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- Original Research Articles
- Opinion Articles
- Report
- Review Articles
- Technical Notes

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6. Main text (subtitles)
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The evaluation of the serum brain natriuretic peptide concentrations in preeclamptic and healthy pregnant women and its potential relationship with mean arterial blood pressure

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Abstract

Objective: In this study, we aimed to investigate the correlation between serum brain natriuretic peptide (BNP) concentrations and blood pressure levels by comparing serum brain natriuretic peptide (BNP) concentrations in preeclamptic and normotensive pregnant women and to assess its potential role in the preeclampsia pathogenesis.

Methods: A total of 48 preeclamptic and 39 normotensive patients were included in the study prospectively. Systolic diastolic and mean arterial blood pressure of the pregnant women were measured. Serum BNP concentrations were measured by enzyme immunoassay method. The variable differences between the groups were analyzed by independent samples t-test. Potential correlations between the variables were assessed by Pearson’s correlation analysis.

Results: There was no difference between the groups in terms of age (26.18±11.49 years vs. 26.04±14.06 years), gestational age (31.59±6.94 weeks vs. 30.17±5.72 weeks), parity (2.62±1.4 vs. 2.53±1.82) and body mass index (30.71±16.33 kg/m² vs. 30.09±13.82 kg/m²) (p>0.05). Systolic (148.66±61.82 mmHg vs. 126.44±97.47 mmHg; p=0.015), diastolic (81.19±52.25 mmHg vs. 97.29±14.27 mmHg; p=0.019) and mean arterial pressure (113.97±41.76 mmHg vs. 96.26±27.25 mmHg; p=0.001) levels were higher in the pregnant women complicated with preeclampsia. In addition, serum BNP concentrations were also higher in the preeclamptic pregnant women than the control group (139.42±62.19 pg/mL vs. 99.28±19.32 pg/mL; p=0.028). BNP levels were significantly associated with only mean arterial pressure (β=0.241, p=0.037). Also, there was a significant positive correlation between BNP levels and mean arterial pressure (r=0.406, p=0.002).

Conclusion: We recommend further prospective studies with wider populations to assess whether BNP levels, which increase in preeclampsia, are associated with blood pressure levels or not.

Keywords: Pregnancy, preeclampsia, brain natriuretic peptide, mean arterial blood pressure.

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Introduction

Preeclampsia is characterized with vascular disorders affecting approximately 3–5% of the pregnancies, seen after 20 weeks of gestation, causing new-onset hypertension, and leading to vessel damage and at least one organ or system damage. Severe preeclampsia is the progressive form of the preeclampsia complicating approximately 0.6–1.2% of the pregnancies, and it results with impaired systemic characteristics such as elevated blood pressure (systolic blood pressure being 160 mmHg or above, and diastolic blood pressure being 110 mmHg and above) or renal failure, liver dysfunction (liver enzymes being two times higher than the normal upper threshold value) and persistent right upper quadrant or epigastric pain not responding to medical treatment, pulmonary edema, thrombocytopenia (platelet number being below 100x10^9/L) or cerebral or visual anomalies. Preeclampsia is a systemic vascular disorder specific to pregnancy only, and may frequently progress to life-threatening clinical conditions such as eclampsia, renal failure and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). Despite many theories asserted, the pathogenesis and etiology of preeclampsia is still unclear and it is believed that it is complex and associated with many factors.\(^1\)\(^-\)\(^3\)

Brain natriuretic peptide (BNP) is a polypeptide released as pre-pro BNP by the cells in ventricular myocardium and its production increases as a response to inflammatory conditions.\(^4\) Ventricular myocytes release BNP and N-terminal pro BNP, which is a product of non-active N-terminal fragment cleavage, into the systemic circulation as a response to stress and over-stress. It has been reported that BNP levels can be used as a sensitive marker in the diagnosis of mild systolic or diastolic cardiac failure and congestive cardiac failure accompanied by left ventricular dysfunction.\(^5\) In addition, it was also reported that plasma BNP levels elevates in preeclamptic women compared to pregnant women and it is a marker of subclinical vascular diseases in these patients. The previous studies also reported that there is a correlation between BNP levels and other complications associated with pregnancy such as the severity of preeclampsia and preterm labor.\(^6\) However, it is not fully known whether this biochemical increase is associated non-specifically or directly with these pathological conditions or not.\(^7\) Therefore, we aimed to investigate the correlation between serum BNP concentrations and blood pressure levels of the pregnant women in our study group by comparing serum BNP concentrations in preeclamptic and normotensive pregnant women and to assess its potential role in the preeclampsia pathogenesis in this study.

Methods

This study was conducted prospectively with the pregnant women between 18 and 38 years old who admitted to the obstetrics and gynecology clinic after getting the approval of ethics committee. The gestational ages of the pregnant women were calculated according to their last menstrual periods and they were confirmed by checking the ultrasonographic measurement data, and recorded as “week + day”. The heights (meter) and body weights (kg) were measured and recorded by using standard and same scales while the pregnant women were wearing casual and light clothes. The systolic and diastolic blood pressure levels were measured of each pregnant women three times by the standard and same sphygmomanometer (OMRON M2 Intellisense HEM-7121-E; OMRON Healthcare Group, Hoofddorp, Netherlands) while they were rested for at least 20 minutes and on sitting position at least for 5 minutes, and the arithmetic means were recorded. The diagnosis of preeclampsia was established as defined in the guidelines of the American College of Obstetricians and Gynecologists (ACOG) with at least one of the following criteria accompanying hypertension (systolic blood pressure <140 mmHg or diastolic blood pressure >90 mmHg) with an onset after the 20 weeks of gestation: proteinuria (creatinine rate ≥30 mg/mmol or ≥300 mg/day or testing in persistent spot urine ≥2+), renal failure (serum creatinine level which is not previous renal disease being >106 μmol/L or above 1.1 mg/dL or doubling serum creatinine level without additional renal disease), at least two-fold elevation in the values of measured serum alanine aminotransferase or aspartate aminotransferase, neurological complications (severe headache, blurred vision or convulsion), hematologic complications (platelet number below 150x10^9/L, coagulopathies), and fetal growth restriction.\(^8\)\(^,\)\(^9\) The pregnant women without additional health problem or proteinuria or any clinical symptoms listed above, the pregnant women with normal laboratory values whose blood pressure levels are within normal limits (blood pressure below 140/90 mmHg) were included in the healthy pregnant women group.
The mean arterial pressure (MAP) was calculated by the formula below:

\[
\text{MAP (mmHg)} = \frac{\text{Systolic blood pressure (mmHg)} + 2 \times \text{Diastolic blood pressure (mmHg)}}{3}
\]

The pregnant women whose gestational age was below 20 weeks of gestation, the cases with multiple pregnancy, intrauterine dead fetuses, fetal or placental anomalies, hypertension without induced proteinuria, diabetes mellitus, eclampsia, and the cases with pregestational hypertension history or chronic hypertension detected before pregnancy were excluded from the study.

After the preeclamptic and healthy groups were established, 5 cc venous blood sample was collected from each volunteer case after minimum 8-hour overnight fasting, and the serum sample was separated by centrifuging the samples. Serum BNP measurements were done by using an appropriate kit (Human Brain Natriuretic Peptide EIA Kit; RayBiotech Inc., Peachtree Corners, GA, USA) via enzyme immunoassay (EIA) method.

### Statistical analysis

The variables were presented as “mean ± standard deviation”. The compliance of the data to the normal distribution was analyzed by Kolmogorov-Smirnov test, and it was seen by the analysis results that the data exhibited normal distribution (p=0.621). The homogeneity of the data was examined by one-way ANOVA analysis and it was seen by the analysis results that the data exhibited homogeneous distribution (p=0.49). The comparisons of the variables in the groups among themselves were analyzed by independent sample t-test. The potential cause-effect relationships between the variables were analyzed by linear regression analysis and the correlations between the variables were analyzed by Pearson’s correlation analysis. All analyses were done by using SPSS v.16 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) software compatible with Microsoft Windows OS. The value of p<0.05 was considered significant.

### Results

The clinical and laboratory findings of the study population are shown in the Table 1. There was no significant difference between the pregnant women in both groups in terms of age, gestational age, parity and body mass index (p>0.05). The systolic blood pressure levels were found significantly higher in the preeclamptic pregnant women (148.66±61.82 mmHg vs. 126.44±97.47 mmHg; p=0.015). The diastolic blood pressure levels were significantly lower in the healthy pregnant women compared to the pregnant women complicated with preeclampsia (81.19±52.25 mmHg vs. 97.29±14.27 mmHg; p=0.019). The mean arterial blood pressure values were significantly higher in the preeclamptic pregnant women (113.97±41.76 mmHg vs. 96.26±27.25 mmHg; p<0.001). Serum BNP concentrations were higher in the preeclamptic pregnant women compared to the healthy pregnant women (139.42±62.19 pg/mL vs. 99.28±19.32 pg/mL; p=0.028).

The potential cause-effect relationships between the variables were evaluated by the linear regression analysis. In the model created, the systolic blood pressure, diastolic blood pressure and mean arterial blood pressure levels were designed as the independent variables, and the BNP levels were designed as dependent variable. According to this model, it was found that BNP levels were only correlated significantly with the mean arterial

### Table 1. The clinical and laboratory findings of the study population.*

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia (n=48)</th>
<th>Healthy (n=39)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26.18±11.49</td>
<td>26.04±14.06</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Gestational age, week±day</td>
<td>31.59±6.94</td>
<td>30.17±5.72</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Parity</td>
<td>2.62±1.49</td>
<td>2.53±1.82</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>30.71±16.33</td>
<td>30.09±13.82</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>148.66±61.82</td>
<td>126.44±97.47</td>
<td>0.015</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>97.29±14.27</td>
<td>81.19±52.25</td>
<td>0.019</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>113.97±41.76</td>
<td>96.26±27.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum BNP concentration, pg/mL</td>
<td>139.42±62.19</td>
<td>99.28±19.32</td>
<td>0.028</td>
</tr>
</tbody>
</table>

*The independent samples t-test was used. The value of p<0.05 was considered significant. BNP: brain natriuretic peptide.
pressure ($\beta=0.241$, $p=0.037$) (Table 2). Also, there was a significant positive correlation between BNP levels and mean arterial pressure ($r=0.406$, $p=0.002$).

### Discussion

In our study, we compared pregnant women without any additional health problem and the preeclamptic pregnant women who were similar in terms of maternal age and gestational age. In this comparison, we found that the serum BNP concentrations were significantly higher in the preeclamptic pregnant women ($139.42\pm62.9$ pg/mL vs. $99.28\pm19.32$ pg/mL; $p=0.028$) while BNP levels were only correlated significantly with the mean arterial pressure ($r=0.406$, $p=0.002$).

Hypertensive diseases may develop during pregnancy as a result of the inadequacies in the compliance of the volume and hemodynamic changes in pregnancy to the pregnancy-specific adaptive changes.\[^6\] It was reported that the maternal serum BNP levels were significantly higher in the preeclamptic pregnant women ($139.42\pm62.9$ pg/mL vs. $99.28\pm19.32$ pg/mL; $p=0.028$) while BNP levels were only correlated significantly with the mean arterial pressure.

<table>
<thead>
<tr>
<th></th>
<th>$\beta$ coefficient</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>0.116</td>
<td>0.52</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.109</td>
<td>0.36</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>0.241</td>
<td>0.037</td>
</tr>
</tbody>
</table>

$*It was evaluated by the linear regression analysis. The BNP levels were designed as dependent variable, and the systolic, diastolic and mean arterial blood pressure levels were designed as the independent variables. The value of $p<0.05$ was considered significant.

They also reported that the serum BNP levels were higher in the preeclamptic pregnant women with severe findings compared to the preeclamptic pregnant women. They suggested that the reason of this elevation in BNP levels may be associated with ventricular stress related with preeclampsia or subclinical cardiac disorders.\[^9\]

On the other hand, there are different data related with the maternal BNP levels in the preeclampsia. Kaaja et al. compared the preeclamptic and healthy pregnant women who had no difference between them in terms of gestational age and parity similar to our study, but they could not find significant difference between two groups in terms of serum BNP levels unlike our study. They explained this result with the impairment of BNP in the normal diurnal variation in which there are also serum aldosterone and urinary prostaglandin metabolites as the other parameters analyzed in their study.\[^14\]

Although mean arterial pressure exhibit decrease in the first periods of pregnancy, blood pressure levels elevate in the further periods of pregnancy and blood pressure levels reach to the pregestational levels as a result.\[^8\] As proven in many studies, arterial blood pressure is a risk factor which is widely accepted for the development of cardiovascular diseases.\[^\]^\[^14\],\[^18\] On the other hand, these studies investigating risk factors for cardiovascular diseases frequently focus only on the impacts of systolic and diastolic blood pressure levels. However, these levels reflect only the fluctuations in extreme conditions.\[^17\]-\[^19\] In addition to the systolic and diastolic blood pressure levels, we also included arterial blood pressure in our study which provides more important data about the daily mean blood pressure levels instead of instant levels. Besides, other studies investigating preeclampsia examined the mean arterial pressure relatively less. The mean arterial pressure as a major component of the blood pressure provides more extensive information for the daily interpretation of blood pressure and does not require an additional cost as it can be obtained in routine clinical practice easily.\[^19\] Cataliotti et al. reported that the conjugated BNP they administered orally decreased the mean arterial pressure significantly. They asserted that this decrease in the mean arterial pressure occurred by the activation of cGMP via orally administered BNP.\[^20\]

There were many limitations in our study. Firstly, relatively small study population caused the results being unable to support study hypothesis completely. Secondly, we could not include eclamptic pregnant women in our study. Lastly, we could not evaluate maternal systolic and diastolic functions echocardiographically.
Conclusion
We found in our study that serum BNP concentrations increased in preeclamptic pregnant women. The BNP concentrations elevated in our study population were associated with the maternal mean arterial pressure. We believe that wider prospective studies evaluating BNP concentrations in the preeclampsia should be conducted to address the relationship between BNP levels and maternal cardiac functions.

Acknowledgement
The authors would like to thank Hasan Taylan Yılmaz, Spec. MD, and Hakan Çelik, Spec. MD., for their helps in the statistical analyses.

Conflicts of Interest: No conflicts declared.

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The evaluation of the retinal findings in the fundoscopic examination of the preeclampsia patients

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Abstract

Objective: We aimed to evaluate and compare the retinal findings of the fundoscopic examination of mild and severe preeclampsia cases in our study.

Methods: The data of 165 patients who admitted to Somalia Mogadishu-Turkey Training and Research Hospital, were hospitalized in the obstetrics and gynecology clinic upon the preeclampsia diagnoses and for whom the eye consultation was requested between January 2017 and January 2020 were evaluated retrospectively. The patients were grouped according to their age, week of gestation, delivery type (cesarean section – normal delivery) and preeclampsia severity (mild – severe). The patients found to have hypertensive retinopathy changes on right or left eye or both eyes were recorded as positive in terms of the findings.

Results: While no pathological finding was observed in 104 (63.1%) of 165 patients who underwent fundoscopic examination, 61 (36.9%) patients had retinal pathology. Of the patients found to have pathology in their fundoscopic findings, 39 (63.9%) were severely preeclamptic and 22 (36.1%) were mildly preeclamptic. The pregnancy of 51 (83.6%) of these 61 patients was terminated at preterm period (<37 weeks of gestation) and of 10 (16.4) at term (≥37 weeks of gestation). Of 61 patients found to have retinal pathology, 36 (59%) had hypertensive retinopathy, 9 (14.8%) had macular edema, 6 (9.8%) had hypertensive hemorrhage, 4 (6.6%) had pigment epithelial detachment, 2 (3.3%) had bilateral retinal detachment, and 2 (3.3%) had edema in bilateral optical disk.

Conclusion: While visual complaints are very common in preeclamptic pregnant women, rare but serious complications such retinal detachment, pigment epithelial detachment, macular edema and papilledema may also develop. Other retinal diseases in addition to hypertensive retinopathy should also be considered during the fundoscopic examination of preeclamptic pregnant women. The clinicians should be aware of these ocular indications and they should work in cooperation to prevent blindness during or after pregnancy. It seems that terminating the pregnancy in preeclamptic pregnant women who develop visual impairment is effective to regain visual capability.

