28%). In the literature, the rates of hemorrhage, blood transfusion, infection, post-procedure placenta retention, uterine rupture, hysterotomy and hystereotomy complications were reported higher in second trimester terminations than first trimester terminations, independent from all risk factors.\textsuperscript{[20]}

Yapar et al. compared Bishop score ≤4, extra-amniotic ethacridine lactate in terminations conducted between 4 and 28 weeks of gestation, intracervical prostaglandin, E2 gel, IV concentrated oxytocin, vaginal misoprostol and balloon procedure in 340 cases in their study. Being unable to complete termination procedure in 48 hours was considered as a failure, and success was achieved in all groups with a success rate of 98.8%. It has been reported that ethacridine lactate, balloon and oxytocin procedures are faster and cheaper methods. Maternal death associated with uterine rupture occurred in a case which underwent oxytocin. It was reported that the extension of induction period in late terminations in particular causes the increase of complications.\textsuperscript{[21]} It is known that prostaglandins are the most effective agents to mature the cervix.\textsuperscript{[22]} There is no sufficient number of studies on the dosage and method of vaginal misoprostol administration during the publication date of the study; we found that the administration of maximum 600 μg misoprostol in a total of 36 hours was insufficient compared to other treatment methods. In the termination procedures performed in our clinic, mean vaginal misoprostol administration dose was 1200 μg.

Yüce et al. evaluated 112 cases of second trimester termination in their recent study, and they administered misoprostol in 50 cases, and used cervical Foley in 32 cases and cervical Foley + single dose of misoprostol in 30 cases. When they compared the methods in terms of efficacy, adverse effects and complications, they observed that the termination duration was significantly shorter in misoprostol group; only the misoprostol group had 2 uterine rupture cases. They claimed that the efficacy increased and complications decreased when misoprostol and intracervical Foley procedure were combined.\textsuperscript{[23]}

In another study conducted in Turkey, the authors separated 337 second trimester termination cases with cesarean section history into three groups which were those with cesarean section history for once, twice and more, and the cases had 200 μg misoprostol administration intravaginally with 4-hour intervals. Intracervical Foley was applied to the cases which did not undergo termination up to 24 hours. The authors observed no difference among the groups in terms of termination completion period within 24 hours, Foley catheter procedures at the end of 24 hours (11.9%) and major complications including uterine rupture. It was reported that Foley catheter procedure in addition to misoprostol was efficient and safe in cases which underwent cesarean.\textsuperscript{[24]}

In our studies, 100 cases had cesarean section history. We did not find any significant difference between scarred and unscarred uterines in terms of termination durations.

In their meta-analysis results, Andrikopoulou et al. found similar efficacy for prostaglandin E1, E2 and mechanical methods in second trimester terminations of scarred cases (1 and more cesarean section histories). In their study, the most commonly used cervical agent was prostaglandin E1 analogue (misoprostol), the vaginal termination rate by misoprostol was 96.8%, the termination rate within 24 hours was 76.3%, and the uterine rupture rate was 0.8%. While uterine rupture rates were similar in the cases that were applied prostaglandin E1 and had one cesarean section during their second trimester terminations, there was a slight increase in the uterine rupture risk of those who had two or more cesarean section previously.\textsuperscript{[25]} In our study, the uterine rupture rate was 0.26% and we did not find any difference in scarred uterines in terms of rupture.

While the clinicians may make termination decision easily in anomalies which are near-fatal or will cause severe disability if the fetus is born, it may be difficult to make termination decision in patient groups which are non-fatal but include additional problems such as trisomy 21 although the opinions of family, podiatrist or physician from relevant field are taken. If the family
decides to terminate the pregnancy, it should be evaluated carefully if there is any severe malformation that will require the termination of the pregnancy or if it is in compliance with the legal regulations. The delayed terminations in particular may introduce many ethical or medicolegal issues. In addition to the laws of country, many factors such as health system, educational level, cultural characteristics, beliefs and socioeconomic status of families and the sex of fetus have an influence on the termination decision.\[31\]

The Maternal-Fetal Medicine and Perinatology Society of Turkey reported in their Ankara Declaration in 2011 that terminations after 24 weeks of gestation are not ethical.\[26,27\] Yet, in accordance with the legal regulations, pregnancies can be terminated under necessary conditions without any upper limit for week of gestation in Turkey. Similar to Turkey, there is no upper limit for the termination of pregnancy in some countries such as Austria, Denmark, Belgium, England, Switzerland and Russia. However, some other countries such as Germany, Iran (upper limit is 16 weeks of gestation), Spain and Poland (upper limit is 12 weeks of gestation) limited termination of pregnancy due to medical reasons up to 22 weeks of gestation. In addition, some states of the USA and some European countries defined obligatory legal periods to reconsider the decision after patients are informed about termination by physicians.\[28\] Turkey does not have such a practice yet. If it is considered that fetus can live after 23 weeks of gestation, neonatal resuscitation and hospitalization at intensive care unit may be decided if it is born alive. Therefore, pregnancy terminations are carried out by performing intrauterine feticide procedure.

Conclusion
In our series, the most common reason for terminations was amniotic fluid anomalies while isolated fetal anomalies were the second most common reason. Chromosomal anomalies were identified in more advanced maternal ages and at earlier weeks of gestation. We observed that isolated structural (cardiac and urogenital anomalies in particular) and multiple congenital anomalies were identified at younger ages and further weeks of gestation.

We believe that detailed analysis of fetal and maternal reasons in the management of termination cases will be beneficial for both current pregnancy of mother and other following pregnancies. We think that considering the ethical, social, psychological, economic and legal results of the termination of pregnancy and carrying out terminations in collaboration with families and physicians will be effective in developing standard approaches for this matter.

Conflicts of Interest: No conflicts declared.

References


Failure of getting intracranial translucency image in posterior fossa in the examination of singleton pregnancies at 11–13 weeks of gestation: reasons and outcomes

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Abstract

Objective: To investigate the reasons and outcomes of being unable to see intracranial translucency (IT), and to determine the sensitivity, specificity, positive and negative predictive values and our diagnostic accuracy rate for the poor outcomes that may follow IT negativity.

Methods: This study was designed as the retrospective assessment of the data of 2670 singleton pregnancies. The evaluation of cerebral structures and posterior fossa was conducted on classical nuchal translucency evaluation plane and the cases, IT of whose could not be seen or measured, were included in the study. The distribution of chromosomal anomalies, malformations and fetal losses which may affect gestational prognosis as well as maternal characteristics of these cases was evaluated and they were compared with the group considered normal.

Results: The rate of the cases whose IT could not be measured in posterior fossa was 4.05%. Compared to the group whose IT could be measured, poor prognosis of gestation, fetal loss or termination of pregnancy, chromosomal markers of early period and the presence of chromosomal anomaly, and the rate of central nervous system and other system malformations were higher in a statistically significant manner in the group whose IT could not be measured. Of the IT non-measurability, the sensitivity was 26.9%, the specificity was 95.9%, the positive predictive value was 21.9%, the negative predictive value was 96.9%, the accuracy rate was 93% and the odds ratio was 8.7 to predict the poor gestational prognosis mentioned above.

Conclusion: The findings of our study make us think that intracranial translucency can be used as a parameter helping classical methods for the early diagnosis of the malformations of central nervous system and other systems, and some chromosomal anomalies, and that it can be useful to use it in routine perinatal assessment.

Keywords: Intracranial translucency, ultrasonography at 11–13 weeks of gestation, central nervous system defect, chromosomal anomaly.

Özet: Tekil gebeliklerin 11–13 hafta incelemesinde posterior fossada intrakraniyal saydamlık görüntüsünün elde edilememesi: Nedenler ve sonuçlar

Amaç: Intrakraniyal saydamlık (IT) görüntülememisinin neden ve sonuçlarını araştırmak, IT negatiftiğinin takip edebilen olumsuzluklardaki düyarılığı, özgünlüğü, pozitif ve negatif belirleyicilikleri ve tanısal doğruluk oranının belirlenmesi.

Yöntem: Bu çalışma 2670 tekil gebeliğin verilerinin retrospektif değerlendirilmesi olarak tasarlandı. Serebral yapılar ve posterior fossa inceleme klasik ense kalınlığında inceleme planında gerçekleştirildi ve IT’nin görüntülememesi veya ölçülememesi olguların doğrulanış grubunu oluşturmaktadır. Bu olgulardaki maternal özellikleri, nihai gebelik prognozu, fetüs kayıplarının dahil olmaksızın anelerin normal olarak kabul edilen grup ile karşılaştırıldır.

Bulgular: Posterior fossada IT ölçülememeyen oğul oranı %4.05 idi. IT ölçülemememiş grup ile karşılaştırıldığında IT ölçülemememiş olan grubun köti gebelik prognozu, fetüs kaybı veya gebelik sonlandırma işlemi, erken döneme ait kromozomopati belirteçleri ile kromozom anomalisi varlığı, merkezi sinir sistem ve diğer sistem malformasyonlarının oranı istatistiksel olarak anlamalı şekilde daha yüksek saptandı. IT görüntülemememinin yukarıda sayılan kötü gebelik prognozu tahmin etmedeki düyarılığı %26.9, özgünlüğü %95.9, pozitif belirleyiciliği %21.9, negatif belirleyiciliği %96.9, doğruluk oranı %93, olasılık oranı 8.7 olarak saptandı.

Sonuç: Çalışmanın sonuçlarında, intrakraniyal saydamlık görüntülememeyi, intrakraniyal saydamlığın merkezi sinir sistem ve diğer sistem malformasyonları ile baza kromozom anomalilerinin erken tanısında klasik yöntemlere yardımcı bir parametre olarak yer alabileceğini ve rutin perinatal incelemenin içinde kullanılmasının faydaları olabileceğini düşündürmektedir.