Keywords: Retinal detachment, pregnancy, hypertension, preeclampsia.

Özet: Preeklampsi hastalarının göz dibi muayenesinde retina bulgularının değerlendirilmesi

Amaç: Bu çalışmada amaç, hafif ve şiddetli preeklampsi hastalarının göz dibi retinal bulgularını değerlendirip ve karĢılaĢtırmaktır.


Bulgular: Göz dibi muayenesi yapulan 165 hastanın 104‘ünde (%63.1) patolojik bulgu gözlenenmek, 61 (%36.9) hastada retinal patoloji gözlenmiştir. Göz dibi bulgularında patoloji saptanan hastaların 39’u (%63.9) şiddetli preeklampsk, 22’si (%36.1) hafif preeklampskti. Bu 61 hastadan 51’inin (%83.6) gebelikte preterm (<37. gestasyonel hafta), 10’unun (%16.4) ise term (%37. gestasyonel hafta) olarak sonlandırılmıştır. Retinal patoloji saptanan 61 hastanın 36’sında (%59) hipertansiyon retinopati, 9’unda (%14.8) maküla ödemi, 6’inda (%9.8) hipertansiyon hemorajis, 4’ünde (%6.6) pigment epitel deteksiyonu, 2’sinde (%3.3) bilateral retina dokunu, 2’inde (%3.3) bilateral optik diskte odem izlenmiştir.


Anahtar sözcükler: Retina dokunu, gebelik, hipertansiyon, preeklampsi.
Introduction

Preeclampsia is a pregnancy-specific disease which affects 5–7% of pregnancies, develops during second or third trimester, and causes fetal mortality rate to increase significantly.\(^\text{[1]}\) Measuring blood pressure before pregnancy and during early period and second trimester of pregnancy is very important in terms of the preeclampsia diagnosis. Although elevated blood pressure and the presence of proteinuria developing after 20 weeks of gestation in a pregnant woman who is considered to be normotensive before pregnancy are defined as preeclampsia, the presence of proteinuria is not always necessary.\(^\text{[2,3]}\) Preeclampsia diagnosis can also be established in case of systemic findings (such as liver dysfunction, renal failure, pulmonary edema, presence of hemolysis and thrombocytopenia, and visual and cerebral findings) coexisting with hypertension in the absence of proteinuria.\(^\text{[1]}\) Preeclampsia affects all organs and systems including visual system. It causes ischemic injury by leading to maternal systemic inflammation and endothelial dysfunction.\(^\text{[4]}\)

The vision system may be affected at different levels in the preeclampsia. Various underlying pathological changes in retina, optic nerve and cerebral cortex cause ocular symptoms developing in the patients.\(^\text{[5]}\) The most common ocular pathological change is the vasoconstriction of arterioles. Serous retinal detachment developing as a result of choroidal vascularization is a rare reason of visual impairment in preeclampsia.\(^\text{[6]}\)

The visual symptoms may include photopsia, hemianopsia, difficulty in focusing, blurry vision, reduced visual acuity and full blindness in severe cases.\(^\text{[5]}\) It has become obligatory to have an ophthalmoscope in delivery rooms according to the efficiency in-place evaluation of obstetrics and pediatrics hospital published in 2018.\(^\text{[7]}\) The recent studies have shown that the women with the history of preeclampsia are under a higher risk of ocular complication during antepartum, intrapartum and postpartum periods compared to the health pregnant women.\(^\text{[8,9]}\) Although most of the ocular changes are physiological (reduced intraocular pressure, increased myopia, bitemporal and concentric defects in the visual field associated with the physiological growth in pituitary gland) during pregnancy, they can be pathological (papilledema, optic atrophy, retinal hemorrhage, macular edema, retinal detachment) in preeclampsia.\(^\text{[8]}\) In addition, preeclamptic retinopathy may present more severely in the presence of underlying diabetes, chronic hypertension and kidney disease.\(^\text{[9]}\)

Somalia is a country with low income which is bordered by Kenya, Ethiopia and Djibouti and located in Sub-Saharan Africa. The fertility rate in Somalia is 6.08 births per woman (2014 estimates). This is also the fourth highest rate in the world. The limited access to antenatal care services in underdeveloped and developing countries increases the rates of sequela and mortality rates associated with preeclampsia and its complications.\(^\text{[10]}\)

In this study, we aimed to evaluate the fundoscopic findings of the pregnant women who were hospitalized in the Obstetrics and Gynecology Clinic of Somalia Mogadishu-Turkey Training and Research Hospital due to the preeclampsia diagnosis in the last 3 years.

Methods

The files of 220 patients who were established with the diagnosis of preeclampsia and delivered at the Obstetrics and Gynecology Clinic of Somalia Mogadishu-Turkey Training and Research Hospital, and for whom the eye consultation was requested during the hospitalization between January 2017 and January 2020 were evaluated retrospectively. The fundoscopic examination findings of 165 of these patients were accessed. The approval was obtained from the Ethics Committee of Somalia Mogadishu-Turkey Training and Research Hospital for the study (Approval No. 218; MSTH/3401, Date: 12.02.2020). The study was conducted in accordance with the principles of Helsinki Declaration.

The diagnosis of preeclampsia was established according to the criteria of the American College of Obstetricians and Gynecologists (ACOG).\(^\text{[11]}\) According to these criteria, (1) the presence of 140–159 mmHg or higher persistent systolic blood pressure or 90–109 mmHg or higher diastolic blood pressure after 20 weeks of gestation in a woman whose blood pressure is within normal limits previously, (2) measuring blood pressure 160/110 mmHg or higher with a 15-minute interval together with systemic findings (proteinuria ≥300 mg/24-hour, platelet count <100,000/dL, at least two times higher transaminase level, creatinine level >1.1 mg/dL, presence of pulmonary edema, and presence of cerebral or visual symptoms) and (3) measuring blood pressure ≥160/110 mmHg with 4-hour interval in addition to at least one systemic finding was considered
preeclampsia. The diagnosis of HELLP syndrome was established when it is found that a preeclamptic patient has hemolysis, lactate dehydrogenase (LDH) >600 IU/L and platelet count <100,000 cell/mm$^3$. The cases found to have new-onset grand mal seizure were considered eclampsia.

The ocular symptoms of consulted cases were (1) blurry vision, (2) headache, (3) photopsia, (4) hemianopsia, (5) difficulty in focusing, (6) reduced visual acuity and (7) full loss of vision in both eyes.

The patients were examined by direct and/or indirect ophthalmoscope at bedside half an hour later after applying 1% tropicamide drop on both eyes.

The patients were grouped according to their age, week of gestation, delivery type (cesarean section – normal delivery) and preeclampsia severity (mild – severe). The patients found to have hypertensive retinopathy changes on right or left eye or both eyes were recorded as positive in terms of the findings.

Hypertensive retinopathy was categorized according to Keith-Wagener classification. According to this classification:

- **Grade 1**: Mild generalized retinal arteriolar narrowing;
- **Grade 2**: Definite focal arteriolar narrowing and arteriovenous nipping in addition to the Grade 1 findings;
- **Grade 3**: Retinal hemorrhages, exudates and cotton-wool spots in addition to the Grade 2 findings;
- **Grade 4**: The presence of papilledema in addition to the Grade 3 findings.$^{[13]}$

The patients with pregestational hypertension, diabetes and kidney disease and the patients with an eye disease preventing fundus imaging (corneal scar and dystrophies, cataract, etc.) were excluded from the study.

![Table 1.](image) Demographic and clinical characteristics of preeclamptic patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean value (min–max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (year)</td>
<td>24.4±5.2 (15–44)</td>
</tr>
<tr>
<td>Week of gestation</td>
<td>33±4.2 (26–38)</td>
</tr>
<tr>
<td>Systolic pressure (mmHg)</td>
<td>161±11.4 (140–185)</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td>102±8.8 (90–115)</td>
</tr>
<tr>
<td>Protein (mg/day)</td>
<td>2204±254 (1300–3300)</td>
</tr>
</tbody>
</table>

For the statistical analyses, IBM SPSS 23.0 (SPSS Inc., Chicago, IL, USA) software was used. The analyses were done by Fisher’s exact test and the value p<0.05 considered statistically significant.

**Results**

Of the patients established with preeclampsia diagnosis, the mean age was 24.4±5.2 (range: 15–44) years and mean week of gestation was 33±4.2 (range: 26–38) weeks. While the mean arterial blood pressure was 153/98 mmHg in the patients with mild preeclampsia, it was 178/110 mmHg in the patients with severe preeclampsia. The mean proteinuria amount in 24-hour urine was 2204±254 mg/l/day (Table 1).

Of 165 patients, the pregnancy was terminated at preterm period (<37 weeks of gestation) in 91 (55.1%) patients and at term (≥37 weeks of gestation) in 74 (44.9%) patients. Fifty-seven (34.5%) patients had severe preeclampsia and 108 (65.5%) patients had mild preeclampsia. While 118 (71.5%) patients delivered by cesarean section, 47 (28.5%) patients delivered by spontaneous vaginal labor.

Fourteen (8.4%) of all cases were previously using alpha-methyldopa (250 mg) 3×1 tablet as an antihypertensive drug due to the preeclampsia diagnosis.

**Table 2.** The distribution of retinal findings in preeclamptic patients.

<table>
<thead>
<tr>
<th>Retinal finding</th>
<th>Mild preeclampsia</th>
<th>Severe preeclampsia</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive retinopathy</td>
<td>16</td>
<td>20</td>
<td>36</td>
<td>0.24</td>
</tr>
<tr>
<td>Hypertensive hemorrhage</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>0.37</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pigment epithelial detachment</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Macular edema</td>
<td>2</td>
<td>7</td>
<td>9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Papilledema</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>–</td>
</tr>
</tbody>
</table>
The most common complaints of the consulted patients were headache, blurry vision and eye floaters, respectively.

While no pathological finding was found in 104 (63.1%) of 165 preeclamptic pregnant women who underwent fundoscopic examination, retinal pathology was observed in 61 (36.9%) preeclamptic pregnant women. Thirty-nine (63.9%) of the patients found to have pathology in their fundus findings had severe preeclampsia while 22 (36.1%) of them had mild preeclampsia. The pregnancy of 51 (83.6%) patients was terminated at preterm period (<37 weeks of gestation) and 10 (16.4%) of them at term (≥37 weeks of gestation).

Of 61 preeclamptic pregnant women found to have retinal pathology, 36 (59%) had hypertensive retinopathy, 9 (14.8%) had macular edema, 6 (9.8%) had hypertensive hemorrhage, 4 (6.6%) had pigment epithelial detachment, 2 (3.3%) had bilateral retinal detachment, 2 (3.3%) had left retinal detachment, and 2 (3.3%) had edema in bilateral optical disc (Table 1). Macular edema, retinal detachment and pigment epithelial detachment were more frequent in the severe preeclamptic cases than the mild preeclamptic cases, and it was statistically significant (p<0.05) (Table 2).

When 61 preeclamptic pregnant women who had retinal pathology were evaluated among themselves, 9 (14.8%) patients in the severe preeclampsia group were followed up in the intensive care unit after labor due to HELLP syndrome. The convulsion was observed in 2 (3.3%) patients. The uterine atony developed in 1 (1.6%) patient during the cesarean section, and it was seen in the follow-up that the patient developed acute renal failure. One (1.6%) patient who developed lung edema after right ventricular failure died.

Of the patients diagnosed with hypertensive retinopathy, 22 (50%) were grade 1, 14 (31.9%) were grade 2, 6 (13.6%) were grade 3 and 2 (4.5%) were grade 4 (Table 3).

<table>
<thead>
<tr>
<th>Hypertensive retinopathy grade</th>
<th>Patient number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>22</td>
<td>50</td>
</tr>
<tr>
<td>Grade 2</td>
<td>14</td>
<td>31.9</td>
</tr>
<tr>
<td>Grade 3</td>
<td>6</td>
<td>13.6</td>
</tr>
<tr>
<td>Grade 4</td>
<td>2</td>
<td>4.5</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>100</td>
</tr>
</tbody>
</table>

Discussion

The preeclampsia, which is a constrictive vasculopathy, is a major reason for maternal and neonatal morbidity and mortality, and it is estimated that visual systems of 30–100% of preeclamptic women are affected.[14] Preeclampsia is seen about 5% of the pregnant women, and ocular complications have been reported in one third of these patients.[15] The blurred vision is the most common complaint in these patients. [16] On the other hand, photopsia, scotoma and diplopia are not rare.[17] These findings are observed after the development of hypertensive retinopathy and optic neuropathy associated with the hyperperfusion of the ocular system. However, there are studies reporting that approximately 40% of the blurred vision complaint of preeclamptic patients are subjective. [18] In our study, the rate of affected visual system in preeclamptic pregnant women was 36.9%. While the blurred vision was the most common complaint, eye floater and temporary loss of vision were not rare.

The retinopathy findings in preeclamptic patients are similar to the hypertension-associated retinopathy. The retinopathy beginning with the generalized weakening of retinal arterioles followed by focal narrowing is the most common finding in the preeclamptic retinopathy.[19] In our study, we found hypertensive retinopathy in 59% of the patients whose visual systems were affected, and it was also the most common finding. Fifty percent of the hypertensive retinopathies was grade 1.

Retinal edema, hemorrhage and exudate, nerve fiber infarcts and neovascularization-associated vitreous hemorrhage and serous retinal detachment are the other pathological changes seen in preeclampsia-associated retinopathy.[19,20] Endothelial injury, abnormal autoregulation and hypoperfusion-associated ischemia are among the potential reasons of these complications. Most of these findings return to normal levels after the recovery from preeclampsia.

The recent studies reported the prevalence of retinal detachment in preeclampsia between 1.5% and 3.7%. [21] In our study, this rate was 6.6%. The retinal detachment is an extraordinary reason of visual loss in preeclampsia. It is usually in bilateral, serous and bullous form. The detachment of neurosensorial retina from retinal pigment epithelium due to severe hypertension causes the loss of vision. The treatment of retinal detachment in preeclampsia is conservative and it includes the treatment of underlying condition. The prognosis is good, and
spontaneous resolution generally occurs by blood pressure control and labor. The development of retinal detachment in a preeclamptic pregnancy is an indication for the necessity of pregnancy termination. After labor, the sub-retinal fluid is resorbed and visual acuity becomes normal within weeks. On the other hand, if there is excessive necrosis in the retinal pigment epithelium, permanent loss of vision may occur. Lee et al. reported that ocular symptoms and visual sequelae usually become reversed with the immediate termination of the pregnancy. In our study, we observed that the retinal detachments of the patients, who were followed up after labor, recovered without the need of surgical procedure. The findings of the patients with pigment epithelial detachment also returned to normal levels during the follow-up. The reason for a higher rate of retinal detachment in our study compared to other countries may be that pregnant women did not undergo routine health screening before pregnancy in Somalia and they admitted to hospital upon pregnancy for the first time. In addition, not performing fundoscopic examination routinely during pregnancy may lead to miss retinal breaks and small peripheral ruptures. According to our observations, the greatest obstacle for the routine screenings is that the country does not have a social healthcare system and the people cannot afford healthcare costs as their income level is low. In addition, maternal morbidity and mortality and perinatal morbidity and mortality may progress severely in the preeclampsia developing in association with chronic hypertension. Not doing routine examinations before the development of preeclampsia in most of the pregnant women in Somalia may lead to miss out hypertensive pregnant women and make preeclampsia complications more frequent and severe.

The retinopathy grade correlates with preeclampsia grade positively. Radha Bai Prabhu showed in their study that retinal detachment and loss of vision are more frequent in the patients with severe preeclampsia. Retinal findings being more frequent in severe preeclampsia and observing retinal detachment more frequently in the patients with severe preeclampsia particularly in our study were consistent with their study.

Pigment epithelial detachment accompanying to central serous chorioretinopathy is detachment of neurosensory layer after the subretinal fluid accumulation on the posterior part of fundus. There are studies showing that this risk increases up to 9 times during third trimester in particular. The increasing cortisol level in the blood circulation particularly during third trimester causes this condition. In our study, we consider that the development of pigment epithelial detachment may be associated with elevated blood pressure because 3 out of 4 cases with pigment epithelial detachment are severe preeclampsia cases.

The loss vision caused by the cortex part of optical paths can be seen rarely in preeclampsia cases. Ischemia, edema and hemorrhage are among the reasons of cortical loss of vision, and they are usually irreversible. Permanent damage at legal blindness level may develop in 1–3% of the patients with preeclampsia/eclampsia. There was no patient with acute cortical blindness in our study.

**Conclusion**

It seems that the greatest obstacle for the regular follow-up of pregnant women in the underdeveloped countries such as Somalia is the incapability of public healthcare organizations and the low income levels. Making free and accessible pregnant follow-up centers more prevalent may decrease the severity and frequency of maternal complications.

Retroorbital evaluations should be made in preeclamptic patients describing loss of vision even though pupil reflex and fundus findings are normal. Therefore, it may be helpful to do examinations by MRI (magnetic resonance imaging) and VEP (visual evoked potential) devices for lesions associated with optic nerve and occipital cortex in addition to direct ophthalmoscope for the preeclamptic pregnant women developing loss of vision.

Although visual complaints are very common in preeclamptic pregnant women, rare but serious complications such as retinal detachment, pigment epithelial detachment, macular edema and papilledema may also develop.

Other retinal diseases should also be kept in mind in addition to the hypertensive retinopathy during the fundoscopic examination of the preeclamptic pregnant women. The clinicians should be aware of these ocular indications and work in cooperation to prevent blindness that may develop during or after pregnancy. It seems that terminating the pregnancy in preeclamptic pregnant women who develop loss of vision is effective to regain visual capability.

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


Persistent right umbilical vein: its incidence and clinical importance

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Abstract

Objective: To investigate the incidence and concomitant findings of persistent right umbilical vein (PRUV).

Methods: The study was conducted by retrospective review of the data of 1856 patients who admitted to the Clinic of Obstetrics and Gynecology of Firat University between December 2018 and December 2019 for the gestational examination between 14 and 28 weeks of gestation. The obstetric characteristics of the patients such as age, number of pregnancy, abortion, parity and body mass index were recorded. The diagnosis of PRUV was established in the conditions where portal vein reaches to stomach abnormally (roughly, course towards stomach instead of parallel course), fetal gall bladder locates in the medial of umbilical vein or umbilical vein connects to right portal vein abnormally instead of left portal vein. In the cases diagnosed with PRUV, the isolated persistent right umbilical vein or its association with other anomalies was recorded. Ultrasonography findings (minor markers) were also recorded in these cases.

Results: During the study period, 1856 pregnant women were evaluated for gestational examination. Five cases were established with the diagnosis of PRUV. Accordingly, PRUV prevalence was 0.27%. The PRUV incidence in the study population was 1/370 in the study population. Chromosome analysis was not performed in any cases. No chromosomal anomaly was found in PRUV cases, but one case had echogenic intracardiac focus, one case had renal cyst was found in one case. When organ systems were evaluated, renal cyst was found in one case. No additional finding was found in one case.

Conclusion: PRUV is the most common form among fetal venous system anomalies. If detected, fetal examination is required in terms of the anomalies that may accompany. Chromosome analysis is not necessary if it is isolated, and it should be evaluated as a variant of normal anatomy.

Keywords: Persistent right umbilical vein, ultrasonography, incidence.

Özet: Persiste sağ umbilik ven: Insidans ve klinik önemi

Amaç: Persiste sağ umbilik ven (PSUV) görülme sıklığı ve eşlik eden bulguların incelenmesi.


Sonuç: PSUV, fetal venöz sistem anomalileri içinde en sık görülen formdur. Tespit halinde eşlik edebilecek anomaliler arasında dikaktal fetal muayene gerekir. İzole olmasa da kromozom incelenmesi gerektirmek; normal anatominin bir varyantı olarak değerlendirilmelidir.

Anahtar sözcükler: Persiste sağ umbilik ven, ultrasonografi, insidans.
Introduction

Umbilical cord anomalies may include the conditions such as the presence of an extra vein in the cord, anomalies seen in vein course or dimension or the presence of a persisting vein. With the development of color Doppler and 3D ultrasonographic imaging methods, it has become easy to establish prenatal diagnosis for umbilical cord anomalies.

Persistent right umbilical vein (PRUV) is the condition where left umbilical vein which should develop normally becomes obliterated and right umbilical vein remains open during the embryological development. The recent studies report its incidence between 0.2% and 0.5%. This incidence makes PRUV the most common form among fetal venous system anomalies.

PRUV can be seen in the transverse plain imaging of fetal abdomen in the routine fetal screening.

PRUV cases are categorized under two groups as intrahepatic variant and the extrahepatic type which bypasses liver completely. In the intrahepatic variant, the umbilical vein proceeds towards stomach on the right side of gall bladder and merges with the portal vein. In the extrahepatic variant, it may proceed directly to the right atrium, inferior vena cava or iliac veins. Intrahepatic variant is the variation which is seen 95% more frequently, and its prognosis is good. On the other hand, extrahepatic type has a poor prognosis due to the hemodynamic changes.

In our study, we aimed to evaluate our PRUV cases that we found within one-year period.

Methods

The study was conducted by retrospective review of the data of 1856 patients who admitted to the Clinic of Obstetrics and Gynecology of Fırat University between December 2018 and December 2019 for the gestational examination between 14 and 28 weeks of gestation. The ethical approval required for the study was obtained from the Ethics Committee of Fırat University. The study was conducted in accordance with Helsinki Declaration. The obstetric and demographic characteristics of all patients such as age, number of pregnancy, abortion, parity and body mass index were recorded.

The ultrasonographic examination was performed in accordance with the recommendations provided in the up-to-date guidelines of International Society of Ultrasound in Obstetrics & Gynecology (ISUOG). For determining the gestational age, the last menstrual period was used in the cases with regular menstruation and fetal crown-rump length at 11–14 weeks of gestation during the first trimester was used in other cases. The fetal biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur diaphysis length (FDL) were measured for the fetal biometry. Fetal abdominal examination was done as defined in the guidelines. Accordingly, abdominal organ situs was determined. Fetal stomach was defined in the normal position on the left. It was found that the intestines were within the abdomen and the umbilical cord reached to fetus through the intact abdominal wall. It was noted that fetal gall bladder was observed on the right upper quadrant beside the liver as well as the left-sided stomach.

The fetus was evaluated in terms of the findings of the ventral wall defects such as omphalocele or gastroschisis on the location where fetal umbilical cord is connected to the abdomen. Cord veins were viewed by using standard ultrasonography and Doppler ultrasonography as a component of routine anatomic examination. The number of veins in the cord and the intrafetal course of the cord were also recorded. The cases found to have two arteries and one umbilical vein in the cord were evaluated as normal cord structure. Abnormal course and persistence in the umbilical vein was considered as the presence of PRUV. Accordingly, the following criteria were used for the diagnosis of PRUV: the conditions where portal vein reaches to stomach abnormally (course towards stomach instead of parallel course), fetal gall bladder locates in the medial of umbilical vein or umbilical vein connects to right portal vein abnormally instead of left portal vein. In addition, the isolated PRUV or its association with other anomalies was recorded. Chromosomal evaluation was recommended for the cases in which additional anomalies were detected.

The fetuses, in which situs inversus, unclear situs and heterotaxia (left and right isomerism) were found, were excluded from the study.

The statistical analysis of the study was done by using SPSS 21.0 package software (SPSS Inc., Chicago, IL, USA). Definitive statistics were used to analyze the data.

Results

Between December 2018 and December 2019, 1856 patients admitted to the clinic for gestational examination. The age, week of gestation, number of pregnancy,
parity, abortion numbers and body mass index values of the patients are shown in Table 1.

The diagnosis of persistent right umbilical vein was established in 5 cases during the study period. When all cases were evaluated, the prevalence was found 0.27% (the incidence of persistent right umbilical vein was found 1/370 in the study population). No major anomaly was found in these cases, but minor ultrasonographic markers were found in four cases. Accordingly, the first case had an advanced maternal age and the echogenic focus was found in the right ventricle. No additional finding was detected in the fetal echocardiography examination. The case did not undergo first trimester screening test and did not accept advanced chromosomal evaluation. The echogenic intestine was found in the second case, and the risk for first trimester combined test was low (1/1500). No additional finding was found in the fetal examination of the third case. A simple 12×12 mm cyst was found on the upper pole of the fetal left kidney in the fourth case, and it was confirmed that the lesion was within kidney in the fetal magnetic resonance imaging which was performed to differentiate potential suprarenal gland pathology. The fifth case admitted at the 26 weeks of gestation and fetal nasal bone shortness [biparietal dimeter (83 mm) / nasal bone (6.9 mm) >12] was found in the ultrasonography examination; the result of the first trimester combined screening test was 1/1000 and the case did not accept chromosomal invasive evaluation. The intrafetal course of umbilical vein in this last case is shown in Fig. 1.

All cases were reached after labor and it was learnt that their infants did not have any structural or chromosomal anomalies. The obstetric characteristics and the additional characteristics found during gestational examinations of the cases who were found to have persistent right umbilical vein are shown in Table 2.

Table 1. The obstetric characteristics of the patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>23.4±1.5</td>
</tr>
<tr>
<td>Week of gestation (week)</td>
<td>22±1.4</td>
</tr>
<tr>
<td>Number of gestation (number)</td>
<td>2.1±0.5</td>
</tr>
<tr>
<td>Parity (number)</td>
<td>1.3±0.8</td>
</tr>
<tr>
<td>Abortion (number)</td>
<td>0.4±0.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.2±1.1</td>
</tr>
<tr>
<td>Total number of cases</td>
<td>1856</td>
</tr>
</tbody>
</table>

BMI: body mass index; Mean±SD: mean ± standard deviation.

**Discussion**

Under normal circumstances, right umbilical vein regresses on the fourth week of embryonal period and completely disappears on the seventh week. Left umbilical vein remains as the single vein moving from placenta to liver. The ultimate course of left umbilical vein is towards the midline of fetal abdomen as it connects to the distal part of the left portal vein. The left umbilical vein disappears when the right umbilical vein per-
The blood proceeds from the placenta to the right umbilical vein, then to the right portal vein, to vena cava through ductus venosus and then heart. PRUV proceeds slightly on the parasagittal plane on the right of the mid-sagittal plane of the fetus. Some studies report PRUV cases usually as isolated anomalies (75% of the cases), and other cord anomalies (single umbilical artery), cardiovascular (ventricular septal defect, tetralogy of Fallot, ARSA), gastrointestinal (omphalocele, esophageus atresia), skeletal (hemivertebra) and urogenital (hydronephrosis, duplicated collecting system, undescended testicle) system problems are among the concomitant anomalies. In our study, all of the cases found to have PRUV were in the form of I-PRUV which is the most common form seen in the literature, and we did not see any concomitant anomaly in any of the cases. We observed minor markers (nasal hypoplasia, echogenic intestine and echogenic cardiac focus) in three of five PRUV cases, anechoic cyst in the upper pole of the left kidney in one case, and no additional finding in one case. We found in the organ system examination that the case with cyst in the renal system was 5-month infant during the time when we were writing our study and that pediatrics and nephrology clinics recommended 6-month follow-ups for the renal cyst and there was no additional pathology.

Whether there is chromosomal anomaly in PRUV cases or not is the subject of another discussion. Some studies stated that they did not observe chromosomal anomaly while some other studies reported that they found anomaly with a rate of 1.3%. When we reviewed the literature, we found that the fetus of a pregnant woman with Noonan syndrome had also Noonan syndrome as well as PRUV after conducting a chromosomal evaluation. Lide et al. investigated 166,548 pregnant women in their systematic review, and they found PRUV in 212 cases. Of these 212 cases, 3 had chromosomal anomaly, 2 had trisomy 18 and 1 had mosaic Turner syndrome. As highlighted in the studies, the incidence of chromosomal anomaly increases as the concomitant anomalies increase. The experience gained throughout the years on the diagnosis of PRUV show that the intrahepatic PRUV with normal ductus venosus connection is a normal anatomic variant without clinical significance in the absence of concomitant anomalies. In our cases, we did not find chromosomal anomaly in any of the cases in the evaluation made after labor.

The differential diagnosis of PRUV involves umbilical vein varicose, gall bladder duplication, portal vein anomalies and intrahepatic cysts. During the diagnosis, gall bladder has a left-sided view due to the course of PRUV. This should not be confused with the ectopic localization where gall bladder locates in the left lobe lateral segment. It has been shown that this view is associated with the alternative course of the persistent umbilical vein instead of an ectopic gall bladder, and that it is not a localization anomaly of gall bladder. As it will prevent diagnostic errors, a careful anatomic evaluation is critical.

Conclusion
The persistent right umbilical vein is the most common form among fetal venous system anomalies. The fetal abdomen should be evaluated carefully for PRUV diagnosis. The recent studies have highlighted that this anomaly does not increase the rate of chromosomal anomaly or syndromic pattern frequency. However, when PRUV diagnosis is established, cardiovascular, gastrointestinal, skeletal and urogenital systems should be examined carefully in terms of the concomitant anomalies. PRUV should be considered as anatomic variant in cases in which ductus venosus has a normal course.

Conflicts of Interest: No conflicts declared.

References


The relationship between psychosocial health and prenatal attachment in pregnant women

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Bucak Health College, Burdur Mehmet Akif Ersoy University, Burdur, Turkey

Abstract

Objective: The aim of this study is to determine the relationship between psychosocial health and prenatal attachment in pregnant women.

Methods: This quantitative and descriptive study was conducted with 241 pregnant women who admitted to the Obstetrics and Gynecology Clinic of a state hospital in the Mediterranean Region between December 2019 and March 2020. The Introductory Characteristics Form, Prenatal Psychosocial Health Assessment Questionnaire and Prenatal Attachment Inventory were used to collect the data.

Results: It was found in the study that 84.9% of the pregnancies were planned, 83.8% of them were at the last trimester, and 31.3% of them were their first pregnancy. The mean score of pregnant women was 4.54±0.18 (range: 3.87 to 4.87) in the Prenatal Psychosocial Health Assessment Questionnaire and 72.24±7.48 (range: 50.00 to 84.00) in the Prenatal Attachment Inventory. It was found that the mean scores obtained in the Prenatal Psychosocial Health Assessment Questionnaire were significantly different between the groups according to age, education level, family type and number of pregnancy. There was also significant difference in the mean scores obtained in the Prenatal Attachment Inventory between the groups according to age, education level, family type, number of child and household income level.

Conclusion: We did not find any statistically significant correlation between the scores of the Prenatal Psychosocial Health Assessment Questionnaire and the Prenatal Attachment Inventory in our study.

Keywords: Pregnant woman, psychosocial health, prenatal attachment.

Introduction

The prenatal psychosocial health refers to a complete wellbeing of pregnant woman psychologically, socially and emotionally. Although women perceive pregnancy as a pleasing and exciting condition and a way to reach a certain maturity, the pregnancy makes mothers feel concerned depending on the stages of pregnancy and some psychosocial factors. The prenatal psychosocial health


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of a woman is affected by many factors such as the socioeconomic status of family, her education level, history of previous pregnancies and labor experiences, pregnancy being planned, number of child, previous and current diseases of mother, wrong and insufficient knowledge of woman about pregnancy, and low self-esteem.\(^{1-4}\) Therefore, pregnancy is a period in which it is more likely to encounter many factors that may cause anxiety and stress. It increases the likelihood of seeing depression in mother.\(^{1-7}\) Pregnant woman being healthy psychologically is very important for maternal and fetal health. It poses a problem in terms of establishing mother-baby attachment if the psychosocial health impaired during pregnancy continues to be impaired during postnatal period.\(^{1,4}\)

Mother-baby attachment is the case where mother cares her baby through unreluctant behaviors and meets its needs in case that the baby needs the mother and where the baby have confidence in the mother. The foundations of mother-baby attachment are laid during pregnancy. Prenatal attachment represents the initial part of mother-baby attachment. The attachment between pregnant woman and fetus is the first important relationship established with the baby and it is determinative for the relationship between mother and baby after labor.\(^{8,9}\) The cases such as not having proper care during prenatal period, skipping the examinations or not going on time, consumption of alcohol, tobacco and tobacco products or other harmful substances, living in an environment where the sex of baby is considered important, miscarriage, preterm labor, undesired pregnancy and prolonged or challenging labor history are the risk factors which have a role on the impairment of psychological health during pregnancy for the development of motherhood role and the improvement of motherhood identity. These risk factors impair the psychological health of mother and hinder her motherhood duty. Addressing the motherhood and prenatal psychological experience at an early period is therefore of vital importance.\(^{10}\)

The level of attachment is related with the psychological health of mother during prenatal period. The mother having a complete wellbeing psychologically is related with the good levels of psychosocial factors. In the studies carried out abroad showed that prenatal depression and high anxiety during pregnancy have a negative impact on mother-baby attachment.\(^{5,11,12}\) The significant determinative of prenatal attachment is related with prenatal and postnatal psychological health,\(^{13,14}\) and there is a significant correlation between hostile approaches of pregnant women towards fetus and mental disorders.\(^{15}\) Although there are studies carried out in Turkey which investigated psychosocial health\(^{16-19}\) and prenatal attachment levels of pregnant women\(^{20-23}\) separately, there are no sufficient studies showing the relationship between them. In this sense, we conducted our study to determine the relationship between psychosocial health and prenatal attachment of pregnant women, and we sought answers to these questions: (i) Do the introductory characteristics of pregnant women have an impact on their psychosocial health levels? (ii) Do the introductory characteristics of pregnant women have an impact on their prenatal attachment levels? (iii) Is there a relationship between the psychosocial health levels and prenatal attachment levels of pregnant women?