Anahtar sözcükler: Intrakraniyal saydamlık, 11–13 hafta ultrasonografi, merkezi sinir sistem içi defekti, kromozom anomalisi.
Introduction

Today, it is considered helpful to use ultrasonography examinations beginning from first trimester for the early diagnosis of fetal defects and malformations.\(^1,2\) Efforts are made and new methods are recommended for more than two decades for the early diagnosis of cranial malformations and other defects related with neural tube in particular.\(^3,4\) The most recent one is the measurement of intracranial translucency defined by Chaoui et al. in 2009, and the authors recommended the assessment between 11 and 13 weeks of gestation.\(^5\) While initial applications were mostly for the early diagnosis of spina bifida,\(^6–8\) further studies reported that this measurement could be used for chromosomal anomalies and other defects.\(^9–11\)

The common point of origin of all these studies is the deviations from normal posterior brains structures examined between 11 and 13 weeks of gestation, and they aim to establish early diagnosis of both spina bifida and other neural tube defects. On the other hand, being unable to see or measure IT in the posterior fossa examination between 11 and 13 weeks of gestation does not always indicate an anomaly.\(^9\)

We carried out some preliminary studies on IT presence in the previous years and generated some nomograms by the weeks of gestation.\(^14–16\) In our present study, we aimed to investigate the reasons and outcomes of being unable to see intracranial translucency (IT), and to determine the sensitivity, specificity, positive and negative predictive values and our diagnostic accuracy rate for the poor outcomes that may follow IT negativity by extending our current series slightly further.

Methods

The data of this study were obtained by the retrospective evaluation of the reports of 2670 singleton pregnancies examined between 11 and 13 weeks of gestation during a 7-year period between July 1st, 2011 and June 30th, 2018. Of the pregnancies, 94.3% were routine cases while 5.7% were referred cases, and 98.8% of the examinations were carried out transabdominally while 1.2% of them were carried out transvaginally. The cases whose crown-rump length (CRL) measurements were between 45 and 84 mm and which underwent detailed anatomic examination were included in the study group, and maternal age, anatomic-pathological characteristics of uterine, image quality, week of gestation, biometric data such as CRL, biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL), nuchal translucency (NT) from genetic markers, nasal bone, the presence of ductus venosus diastolic flow, and also the presence of major malformation, if any, were noted for each case. NT and other genetic marker measurements were carried out in accordance with the guidelines of the Fetal Medicine Foundation (London, UK).\(^17\)

The examination of cerebral structures and posterior fossa was carried out on classic NT examination plane as described by Chaoui et al.,\(^6\) and the distance between the external echogenic line of inferior border of brain stem and the internal echogenic line of choroid plexus of the fourth ventricle was measured twice for IT measurement, and the mean value of these two measurements was calculated. In cases where sagittal plane view of IT was suspected, it was confirmed by transverse plane examination. The cases whose IT could not be seen or measured were not accepted pathologically for clinical follow-ups, the clinical follow-up protocol was not changed, and karyotyping procedures were carried out only according to the classical screening findings.

Second trimester examination was performed in all singleton pregnant women (n=1914) who did not found to have any pathology in the first trimester examination, whose pregnancies were not terminated and admitted for the follow-up, and the progress and results (defects and malformations, karyotype and microarray anomalies, fetal losses and terminations) of the cases whose IT could not be seen in particular were investigated. The cases whose IT could not be seen were noted if they had malformations in central nervous system (CNS) and other organs or were normal. Karyotype, extracellular (free) DNA, third trimester ultrasonography or delivery reports of the followed-up cases, if any, were accessed and their gestational progresses were found. A total of 752 cases who did not show up to their follow-ups and whose prognosis could not be reached were excluded from the study. Second trimester ultrasonography examination was carried out in accordance with the guidelines of International Society of Ultrasound in Obstetrics & Gynecology Education Committee (ISUOG) published in 2007.\(^18\)

Sonography examinations for both trimesters were carried out by a perinatologist via GE-patented Voluson 730 Expert E8 and E10 devices (GE Healthcare,
Chicago, IL, USA) with the help of linear or 4-D probes (RAB 2-5, AB 2-7, RM6C, RIC 5-9, IC5-9, C1-5D).

SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The definitive statistics were given as mean and standard deviation for numerical variables and as number and percentage for categorical variables. Normal distribution analysis was performed by Kolmogorov-Smirnov test, and Student’s t-test was used to compare group mean values and chi-square test was used to obtain the rates of categorical variables among the groups. p<0.05 was considered statistically significant. OR, sensitivity, specificity, positive and negative predictive values and diagnostic accuracy rate were used to evaluate the risk level of not getting IT image between the groups.

Results
In a total of 2670 singleton pregnancies which underwent first trimester examination, 752 cases were not followed up, 1832 cases were normal, 56 cases had classical karyotype or chromosomal microarray anomaly, 22 cases had fetus loss without chromosomal anomaly, and 4 cases had acrania. The cases with acrania were excluded from the study.

The rate of the cases whose IT could be measured in posterior fossa was 95.95% while the rate of those whose IT could not be measured was 4.05% (108/2666). IT measurement was not performed in 3.61% of the routine examination group and in 13.56% of the referred case group. This 3.7 times higher difference between the groups was considered statistically significant (p<0.001). Of the entire group, 28.21% did not undergo a second examination, and this “non-followed-up” group was excluded from the study. Among the cases who came for a second examination, the rate of IT(-) cases was 3 times higher than those who did not come for the second examination, and this difference was statistically significant (p<0.05). The distribution of followed-up and non-followed-up cases according to whether they were referred cases or not is given in Table 1.

Weeks of gestation and mean CRL values of IT(+) and (-) groups were similar. However, mean NT values were significantly higher in IT(-) group (p<0.001) (Table 2).

The findings showing the relationship between IT measurability and prognosis are shown in Table 3. The rate of poor gestational prognosis in IT(-) group was higher than IT(+) group which was statistically significant (about 7 times higher: 3.14% vs. 21.87%; p<0.001).

When the demographic and biometric characteristics of the cases whose IT could be measured were compared between the groups with normal and abnormal prognosis, it was found that maternal age and mean CRL, NT, IT, BPD and HC values were higher which were statistically significant although examina-

| Table 1. The distribution of the cases according to their referral and follow-up status before and after intracranial translucency (IT) examination at 11–13 weeks of gestation. |
|---------------------------------|----------------|----------------|----------------|----------------|
| Total n (%)                      | 2666 (100%)    | 2548 (95.57%)  | 118 (4.42%)    | 752 (28.21%)   |
| IT(+) n (%)                      | 2558 (95.95%)  | 2456 (96.39%)  | 102 (86.44%)   | 740 (98.40%)   |
| IT(-) n (%)                      | 108 (4.05%)    | 92 (3.61%)     | 16 (13.56%)    | 12 (1.60%)     |
| Statistical significance         |               |               |               |               |
| p<0.001                          |               |               |               |
| p<0.05                           |               |               |

| Table 2. Intracranial translucency (IT) at 11–13 weeks of gestation: biometric data of the followed-up cases. |
|---------------------------------|----------------|----------------|----------------|----------------|
| CRL: crown-lump length; NT: nuchal translucency. |
| Total n (%)                      | 1914 (100%)    | 12.28±0.73     | 62.08±6.88     | 1.83±0.81      |
| IT(+) n (%)                      | 1818 (94.98%)  | 12.28±0.53     | 62.16±6.76     | 1.78±0.68      |
| IT(-) n (%)                      | 96 (5.02%)     | 12.25±0.60     | 60.46±8.49     | 2.63±2.09      |
| Statistical significance         | p>0.05         | p>0.05         | p<0.001        |               |
Failure of getting intracranial translucency image in posterior fossa in the examination of singleton pregnancies at 11–13 weeks

Table 1. The distribution of the cases with normal and abnormal prognosis after intracranial translucency (IT) examination at 11–13 weeks of gestation.

<table>
<thead>
<tr>
<th>Followed-up cases</th>
<th>Normal prognosis</th>
<th>Abnormal prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n (%)</td>
<td>1914 (100%)</td>
<td>1836 (95.92%)</td>
</tr>
<tr>
<td>IT(+) n (%)</td>
<td>1818 (94.98%)</td>
<td>1761 (96.86%)</td>
</tr>
<tr>
<td>IT(-) n (%)</td>
<td>96 (5.02%)</td>
<td>75 (78.13%)</td>
</tr>
<tr>
<td>Chi-square test</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

*Those with normal findings in second trimester perinatal ultrasonography, cfDNA, karyotype or delivery. †Those with abortion, fetal loss or anomaly, karyotype or chromosome pathology.

Of the IT non-measurability, the sensitivity was 26.9%, the specificity was 95.9%, the positive prediction value was 21.9%, the negative prediction value was 96.9%, the accuracy rate was 93%, the odds ratio was 8.7 and the confidence interval was 5.0–15.0 to predict the poor gestational prognosis. Diagnostic performance results related with various system anomalies, chromosomal anomalies, abortions and gestational losses which establish the poor prognosis are shown in Table 7.

When technical and imaging conditions during the examination are taken into consideration in all cases of the main group, the maternal age, reported obesity, uterine anomalies, myomas and position disorders, and posture disorders of fetus were statistically different in

Table 4. The comparison demographic and biometric data of intracranial translucency (IT)-measured cases (n=1818) between the groups with normal and abnormal prognoses.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Age</th>
<th>Week of gestation</th>
<th>CRL</th>
<th>NT</th>
<th>IT</th>
<th>BPD</th>
<th>HC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal prognosis</td>
<td>1761 (96.86%)</td>
<td>31.74±3.89</td>
<td>12.28±0.52</td>
<td>62.26±6.71</td>
<td>1.72±0.47</td>
<td>1.82±0.29</td>
<td>20.37±.21</td>
</tr>
<tr>
<td>Abnormal prognosis</td>
<td>57 (3.14%)</td>
<td>34.39±.77</td>
<td>12.2 ±0.70</td>
<td>58.67±8.23</td>
<td>3.79±2.13</td>
<td>1.94±0.45</td>
<td>19.57±2.80</td>
</tr>
<tr>
<td>Statistical significance</td>
<td>p&lt;0.001</td>
<td>p&gt;0.05</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

BPD: biparietal diameter; CRL: crown-lump length; HC: head circumference; NT: nuchal translucency.

Table 5. The distribution of prognosis according to the sub-groups after intracranial translucency (IT) examination at 11–13 weeks of gestation.

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Chromosomal anomaly</th>
<th>Abortion or losses*</th>
<th>Temporary finding†</th>
<th>Normal‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1914 (100%)</td>
<td>56 (2.93%)</td>
<td>22 (1.15%)</td>
<td>1772 (92.58%)</td>
</tr>
<tr>
<td>IT(+)</td>
<td>1818 (94.98%)</td>
<td>44 (2.42%)</td>
<td>13 (0.72%)</td>
<td>1701 (93.56%)</td>
</tr>
<tr>
<td>IT(-)</td>
<td>96 (5.02%)</td>
<td>12 (12.5%)</td>
<td>9 (9.38%)</td>
<td>71 (73.96%)</td>
</tr>
<tr>
<td>Chi-square test</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.05</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

*Abortions or intrauterine fetal losses with unknown or normal karyotype. †Temporary finding: The cases which exhibit changes within physiological borders in the cerebral ultrasonography but have normal prognosis. ‡The cases which have at least a second ultrasonography examination and/or fetal genetic analysis and/or delivery results.

Chromosomal anomalies, fetal loss or termination of pregnancy were higher in the group with non-measured IT than the group with measured IT (p<0.001). No negative finding was found in 73.96% (71/96) of the group which was IT(-) and followed up, and cerebral findings (Blake’s pouch cyst, mild ventriculomegaly, etc.) which require follow-up but do not affect the prognosis were observed in 4.17% (4/96) of them. The IT negativity in the initial findings of 71 cases, which were considered normal, was interpreted as false negativity. In this case, the impact of actual IT negativity (n=25) on poor prognosis was calculated 84% (Table 5).

When ultrasonography examinations of IT(-) cases were assessed as sub-groups, the rates of chromosomal markers of early period (NT, nasal bone, ductus venosus), and CNS and non-CNS malformations and defects were found higher than the IT(+) group (p<0.001). The markers and malformations which can be seen after 13 weeks of gestation were similar in both groups. Karyotype and cfDNA analyses were also referred much more in IT(-) group and more chromosomal pathologies were found in this group (p<0.001) (Table 6).
IT(-) cases than IT(+) cases. The details can be seen in Table 8. It was found that these factors are prominent and there is no fetal pathological results in the cases (n=71) which are false negative in particular. When these cases causing false negativity are excluded, the rates of chromosomal anomaly, malformation and negative prognosis increase to 48%, 68% and 84%, respectively. Some cases with normal and abnormal findings are shown in Figs. 1–4.

Discussion

Most of the studies conducted on the intracranial translucency are for the early diagnosis of open spina bifida.[6–8] In our study, we aimed to investigate the reasons for non-measurability of IT and what outcomes are introduced in the presence of other findings following this finding.

We found in our study that IT measurement was not done in approximately 4% of all cases during early period examination. This rate was between 0% and 5% in other series.[4,19–21] When we reviewed the literature, we found out that many studies on IT issue were rather archive studies which investigated recorded images retrospectively.[13,22,23] When these examinations were re-evaluated, it was found that any fluid image seen in posterior fossa of some fetuses could be measured as IT by accident.[8] We did not scrutinize false positivity as it may be difficult to carry out prospective investigation on archived images in the studies with wide series such as ours; however, we decreased the negative influence of this matter on our results by investigating the follow-ups and prognoses of IT(+) cases.

Considering the followed-up cases (n=96) in our series, we found that 73.9% of IT(-) cases were completely normal, 4.2% of them had normal prognoses together with mild findings such as Blake’s pouch cyst, and 21.87% of them had significant issues. When we excluded the cases that we interpreted as false negative, the rate of actual IT(-) cases was 1.3% (25/1914). We revised the rate of ending with a poor prognosis as 84%.

In our study series, the number of IT(-) cases among the pregnant women referred with other reasons was not high. The majority of pregnant women referred with other reasons were chromosomal abnormalities (14% of whole cases). When we reviewed the literature, we found that many studies on IT issue were rather archive studies which investigated recorded images retrospectively.[13,22,23] When these examinations were re-evaluated, it was found that any fluid image seen in posterior fossa of some fetuses could be measured as IT by accident.[8] We did not scrutinize false positivity as it may be difficult to carry out prospective investigation on archived images in the studies with wide series such as ours; however, we decreased the negative influence of this matter on our results by investigating the follow-ups and prognoses of IT(+) cases.

Table 6. Intracranial translucency (IT) examination at 11–13 weeks of gestation and the findings of malformation and karyotype obtained afterwards.

<table>
<thead>
<tr>
<th></th>
<th>Total n (%)</th>
<th>IT(+) n (%)</th>
<th>IT(-) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>1914 (100%)</td>
<td>1818 (94.98%)</td>
<td>96 (5.02%)</td>
</tr>
<tr>
<td>Cases with (+) markers at 11–13 weeks</td>
<td>51 (2.66%)</td>
<td>29 (1.59%)</td>
<td>22 (22.92%)</td>
</tr>
<tr>
<td>Malformations at 11–13 weeks</td>
<td>38 (1.98%)</td>
<td>21 (1.15%)</td>
<td>17 (17.71%)</td>
</tr>
<tr>
<td>CNS malformations at 11–13 weeks</td>
<td>24 (1.25%)</td>
<td>14 (0.77%)</td>
<td>10 (10.42%)</td>
</tr>
<tr>
<td>Malformations except CNS at 11–13 weeks</td>
<td>27 (1.41%)</td>
<td>13 (0.71%)</td>
<td>14 (14.58%)</td>
</tr>
<tr>
<td>Malformations at 14–27 weeks</td>
<td>22 (1.15%)</td>
<td>21† (1.18%)</td>
<td>1† (1.39%)</td>
</tr>
<tr>
<td>Genetic analyses</td>
<td>169 (8.83%)</td>
<td>140 (7.00%)</td>
<td>29 (30.21%)</td>
</tr>
<tr>
<td>Karyotype-chromosome anomalies</td>
<td>56 (2.93%)</td>
<td>44 (2.24%)</td>
<td>12 (12.50%)</td>
</tr>
</tbody>
</table>

Statistical significance: p<0.001, p<0.001, p<0.001, p<0.001, p>0.05, p<0.01, p<0.001.

*Early genetic markers: nuchal translucency, nasal bone and ductus venosus abnormalities. †The data calculated on the basis of second trimester examination finding.

Table 7. Sensitivity, specificity, positive and negative predictivity, accuracy rates and odds ratio of intracranial translucency (IT) negativity to predict various anomalies, fetal losses and final poor prognosis.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>11–13 week anomaly</td>
<td>44.7%</td>
<td>95.8%</td>
<td>17.7%</td>
<td>98.8%</td>
<td>94.8%</td>
<td>18.4</td>
<td>9.3–36.3</td>
</tr>
<tr>
<td>Non-CNS anomalies</td>
<td>51.9%</td>
<td>95.7%</td>
<td>14.9%</td>
<td>93.9%</td>
<td>95.0%</td>
<td>23.7</td>
<td>10.8–52.0</td>
</tr>
<tr>
<td>CNS anomalies</td>
<td>41.7%</td>
<td>95.4%</td>
<td>10.4%</td>
<td>99.2%</td>
<td>94.8%</td>
<td>15</td>
<td>6.5–34.7</td>
</tr>
<tr>
<td>Chromosomal anomalies</td>
<td>21.4%</td>
<td>95.5%</td>
<td>12.5%</td>
<td>97.6%</td>
<td>93.3%</td>
<td>5.8</td>
<td>2.9–11.3</td>
</tr>
<tr>
<td>Abortion - loss</td>
<td>29.2%</td>
<td>95.9%</td>
<td>21.8%</td>
<td>97.2%</td>
<td>93.4%</td>
<td>9.7</td>
<td>5.6–17.0</td>
</tr>
<tr>
<td>Poor prognosis</td>
<td>26.9%</td>
<td>95.9%</td>
<td>21.9%</td>
<td>96.9%</td>
<td>93.1%</td>
<td>8.7</td>
<td>5.0–15.0</td>
</tr>
</tbody>
</table>

CI: confidence interval; NPV: negative predictive value; OR: odds ratio; PPV: positive predictive value.
sons not related with IT was higher in a statistically significant manner. Also, the rate of being not followed up of IT(-) cases was lower than IT(+) cases (p<0.05). Although the families in this group were not recommended any procedure or examination which may affect prognosis as IT could not be seen, the presence of other reasons required a second examination or an invasive procedure. We interpreted our two findings as an indicator that IT negativity might accompany other pathologies.

When we compared fetal clinical findings and biometric parameters in IT(-) and IT(+) groups, we observed that mean weeks of gestation and CRL measurements were similar but mean NT was higher in IT(-) group. Similarly, maternal age was also higher in this group. When we interpreted our findings together with further examinations, we determined that this was caused by chromosomal anomalies in particular. Martinez-Ten et al. reported in their study that there was an increase in NT in 50% of IT(-) cases and 71% of the entire group had major chromosomal anomalies. When we excluded false negative cases, the rate of major chromosomal anomaly was 48%.

On the other hand, when we excluded IT(-) cases and took only IT(+) cases into consideration, we found that the mean values of NT, IT and other biometric parameters deviated in a statistically significant manner among the case groups with normal and abnormal prognoses. While maternal age, NT and IT had higher values at similar weeks of gestation, CRL, BPD and HC values were lower. The reason for these findings was the presence of chromosomal anomalies in the same group and we interpreted that posterior fossa expansion accompanied other typical findings of chro-

<p>| Table 8. Intracranial translucency (IT) finding at 11–13 weeks of gestation and the relationship between technical and maternal characteristics. |
|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Maternal age</th>
<th>Technical difficulty*</th>
<th>Uterine reasons†</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2666</td>
<td>31.57±4.00</td>
<td>31 (1.16%)</td>
<td>151 (5.66%)</td>
<td>182 (6.82%)</td>
</tr>
<tr>
<td>IT(+)</td>
<td>2558</td>
<td>31.86±3.97</td>
<td>12 (0.47%)</td>
<td>121 (4.73%)</td>
<td>133 (5.20%)</td>
</tr>
<tr>
<td>IT(-)</td>
<td>108</td>
<td>33.16±4.09</td>
<td>19 (17.59%)</td>
<td>30 (27.78%)</td>
<td>49 (45.37%)</td>
</tr>
<tr>
<td>Statistical significance</td>
<td>-</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

*Difficulty in imaging, inconvenient fetal position. †Uterine anomaly, retroversion, myoma.

Fig. 1. (a) Normal intracranial translucency (IT) image and (b) drawing in posterior fossa imaging.
mosomopathy. Volpe et al.\textsuperscript{[13]} highlighted in their study that the reason of fluid increase seen in IT-like areas in the posterior fossa could be the presence of various minor and major chromosomal anomalies.