**Methods**

This quantitative and descriptive study was conducted with the pregnant women who admitted to the Obstetrics and Gynecology Clinic of a state hospital in the Mediterranean Region between December 2019 and March 2020. The population of the study comprises the pregnant women (N=651) who admitted to the Obstetrics and Gynecology Clinic of a state hospital in the Mediterranean Region during 2019. The sample size of the study was calculated by using the formula \(n=\frac{Ni^2pq/(d2)(N-1)+pq}{pq}\) and the minimum sample size was found 241 with 95% confidence interval and 5% error margin. The study was completed with a total of 265 pregnant women who did not have any visual or hearing loss, spoke Turkish, open for verbal communication, completed in the questionnaire during the study period and accepted to participate in the study.

“Introductory Characteristics Form”, “Prenatal Psychosocial Health Assessment Questionnaire” and “Prenatal Attachment Inventory” were applied to the pregnant women. The Introductory Characteristics Form which aims to understand the socio-demographic characteristics of the pregnant women consist of 9 questions investigating their age, education level, place of residence, family type, delivery type, gestational month, number of pregnancy, number of child and household income level.

The Prenatal Psychosocial Health Assessment Questionnaire (PPHAQ) developed by Yıldız is used to evaluate the psychosocial health during pregnancy. The questionnaire includes 46 items and 6 sub-sections. The mean score is obtained by dividing the total score of the questionnaire by the number of items, and a score.
between 1 and 5 is obtained. The more the total score moves towards 1 from 5, the more the prenatal psychosocial health is impaired, and 1 means that the psychosocial health is at the worst level. The same assessment applies to the sub-sections, and as the score moves towards 1, it means that there is a problem related with that factor.\[^{3}\]

The Prenatal Attachment Inventory (PAI) developed by Muller is used to measure the attachment levels of pregnant women to their unborn babies.\[^{14}\] The PAI was adapted to Turkish in 2013 by Duyan et al. and it has a total of 21 items aiming to measure the emotional attachment to the fetus. The participants are asked to select one of the following options for each of the statements given in the items: “Almost never = 1 point”, “Sometimes = 2 points”, “Usually = 3 points”, and “Almost always”. None of the statements in the inventory are not scored in a reverse way. The total score that participants may have in the inventory varies between 21 and 84, and higher scores show that the prenatal attachment level is high while lower scores show that the prenatal attachment level is low. No norm determination study was conducted regarding to the inventory, and therefore the inventory enables to make comparison between the prenatal attachment levels of the pregnant women from a different group.\[^{12}\]

The data were obtained via the face-to-face interview technique by the researchers in the waiting room before the examinations of the pregnant women who visited the Obstetrics and Gynecology Clinic of a state hospital in the Mediterranean Region between December 2019 and March 2020. The aim and the methods of the study were explained to the pregnant women before their participation in the study, and it was stated that the data would be used only for scientific purposes. It took approximately 10–15 minutes to complete the questionnaire.

SPSS 20.0 (Spss Inc., Chicago, IL, USA) was used to analyze the data obtained in the study, and descriptive statistical analysis (mean, standard deviation, percentage, frequency), one-way ANOVA test, Kolmogrov Smirnov test and independent samples t-test were used. The value p<0.05 was considered significant.

In order to conduct the study, the ethics approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Burdur Mehmet Akif Ersoy University before the study. In addition, the pregnant women who participated in the study read and signed the informed consent forms, and their written and verbal consents were obtained. This study does not reflect all pregnant women in Turkey and it is only limited to the pregnant women who came to the study hospital for examination.

<table>
<thead>
<tr>
<th>Table 1. The distribution of the pregnant women by the introductory characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introductory characteristics (n=265)</td>
</tr>
<tr>
<td><strong>Age (year)</strong></td>
</tr>
<tr>
<td>15–20</td>
</tr>
<tr>
<td>21–28</td>
</tr>
<tr>
<td>29–35</td>
</tr>
<tr>
<td>36–42</td>
</tr>
<tr>
<td>43 or above</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
</tr>
<tr>
<td>Primary school</td>
</tr>
<tr>
<td>Secondary school</td>
</tr>
<tr>
<td>High school</td>
</tr>
<tr>
<td>Higher education or above</td>
</tr>
<tr>
<td><strong>Place of residence</strong></td>
</tr>
<tr>
<td>City</td>
</tr>
<tr>
<td>District</td>
</tr>
<tr>
<td>Village</td>
</tr>
<tr>
<td><strong>Family type</strong></td>
</tr>
<tr>
<td>Nuclear family</td>
</tr>
<tr>
<td>Extended family</td>
</tr>
<tr>
<td><strong>Pregnancy type</strong></td>
</tr>
<tr>
<td>Planned pregnancy</td>
</tr>
<tr>
<td>Unplanned pregnancy</td>
</tr>
<tr>
<td><strong>Month of gestation</strong></td>
</tr>
<tr>
<td>4, 5, 6 months</td>
</tr>
<tr>
<td>7, 8, 9 months</td>
</tr>
<tr>
<td><strong>Number of pregnancy</strong></td>
</tr>
<tr>
<td>One</td>
</tr>
<tr>
<td>Two</td>
</tr>
<tr>
<td>Three</td>
</tr>
<tr>
<td>Four</td>
</tr>
<tr>
<td>Five or more</td>
</tr>
<tr>
<td><strong>Number of child</strong></td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>1–2</td>
</tr>
<tr>
<td>3 or more</td>
</tr>
<tr>
<td><strong>Income level</strong></td>
</tr>
<tr>
<td>Good</td>
</tr>
<tr>
<td>Medium</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

**Results**

The distribution of the introductory characteristics of the pregnant women in our study are given in Table 1. Accordingly, 62.6% of the pregnant women are between 21 and 28 years old, 44.2% of them are graduated from high school, 50.9% of them reside in a district, and 81.5% of them have nuclear family. It was found that 84.9% of the pregnancies are planned, 83.8% of them are at the last trimester, 31.3% of them are the first pregnancy, 45.7% of them have no child, and the 62.6% of them have a medium income level.
The mean scores of the pregnant women were 4.54±0.18 (range: 3.87 to 4.87) for PPHAQ and 72.24±7.48 (range: 50.00 to 84.00) for PAI (Table 2).

The mean scores of the pregnant women according to the introductory characteristics are given in Table 3. Accordingly, the mean PPHAQ scores of those

**Table 2.** The mean scores of the pregnant women obtained from the Prenatal Psychosocial Health Assessment Questionnaire and the Prenatal Attachment Inventory.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Minimum score</th>
<th>Maximum score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal Psychosocial Health Assessment Questionnaire (PPHAQ)</td>
<td>4.54</td>
<td>0.18</td>
<td>3.87</td>
<td>4.87</td>
</tr>
<tr>
<td>Prenatal Attachment Inventory (PAI)</td>
<td>72.24</td>
<td>7.48</td>
<td>50.00</td>
<td>84.00</td>
</tr>
</tbody>
</table>

**Table 3.** The mean scores of the pregnant women obtained from the Prenatal Psychosocial Health Assessment Questionnaire according to the introductory characteristics.

<table>
<thead>
<tr>
<th>Introductory characteristics (n=265)</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Test statistics</th>
<th>p-value</th>
<th>Significant difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (year)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–20</td>
<td>a</td>
<td>4.53</td>
<td>0.17</td>
<td>0.537</td>
<td></td>
</tr>
<tr>
<td>21–28</td>
<td>b</td>
<td>4.56</td>
<td>0.17</td>
<td>0.002</td>
<td>a &gt; d, e</td>
</tr>
<tr>
<td>29–35</td>
<td>c</td>
<td>4.48</td>
<td>0.17</td>
<td>0.063</td>
<td>b &gt; c, d</td>
</tr>
<tr>
<td>36–42</td>
<td>d</td>
<td>4.40</td>
<td>0.15</td>
<td>0.887</td>
<td></td>
</tr>
<tr>
<td>43 or above</td>
<td>e</td>
<td>4.40</td>
<td>0.15</td>
<td>0.737</td>
<td></td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>a</td>
<td>4.45</td>
<td>0.22</td>
<td>3.521</td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>b</td>
<td>4.54</td>
<td>0.16</td>
<td>0.016</td>
<td>b &gt; a</td>
</tr>
<tr>
<td>High school</td>
<td>c</td>
<td>4.52</td>
<td>0.18</td>
<td>0.063</td>
<td>b &gt; a, d &gt; c</td>
</tr>
<tr>
<td>Higher education or above</td>
<td>d</td>
<td>4.59</td>
<td>0.15</td>
<td>0.887</td>
<td></td>
</tr>
<tr>
<td><strong>Place of residence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>City</td>
<td>4.53</td>
<td>0.15</td>
<td>2.411</td>
<td>0.092</td>
<td></td>
</tr>
<tr>
<td>District</td>
<td>4.56</td>
<td>0.18</td>
<td>0.092</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Village</td>
<td>4.49</td>
<td>0.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Family type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear family</td>
<td>4.55</td>
<td>0.17</td>
<td>0.110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended family</td>
<td>4.47</td>
<td>0.18</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pregnancy type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planned pregnancy</td>
<td>4.56</td>
<td>0.16</td>
<td>2.448</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unplanned pregnancy</td>
<td>4.38</td>
<td>0.18</td>
<td>0.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Month of gestation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4, 5, 6 months</td>
<td>4.53</td>
<td>0.18</td>
<td>1.185</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7, 8, 9 months</td>
<td>4.54</td>
<td>0.17</td>
<td>0.905</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>a</td>
<td>4.53</td>
<td>0.15</td>
<td>0.472</td>
<td></td>
</tr>
<tr>
<td>Two</td>
<td>b</td>
<td>4.52</td>
<td>0.20</td>
<td>0.005</td>
<td>c &gt; a, b, d, e</td>
</tr>
<tr>
<td>Three</td>
<td>c</td>
<td>4.59</td>
<td>0.17</td>
<td>0.034</td>
<td></td>
</tr>
<tr>
<td>Four</td>
<td>d</td>
<td>4.48</td>
<td>0.15</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Five or more</td>
<td>e</td>
<td>4.42</td>
<td>0.16</td>
<td>0.220</td>
<td></td>
</tr>
<tr>
<td><strong>Number of child</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>a</td>
<td>4.53</td>
<td>0.17</td>
<td>0.220</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>b</td>
<td>4.56</td>
<td>0.19</td>
<td>0.034</td>
<td></td>
</tr>
<tr>
<td>3 or more</td>
<td>c</td>
<td>4.48</td>
<td>0.16</td>
<td>b &gt; c</td>
<td></td>
</tr>
<tr>
<td><strong>Income level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>a</td>
<td>4.56</td>
<td>0.15</td>
<td>0.203</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>b</td>
<td>4.52</td>
<td>0.18</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>c</td>
<td>4.61</td>
<td>0.25</td>
<td>a &gt; b</td>
<td></td>
</tr>
</tbody>
</table>

*One-way ANOVA; †Independent samples t-test.
in 21–28 age range were significantly higher than those who are 29 years old or above, and the mean PPHAQ scores of those in 15–20 age range were significantly higher than those who are 36 years old or above. The mean PPHAQ scores of those graduated from secondary school were significantly higher than those graduated from primary school, and the mean PPHAQ scores of those with higher education levels were significantly higher than those graduated from primary school and high school. It was found that the mean PPHAQ scores of those who have nuclear family were higher than those who have extended family, and the mean PPHAQ scores of those with planned pregnancy were higher than those with unplanned pregnancy, which were all statistically significant. It was also found that the mean PPHAQ scores of those with three pregnancies were higher than those with other numbers of pregnancy, and the mean PPHAQ scores of those with high level of household income were higher than those with medium level of household income, which were all statistically significant.

Table 4. The mean scores of the pregnant women obtained from the Prenatal Attachment Inventory according to the introductory characteristics.

<table>
<thead>
<tr>
<th>Introductory characteristics (n=265)</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Test statistics</th>
<th>p-value</th>
<th>Significant difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (year)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>15–20</td>
<td>a</td>
<td>76.17</td>
<td>4.39</td>
<td>5.323</td>
<td>a, e &gt; b, c, d</td>
</tr>
<tr>
<td>21–28</td>
<td>b</td>
<td>71.33</td>
<td>7.32</td>
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</tr>
<tr>
<td>29–35</td>
<td>c</td>
<td>72.90</td>
<td>8.15</td>
<td></td>
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<tr>
<td>36–42</td>
<td>d</td>
<td>67.45</td>
<td>10.86</td>
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<td>43 or above</td>
<td>e</td>
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<td>0.81</td>
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<tr>
<td>Primary school</td>
<td>a</td>
<td>76.26</td>
<td>6.18</td>
<td>3.401</td>
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<td>Secondary school</td>
<td>b</td>
<td>70.83</td>
<td>7.94</td>
<td>0.018</td>
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<tr>
<td>High school</td>
<td>c</td>
<td>72.19</td>
<td>7.53</td>
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<tr>
<td>Higher education or above</td>
<td>d</td>
<td>72.20</td>
<td>6.81</td>
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<tr>
<td><strong>Place of residence</strong></td>
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<td><strong>Family type</strong></td>
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<td>Nuclear family</td>
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<td>0.001</td>
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<td>Extended family</td>
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<tr>
<td>Planned pregnancy</td>
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<td>Unplanned pregnancy</td>
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<tr>
<td><strong>Month of gestation</strong></td>
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<tr>
<td>4, 5, 6 months</td>
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<td>0.014</td>
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<tr>
<td>7, 8, 9 months</td>
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<tr>
<td><strong>Number of pregnancy</strong></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>One</td>
<td>a</td>
<td>73.21</td>
<td>6.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two</td>
<td>b</td>
<td>72.52</td>
<td>7.04</td>
<td>0.263</td>
<td></td>
</tr>
<tr>
<td>Three</td>
<td>c</td>
<td>72.12</td>
<td>8.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Four</td>
<td>d</td>
<td>69.75</td>
<td>8.15</td>
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<tr>
<td>Five or more</td>
<td>e</td>
<td>70.66</td>
<td>10.44</td>
<td></td>
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<tr>
<td><strong>Number of child</strong></td>
<td></td>
<td></td>
<td></td>
<td>3.452</td>
<td></td>
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<tr>
<td>None</td>
<td>a</td>
<td>73.14</td>
<td>6.40</td>
<td></td>
<td></td>
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<tr>
<td>1–2</td>
<td>b</td>
<td>72.13</td>
<td>7.85</td>
<td>0.033</td>
<td>a &gt; c</td>
</tr>
<tr>
<td>3 or more</td>
<td>c</td>
<td>69.28</td>
<td>9.20</td>
<td></td>
<td></td>
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<tr>
<td><strong>Income level</strong></td>
<td></td>
<td></td>
<td></td>
<td>4.560</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>a</td>
<td>71.11</td>
<td>8.27</td>
<td></td>
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<tr>
<td>Medium</td>
<td>b</td>
<td>72.36</td>
<td>7.14</td>
<td>0.011</td>
<td>c &gt; a, b</td>
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<td>Low</td>
<td>c</td>
<td>77.33</td>
<td>8.27</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*One-way ANOVA; †Independent samples t-test.
The mean PAI scores of the pregnant women according to the introductory characteristics are given in Table 4. Accordingly, the mean PAI scores of those in 15–20 age range and those who are 43 years old or above were significantly higher than those in other age groups in a statistically significant way. The mean PAI scores of those graduated from primary school were higher than those with other educational levels in a statistically significant way. It was found that the mean PAI scores of those who have nuclear family were higher than those who have extended family, and the mean PAI scores of those with no child were higher than those with 3 or more children, which were all statistically significant. Also, the mean PAI scores of those with low level of household income were higher than those with medium and high levels of household income in a statistically significant way. There was no statistically significant relationship between PPHAQ and PAI scores of the pregnant women (Table 5).