When we investigated the cases, whose IT could not been in the posterior fossa examination during the first trimester, at that and further weeks of gestation, we noticed that the rates of chromosomal anomalies, fetal defects, fetal losses and termination of pregnancy were higher. For example, CNS defects increased 15 times, abortion and fetal losses increased 10 times, and chromosomal anomalies increased 6 times. The frequency of occurrence for any of them increases approximately 9 times. In fact, Ferreira et al.,\textsuperscript{[10]} Bornstein et al.,\textsuperscript{[12]} Volpe et al.,\textsuperscript{[13]} Fong et al.,\textsuperscript{[20]} Martinez-Ten et al.,\textsuperscript{[23]} and Volpe et al.\textsuperscript{[24]} showed that posterior fossa examinations may help to diagnose chromosomopathy and CNS defects.

The most significant and prominent finding in our study was the significant increase (8.7 times) in the rates of poor prognostic criteria such as chromosomopathy, fetal defect and pregnancy loss mentioned above when other findings accompanying the failure of seeing or measuring IT are present. Volpe et al.\textsuperscript{[13]} expressed that the pregnancy was terminated in 71\% (12/17) of the cases who had abnormal image in the posterior fossa. In the study of Martinez-Ten et al.,\textsuperscript{[23]} the rate of ended or terminated case was 82\% (23/28) after similar findings. In our series, the rate of ended-terminated cases we found after actual negatives were determined was 84\% (21/25), and it was similar to other studies.

Volpe et al.\textsuperscript{[24]} described 3 pathognomonic markers which also included posterior fossa abnormalities in the brain, and they highlighted that cerebral or chromosomal anomalies increased in the presence of any of them and that they affected gestational prognosis negatively. The same authors reported in another study\textsuperscript{[13]} that 9 of 17 cases, who had abnormal images in the posterior fossa, had chromosomal anomalies, 7 of them had cranial malformation, 5 of them had extracranial...
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malformation, and only 5 cases had good prognosis. Martinez-Ten et al.\textsuperscript{[39]} studied 28 cases whose choroid plexus of 4th ventricle could not be seen, and found karyotype anomaly in 20 of them, and systemic malformation in a total of 19 cases in which 12 of them were CNS anomaly, and only 5 cases had normal prognosis.

Some studies highlighted that the examination of IT during the early periods of pregnancy could be effective to detect chromosomopathies, malformations and poor gestational prognosis, and that it may indicate cerebral malformations such as Dandy-Walker and Blake’s pouch cyst persistence which may develop at late period.\textsuperscript{[11–13,25]} The findings of the early period in our study are also similar. We did not obtain a significant result when we distributed other 22 malformations, which we found at and after 14 weeks of gestation, by the groups.

Although the examination of IT and therefore posterior fossa during this period does not completely supersede NT and other genetic markers used for the early diagnosis of trisomy 21, it is powerful enough to help for suspecting trisomies and other karyotype anomalies in some cases.\textsuperscript{[4,6–8,15]} In fact, some studies\textsuperscript{\[9–13\]} showed that posterior fossa abnormalities were apparent not in trisomy 21 cases but in triploidy and trisomy 13 and 18 cases. In our study, we did not investigate chromosomal anomalies by establishing sub-groups, but we found that IT image and measurements in chromosomopathies differed from the cases in the normal group. We detected more chromosome markers in the ultrasonography examinations of IT(-) cases than IT(+) cases, and we found more procedures performed for genetic evaluation and a higher rate of abnormal karyotype results obtained. However, we did not find any difference between the groups in terms of markers and malformations which can be seen after 14 weeks of gestation.

The first point of origin for IT measurement was for the early diagnosis of open spina bifida and there were different study results.\textsuperscript{[6,8–11]} The further investigations showed that IT screening could help not only spina bifida but also other anomalies.\textsuperscript{[9–11]} In our series, we found IT negativity in 2 spina bifida cases as well as 8 CNS cases, and the early detection of CNS anomalies by IT screening had a sensitivity of 42% with a 95% accuracy rate. In other series, this rate varied between 0% and 100%.\textsuperscript{[6,8–11]}

While the positive relationship between poor prognosis and the failure of seeing IT was apparent in our study, the impact of the measurement IT distance range on the prognosis exhibited only a statistically poor relationship. In other words, IT values of the cases with poor prognosis may conflict with normal values. Therefore, being able to measure IT is not a strong parameter to predict prognosis, but the view of IT and its relationship with its vicinity are more important.

On the other hand, posterior fossa may have a cystic appearance between 15 and 18 weeks of gestation in 10% of normal fetuses. They can later be interpreted as 4th ventricle or Blake’s pouch cyst.\textsuperscript{[22]} The presence of similar image also during earlier weeks of gestation is also an expected finding. Therefore, establishing posterior fossa cyst diagnosis during very early periods can be qualified as a malpractice. In our study, we found posterior fossa cyst in 45 cases, and 24% of them resulted in poor prognosis. None of the cases with isolated findings underwent an invasive procedure that would change routine follow-up, and only second examination time was moved to an earlier time.

Volpe et al.\textsuperscript{[3]} stated that posterior fossa examination can be a guiding parameter for malformations in this region and chromosomal anomalies. In our study, the sensitivity of IT negativity for chromosomal anomalies was 21%, and the odds ratio was 5.8. The findings of our study were guiding parameters for CNS and systemic malformations rather than chromosomal anomalies.

Lafouge et al.\textsuperscript{[11]} reported that Blake’s pouch could be seen by sonographic images similar to the lack of IT, but differential diagnosis could be established by the examinations during following weeks and prognosis was good. Martinez-Ten et al.\textsuperscript{[39]} found the rate of Blake’s pouch persistence in 7.1% (2/28) in their series similar to our study. In our study, the rate to detect Blake’s pouch was 16% (4/25) in our actual IT(-) cases.

Also, we did not find IT negativity in any of the cases with conditions which may be temporary and do not affect prognosis negatively such as mild ventriculomegaly. Some studies reported that the distance with brain stem and occipital bone can be more helpful in the early diagnosis of open spina bifida and Dandy-Walker malformation.\textsuperscript{39,26–28} While this distance becomes narrow in spina bifida, it increases in Dandy-Walker malformation.
When we considered all examined studies, we observed that the rates of maternal age, obesity, uterine anomalies, myoma and position disorders, and fetal posture disorders were higher in IT(−) cases than IT(+) cases. We noticed that these factors are prominent and there is no fetal pathological results in the cases (n=71) which are false negative in particular. Papastefanou et al.\(^9\) and Fong et al.\(^{20}\) also reported similar results.

The research of intracranial translucency has been in our agenda over the last decade, and it has become one of the cornerstones for better assessment of fetal anatomy. The results that we obtained in our study in which we aimed to investigate the rates, reasons and results for being unable to see or measure this image during perinatal examination are:

- Intracranial translucency can be seen and measured during routine perinatal examination with a rate of 96%, and this rate is almost 99% when we exclude false negative cases,
- Uterine anomalies, myomas, and the changes in fetal posture may cause technical difficulties and false negative findings,
- The cases whose IT cannot be seen are, independent from this finding, are examined much more during further weeks of gestation and they expose to more genetic researches,
- The negative variances in fetal biometric parameters, NT and similar genetic markers, CNS and non-CNS anomalies, genetic disorders, fetal losses and abortions have higher rates in IT(−) cases.
- When the cases which are false negative for IT are ruled out, the prognosis rate is 84%.

Not assessing false positivity, not repeating the measurements by a second specialist and performing postmortem examination in few cases are the weak points of our study.

**Conclusion**

The findings of our study make us think that the examination and measurement of intracranial translucency can be used as a parameter helping classical methods for the early diagnosis of CNS or systemic malformations and some chromosomal anomalies, and that it can be a part of perinatal assessment.

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

**References**

Failure of getting intracranial translucency image in posterior fossa in the examination of singleton pregnancies at 11–13 weeks


The impact of ursodeoxycholic acid treatment on myocardial performance index in the obstetric cholestasis cases

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Abstract

Objective: It is asserted that the reason of sudden fetal death in obstetric cholestasis cases is the disruption of fetal cardiac conduction by bile acids. In our study, we aimed to investigate the impact of ursodeoxycholic acid treatment on fetal cardiac functions.

Methods: The prospective cohort study was planned in a tertiary center. The cases diagnosed with obstetric cholestasis were included in the study. Fetal cardiac functions were assessed before and after ursodeoxycholic acid treatment. Fetal myocardial performance index (MPI), AV conduction time (mechanical PR interval), and E/A ratios were evaluated.

Results: Ursodeoxycholic acid treatment provides an improvement in the myocardial performance index of right and left ventricles. While the MPI of right ventricle was 0.44±0.02 ms before the treatment, it was 0.43±0.01 ms after the treatment. These values were and 0.45±0.02 ms and 0.43±0.02 ms, respectively for the MPI of left ventricle. It was found that AV conduction time was shortened after ursodeoxycholic acid treatment (116.4±4.1 vs. 112.2±4.1). E/A ratios and peripheral and central Doppler resistance indices were affected by the treatment.

Conclusion: The MPI improves after ursodeoxycholic acid treatment. The clinical impact of this improvement on perinatal morbidity and mortality can only be shown by conducting prospective studies with more cases.

Keywords: Obstetric cholestasis, myocardial performance index.

Introduction

The incidence of obstetric cholestasis varies among the studied populations, ranging from 0.3% to 10%. It is one of the most important complications of sudden fetal death. Although complete pathophysiology is not known, increased bile acid is considered to be the reason of the complications. Bile acids accumulate in the cardiac conduction system and cause conduction disor-
The impact of ursodeoxycholic acid treatment on myocardial performance index in the obstetric cholestasis cases

ders. The standard treatment for obstetric cholestasis is ursodeoxycholic acid (UDC). Bile acids have arrhythmic effect and UDC antagonizes this effect. There are many studies investigating fetal circulation changes in obstetric cholestasis. No change was found before sudden fetal death in peripheral and central Doppler studies. In the recent studies, prolonged fetal cardiac AV conduction time was found in the cases with cholestasis. Myocardial performance index (MPI) is one of the indications of fetal well-being. It is the ratio of the time out of the duration where heart spends for ejection during systole to the ejection time. As the cardiac functions fail, ejection time during systole duration will also get shorter since the contraction strength of myocardium will decrease. MPI fails in the cases with obstetric cholestasis. Although UDC treatment improves liver function tests, it is not known if it has an impact on cardiac functions or not. In our study, we aimed to investigate the impact of UDC treatment on MPI.