Discussion

In our study, the mean PPHAQ score of the pregnant women was 4.54±0.18 (range: 3.87 to 4.87). Aksay et al. reported in their study that the pregnant women had a medium level of psychosocial health and their mean PPHAQ score was 3.13±0.33.[16] Yıldız reported that the mean PPHAQ score of the pregnant women was 3.84±0.51 and they had a medium level of psychosocial health.[1] In the study of Özişahin et al., this mean score was 3.20±0.50 and the level of psychosocial health was medium.[17] The level of psychosocial health was medium in relevant studies, but it was at a high level in our study. In parallel with our study, Koyuncu reported in their study that the mean PPHAQ score was 3.95±0.45 and the level of psychosocial health was high.[18] In the study of Değirmenci, the mean PPHAQ score was 4.02±0.41 and the level of psychosocial health was high.[19] In the study of Derya et al., the psychosocial health level of the pregnant women was high with a mean PPHAQ score of 4.0±0.4.[24] We believe that the high psychosocial health levels in our study may be associated with the high rate of planned pregnancies (84.9%) of the women who participate in our study. We consider that the high rate of planned pregnancies may show that the number of women who are ready for pregnancy psychologically is high and being ready psychologically for pregnancy may affect psychosocial health positively.

In our study, we found that the mean PPHAQ scores of those graduated from secondary school were higher than those graduated from primary school, and the mean PPHAQ scores of those with higher education levels were significantly higher than those graduated from primary school and high school in a statistically significant way. Similar to our study, Özişahin et al. found that the mean PPHAQ scores of those graduated from primary school were significantly lower than those graduated from secondary school, high school and university.[17] Değirmenci did not find any significant difference between educational levels and mean PPHAQ scores.[19]

The pregnancy is a period during which women most frequently benefit from the healthcare services and are more open to learn health related information and behaviors. In the study of Filiz, the authors reported a positive correlation between health perception and health literacy.[25] Also, some studies in the literature emphasize that the health literacy level increases as educational levels increase.[26] We consider that the difference in psychosocial health levels according to the educational levels in our study may be associated with health literacy.

We found in our study that the mean PPHAQ scores of those with planned pregnancy were higher than those with the unplanned pregnancy, which was statistically significant. Özişahin et al. did not find a significant difference between the mean PPHAQ scores of those with planned pregnancy and those with the unplanned pregnancy.[17] We consider that the woman being in control of the pregnancy planning shows the readiness of woman for the pregnancy and therefore the stress during pregnancy will decrease and their psychosocial health will be affected positively.

We found in our study that the mean PPHAQ scores of those with high level of household income were higher than those with medium level of household income, which is statistically significant. The studies in the liter-

### Table 5.
The correlation between the scores of the pregnant women obtained from the Prenatal Psychosocial Health Assessment Questionnaire and the Prenatal Attachment Inventory.*

<table>
<thead>
<tr>
<th>Prenatal Attachment Inventory (PAI)</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal Psychosocial Health Assessment Questionnaire (PPHAQ)</td>
<td>0.072</td>
<td>0.111</td>
</tr>
</tbody>
</table>

*Pearson correlation.
ature show that there is a positive correlation between the psychosocial health and high level of household income. Koyuncu reported in their study that the mean PPHAQ scores of those perceiving their income level high are significantly higher than the other groups[19]. Değirmenci found in their study that the mean PPHAQ scores of those with lower income than their expenses were significantly lower than the other groups. In a study performed, it was found that the depression symptoms are more common in women with low socio-economic levels.[25] The authors believed that there is a correlation with income level and the care of baby and preparing for future, and this may affect the psychosocial health of mother.

The prenatal attachment is a term used to define the emotional bond which is established between woman and fetus during pregnancy and exists emotionally, cognitively, and behaviorally.[28] Maternal age is also among the factors affecting mother-baby attachment.[30] We found in our study that the mean PAI scores of those in 15–20 age range and who are 43 years old or above are higher than those in other age groups in a statistically significant way. In a study conducted on pregnant women with high risk, the authors reported that the median PAI scores of the pregnant women between 18 and 30 years old were higher than those who are 31 years old or above in a statistically significant way.[28] Hjelmstedt et al. found that the PAI scores of young mothers are higher.[30] Damato also reported that the prenatal attachment level is higher in young pregnant women.[30] Özkan et al. found in their study that the mean PAI scores of women who are 31 years old or above are significantly higher than those who are between 18 and 30 years old.[31] The studies conducted on various sample groups show that there is a correlation between age and prenatal attachment.

We found in our study that the mean PAI scores of those graduated from primary school were higher than those with other educational levels in a statistically significant way. Bakır et al. reported in their study that the median PAI scores of those graduated from secondary school or with higher education levels were higher than those graduated from primary school in a statistically significant way.[32] In the study of Küçükkaya et al., the authors found that the prenatal attachment level of those graduated from high school or with higher education levels was significantly higher than those graduated from primary school or with lower education levels.[31] While these two studies are not similar to our study, Özkan et al. reported in their study similar to our study that the prenatal attachment level of the pregnant women graduated from primary school was higher than the other pregnant women.[25] The studies conducted show that the educational level affects prenatal attachment differently.

We found in our study that the mean PAI scores of those who have nuclear family were higher than those who have extended family in a statistically significant way. Although it was not statistically significant, Bakır et al. reported in their study that the median PAI scores of the pregnant women who have nuclear family are higher than those who have extended family.[26]

In our study, we found that the mean PAI scores of those who have no child were higher than those with 3 or more children in a statistically significant way. Bakır et al. reported in their study that the median PAI scores of those with no child were higher than the pregnant women with one or more children in a statistically significant way.[26] It can be said that the women without any child are more willing to have a child, and therefore their prenatal attachment levels are higher.

In our study, we found that the mean PAI scores of those with low level of household income were higher than those with medium and high levels of household income in a statistically significant way. Unlike our study, Elkin reported in their study that the median PAI scores of those whose incomes are higher than their expenses were significantly higher than those with other income levels.[28] Küçükkaya et al. also found in their study that the prenatal attachment level of those whose incomes are higher than or equal to their expenses were higher than those whose incomes are lower than their expenses.[22] While the results of these two studies are not in parallel with our study, Damato reported similar to our study that the prenatal attachment level of those with low income level was higher.[29]

Mental and emotional conditions of a pregnant woman affect the course of pregnancy. Biological and psychological changes during pregnancy and labor may decrease the prenatal attachment level by affecting psychosocial health negatively. Feelings such as worry, nervousness and self-depreciation may prevent pregnant women to establish attachment with fetus.[32] In a study investigating the pregnant women dealing with stress, depression and prenatal attachment levels and the factors affecting them, the authors found that the pregnant women with low economic levels, low educational levels and who consider to terminate pregnancy
show more depression symptoms, but there is no statistically significant difference between them and attachment levels. We did not find any statistically significant correlation between PPDAQ and PAI scores in our study.

**Conclusion**

In our study, we found statistically significant difference between PPDAQ scores in terms of age, educational level, family type, number of pregnancy and household income level. We also found statistically significant difference between PAI scores in terms of age, educational level, family type, number of child and household income level. On the other hand, there was no statistically significant correlation between PPDAQ and PAI scores. In terms of the limitations of our study, the study population reflects the pregnant women who participated in our study only from a single hospital, we recommend conduct further studies with pregnant women from different regions to investigate the correlation between psychosocial health and prenatal attachment level. Also, we recommend healthcare professionals help pregnant women to express themselves in the best way and identify current problems through therapeutic communication to be established with them considering that fact that various factors affect the psychosocial health and prenatal attachment levels of pregnant women. In addition, we recommend organizing multidisciplinary trainings in order to eliminate the problems regarding psychosocial health and prenatal attachment levels and to improve health.

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

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The relationship between psychosocial health and prenatal attachment in pregnant women


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Abstract

Objective: We aimed to investigate the characteristics of early and late gestational termination cases by evaluating the cases undergone gestational termination in our clinic.

Method: All pregnant women who had singleton pregnancy and underwent gestational termination due to fetal indications between January 2017 and December 2019 were included in the study.

Results: A total of 341 cases, of which 263 were with early gestational termination (Group 1) and 73 were with late gestational termination (Group 2) were included in the study. No difference was observed between the demographic characteristics of the groups. The ultrasonicographic structural anomaly was observed in 273 (80.1%) of 341 cases and no structural anomaly was observed in 68 (19.9%) cases. Of the cases with structural anomaly, 200 (73%) had isolated system anomaly and 73 (26.7%) had multiple system anomaly. Karyotype analysis was performed in 68% of the cases, and chromosomal anomaly was found in 52.6% of them. Among the cases with normal karyotype analysis results, 22 cases had single gene disorder, which mostly had thalassemia. While the incidence of structural anomaly was significantly high in the late termination cases (91% vs. 76.8%), the incidence of isolated cardiovascular anomaly was significantly high in the late termination cases similarly (37.5% vs. 13.8%). The autopsy was performed on 16.7% of the cases after termination and the findings were consistent with the prenatal ultrasonographic results in 86% of the cases, and additional findings were found in 22.4% of the cases in the autopsy.

Conclusion: When the late gestational terminations performed in our clinic are compared to the early gestational terminations, we believe that conducting ultrasonographic anomaly screening to all pregnant women including echocardiography even at a less rate, and also making screening programs in the early gestational periods such as aneuploidy screening easily accessible for all pregnant women may help to maintain maternal health by decreasing the rates of the cases with late gestational termination.

Keywords: Gestational termination, prenatal screening, fetal structural anomaly.

The assessment of early and late gestational termination cases

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Original Article

Özet: Erken ve geç gebelik terminasyonu olgularının değerlendirilmesi

Amaç: Klinikimizdeki gebelik terminasyonu uygulanan olguların incelenerek erken ve geç gebelik terminasyonu olgularının özelliklerinin araştırılması amaçlandı.


Bulgular: Çalışmaya 263’ü erken gebelik terminasyonu (Grup 1) ve 78’i geç gebelik terminasyonu (Grup 2) olmak üzere 341 olgu dahil edildi. Grupların demografik özellikleri arasında fark izlenmedi. Grupların %80.1’inde ultrasonografide yapışal anomaliler saptanırken, %19.9’unda anomaliz izlenmedi. Yapısal anomalilerin %73’ünde (%73) izole sistem anomalisi saptanırken, 73 olguna (%26.7) çoklu sistem anomalisi bulundu. Olguların %68’sine karyotip analizi uygulandı ve bunların %52.6’sında kromozom anomalisi saptandı. Karyotip analizi sonucu normal olan olgular arasında çoğunlukla talel olunan verilerin %22’ü taraflı hastalığı saptandı. Geç terminasyon olgularının %91’inde Karşı %76.8’lik sıklığı olanları olarak yüksek saptanırken benzer şekilde izole kardiyovasküler anomalilerin %37.5’te karşı %13.8’lik sıklığa da geç terminasyon olgularında anlamalı yükseklikleri. Terminasyon sonrası olguların %16.7’sine otopsi uygulandı ve bunların %86’sında prenatal ultrasonografik bulgularla uyuşan zerre orantılı olup bu zerre saptandı.

Sonuç: Klinikimizde uygulanan geç gebelik terminasyonları erken gebelik terminasyonlarından daha az olmaktadır. Çünkü ekoardiografide ki dahil edildiği ultrasonografide anomalilerin tüm masının tüm gebelerde uygulanması ve aynı zamanda anıptoldi tarama gibi erken gebelik haftalarındaki taraflı programların tüm gebeler için kolay ulaşılabilirlictsini geçe gebelik terminasyonu olgularının daha da azalmaması sağlayarak maternal sağlığın korunmasında katkı sağlayabilir.

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

Fetal malformations have been an important issue in fetal medicine and become one of the significant reasons of perinatal deaths.[1] The incidence of gestational termination associated with fetal malformation has been reported 5.2 per 10,000 live births and its incidence has been increasing.[2] As the ultrasonographic anomaly screening performed in the second trimester of pregnancy has become prevalent, the rate of detecting fetal anomalies during prenatal period has increased.[3] With the addition of ultrasonographic, biochemical and genetic examinations into the first trimester screening programs and the technological developments in ultrasound devices and equipment, diagnosing many fetal anomalies (structural, genetic, and chromosomal) during early weeks of gestation has become possible. Thus, it has been contributed to the maintenance of maternal health by conducting gestational termination during early weeks of gestation in necessary cases.[4–6]

The rights regarding gestational termination have been determined within the limits of the law, and they vary by countries. In Turkey (Law No 2827, 1983), voluntary gestational termination is allowed in the first 10 weeks of gestation while it is possible after 10 weeks of gestation only in the cases where the life of mother is endangered or in the presence of lethal diseases or severe disability which are incurable for the fetus, regardless of the week of gestation.

In our study, we evaluated the records of the cases which underwent gestational termination in our perinatology clinic. In addition to the indications of gestational termination, we assessed the characteristics of the early and late gestational termination cases to raise awareness regarding the early diagnosis of fetal structural, chromosomal and genetic anomalies during prenatal period.

Methods

In this study, we retrospectively evaluated 341 cases which underwent gestational termination for medical purposes in the Perinatology Clinic of the Faculty of Medicine at Akdeniz University between January 2017 and December 2019. The ethics committee approval was obtained from the Clinical Research Ethics Committee of the Faculty of Medicine of Akdeniz University with the decision no. 70904504/544. All fetal ultrasonographic examinations were carried out by maternal-fetal medicine specialists by using Toshiba Applio 500 (Toshiba Medical Systems, Co., Ltd., Otawara, Japan) ultrasonography device. Karyotype analysis was offered to all cases who were found to have anomaly in the ultrasonographic examination or who were in the high risk group in the prenatal aneuploidy screening tests. After clinical evaluations of the cases were completed, the families were informed about potential fetal and postnatal prognosis by a board consisting of perinatology, medical genetic, pediatrics and relevant pediatric sub-specialty experts. In the presence of lethal anomalies and anomalies with the expectations of postnatal severe disability, the gestational termination was performed after informing families in detail and obtaining their consents. The terminations performed due to maternal indications and multiple pregnancies were excluded from the study.

The cases included in the study were categorized in two groups according to the week of gestation at which gestational termination was performed. The patients who underwent termination before 23 weeks of gestation were included in the Group 1 (early termination) while the patients who underwent termination at and after 23 weeks of gestation were included in Group 2 (late termination). The fetocide was performed in all late termination cases by administering intracardiac potassium chloride guided with ultrasonography before termination. Autopsy after termination was offered to all cases.

SPSS version 23 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis of the data. The descriptive statistics were given as mean ± standard deviation, median (minimum–maximum) and number (percentage). Normal distributions of continuous variables were tested by Kolmogorov-Smirnov test. The numerical variables not conforming normal distribution were compared by Mann-Whitney U test. Categorical variables were compared by chi-square test or Fisher’s exact probability test between the groups. The statistical significance level was considered 0.05.

Results

While 263 (77.1%) of 341 cases, who were included in the study, underwent early gestational termination, 78
(22.9%) cases underwent late gestational termination. Mean maternal age of the cases was 31.1 years and mean week of gestation during termination was 18.6 weeks. There was no significant difference between the groups in terms of maternal age, gravida, parity and abortion (p>0.05). The demographic characteristics of the cases are given in Table 1.

The structural anomaly was observed in 273 (80.1%) of 341 cases, who were included in the study, in the ultrasonographic examination and no structural anomaly was observed in 68 (19.9%) cases. While the structural anomaly incidence was 76.8% in the early termination cases, the structural anomaly was found in 91% of the late termination cases ultrasonographically (p=0.006). Of 273 cases found to have structural anomaly in the ultrasonographic examination, 200 (73.3%) had isolated system anomaly and 73 (26.7%) had multiple system anomaly. Isolated system anomaly was found in 75.2% of the early termination cases and in 67.6% of the late termination cases (p=0.05). When the distribution of isolated anomalies was evaluated according to the systems, the incidence of isolated cardiovascular system anomaly was significantly higher in the late termination cases (37.5%) compared to the early termination cases (13.8%). The distribution of structural anomalies found in the cases according to the systems is shown in Table 2.

Karyotype analysis was performed in 232 (68%) of 341 cases. Chromosomal anomaly was found in 122 (52.6%) of the cases which underwent karyotype analysis. Twenty-two cases, of which 72.7% had thalassemia, had single gene disorder among 110 cases with normal karyotype analysis results. The karyotype analysis results of the cases are summarized in Table 3.

The autopsy was performed on 57 cases (16.7%) after termination. In 49 (86%) of these cases, autopsy findings were fully or partially consistent with the ultrasound findings while there were inconsistencies between the findings in 8 (14%) cases. The additional findings were found in 11 (22.4%) of the cases in which autopsy and prenatal findings were consistent.

**Discussion**

The congenital anomalies are the major reasons of infant deaths and 2% of the infants have congenital anomaly.[4] Ultrasonographic fetal anomaly screening has been a significant tool for the prenatal diagnosis of congenital anomalies, it has made possible to detect most of the congenital anomalies prenatally. While the sensitivity of routine ultrasonographic screening for major anomalies is 74%, it is 46% for minor anomalies.[7] The rate of detecting fetal anomaly by ultrasonography varies according to the number and structure of anomalies, and the affected organ system.[4,8,9] While the sensitivity of the ultrasonography has higher values with the rates of 83% in the major anomalies of central nervous system (CNS) and 85% in the major anomalies of urinary system, it is 38.8% in cardiovascular system (CVS) anomalies.[7] With the contribution of technological developments in the devices in addition to the prevalent use of ultrasonography and screening tests to determine the risk of chromosomal anomaly in all pregnant women at early weeks of gestation, it has become possible to examine fetal anatomy in more detail and the progress has been made for the early diagnosis of chromosomal anomalies.[10]

Considering the elevation in the complications at the end of each completed week of gestation and additional burden for maternal emotional state caused by the gestational termination, performing the termination as early weeks of gestation as possible is important for the maternal health.[11–13]

Vaknin et al. performed gestational termination on 462 cases (328 early gestational termination cases and 134 late gestational termination cases) and found that the

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**Table 1. The demographic characteristics of the cases.**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=263)</th>
<th>Group 2 (n=78)</th>
<th>Total (n=341)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>31.2±5.5</td>
<td>31.0±5.5</td>
<td>31.1±6.3</td>
<td>0.903</td>
</tr>
<tr>
<td>Gravida (n)</td>
<td>2 (1–8)</td>
<td>2 (1–7)</td>
<td>2 (1–8)</td>
<td>0.175</td>
</tr>
<tr>
<td>Parity (n)</td>
<td>1 (0–3)</td>
<td>1 (0–3)</td>
<td>1 (0–3)</td>
<td>0.306</td>
</tr>
<tr>
<td>Week of gestation at termination (week)</td>
<td>16.7±2.7</td>
<td>25.0±1.3</td>
<td>18.6±4.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The data are presented as mean ± SD and median (minimum–maximum).
The presence of fetal structural anomaly was significantly high in the late termination group (62% vs. 54%) and fetal chromosomal and genetic diseases were significantly high in the early termination group (40% vs. 29%).

In another study involving 144 late termination cases, the authors found fetal structural anomaly incidence 63% and reported it as the most common indication in the late termination group.\(^{14}\)

Similarly, we found structural anomaly ultrasonographically in 80.1% of 341 cases, which underwent term-
mination, and did not find any finding in 19.9% in our study. The cases without structural anomaly were mostly the patients which underwent aneuploidy screening tests or invasive diagnostic tests due to family history of genetic disease and underwent termination at early weeks of gestation and therefore did not have optimum ultrasonographic anomaly screening. In this context, when we compared early termination cases due to the presence of structural anomaly and late termination cases, we found that the structural anomaly incidence was significantly high in late termination cases which underwent optimum ultrasonographic anomaly screening (76.8% vs. 91%).

In the studies conducted in the same center, Çorbacıoğlu et al. found CNS anomaly as the most common anomaly (52%) in 498 termination cases and reported the incidence of the multiple system anomaly 10% while Aslan et al. found CNS as the most common anomaly with a rate of 58% and reported the incidence of the multiple system anomaly 8.4%. Moreover, Tayyar et al. also found CNS anomaly as the most common anomaly with a rate of 45% in the cases which underwent late termination, and they reported multiple system anomaly 8% in their study, which was conducted in the same center as well. In our study, isolated anomalies were 73.3% of the structural anomalies while multiple system anomalies were 26.7% of them. CNS anomaly (45%) was the most common isolated system anomaly while CVS anomaly (19.5%) was the other most common isolated anomaly. Considering the multiple system anomalies, CNS and CVS were the most common accompanying systems. The higher rates of multiple system anomalies in our study than the literature can be associated with the addition of the multiple anomalies encountered in the chromosomal anomalies into the date.

When we compare the early termination cases and the late termination cases in our cases, we see that CNS anomalies are the most common anomaly in both groups followed by CVS anomalies. However, we found that CVS anomaly rates were significantly higher in the late termination cases. In consistence with the literature, we may associate it with the fact that the ultrasonographic diagnosis of the cardiac anomalies is established in later weeks.

While Vaknin et al. reported the rates of chromosomal diseases in the cases which underwent termination 35% for the early terminations and 26% for the late terminations, Tayyar et al. reported it 19% for the late terminations. Çorbacıoğlu et al. compared the rates of chromosomal diseases in cases which underwent termination between 2002–2006 and 2007–2010, they found that the rates were significantly higher between 2007 and 2010 and associated it with the prevalent use of aneuploidy screening tests.

In our study, 68% of the cases underwent karyotype analysis, and we found chromosomal anomaly in 52.6% of the cases which underwent karyotype analysis, and 35.8% of 341 termination cases consisted of chromosomal diseases. The distribution of chromosomal anomalies we found in our study was consistent with the literature, and trisomy 21 was the most common anomaly. The majority of the cases with normal karyotype results consisted of single gene diseases associated with thalassemia in particular, and single gene diseases were responsible for 6.5% of all terminations. The ter-

### Table 3. The distribution of the genetic examination results of the cases.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chromosomal anomalies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>60</td>
<td>7</td>
<td>67 (54.9%)</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>14</td>
<td>3</td>
<td>17 (13.9%)</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>2</td>
<td>1</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>45,X</td>
<td>9</td>
<td>2</td>
<td>11 (9%)</td>
</tr>
<tr>
<td>Triploidy</td>
<td>4</td>
<td>1</td>
<td>5 (4.1%)</td>
</tr>
<tr>
<td>Other numerical chromosomal anomalies</td>
<td>5</td>
<td>4</td>
<td>9 (7.4%)</td>
</tr>
<tr>
<td>Structural chromosomal anomalies</td>
<td>5</td>
<td>5</td>
<td>10 (8.2%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>99</td>
<td>23</td>
<td>122 (100%)</td>
</tr>
</tbody>
</table>

| **Genetic diseases** |         |         |
|                      | Thalassemia and other single gene diseases | 19 | 3 | 22 |
mination rate associated with single gene diseases was the main termination rate in our study compared to the literature.[14,16] We believe that this difference originates from the fact that the patients included in the study live in the Mediterranean Region and thalassemia incidence is high in this region. We found that the chromosomal anomaly rate was higher in the early termination cases compared to the late termination cases in consistence with the literature (37.6% vs. 29.5);[14,17] however, the difference was not statistically significant. It seems that this difference depends on whether the cases underwent early gestational termination involve the terminations performed due to chromosomal anomaly as a result of aneuploidy screening tests and being able to accomplish this process at earlier weeks of gestation.

The autopsy rate of 341 cases included in our study is 16.7%, which is quite low. There is a significant reduction in the numbers of both adult autopsies and pediatric and fetal autopsies in 21st century in the literature.[21] While the increase of complicated methods is responsible for this reduction, the attitudes of clinical physicians and pathologists also have an impact. A reduction more than 50% in pediatric autopsies in our institution in the last 3 years is remarkable. While autopsy findings were fully or partially consistent with the ultrasound findings in our cases with a rate of 86%, the rate of inconsistency was 14%. Considering that there are also partial inconsistencies, the reduced number of autopsy for the detection of concurrent anomalies causes a serious data loss. Awareness on the importance of autopsy should be raised not only among the physicians but also the families. The increase of autopsy rates may help to obtain a significant amount of data which can change patient follow-up and management.

The low rates of autopsy after termination, low numbers of cases in the late termination group and also the retrospective design of the study are among the limitations of our study. The high karyotype analysis rates of the cases can be considered as the powerful aspect of our study.

**Conclusion**

The prenatal diagnosis of fetal anomalies can be established in the earlier weeks of gestation with a higher accuracy by the increase of the numbers of centers and personnel experienced in this field, making ultrasonographic anomaly screening and aneuploidy screening tests a routine practice in all pregnant women and also including advanced technology and new screening tests such as extracellular DNA into the program. In conclusion, early prenatal diagnosis and intervention would provide significant contributions in terms of maternal health.

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

**References**


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Evaluation of anxiety levels of pregnant women with gestational diabetes mellitus

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Abstract

Objective: The aim of this study was to investigate the anxiety levels of pregnant women with gestational diabetes mellitus (GDM) followed by different treatment methods.

Methods: Our study was carried out with 141 cases whose pregnancy follow ups were made in Gynecology and Obstetrics Clinic. Cases which had GDM screening with 75-g oral glucose tolerance test (OGTT) were divided into 3 groups. Group 1 (control group) consisted of 50 cases with 75-g OGTT results in normal range, Group 2 consisted of 50 cases which had significant 75-g OGTT results and followed up by diet (A1), and Group 3 consisted of 41 cases which were diagnosed with GDM as a result of 75-g OGTT and received diet as well as medical therapy (A2). Beck anxiety inventory (BAI) was administered to the patients in Group 1 in 24th week, and to patients in Groups 2 and 3 in the 24th and 32nd weeks.

Results: In the first evaluation of the patients, BAI scores of the control group were statistically found to be significantly lower than the patients with GDM (p=0.001). There was no significant difference in BAI scores among patients diagnosed with GDM, and high anxiety scores were found in both groups. There was a significant decrease in anxiety levels in the Groups 2 and 3 after the treatment (p=0.01). In the Group 2, the BAI scores were observed to decrease from 51.76±4.47 to 45.62±3.65, and from 51.73±5.27 to 41.48±3.29 in the Group 3 (p<0.001).

Conclusion: In addition to the metabolic disorders brought by the disease itself, GDM can cause various problems by increasing the levels of anxiety in patients. With an effective treatment for glycemic control, anxiety levels of patients can be reduced.

Keywords: Anxiety, gestational diabetes mellitus, Beck anxiety inventory.

Özet: Gestasyonel diabetes mellituslu gebelerde anksiyete seviyelerinin değerlendirilmesi

Amaç: Bu çalışmanın amacı, farklı tedavi yöntemleri sonrasında gestasyonel diabetes mellitus (GDM) gebelerde anksiyete seviyelerini araştırarak, anksiyete seviyelerinin tedavi sonrasıda azalmasını belirlemektir.

Yöntem: Çalışmamız, Kadın Hastalıkları ve Doğum Kliniğinde gebelik takipleri yapılan 141 olgu ile gerçekleştirilmiştir. 75 g oral glikoz tolerans testi (OGTT) ile GDM taraması yapılan olguların 3 grubu oluşturuldu. Grup 1 (kontrol grubu) 75 g OGTT bulguları normal aralığındaki 50 olgudan, Grup 2 anlamlı 75 g OGTT bulguları olan ve diyet uygulayan 50 olgudan (A1) ve Grup 3 ise 75 g OGTT sonucunda GDM tanısı alan ve tıbbi tedavinin yanı sıra diyet uygulayan 41 olgudan (A2) oluşmaktadır. Beck anksiyete ölçeği (BAÖ) Grup 1’deki olgulara 24. haftada, Grup 2 ve 3’teki olgulara ise sırasıyla 24. ve 32. haftalarda uygulanmıştır.

Bulgular: Hastaların ilk değerlendirme tarihlerinde, kontrol grubunun BAÖ puanları istatistiksel olarak anlamalı şekilde GDM’li olgulardan daha düşük bulunmuştur (p<0.001). GDM tanısı alan hastalar arasında BAÖ puanlarının yönünden anlamlı bir fark yoktu ve her iki grupta yüksek anksiyete puanları bulundu. Tedavi sonrasında Grup 2 ve 3’te anksiyete seviyelerinde anlamlı bir düşüş gözlenmişti (p<0.01). Grup 2 ve 3’te BAÖ puanlarının sırasıyla 51.76±4.47’den 45.62±3.65’e ve 51.73±5.27’den 41.48±3.29’a düştü (p<0.01).

Sonuç: Hasılağın kendisinin sebep olduğu metabolic bozuklukları ve GDM’nin hastaların anksiyete seviyelerinin arttırmış olduğu görülüyor. Glikemik kontrol için erken bir tedavi ile hastaların anksiyete seviyeleri azaltılabilir.

Anahtar sözcükler: Anksiyete, gestasyonel diabetes mellitus, Beck anksiyete ölçeği.
Introduction

Gestational diabetes mellitus (GDM) is one of the most important metabolic diseases of pregnancy.[1] The incidence of GDM in our country varies between 6.9–8.9%.[2] GDM is very important because it has negative effects on the fetus as well as negative maternal effects and may also cause complications in postpartum period.[1] In this period, depression and anxiety disorders can be triggered due to the medical problems caused by the disease as well as the increasing anxiety of the mother about her baby.[3]

Along with changes in social relationships and roles within the family, pregnancy also leads to changes in body image.[4] In addition to hormonal changes, changes of roles in social life also cause anxiety in pregnancy and other procedures in gynecology.[1–7] Unhappiness, pessimism, fatigue, malaise and sleep disorders experienced by pregnant individuals are generally seen as the nature of pregnancy, and can often be overlooked.[8–10] In studies performed, it has been reported that antenatal depression rates are between 9.9–45% and anxiety rates are around 6.6–75%.[11,12] There are many studies showing that anxiety and depression lead to complications such as premature birth, low birth weight, and nutrition disorders during pregnancy.[11,14]

In our study, we aimed to examine the anxiety states of pregnant women who had GDM and were managed with different treatment methods.

Methods

Our study was carried out with 141 cases whose pregnancy follow-ups were made in Gynecology and Obstetrics Clinic. Ethical approval for the study was obtained from the Ethics Committee, Kuru Ankara Hospital (Ethics Committee protocol code: 13/11/2018-17). GDM screening was performed in one step with 75-g OGTT. For 75-g OGTT, it was based on recommendation values (pre-prandial blood glucose: 92 mg/dl, postprandial 1st hour: 180 mg/dl, postprandial 2nd hour: 153 mg/dl) of the International Association of Diabetes and Pregnancy Study Groups (IADPSG). A single high value was considered diagnostic for GDM.[15] All cases were divided into 3 groups. Group 1 (control group) with 75-g OGTT results in normal range consisted of 50 cases. Group 2 also consisted of 50 cases which had significant 75-g OGTT results, namely diagnosed as GDM, and followed up by diet without any medical treatment (A1). Group 3 consisted of 41 cases which were diagnosed with GDM as a result of 75-g OGTT and received diet as well as medical therapy (insulin treatment) (A2). All patients with GDM were followed up with a multidisciplinary approach by consulting the Endocrine and Metabolic Diseases and Psychiatry Polyclinics.