Methods

The study was designed as a prospective cohort study between April 2018 and December 2018 after obtaining the approval of the ethics committee. The cases with obstetric cholestasis were included in the study. The clinical and laboratory diagnoses of obstetric cholestasis were established. Among the patients referring with itching complaint, the cases without rash and dermatologic condition findings in the physical examination, the cases with itching on hands and feet, increased itching at nights, two times or more increases in ALT and AST values in liver function tests and increased preprandial bile acid (>10 mmlmol/dl) were considered as the cases with obstetric cholestasis. The cases with growth and developmental delay, gestational hypertension, affected alloimmunization, preeclampsia, gestational diabetes, and fetal cardiac anomaly were excluded from the study.

Left MPI was calculated through pulse Doppler flow - time diagram obtained by placing Doppler cursor so as to cover the internal cusp of mitral valve and aortic valve on five-chambered view. The measurements were done by keeping angular correction below 20 degrees. The right ventricular outflow velocity vs. time diagram was obtained by placing Doppler cursor on right ventricular outflow plane. Isovolumic contraction time was considered as the time beginning from the moment when pulse Doppler flow on mitral valve ends up to the moment when aortic ejection starts. Ejection time was considered as the time between the start and end of ejection flow on aortic valve at pulse Doppler. Isovolumic relaxation time was calculated as the time beginning from the end of aortic ejection up until mitral valve is opened (Fig. 1). The measurements were carried out by a researcher using Toshiba Apio 500 (Canon Medical Systems USA, Inc., Tustin, CA, USA) 4.5–6 Hz 3D probe. In order to eliminate errors, device speed 5 was used which displays pulse image at maximum width. Valve opening clicks were ignored when conducting the measurements between wave phases. The measurements of the patients were carried out on 3rd pre- and post-treatment days. Since there was only one researcher for each patient, minimum 5 different measurements were done and mean values were calculated. Doppler cursor was placed between left ventricular outflow and anterior cusp of mitral valve to measure AV conduction time. E and A waves were calculated by velocity - time image obtained via mitral valve pulse Doppler. The maximum peaks of first and second waves were calculated as E and A waves, respectively. AV conduction time was considered as the time from the start of A wave of mitral valve up to the beginning of ventricular systole (Fig. 1). The pulsatility indices of umbilical and middle cerebral arteries were used for the peripheral and central Doppler flow study.

The Statistics Package for Social Sciences, 18.0 (SPSS Inc., Chicago, IL, USA) was used for statistical calculations. In order to determine the distribution of the data, Kolmogorov-Smirnov and Shapiro-Wilk tests and Q-Q plot were used. The changes of dependent

Fig. 1. Measurement of fetal cardiac pulse doppler parameters used in MPI calculation. ET: ejection time; IVCT: isovolumic contraction time; IVRT: isovolumic relaxation time.
variables before and after the treatment were evaluated by the paired sample t test. p<0.05 was considered as significant level. Wilcoxon signed-rank test was used for the data which did not conform to the parametric test conditions. The values were expressed as mean and standard deviation.

Results
During study period, 12 patients were included in the study. The demographic characteristics are shown in Table 1. The mean age of the study group was 26.4. Mean week of gestation was 37. BMI value of the study group was 25.8±3.2. The rate of cesarean section was 66% which was 30% higher than the rate of the hospital where this study was conducted. Preprandial bile acid level was 22.1 mmol/l in the study group.

Cardiac functions before and after UDC treatments are shown in Table 2. It was found that the isovolumic contraction time and isovolumic relaxation time got shortened, and ejection time prolonged after UDC treatment. It was found that UDC treatment shortened MPI (right ventricle 0.44±0.02 ms vs. 0.43±0.01 ms, left ventricle 0.45±0.02 ms vs. 0.43±0.02 ms).

The E/A ratio of the right ventricle was 0.72±0.15 before the treatment and 0.73±0.14 after the treatment, and the E/A ratio of the left ventricle was 0.74±0.19 before the treatment and 0.73±0.18 after the treatment.

Table 1. Demographic characteristics of the study group.

| Age (year) | 26±4.3 |
| Delivery week | 37±3.2 |
| BMI (kg/m²) | 25.8±3.2 |
| C/S ratio (%) | 66.6 |
| Birth weight (g) | 3045±3.46 |
| Preprandial bile acid (mmol/dl) | 21.2±8.5 |
| ALT (IU/L) | 74.8±32.5 |
| AST (IU/L) | 65.6±29.4 |

BMI: body mass index; C/S: cesarean section.

Table 2. Fetal cardiac functions before and after the treatment of ursodeoxycholic acid.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Change Δt, ΔIU/dl*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVIVCT (ms)</td>
<td>34.5±2.5</td>
<td>33.2±2.3</td>
<td>-1.3±1.07</td>
<td>0.00</td>
</tr>
<tr>
<td>RVET (ms)</td>
<td>168.7±1.5</td>
<td>169.1±2.5</td>
<td>0.6±1.9</td>
<td>0.03</td>
</tr>
<tr>
<td>RVIVRT (ms)</td>
<td>41.4±2.6</td>
<td>39.5±2.3</td>
<td>-1.6±2.3</td>
<td>0.04</td>
</tr>
<tr>
<td>RVMPI</td>
<td>0.43±0.02</td>
<td>0.43±0.01</td>
<td>0.015±0.013</td>
<td>0.02</td>
</tr>
<tr>
<td>LVIVCT (ms)</td>
<td>35.0±3.8</td>
<td>34.4±2.3</td>
<td>-0.6±2.3</td>
<td>0.02</td>
</tr>
<tr>
<td>LVET (ms)</td>
<td>169.7±1.5</td>
<td>170.2±2.5</td>
<td>0.5±2.3</td>
<td>0.02</td>
</tr>
<tr>
<td>LVIVRT (ms)</td>
<td>42.5±1.5</td>
<td>41.7±2.0</td>
<td>-0.8±1.2</td>
<td>0.02</td>
</tr>
<tr>
<td>LVMPI</td>
<td>0.45±0.02</td>
<td>0.43±0.02</td>
<td>0.015±0.014</td>
<td>0.01</td>
</tr>
<tr>
<td>RV E/A ratio</td>
<td>0.72±0.15</td>
<td>0.73±0.14</td>
<td>0.01±0.01</td>
<td>0.78</td>
</tr>
<tr>
<td>LV E/A ratio</td>
<td>0.74±0.19</td>
<td>0.73±0.18</td>
<td>0.01±0.01</td>
<td>0.82</td>
</tr>
<tr>
<td>Mechanical PR interval</td>
<td>116±4.6</td>
<td>112.2±4.1</td>
<td>-4.1±3.2</td>
<td>0.01</td>
</tr>
<tr>
<td>UMA PI</td>
<td>0.81±0.09</td>
<td>0.82±0.07</td>
<td>0.01±0.001</td>
<td>0.76</td>
</tr>
<tr>
<td>MCA PI</td>
<td>1.71±0.22</td>
<td>1.72±0.23</td>
<td>0.010±0.001</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Δt value was given as the mean difference obtained in the paired sample test. It was given as ms and ratio in the parameters where the measurements were millisecond and ratio, respectively. LV: left ventricle; LVET: left ventricular ejection time; LVIVCT: left ventricular isovolumic contraction time; LVIVRT: left ventricular isovolumic relaxation time; LVMPI: left ventricular myocardial performance index; MCA: middle cerebral artery; PI: Pulsatility index; RV: right ventricle; RVET: right ventricular ejection time; RVIVCT: right ventricular isovolumic contraction time; RVIVRT: right ventricular isovolumic relaxation time; RVMPI: right ventricular myocardial performance index; UMA: umbilical artery.

Discussion
Obstetric cholestasis is clinically characterized as increase in liver enzymes (2 times or more increase in ALT and AST values), increase in preprandial bile acids and itch-
ing especially on hands and feet at nights. The most significant complication of obstetric cholestasis is sudden fetal death. Fetal death risk increases especially after 37 weeks of gestation, and up-to-date treatment protocols recommend carrying out delivery after 37 weeks of gestation.\(^\text{[13]}\) However, this approach is not based on strong scientific evidence.\(^\text{[15]}\) Although the reason of sudden fetal death is not known certainly, some hypotheses were developed. The most accepted hypothesis is the blockage of cardiac conduction system by bile acids. Previous studies found a prolongation in the fetal cardiac conduction in the cases with obstetric cholestasis.\(^\text{[3,14]}\) In autopsy studies, bile acid accumulation was found in the fetal cardiac conduction system.\(^\text{[13,14]}\) Molecular studies showed that the basic reason of conduction block in the cases with obstetric cholestasis was bile acids.\(^\text{[19]}\) In cases with obstetric cholestasis, plasma tauric acid level increases. Tauric acid inhibits L and T types of Ca\(^++\) channels, but it also activates the channels which enable Na\(^+\)-Ca\(^++\) change. This causes cardiac conduction slowdown and re-entrant tachycardia in addition to the disruption in the contraction of cardiac myocytes.\(^\text{[6,16]}\) Bile acids inhibit calcium-mediated conductions and UDC treatment prevents this effect in adult patients.\(^\text{[17]}\) UDC treatment decreases the level of serum bile acids and improves hepatic functions. It increases depolarization in L-type Ca\(^++\) channels and restores cardiac conduction.\(^\text{[14,17]}\) On the other hand, in addition to the conduction, it also decreases the activation of p53 and HIF-1 alpha activation which are the factors responsible for tissue damage during the hypoxia in cardiac myocytes.\(^\text{[18]}\) In consistent with the literature, we found in our study that the prolonged fetal AV conduction time associated with the obstetric cholestasis was shortened by UDC treatment.\(^\text{[15]}\)

MPI shows both systolic and diastolic cardiac functions. MPI is used to detect cardiac dysfunctions secondary to the disorders in fetal well-being.\(^\text{[19]}\) It displays an increase in conditions which cause disorder in fetal well-being.\(^\text{[20–22]}\) MPI was found to increase in obstetric cholestasis.\(^\text{[11]}\) However, the authors of this study did not investigate if the medical treatment improved fetal cardiac functions or not. In our study, we found that the medical treatment improved fetal cardiac functions. UDC treatment provides an improvement in both systolic and diastolic parts of fetal cardiac functions. We found that the treatment increased systolic ejection time and shortened isovolumic relaxation time. Isovolumic contraction is an indication of the diastolic function of ventricles and UDC treatment improves this function. We did not find any change in E/A ratios in our study. E/A ratio shows atrium function and it exhibits disorder in case of severe asphyxia. Previous studies reported that E/A ratio did not change in the cases with obstetric cholestasis.\(^\text{[15]}\) It was found that the increase in peripheral Doppler resistance indices, which are the findings of hypoxia and asphyxia, did not fail in the cases with obstetric cholestasis. These findings show that there was a cardiac dysfunction in obstetric cholestasis but this dysfunction did not cause a prenatal asphyxia or hypoxia. It can be considered that primary hypoxia and asphyxia are not the reasons for prenatal loss in obstetric cholestasis. The first expected abnormality can be cardiac conduction disorder. Conduction disorder might lead to diastolic dysfunction and then systolic dysfunction. Fetal cardiac conduction disorder might cause cardiac dysfunction as well as sudden fetal death.

The significance of the improvement that we found has some limitations. The studies performed found many factors affecting the optimal measurement of MPI.\(^\text{[24]}\) These factors cause intermeasurement and intraobserver variations which may affect the result of the study.\(^\text{[22–25]}\) The previous studies found interclass correlation coefficient 0.7–0.9 for MPI.\(^\text{[22–25]}\) Similarly, although we found a shortening in AV conduction time, this finding should be evaluated carefully. AV conduction time exhibits a certain interobserver variability and does not reflect actual PR distance.\(^\text{[16–19]}\) Since the mean differences we found are very small, the result should be evaluated carefully. In our study where measurement difference is very small, working with a parameter which has a low interclass correlation coefficient may significantly affect the results. In order to obtain more precise and accurate results, the same measurement should be performed by different researchers, interclass correlation coefficient should be provided and more patients should be studied.

**Conclusion**

The fetal MPI improves after ursodeoxycholic acid treatment. However, it is difficult to predict if sonographic recovery causes clinical recovery or not. To answer this question, further prospective studies are required where clinical variables are also evaluated with more patients.

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


Multimedia education on the day of elective cesarean section increases anxiety scores

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Abstract

Objective: Multimedia-based preoperative education to enhance patient knowledge improves anxiety and satisfaction rates in different clinical scenarios, but the ideal method to decrease pre- and perioperative anxiety remains unclear. In this study, we aimed to find out the effects of operation day multimedia education (MME) on anxiety and satisfaction rates of patients who underwent cesarean section (CS) under general anesthesia.

Methods: One hundred and thirty-two patients were assessed for eligibility and 106 patients who were scheduled for elective CS under general anesthesia were randomized to MME group three hours before the operation or to controls who received solely brief verbal information. After randomization, all patients were asked to fill out State and Trait Anxiety Inventory (STAI). MME patients watched an education video about general anesthesia explaining the procedure in details and also risks and benefits. After video education, all patients in both groups asked to complete STAI-state again. All patients in both groups asked to complete STAI-state again. All patients were operated under general anesthesia and after the operation, all patients were asked to fill out a 5-point Likert scale to measure satisfaction level.

Results: There were no statistically significant differences among baseline STAI-state and STAI-trait values and the number of satisfied patients (p>0.05 for all comparisons). STAI-state scores following education were significantly increased in group MME group compared to controls (40.3±9.4 vs. 44.5±10.2 respectively, p<0.05).

Conclusion: Multimedia education on operation day increases anxiety scores in elective CS patients who were operated with general anesthesia. Further studies are required to address the adequate timing and method of patient education in women undergoing CS under general anesthesia.

Keywords: Anesthesia, patient education, preoperative information, cesarean section.

Özet: Elektif sezaryen günündeki multimedya eğitimi kaygı puanlarını artırarakta

Amaç: Hasta bilgisi artırmaya yönelik multimedya tabanlı preoperatif eğitim, farklı klinik senaryolarda kaygı ve memnuniyet oranlarını artırarakta, fakat preoperatif ve perioperatif kaygıyı azaltmaya yönelik ideal yöntem hâlâ belirsizdir. Çalışmamızda, operasyon günü multimedya eğitiminin (MME) genel anestezeli alında sezaryen doğum gerçekleştiren hastaların kaygı ve memnuniyet oranları üzerindeki etkilerini araştırmayı amaçladık.

Yöntem: Çalışmaya uygunluk için 132 hızlı değerlendirilerek ve genel anestezeli altında elektif sezaryen için planlanan 106 hasta, operation-onan üç saat önce MEE grubuna veya sadece özet sözlü bilgi alan kontrol grubuna rastgele olarak ayrıldı. Rastgele gruplandırma sonrası MME hastaları, genel anestezli durumda riskleri ile faydalarını detaylı şekilde anlatan bir eğitim videosu izledi. Video eğitimi önünde sonra her iki gruptaki hastalardan STAI-durumlu ölçeğini tekrar doldurdukları istendi. Tüm hastalar genel anestezeli altında operasyona alındı ve operasyon sonrasında tüm hastalardan, memnuniyet seviyelerini öne çekmek için 5’li Likert ölçeği doldurdukları istendi.

Bulgular: Başlangıç STAI-durumlu ve STAI-sürekli değerleri ve memnun hastaların sayısı arasında istatistiksel olarak anlamli bir fark yoktu (tüm karşılaştırmlar için p>0.05). Eğitim sonrası STAI-durumlu puanlar, kontrol grubuna kıyasla MME grubunda anlamlı şekilde arttı (40.3±9.4'e karşı 44.5±10.2, p<0.05).

Sonuç: Operasyon gününde multimedya eğitimi, genel anestezeli altında operasyonu geçiren elektif sezaryen hastaların kaygı puanlarını artırarakta. Genel anestezeli altında sezaryen operasyonu geçen kadınların yeterli zannedilme ve hasta eğitimi yönteminin araştırılması için çok çalışmalara ihtiyaç duyulmaktadır.

Anahtar sözcükler: Anestezeli, hasta eğitimi, preoperatif bilgi, sezaryen.

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Please cite this article as: Yılmaz G, Akça A, Esen O, Salıhoğlu Z. Multimedia education on the day of elective cesarean section increases anxiety scores. Perinatal Journal 2019;27(1):38–42. doi:10.2399/prn.19.0271006

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Introduction

Anxiety before and during operation is an essential issue affecting more than 60% of surgical patients that might cause different pathophysiological circumstances including hypertension, dysrhythmia, the risk of awareness, changes in perception of pain, difficulties in postoperative analgesia and also decline in overall satisfaction rates.[1–4] Focusing to decrease pre- and perioperative anxiety might enhance postoperative outcome including hospital stay and lifestyle disruption.[5,6]

Anxiety is highly prevalent during pregnancy and the mode of delivery may also be related to anxiety thus elective cesarean section (CS) patients are vulnerable to high anxiety levels.[7,8] Focusing on decreasing maternal anxiety has shown to have favorable effects on fetal health and maternal satisfaction in elective CS patients. Multimedia-based preoperative education to enhance patient knowledge improves anxiety and satisfaction rates in different clinical scenarios but the ideal method and timing of effective preoperative information to decrease pre- and perioperative anxiety remains unclear.[9–11]

In the majority of multimedia education (MME) studies, the timing of information was within one week before operation and the information was not given on operation day in any of these studies.[8,11] In this study, we aimed to find out the effects of operation day MME on anxiety and satisfaction rates of patients who underwent cesarean section with general anesthesia.

Methods

Subject selection

One hundred and thirty-two patients scheduled for elective cesarean section under general anesthesia in our institute were assessed for eligibility. Age below 18 years, contraindication for regional anesthesia (allergy to local anesthetics, severe hypovolemia, infection at the site of injection, patient refusal, severe valvular heart disease) history of previous surgery, psychiatric disease, treatment with antidepressant drugs, visual, cognitive or speech disorders and being illiterate were exclusion criteria. Using a random allocation software (www.randomization.com) 106 patients who were eligible for the study were randomly assigned to one of the study groups: group 1 involved patients receiving multimedia education (MME) and group 2 involved control patients who did not receive a multimedia education but given a brief verbal information regarding the procedure before the surgery. The study protocol was approved by the Institutional Ethics Committee (KAEEK/2018.5.03) and registered to the National Ministry of Health, Health Sciences University (Istanbul, Turkey).

Study setting

After randomization, all patients were asked to fill out State and Trait Anxiety Inventory (STAI) which is a validated and widely used self-report questionnaire assessing both state and trait anxiety.[12] STAI consists of two parts with 20 questions in each; state anxiety (STAI-S) intended to measure anxiety at a specific time and trait anxiety (STAI-T) measures long term anxiety levels and each answer was scored on a scale of 1–4 (ranging from “not at all to very much so”). The overall score is 20–80, a score ≤35 indicates no anxiety, 26–41 moderate anxiety, and ≥42 severe anxiety. A randomization envelope was then opened to identify the study group of the index patient.

Multimedia education patients watched an information video about general anesthesia explaining the procedure in details and also risks and benefits of the surgical procedure for 4 minutes 15 seconds in a personal computer with headphones with an accompanying anesthesiologist. After video education, all patients asked to complete STAI-S again. All patients were operated under general anesthesia by the same operation team and by the same anesthesiologist. Three hours after the recovery, all patients were asked to fill out a 5-point Likert scale to measure satisfaction level (1; dissatisfied, 5; most satisfied).

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 17 (SPSS, Chicago, IL, USA). Kolmogorov-Smirnov test was used to determine whether or not the variables are normally distributed. Comparisons among groups with respect to STAI scores were evaluated using Student’s t-test and distribution of STAI scores and satisfaction scores were evaluated using chi-square or Fisher’s exact test where appropriate. Power calculations based on our pilot study with 50 patients to detect a significant difference in postoperative STAI scores indicated that at least 40 patients were needed in each group (G power 3, Dusseldorf University, Dusseldorf, Germany). Two-sided p≤0.05 was interpreted as statistically significant.
Results

A total of 106 patients (mean age 31.4±5.4 years) were enrolled in the study (Fig. 1). MME was given to 55 patients and there were 51 control patients who did not receive MME. Demographic variables including age, body mass index, American Society of Anesthesiologists (ASA) scores, and cesarean section indications are shown in Table 1. There were no significant differences among groups in terms of the demographic characteristics (p>0.05 for all comparisons).