Data collection tools

The patient polyclinic anamnesis information screen where socio-demographic data was recorded was used as the primary measurement instrument. Age, gravida and parity numbers, educational status, employment status and body mass index (BMI) of the patients were recorded in the socio-demographic data form. Beck anxiety inventory was used as a secondary measurement instrument. These forms were filled out during antenatal pregnancy follow-up in the specified week.

Beck anxiety inventory (BAI), which was developed by Beck et al. in 1988, is being used to determine the frequency of anxiety symptoms.[16] The scale is composed of 21 items, it is four Likert type and each item is evaluated with a score of 0–3. The Turkish validity and reliability study of the scale was conducted by Ulusoy et al. in 1998.[17] The highest score obtainable in the scale is 63. Being high of the overall score indicates a high level of anxiety or severity.

Application of research

The 1st questionnaire study for all 3 groups was performed on a pregnancy visit immediately after the 75-g OGTT was concluded. No recurrent questionnaire evaluation was performed for the Group 1. The patients with GDM in the Groups 2 and 3 were also evaluated by the psychiatrist and taken under follow-up. The 2nd questionnaires applied for all pregnant women in the Groups 2 and 3, whose follow-up and treatment regimens were planned by the endocrine and metabolic diseases specialist, were performed about at 8th week (about 32nd week of gestation) following the GDM diagnosis. In all the cases with GDM in the Groups 2 and 3 included in the study, glycemic follow-ups were normal and no additional fetal or maternal problems were observed during application of the 2nd questionnaire.

Inclusion and exclusion criteria in research

Patients who were diagnosed with GDM as a result of OGTT and had no exclusion criteria were included in the study. Patients in low risk group (being of normal
weight before pregnancy, age <25, no known DM in first degree relatives, nonexistence of bad obstetric history) and without OGTT, who had a psychiatric disease history in their anamnesis, who had other stressors such as fetal (oligohydramnios, polyhydramnios, growth retardation, macrosomia, affected rh incompatibility, etc.) or maternal (myoma, premature birth history, smoking, history of late abortion or fetal loss, recurrent pregnancy loss history, blood pressure, pregestational DM, etc.) which could cause anxiety during pregnancy follow-ups were excluded from 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. It was observed that none of the data groups except age was distributed normally. Because there were more than two independent groups and they did not fit the normal distribution, the difference between the groups was investigated by Kruskal-Wallis H test. One-way ANOVA test was used to evaluate the age group since it distributed normally. In cases where the difference was significant, pair wise comparisons after Bonferroni correction for multiple tests were obtained. Wilcoxon test was used to compare anxiety scores at 24th and 32nd weeks. Descriptive statistics were used to calculate the frequency, mean, median, mode and dispersion (range, variance, SD, maximum, minimum) for each variable when appropriate. Mann-Whitney U test was used to evaluate the BAI results between the groups. A p<0.05 value was accepted as significant statistically.

Results
Of the 141 patients included in the study, 50 were women diagnosed without GDM and 91 with GDM. The sociodemographic data of the patients was shown in Table 1. Comparing maternal age-pregnancy and birth number, body mass indexes and educational status, there was no statistically significant difference between the groups (p>0.05).

In the first evaluation of the patients, BAI scores in the control group (Group 1) were found to be significantly lower than those of patients with GDM (Kruskal-Wallis test p<0.001). This difference was observed to be between the Groups 1 and 2 (MWU test p=0.001) and between the Groups 2 and 3 (MWU test p=0.001). There was no significant difference in BAI scores among patients diagnosed with GDM (Group 2 and Group 3), and high anxiety scores were found in both groups (MWU test p=0.997). The group with the diagnosis of GDM, the group whose blood glucose was regulated by diet (Group 2), and also the group with insulin regula-

<table>
<thead>
<tr>
<th>Table 1. Demographic characteristics of the groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group GDM A1 GDM A2 p-value</td>
</tr>
<tr>
<td>(n=50) (n=50) (n=41)</td>
</tr>
<tr>
<td>Age (mean±SD deviation)</td>
</tr>
<tr>
<td>Gravida (median, min–max)</td>
</tr>
<tr>
<td>Parity (median, min–max)</td>
</tr>
<tr>
<td>BMI (mean±SD deviation)</td>
</tr>
<tr>
<td>OGGT week (mean±SD deviation)</td>
</tr>
<tr>
<td>Employment status of the mother in pregnancy n (%)</td>
</tr>
<tr>
<td>Working</td>
</tr>
<tr>
<td>Not working</td>
</tr>
<tr>
<td>Educational status</td>
</tr>
<tr>
<td>Primary school n (%)</td>
</tr>
<tr>
<td>Middle school n (%)</td>
</tr>
<tr>
<td>High school n (%)</td>
</tr>
<tr>
<td>University n (%)</td>
</tr>
<tr>
<td>Week of the first survey</td>
</tr>
<tr>
<td>Week of the second survey</td>
</tr>
</tbody>
</table>

SD: standard deviation. *One-way test; †Kruskal-Wallis test.
tion (Group 3) showed a significant decrease in anxiety levels after treatment. Comparing the 24th and 32nd weeks, it was seen that BAI scores in the group followed by the diet (Group 2) were decreased from 51.76±4.47 to 45.62±3.65; in the group followed by diet and insulin treatment (Group 3) from 51.43±5.29 to 41.48±3.29, and that the difference was statistically significant (Wilcoxon test p=0.001). Details of anxiety levels of patients are shown in Table 2.

Discussion

GDM is a situation which is increasing in frequency all over the world and has a significant effect on maternal and fetal health.[18] In addition to GDM, situations such as treatment originated problems, possible complications, future anxiety, anxiety of being dependent on others may cause problems on the cognitive and social life of pregnant women.[19] In addition to the concerns about the fetus in pregnant individuals, the increase of concerns about the development of the fetus and possible problems may have led to an increase in the anxiety levels of patients.[20] This explains the difference in anxiety levels between mothers with GDM and without GDM. The aim of this study was to investigate the anxiety levels of pregnant women diagnosed with GDM and to evaluate the effect of treatment method on anxiety levels.

In our study, when the socio-demographic data of the pregnant women who were diagnosed with GDM were compared to individuals without GDM, it was observed that there was no statistically significant difference between two groups. In the study of Lao et al., increased maternal age is reported to be a risk factor for GDM.[21] While the prevalence of GDM is reported to be between 0.4–0.8% in individuals below 25 years of age, this rate is reported as 4.3–5.5% in the group above 25 years of age.[21] All the pregnant women included in our study were found to be in the group with risk of GDM due to age.

In many studies performed, it was reported that GDM may cause antenatal depression and anxiety.[9,20,22–25] In the study of Daniells et al., although anxiety and depression levels were found to be high in individuals with GDM at the time of diagnosis, it was reported that this difference lost its significance in follow-ups and that there was no difference in anxiety levels between those with GDM and without GDM.[20] Also in our study, anxiety levels of patients in Group 2 and Group 3 decreased with time. However, the control group (Group 1) did not have the anxiety scale again. This is a restriction of our study. In a study by Ferrari et al., it was found that 13% of patients with GDM had moderate-severe depressive symptoms, and that body mass index, blood pressure and visceral fat volume were higher in this group.[24] In a study performed by Orbay et al. in our country with 281 pregnant women, anxiety scores were reported to be higher in individuals with GDM.[26] However, in this study, Hospital anxiety and depression (HAD) scale was used, and patients diagnosed with GDM were not divided into groups. In our study, the exclusion of individuals with known psychiatric diseases from the study provided the identification of mild-moderate anxiety symptoms in patients with the help of a scale based on their own reports.

The pregnancy itself is a period in which the mother experienced many physical and mental changes and may have been very anxious for both herself and her baby.[27] In the study performed by Felice et al., the incidence of psychiatric disorders in pregnancy was found to be about 19.2%, and 14.8% of this were found to be the pregnancy anxiety and depression.[28] The pregnancy anxiety and depression were associated with low birth weight, premature birth and infant nutrition problems.[27,29] In our study, patients with high anxiety scores were followed up multidisciplinary in the antenatal period, but the postnatal results were not evaluated. This is another restriction of our study.

Table 2. Evaluation of anxiety levels of the groups.

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=50)</th>
<th>GDM A1 (n=50)</th>
<th>GDM A2 (n=41)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 weeks</td>
<td>38.72±4.76</td>
<td>51.76±4.47</td>
<td>51.73±5.27</td>
<td>0.001*</td>
</tr>
<tr>
<td>32 weeks</td>
<td>-</td>
<td>45.62±3.65</td>
<td>41.48±3.29</td>
<td>0.001†</td>
</tr>
</tbody>
</table>

*One-way test; †Kruskal-Wallis test.
In our study, a multidisciplinary treatment approach was applied to mothers diagnosed with GDM by having been directed to endocrine and metabolic diseases and psychiatry polyclinics. The patients were informed about diabetes and some of them were followed up with only diet and some others with diet+insulin treatment. The patients were evaluated by psychiatrist and followed up with psychoeducation as well as supportive interviews. In spite of the high anxiety scores of the patients, having no significant deterioration in their functionalities allowed them to be followed up without medical treatment. It was found that there was a significant decrease in anxiety levels because of improvement provided in blood glucose levels in the process (Table 2, p<0.01). Regardless of the treatment method, besides providing the blood glucose regulation of the patients, psychoeducation and supportive interviews are thought to contribute to the decrease in anxiety levels of patients. In a study investigating stress coping methods in pregnant women with GDM, it was found that HbA1c levels were lower in those who exhibited more optimistic and positive views. In spite of the high anxiety scores of the patients, no difference was found between the groups. 

Conclusion
In this study, we only evaluated anxiety levels of the patients. A measurement method was not used to assess depressive symptoms. The relationship between the clinical variables and the anxiety levels of the patients was not examined, and this is among the important restrictions. In this area, prospective studies with longer follow-up of patients are needed.

Conflicts of Interest: No conflicts declared.

References


Investigating the factors affecting postpartum diabetes screening in the patients with gestational diabetes mellitus: a reference tertiary center experience

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Abstract

Objective: The pregnant women with gestational diabetes mellitus (GDM) are under the risk of developing type 2 diabetes mellitus and cardiovascular disease after labor. The postpartum diabetes screening has a key role to establish the diagnosis of type 2 diabetes and to start necessary treatment at an earlier period. For that purpose, we aimed to investigate the rates of postpartum diabetes screening and the factors affecting these rates in the pregnant women with GDM diagnosis at Kayseri City Hospital which is a reference center.

Methods: This study was conducted retrospectively in a tertiary center by investigating pregnant women between 18 and 45 years old whose pregnancy follow-ups were done between June 2018 and January 2020. A total of 2652 pregnant women were screened for GDM by 75-g oral glucose tolerance test (OGTT) during routine clinical follow-up and GDM was found in 425 (16%) of these pregnant women. Of these 425 pregnant women, 225 who continued their postpartum follow-ups and whose contact information was accessed were included in the study. The patients were separated into two groups according to their preference of undergoing postpartum diabetes screening. The demographic characteristics, follow-up numbers and gestational complications of the groups were compared statistically.

Results: We found that only 34.6% (78/225) of the patients included in the study underwent postpartum diabetes screening and 147 (65.4%) of them did not prefer to undergo postpartum screening. There was no difference between the groups in terms of maternal demographic characteristics. It was found that the patients underwent more postpartum diabetes screening tests in a statistically significant way in cases of the need for antenatal insulin treatment, antenatal visit being more than 10 and the presence of antenatal complication (p=0.001, p=0.001, p=0.001, respectively) which are among the gestational characteristics.

Conclusion: We found that only 34.6% (78/225) of the pregnant women with GDM diagnosis underwent postpartum diabetes screening, and the need for antepartum insulin treatment, antenatal visit number being more than 10 and the presence of antenatal complications were the important factors affecting screening rates. The patients with GDM should be informed again about the importance of undergoing postpartum diabetes particularly near the labor period and during discharge after labor and the type 2 diabetes risk should be explained in detail after labor.

Keywords: Gestational diabetes, diabetes screening, postpartum.
Introduction

Gestational diabetes mellitus (GDM) is the glucose intolerance starting at the second and third trimesters of the pregnancy and it is one of the most common poor outcomes of pregnancy.\(^1\) GDM incidence has been increasing globally as a result of the increase of obesity and maternal age, and it causes a great economic burden on the public healthcare system.\(^1–3\) The perinatal complications associated with GDM include cesarean section, shoulder dystocia, preterm labor, macrosomia, birth trauma, stillbirth and neonatal hypoglycemia.\(^4\) In addition, the women with GDM are under the risk of developing type 2 diabetes mellitus and cardiovascular disease after labor.\(^5\) The GDM prevalence varies between 1.2% and 27.9% in various studies conducted in Turkey regionally.\(^6\) Type 2 diabetes may be found in about half of these patients diagnosed with GDM many years after pregnancy.\(^7\) The study bulletins of American Diabetes Association (ADA) and American College of Obstetricians and Gynecologists (ACOG) recommend type 2 diabetes screening via preprandial plasma glucose or 2-hour oral glucose tolerance test (OGGT) at postpartum 4–12 weeks after GDM diagnosis.\(^8,9\) The diabetes screening at postpartum period has a key role to establish early diagnosis of type 2 diabetes and to start necessary treatment at an earlier period. The association of undiagnosed and untreated diabetes with microvascular and macrovascular complication risk was reported.\(^10\) It was reported in the literature that there is lack of information for postpartum screening in the pregnant women with GDM in addition to the lack of time and motivation and that additional support is needed to reach these goals.\(^11,12\) The programs supporting lifestyle changes after GDM may decrease the development risk of type 2 diabetes later.\(^13\) In the light of these information, we aimed to investigate the rates of postpartum diabetes screening and the factors affecting these rates in the pregnant women who were diagnosed with GDM at Kayseri City Hospital which is a reference center.

Methods

This study was conducted retrospectively to evaluate the pregnant women between 18 and 45 years old whose pregnancy follow-ups were carried out at the Obstetrics and Gynecology Clinic of Kayseri City Hospital between June 2018 and January 2020. All stages of the study were conducted in accordance with the Declaration of Helsinki, and its ethical approval was obtained from the Ethics Committee of Erciyes University. A total of 2652 pregnant women were screened for GDM by 75-g OGTT during routine clinical follow-up and GDM was found in 425 (16%) of these pregnant women. In accordance with the routine approach of our clinic, all pregnant women with GDM are discharged by recommending type 2 diabetes screening via preprandial plasma glucose or 2-hour OGTT at postpartum 4–12 weeks. Of these 425 pregnant women, 225 who continued their postpartum follow-ups at Kayseri City Hospital and whose contact information was accessed were included in the study. The patients were separated into two groups according to their preference of undergoing postpartum diabetes screening. The flow chart of the patients is shown in Fig. 1.

The patients who were diagnosed with type 1 and type 2 diabetes previously, those with the history of endocrine diseases affecting carbohydrate metabolism (Cushing disease, Addison’s disease, hypopituitarism, acromegalia, etc.) or the patients using drugs that may affect their blood sugar levels (steroids, etc.) were excluded from the study. The last menstrual date was used to
determine the weeks of gestation of the patients. The gestational ages of those with unknown last menstrual date were calculated according to the ultrasonographic measurements. The patients were screened by one-step 75-g OGTT, and the criteria of IADPSG (The International Association of Diabetes and Pregnancy Study Groups) were used for the diagnosis. The Guidelines of Turkish Perinatal Society recommends 75-g OGTT for each pregnant woman and those consent the test as we have a risky ethnic group. After 12-hour fasting, plasma glucose of the patients were measured, and then 75g glucose was administered orally. The venous blood samples were collected one and two hours later. The upper limits of fasting state and first and second hours plasma glucose values following glucose intake were 91, 179 and 152 mg/dL, respectively. Any value above the threshold values was considered as positive test. GDM prevalence was determined according to the results of this one-step screening test. Chronic hypertension, gestational hypertension, preeclampsia, fetal growth restriction, macrosomia and polyhydramnios were defined as poor perinatal outcomes.