STAI-S baseline, STAI-T baseline and STAI-S after multimedia education are shown in Table 2. There were no statistically significant difference among baseline STAI-S and STAI-T values and the number of satisfied patients (p>0.05 for all comparisons). However, STAI-S scores after video education was significantly higher in MME group compared to group controls (40.3±9.4 vs. 44.5±10.2 respectively, p<0.05; Table 2).

Discussion

We hypothesized that multimedia-based education program on operation day might affect the anxiety and satisfaction score of cesarean section patients who were operated with general anesthesia. Our findings show that operation day MME given just prior to surgery significantly increases STAI-S scores compared to that of the control group.

Multimedia patient education is increasingly used preoperatively in different surgical operations including obstetric, urologic, cardiac, orthopedic surgeries under different kinds of anesthesia techniques varying from general anesthesia to regional techniques. However, studies investigating the role of preoperative patient education provided conflicting results.[13–15] Comparing this kind of studies is problematic due to differences in duration, purpose, content, and timing. In many of the above-mentioned studies with favorable results on behalf of anxiety and satisfaction, multimedia informa-
tion were given in one or two weeks before operation during pre-anesthetic evaluation, thus, it might give the patient an acceptable time to understand the procedure or the techniques. Also, places that are used for education in the studies showing favorable results with MME were mostly pre-anesthetic evaluation room, not a chaotic, populated waiting room in an operation theatre.

Anesthesia technique itself might also affect the anxiety level. We suggest that general anesthesia might have a positive effect on patients who already have an increased anxiety level. Indeed, despite the proven advantages on patient outcomes of regional anesthesia, many patients have special concerns related to regional anesthesia including permanent paralysis, back pain or being awake during the procedure and this subgroup of patients might require more information about anesthesia technique and they might benefit most from a multimedia education program.

Due to unique characteristics of the obstetric patient population who experience increased anxiety level compared to other patients groups, special effort to decrease anxiety is essential. Lower preoperative anxiety has been shown to be associated with greater maternal satisfaction and better recovery in patients undergoing elective cesarean section. Preoperative multimedia education program in obstetric patients is limited and majority of studies were in elective CS patients who were operated under regional anesthesia.

Several studies focusing on multimedia education program have revealed decreased anxiety and increased satisfaction level in patients operated with spinal anesthesia. In a previous study conducted by Eley et al., video information given prior to surgery did not provide a decrease in preoperative anxiety in patients undergoing cesarean section with regional anesthesia. However, there are also a few studies consistent with our findings which did not show a favorable impact of MME on preoperative anxiety. Our results indicate that detailed multimedia education in operation theatre on operation day shows no favorable influence on behalf of anxiety and satisfaction scores in our study. Our findings are somewhat conflicting with the results of the previous studies. We suppose that the main factors that increased anxiety scores in our study might be attributed to timing, place and the content of the used multimedia. We suggest that MME should be performed days before the surgery in a comfortable and relaxing room with a calming content.

| Table 1. Demographic variables of the study group.* |
|-----------------|----------------|----------------|
|                | MME (n=55) | Controls (n=51) | p-value |
| Age (years)    | 31.2±5.3 | 31.6±5.6 | 0.476 |
| Body mass index (kg/m²) | 31.5±5.8 | 30.5±5.6 | 0.346 |
| ASA (n,%):      |          |                |        |
| 1               | 14 (25%) | 17 (33%) | NS |
| 2               | 29 (53%) | 28 (55%) | NS |
| 3               | 12 (22%) | 6 (12%) | NS |

*Data are presented as mean ± standard deviation. ASA: acetyl salicylic acid; MME: multimedia education; NS: not significant.

Several limitations of this study should be considered including (i) the lack of participation of illiterate patients who might have benefited the most from multimedia education, (ii) not evaluating the newborn outcome, (iii) and the limited number of anxiety evaluation, and (iv) not comparing hemodynamic data. Finally, the lack of power calculation is an important limitation of this study. Elimination of the limitations mentioned above would provide valuable information concerning the benefit of MME on pregnancy outcomes, maternal outcomes, and intraoperative hemodynamic changes. Further studies evaluating the effect of multimedia education programs on maternal and newborn parameters in different timing with different contents are needed.

| Table 2. State and Trait Anxiety Inventory (STAI) scores and satisfied patients.* |
|-----------------|----------------|----------------|
|                | MME (n=55) | Controls (n=51) | p-value |
| STAI-T baseline | 45.4±6.9 | 44.1±8.9 | 0.45 |
| STAI-S baseline | 40.9±7.4 | 40.6±8.6 | 0.36 |
| STAI-S after video | 44.5±10.2 | 40.3±9.4 | 0.03 |
| Satisfied with operation (n, %) | 47 (85%) | 46 (90%) | 0.71 |

*Data are presented as mean ± standard deviation. MME: multimedia education; STAI-T: State and Trait Anxiety Inventory-Trait; STAI-S: State and Trait Anxiety Inventory-State.
thea technique. However, appropriate timing and content of MME are critical to getting the desired favorable effects. Our findings demonstrate that MME given on the day of surgery increases the anxiety score of patients who underwent elective CS under general anesthesia. Further studies are required to address the adequate timing and the method of patient education in women undergoing cesarean section under general anesthesia.

Conflicts of Interest: No conflicts declared.

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12. Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). Arthritis Care Res (Hoboken) 2011;63(Suppl 11):S467–72.

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Does parity and labor influence anxiety levels of pregnant women?

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Abstract

Objective: Our aim for this study is to examine state anxiety levels in the prenatal period in the presence of different forms of parity and birth types.

Methods: A retrospective study was conducted to collect the results of pregnant woman which has different parities and type of deliveries in our tertiary center between June and December 2013. 186 cases were divided into 3 groups. Group 1 (n=60) consists of primiparous pregnant women who are expected to give birth spontaneously. Group 2 (n=64) consists of multiparous pregnant women whose will be their second birth with spontaneous vaginal delivery and Group 3 (n=62) consists of elective cesarean section and second-trimester pregnant women. State and Trait Anxiety Inventory (STAI) analysis was made during antenatal pregnancy follow-up at 37 weeks of gestation.

Results: When patients were divided into groups of normal, mild anxiety, moderate anxiety and severe anxiety, 124 (66.6%) of the patients were found to be anxious. In the group of anxious patients, it was found that 95.9% of the patients had mild anxiety. No patient is severely anxious. Especially in Group 1, the patient ratio was higher than the other groups with 85%. In Group 3, it was shown that the majority of the patients (50%) evaluated as normal compared to other groups.

Conclusion: The anxiety levels of pregnant women are generally mild and women who have already experienced birth and did not experience pain have reduced anxiety levels.

Keywords: Anxiety, elective cesarean section, STAI.

Introduction

During pregnancy, many physiological, psychological and anatomical changes are seen in the female body. These changes nurture the development of fetus and prepare the mother for labor.¹ Also childbirth, aside from the pregnancy process, is an important experience. Sometimes it can be one of the serious traumas.²

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anxiety. The severity of this anxiety varies. For women, not knowing how the birth process and the type of birth are going to be and the fear of pain related to birth, are the reasons that can cause anxiety.[3,4] Also, the fear of harm or death of the baby or the mother, fear of extreme pain, distrust of the medical personnel, the thought of losing control can be the common causes of anxiety.[5–8]

Excessive anxiety and stress before birth can cause prolonged labor and as a result, it causes operative births and the fetus to be adversely affected.[9] Furthermore, anxiety is very important in terms of increasing the severity of birth pain. In the literature, anxiety is classified as two different types; continuous and state anxiety. In our study, state anxiety levels of women were measured. State anxiety; is a type of anxiety that occurs when a dangerous, undesirable situation is encountered.[10]

It is important that the nurse, midwife and obstetricians, who are in charge before and during birth, should be aware of the level of anxiety of the expectant and should plan their approaches to manage childbirth. This is why further studies on the state anxiety before birth are needed. Our aim for this study is to examine state anxiety levels in the prenatal period in the presence of different forms of parity and birth types.

Methods
Our study was designed on 186 patients who were done pregnancy follow-up at Private Koru Ankara Hospital, Obstetrics and Gynecology Clinic. Ethical approval for the study was obtained from the Ethics Committee of Koru Ankara Hospital (Ethics Committee protocol code: 13/11/2018-16). The study was conducted in accordance with the Helsinki declaration. 186 cases were divided into 3 groups. Group 1 (n=60) consists of primiparous pregnant women who are expected to give birth spontaneously, Group 2 (n=64) consists of multiparous pregnant women whose will be their second birth with spontaneous vaginal delivery and Group 3 (n=62) consists of elective cesarean section and second-trimester pregnant women.

Data collection
As a primary measurement tool, “patient polyclinic history information screen” which all sociodemographic data was recorded, was used. As a secondary measurement tool STAI (State-Trait Anxiety Inventory) FORM TX-1 was used. These forms were filled during antenatal pregnancy follow-up at 37 weeks of gestation.

Data collection tools
STAI-1 (State-Trait Anxiety Inventory)
In order to measure the level of preoperative anxiety, many survey studies were conducted. These studies need to be renewed in parallel with the differences between countries and regions and sociocultural changes in society. The most commonly used test for the measurement of anxiety in medicine is the State-Trait Anxiety Inventory (STAI) scale.[10] With the inventory, which was started to be developed by Spielberger and Gorsuch in 1964, it was aimed to measure continuous and state anxiety levels in normal and non-normal individuals.[11] In preparation of inventory articles, Cattell and Scheier’s Anxiety Scale, Taylor’s Manifest Anxiety Scale and Welsh’s Anxiety Scale articles were used.[12] The validity in Turkish population was demonstrated by Le Compte and Oner.[13]

In order to perform STAI-1 test in our study, the participants were asked to mark the best expression on the scale that is numbered from 1 to 4, with the options “none”, “a little”, “a lot” and “completely”. In the scales, there are two kinds of expressions. We can also call them direct and reverse expressions. Direct expressions express negative feelings and reverse expressions express positive feelings. While this second round is scored, 1 weight value changes to 4, and 4 weight value changes to 1. In direct expressions, 4 valued answers show that the anxiety is higher. In reverse expressions, 1 valued answers show high anxiety, 4 valued answers show low anxiety.[9]

In the state anxiety scale, there are ten reverse expressions. Those are articles 1, 2, 5, 8, 10, 11, 15, 16, 19 and 20. In these articles, 4 points are given to 1, 3 points to 2, 2 points to 3 and 1 point to 4.[9] In state anxiety scale, there are ten direct expressions. Those are articles 3, 4, 6, 7, 9, 12, 13, 14, 17, and 18. In these articles, 1 point is given to 1, 2 points to 2, 3 points to 3 and 4 points to 4. In order to calculate state anxiety, the results obtained from direct and reverse expressions are collected. 40 and below 40 results are evaluated as normal, 41–60 mild anxiety, 61–80 moderate anxiety, 80 and above are evaluated as severe anxiety.

In our study, values 40 and below are evaluated as normal, values 41 and above evaluated as anxious and are categorized to be mild, moderate, severe anxiety.
Implementation of the research

The 1st study group consisted of 71 pregnant women who were monitored, 37 weeks of gestation and who were expected to have primiparous and normal birth in our polyclinic. The survey study was conducted to the 2nd study group consisted of 68 multiparous women whose spontaneous vaginal delivery was delivered spontaneously. The survey study was conducted to the 3rd study group of 69 multiparous women whose first delivery was performed by cesarean section and the current birth was planned by cesarean delivery. 15 pregnant women from Group 1 and 4 from Group 2 were excluded because of interventions during childbirth. Due to an emergency cesarean section was performed before the planned date, 7 pregnant women from Group 3 were excluded from the study. Pregnant women who have a history of psychiatric disease or diagnosis; pregnant women with maternal metabolic diseases such as hypertension, gestational diabetes mellitus (GDM); pregnant women with fetal antenatal problems such as growth retardation, polyhydramnios, and oligohydramnios were not included in the study.

Statistical analysis

All statistical analyses were performed using the SPSS ver. 25.0 (SPSS Inc., Chicago, IL, USA). The data were evaluated by the Kolmogorov-Smirnov test for normal distribution. No data group was found to be suitable for normal distribution. Because there were more than two independent groups and they were not suitable for normal distribution, the difference between the groups was investigated by Kruskal-Wallis H test. In case of significant difference, pairwise comparisons after Bonferroni correction for multiple tests were obtained. Comparisons of percentages between literature and the current study were performed by “chi-square test for goodness of fit”. Descriptive statistics were used to calculate the frequency, central tendency (mean, median & mode) and dispersion (range, variance, SD, maximum & minimum) for each variable when appropriate. A p-value <0.05 has been considered statistically significant.

Results

No statistically significant difference found between the three groups in terms of mother’s working status, data collection weeks, birth weeks and newborn weight (Table 1). When age is evaluated, also there is no statistically difference between three groups (Group 1: 28.38±1.74, Group 2: 27.96±1.16, Group 3: 28.21±2.01; p=0.454) (Table 1). When BMI is evaluated, also there is no statistically difference between three groups (Group 1: 21.72±3.16, Group 2: 22.18±3.01, Group 3: 21.88±2.92; p=0.436) (Table 1).

In the Kruskal-Wallis test, there was statistically significant difference between at least two groups (p<0.001). To find out which groups were different, we followed pairwise comparisons. As a result, 1–2 (p=0.001) and 1–3 (p=0.014) groups were found to be different (Table 2). In Group 1, anxiety levels was 49.9±8.44; in Group 2 it was 47.2±7.52.

Table 1. Baseline characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Primiparous (n=60)</th>
<th>Group 2 Multiparous (n=64)</th>
<th>Group 3 Elective cesarean section (n=62)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.38±1.74</td>
<td>27.96±1.16</td>
<td>28.21±2.01</td>
<td>0.454</td>
</tr>
<tr>
<td>Gravidity (n)</td>
<td>1 (1–2)</td>
<td>2 (2–4)</td>
<td>2 (2–4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Parity (n)</td>
<td>0 (0–0)</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.72±3.16</td>
<td>22.18±3.01</td>
<td>21.88±2.92</td>
<td>0.436</td>
</tr>
<tr>
<td>Working during pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working n (%)</td>
<td>39 (65)</td>
<td>40 (62.5)</td>
<td>39 (62.9)</td>
<td>0.310</td>
</tr>
<tr>
<td>Not working n (%)</td>
<td>21 (35)</td>
<td>24 (37.5)</td>
<td>23 (37.1)</td>
<td>0.082</td>
</tr>
<tr>
<td>Data collection week (weeks)</td>
<td>37.12±0.28</td>
<td>37.32±0.81</td>
<td>37.28±0.71</td>
<td>0.814</td>
</tr>
<tr>
<td>Birth week (weeks)</td>
<td>39.2±0.24</td>
<td>39.14±0.31</td>
<td>38.66±0.45</td>
<td>0.097</td>
</tr>
<tr>
<td>Newborn weight (g)</td>
<td>3450±172.12</td>
<td>3400±180.23</td>
<td>3440±167.48</td>
<td>0.111</td>
</tr>
</tbody>
</table>

*p<0.001
When patients were divided into groups of normal, mild anxiety, moderate anxiety and severe anxiety, 124 (66.6%) of the patients were found to be anxious (Table 3). In the group of anxious patients, it was found that 119 (95.9%) of the patients had mild anxiety, 5 (2.68%) of the patients moderate anxiety and no patient was severely anxious (Table 3). In Group 1, the patient ratio was higher than the other groups with 51 (85%), but most of the anxious patients was mild (90.2%) (Table 3).

All patients with moderate anxiety (5 patients) were in Group 1 (Table 3). In Group 3, it was shown that the half of the patients (50%) evaluated as Normal, other half of the patients (%50) was mild anxiety (Table 3).

Discussion

Fear is defined as the usual reaction to a perceived or existing danger. This reaction motivates people to warn themselves in the face of danger and to show convenient behavior towards it. Obstetricians and gynecologists observe the fears and anxiety of the patients during their examinations and interventional procedures (hysterosalpingography, amniocentesis, cordocentesis, etc.) in their daily practices.

Childbirth is a process in which the results are unpredictable and there are uncertainties. Many women face the fear of childbirth. This fear, like other physiological changes, prepares the pregnant woman for the postpartum period. Childbirth appearing in many different levels and reasons, may adversely affect the course of labor and prepare maternal and neonatal complications, if in severe stage.

Mild or moderate fear of childbirth is very common in many women. Studies show that some women face severe fear of childbirth. In the studies of Kjærgaard et al., it was shown that 10% of pregnant women face severe fear of childbirth and in the studies of Spice et al., 9.1% of pregnant women face severe fear of childbirth. In our study, it was found that 2.68% of the patients face moderate anxiety and none of the patients face severe anxiety (chi-square test for goodness of fit; p=NA).

Age is one of the factors known to be effective in the development of anxiety related to birth. In our study, the average age of women in three groups was 28.38±1.74, 27.96±1.16 and 28.21±2.01, respectively. In the evaluation of women facing anxiety related to childbirth, 97.31% of the patients were found to have normal or mild anxiety. In some studies, it was reported that the levels of anxiety were higher in pregnant

### Table 2. Evaluation of anxiety levels according to groups.

<table>
<thead>
<tr>
<th>Anxiety levels</th>
<th>Group 1 Primiparous (n=60) Mean±SD</th>
<th>Group 2 Multiparous (n=64) Mean±SD</th>
<th>Group 3 Elective cesarean section (n=62) Mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety levels</td>
<td>49.9±8.44</td>
<td>43.4±5.73</td>
<td>45.58±5.25</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Kruskal-Wallis test: To find out which groups were different we followed pairwise comparisons. As a result, 1–2 (p=0.001) and 1–3 (p=0.014) groups were found to be different.

### Table 3. Anxiety levels of groups.

<table>
<thead>
<tr>
<th>Anxiety levels</th>
<th>Group 1 Primiparous (n=60)</th>
<th>Group 2 Multiparous (n=64)</th>
<th>Group 3 Elective cesarean section (n=62)</th>
<th>Total (n=186)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>9 (15%)</td>
<td>22 (34.37%)</td>
<td>31 (50%)</td>
<td>62 (33.33%)</td>
</tr>
<tr>
<td>Mild</td>
<td>46 (76.66%)</td>
<td>42 (65.62%)</td>
<td>31 (50%)</td>
<td>119 (63.97%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (8.33%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (2.68%)</td>
</tr>
<tr>
<td>High</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
women with advanced maternal age and adolescent pregnant women. It is thought that because pregnant women in our study are 25–30 years of age and that the pregnancy is planned and the family may be more ready for the pregnancy, they experience less anxiety.

In the study of Arslan et al., 26.5% of the pregnant women were found to work. According to the Turkey Demographic and Health Survey (TNSA) 2013 data, the rate of working women was defined as 31%. The rate of working women in our study was 63.44% (chi-square test for goodness of fit; p=0.362). We think that the reason why we have higher number of working pregnant women compared to the data of Arslan et al. and TNSA 2013 is because our hospital is preferred by patients with higher income. Therefore, it is difficult to evaluate the population of our patients according to the average of our country. This is a limitation of our study.

In the study of Arslan et al., a significant relationship between the number of pregnancies and anxiety and depression scores of the pregnant women participating in the study was found; as the total number of pregnancies increased, anxiety and depression scores also increased (p=0.004). On the contrary, in our study, it was found that the anxiety in the primiparous pregnant women was more common than the multiparous group and the planned cesarean section (p=<0.001). The average patient with normal anxiety score was the most common in Group 3 (multiparous patients with elective cesarean section) (50%). We think that this case has occurred because the patients have experienced birth psychology before and have not experienced pain. These data is supported by Alehagen et al. with a limited number of patients and their work during the follow-up of nurses.

In the literature, it is reported that the care and education service received in the antenatal period reduces the fear of childbirth. In recent years, the rate of cesarean delivery is increasing all over the world, especially in our country. In the study of Burns et al., it was determined that maternal cesarean delivery was due to doctor referral. In the hospital, where our study takes place, “Pregnancy Education Classes” are created by doctors, many social activities are carried out with pregnant women. We think this situation reduces the fear of birth of patients.

Conclusion
The aim of this study was to determine the levels of anxiety during the birth of pregnant women with different parity history. According to the research results, we think that the anxiety levels of pregnant women are generally mild and women who have already experienced birth and did not experience pain have reduced anxiety levels. Also in the hospital where the study takes place, antenatal care is performed regularly and pregnant women are given regular training by doctors and auxiliary health personnel. We think this situation reduces birth anxiety. Our study was performed on a homogeneous patient population. The comparison of our results with more heterogeneous populations and studies on more patients will be more valuable in terms of interpretation of results.

Conflicts of Interest: No conflicts declared.

References


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