The data were analyzed by using Minitab 16 (Minitab Inc., State College, PA, USA) to compare the groups. Shapiro-Wilk test was used to determine the normality of data and to compare two groups. The assumption of homogeneity of variance was tested by Levene’s test. The values were presented as mean ± standard deviation and n (%). Parametric comparisons were done by Student-t test and non-parametric comparisons were done by Mann-Whitney U test. Percentage and n values were analyzed by using Pearson’s chi-squared test. When the difference between the groups was p<0.05, it was considered statistically significant.

### Results

A total of 225 pregnant women were evaluated in the study. Of these cases, 78 (34.6%) were included in the group referring for postpartum diabetes screening and 147 (65.4%) were included in the group not preferring postpartum diabetes screening. The maternal demographic characteristics of two groups are shown in Table 1. The groups were similar when they were compared for the mean maternal age (p=0.126), body mass index >30 kg/m2 values (p=0.885), ethnicity (p=0.835), parity (p=0.436), previous cesarean delivery (p=0.822) and the rates of family history of diabetes (p=0.877). The gestational characteristics of the groups were compared in Table 2, and it was found that the patients underwent more postpartum diabetes screening tests in a statistically significant way in cases of the need for antenatal insulin treatment.

### Table 1. The comparison of the maternal demographic characteristics between the groups.

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>The group undergoing postpartum diabetes screening (n=78)</th>
<th>The group not undergoing postpartum diabetes screening (n=147)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (year)</td>
<td>32.35±2.66</td>
<td>32.95±2.85</td>
<td>0.126</td>
</tr>
<tr>
<td>BMI&gt;30 kg/m²</td>
<td>20 (25.6%)</td>
<td>39 (26.5%)</td>
<td>0.885</td>
</tr>
<tr>
<td>Ethnicity (Caucasian)</td>
<td>71 (91.0%)</td>
<td>135 (91.8%)</td>
<td>0.835</td>
</tr>
<tr>
<td>Parity</td>
<td>3 (2–5)</td>
<td>3 (2–5)</td>
<td>0.436</td>
</tr>
<tr>
<td>Previous cesarean delivery</td>
<td>18 (23.0%)</td>
<td>32 (21.7%)</td>
<td>0.822</td>
</tr>
<tr>
<td>Family history of diabetes</td>
<td>21 (26.9%)</td>
<td>41 (27.8%)</td>
<td>0.877</td>
</tr>
</tbody>
</table>

The values are presented as median (min–max), mean ± standard deviation, and n (%). BMI: body mass index.

### Table 2. The comparison of the gestational characteristics between the groups.

<table>
<thead>
<tr>
<th>Gestational characteristics</th>
<th>The group undergoing postpartum diabetes screening (n=78)</th>
<th>The group not undergoing postpartum diabetes screening (n=147)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for antenatal insulin treatment</td>
<td>23 (29.4%)</td>
<td>26 (17.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antenatal visit number &gt;10</td>
<td>69 (88.4%)</td>
<td>115 (78.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of antenatal complications*</td>
<td>26 (33.3%)</td>
<td>30 (20.4%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Chronic hypertension, gestational hypertension, preeclampsia, fetal growth restriction, macrosomia and polyhydramnios. The values are presented as n (%).
insulin treatment, antenatal visit number being >10 and the presence of antenatal complication (p<0.001, p<0.001, and p<0.001, respectively). The labor characteristics of the patients are presented in Table 3, and it was found that the week of gestation during labor (p=0.952), need for labor induction (p=0.850), spontaneous vaginal delivery rates (p=0.784), fetal weight (p=0.920) and fetal male sex rates (p=0.740) were similar when the groups were compared.

Discussion

Postpartum OGTT is an important approach in the management of the pregnant women diagnosed with GDM, and it is known that the likelihood of developing type 2 diabetes is seven times higher in women with GDM history than the women without GDM history throughout their lives. These women are also under the risk of early diabetes in their next pregnancies. Ekelund et al. reported in their study that 51% of the patients with GDM have impaired glucose tolerance and 30% of them develop type 2 diabetes within 5 years. Many clinical studies showed that it is possible to decrease or delay diabetes incidence among women with high disease risk with the help of diet and exercise or a pharmacological agent during postpartum period.

Considering the results of our study, we did not find any correlation between postpartum diabetes screening and maternal age, body mass index, ethnicity, parity, previous cesarean delivery and the presence of family history of diabetes. In addition, there was no correlation between postpartum diabetes screening and the week of gestation during delivery, labor induction, spontaneous vaginal delivery rates, fetal weight and fetal sex. We found that the patients underwent more postpartum diabetes screening tests in cases of the need for antenatal insulin, antenatal visit number being more than 10 and the presence of antenatal complication. We found out that only 34.6% (78/225) of the pregnant women underwent postpartum diabetes screening. Werner et al. evaluated 300 patients diagnosed with GDM in their prospective study, and they reported that 42% of the pregnant women underwent postpartum diabetes screening, and educational status, income level, mothers having a job and the use of insulin during pregnancy were the factors affecting the screening. Similar to our results, the authors did not find any correlation between postpartum diabetes screening and maternal age, parity, ethnicity, family history of diabetes, delivery type, delivery characteristics and fetal outcomes. In another study investigating postpartum diabetes screening, Korkmazer et al. evaluated 738 pregnant women with GDM and reported that only 30.7% of the pregnant women completed postpartum diabetes screening. They also showed that 65.9% of the patients did not know screening test, and 19.1% of them did not apply for the test due to financial difficulties and 7.8% of them due to family problems. Bennett et al. reported that only 6–11% of the pregnant women underwent postpartum diabetes screening within the first 3 months after labor and 15–21% of them underwent the screening test within the 1 year after labor. It was reported in the USA that less than 20% of women with GDM underwent diabetes screening by OGTT within the first 6 months after labor.

The following question comes to mind considering the current screening rates: Why do not these patients come back for diabetes screening test after labor? Traditionally, pregnant women concern about potential fetal complications in the presence of GDM and they do not skip their antenatal follow-ups; however, the disappearance of these concerns after labor cause failures in

<table>
<thead>
<tr>
<th>Labor characteristics</th>
<th>The group undergoing postpartum diabetes screening (n=78)</th>
<th>The group not undergoing postpartum diabetes screening (n=147)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week of gestation during labor (week)</td>
<td>38 (37–39)</td>
<td>38 (37–39)</td>
<td>0.952</td>
</tr>
<tr>
<td>Labor induction</td>
<td>45 (57.6%)</td>
<td>80 (54.4%)</td>
<td>0.850</td>
</tr>
<tr>
<td>Spontaneous vaginal delivery</td>
<td>36 (46.1%)</td>
<td>65 (44.2%)</td>
<td>0.784</td>
</tr>
<tr>
<td>Fetal weight at birth (g)</td>
<td>3350 ± 170</td>
<td>3300 ± 150</td>
<td>0.920</td>
</tr>
<tr>
<td>Fetal male sex</td>
<td>42 (53.8%)</td>
<td>83 (56.4%)</td>
<td>0.740</td>
</tr>
</tbody>
</table>

The values are presented as median (min–max), mean ± standard deviation, and n (%).
postpartum follow-ups. It is reported that the most of women with GDM perceived themselves as healthy and did not need to undergo the test or were afraid of the diagnosis and therefore avoided the screening.\[22,25,26\] In addition, there are studies reporting that the training of pregnant women diagnosed with GDM during the postpartum period may be insufficient considering the restrictions of intense clinic practices.\[22,27\]

The number of studies aiming to develop postpartum diabetes screening increases gradually. In their study, Hunt et al. explained the necessity of postpartum OGTT to the patients by contacting them at least three times during postpartum period via a managing nurse who provides postpartum training and follows up the patients in a population with the postpartum diabetes screening rate of 18%. All patients interacted with this case manager nurse at least three times during pregnancy and right after labor, and the laboratory needs for postpartum OGTT were met. The case manager nurse contacted the patients who did not visit for OGTT once more and conducted the OGTT test at home when necessary. Yet, 400 (57%) of 707 women come back for postpartum visit, but 288 (41%) of them did not complete OGTT.\[29\] Similarly, Stasenko et al. retrospectively investigated the impact of educational intervention on the postpartum diabetes screening in the women with GDM. In this study conducted with the diabetes trainer, postpartum patients received consultancy for 3 months, and the authors reported that the rate of undergoing postpartum preprandial plasma glucose or OGTT increased from 33.4% to 52.7%.\[30\] In 2014, Mendez-Figueroa et al. defined a program for the postpartum period in order to define the patients with GDM and arrange test appointments, follow up the completion of the test, provide reminders for participation and reschedule the missed appointments with the help of a special nurse or social support official working with the patients directly. When the authors compared the postpartum diabetes screening rates before and after the program, they found that the screening rates increased from 43.1% (78/181) to 59.4% (123/217).\[30\]

**Conclusion**

Considering the results of our study, we found that only 34.6% (78/225) of the pregnant women underwent postpartum diabetes screening, and the need for antepartum insulin treatment, antenatal visit number being more than 10 and the presence of antenatal complications were the important factors affecting screening rates. The patients with GDM should be informed about the importance of undergoing postpartum diabetes particularly near the labor period and during discharge after labor and the type 2 diabetes risk should be explained in detail after labor.

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

**References**


Does mobile phone use of women during pregnancy cause hearing problems in infants? Preliminary observation

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Introduction

In recent years, exposure to radiofrequency radiation (RFR) emitted from wireless devices such as mobile phones, game consoles, internet service providers, etc., has significantly increased due to the widespread usage these devices. Various studies regarding this topic have reported that exposure to RFR could influence neurodevelopment, the blood-brain barrier, demyelination, and hearing. However, the impact of this radiation on the developing fetus is less understood.

Abstract

Objective: Some studies have claimed that long-term conversation with mobile phones can cause hearing loss. However, it has not been investigated whether exposure to mobile phones during pregnancy affects the hearing of babies in the womb. Therefore, the aim of this human study was to investigate the effects of intrauterine radiofrequency radiation (RFR) exposure emitted from mobile phones on the hearing of newborns.

Methods: The study population comprised 149 newborns. Pregnant women in this study were divided into 4 groups according to RFR exposure duration, such as non-exposure to RFR, exposure to RFR for 2–15 min/day, exposure to RFR for 15–60 min/day, and exposure to RFR for more than 60 min/day. The results of the hearing screening analyses of the newborns, which were performed using transiently evoked otoacoustic emission and automated auditory brainstem response, were investigated retrospectively.

Results: The results of this study indicated that 900 and 1800 MHz RFR exposure during pregnancy did not cause hearing loss in newborns.

Conclusion: In conclusion, we observed that the hearing sensitivity and peripheral sound perception of newborns were not affected by RFR exposure emitted from mobile phones during the intrauterine period. Further studies should be performed to illuminate the subject.

Keywords: Radio frequency radiation, mobile phone, pregnant women, infant, hearing loss.
tion, neurotransmitter release, lead to alterations in the regulation of the cell cycle, and change intracellular and some molecular pathways, and cause alterations in the central nervous system.\cite{5}

The most important groups in terms of health problems that electromagnetic field (EMF) exposure can affect are pregnant women and children. In a workshop organized by the World Health Organization in Istanbul, Turkey, in 2004, the sensitivity of children to EMFs was discussed and it was emphasized that studies on this subject should be increased.\cite{2}

The studies have shown that RFR may disrupt the structure of biomolecules, such as proteins, lipids, and DNA,\cite{3–6} change gene expression\cite{7} and result in oxidative stress during the early pregnancy period. The amount of RFR absorbed by the body has shown alterations during the gestation period due to changes in the amount of water in the body.\cite{8} The nervous system of a baby forms rapidly during the prenatal period and the brain tissues have high conductivity owing to their high water content.\cite{9} Maskey et al.\cite{10} reported that the auditory brainstem region is sensitive to chronic exposure to RFR [835 MHz, 4.0 W/kg specific absorption rate (SAR)], which may influence the function of the central auditory system. Moreover, the results of ABR tests on rats exposed to RFR also displayed a significant threshold elevation that might have originated from auditory dysfunction.\cite{10}

Hearing loss, which is loss of the sense of auditory partially or completely, originates from some defects in the outer or middle ear. These defects may slow the transfer of sound waves and even prevent them from transferring. Another type of the hearing loss originates from damage to hair cells in the inner ear. Damage in the auditory nerve itself or in the brain pathways may cause central hearing loss. The incidence of hearing loss in live birth newborns in was reported as 1–6/1000 babies, and this rate increased up to 10/1000 in newborns in risk groups.\cite{11} About 50%–60% of congenital hearing loss are hereditary. It was reported that 40%–50% of congenital hearing losses arise from disorders, such as intrauterine infections, hypoxia, hyperbilirubinemia, prematurity, low birth weight, ototoxic drug usage, hypothyroidism, sepsis, meningitis, and persistent pulmonary hypertension.\cite{12} These risk factors adversely affect cochlea.

Transient evoked otoacoustic emissions (TEOAE) and auditory brainstem response (ABR) tests are analyses that are used to detect hearing loss in infants during the early period. These tests are non-invasive and they ensure objective and physiological measurements.\cite{13} Eighth nerve and auditory brain stem dysfunction cannot be detected by the TEOAE test. Despite hearing loss, a normal TEOAE response may be received in these types of pathologies. Therefore, TEOAE is not an adequate screening test for infants with neurological hearing loss risk factors. ABR has been used for many years as an electrophysiological measurement that evaluates the hearing function in the section from the 8th nerve to the brainstem. In the ABR test, the electrical responses of the brainstem auditory way and auditory nerve are evaluated against click stimulus given by electrodes placed on the forehead, mastoid, and neck of the patient. Nowadays, the TEOAE and ABR tests are generally used together in newborn clinics for hearing loss screening. If the newborn does not pass the TEOAE test at least twice, the ABR test needs to be applied 3 months afterwards. However, if one or more of the hearing loss risk factors are present in the newborn, it is appropriate to perform the ABR test without waiting.

Studies carried out on the effects of RFR emitted from mobile phones on the auditory systems of fetuses and newborns are very limited. Investigations regarding this issue, the majority of which were carried out on animals, have had differences in terms of parameters, such as experimental setups, techniques, and SARs. These differences in the experimental setups and inconsistencies in the results of the studies have led to contradictions.

Some of previous studies have shown that RFR can cause hearing loss in both humans and animals.\cite{1,10,14–22} The aim of the current study was to reveal whether the auditory system development of babies in the womb was affected by the mobile phone usage of their mothers during pregnancy. The mobile phones used by pregnant women in this study consisted of smart phones (SAR values were between 0.57–0.65 W/kg). 3G technology was used in Turkey at the time of this study. Digitally enhanced cordless telecommunication was not used by the pregnant women. The results of the TEOAE and ABR tests carried out on infants who met the acceptance criteria, which had previously been determined for this study, were used.
Methods
The study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the Ethics Committee of the Medical Faculty, Van Yüzüncü Yıl University (Report No: 2019/14-04). Primarily, the pregnant women accepted into the study were identified by excluding women who had received any medical treatment, had a chronic systemic disease, multiple pregnancies, hearing loss in their families, and consanguineous marriage. The study comprised 149 volunteer pregnant women aged between 18 and 40 years. All of the pregnant women gave their signed informed consent prior to beginning the study. The pregnant women were divided into 4 groups depending on the daily usage time of their mobile phones. Control Group: Non-mobile phone users during pregnancy (n=37), Group 1: Mobile phone users for 2–15 min per day (n=39), Group 2: Mobile phone users for 15–60 min per day (n=37), Group 3: Mobile phone users for more than 60 min per day (n=36). Daily mobile phone usage times of the pregnant women were confirmed using the bills obtained from their GSM service providers.

Before the babies were discharged, TEOAE tests (TEOAE1 and TEOAE2), which were first hearing tests used, were conducted. The tests were administered with an Ero-scan (Madsen Accuscreen, Natus Medical Denmark ApS., Taastrup, Denmark) in a test environment of self-noise at <45 dB. The probe was inserted into the external auditory canal of the patients for calibration and then the test was started. The stimulus intensity given in the TEOAE was 26–36 dB. The screening results were automatically determined by the Ero-scan with passed/failed criteria. If Pass was displayed, the hearing screening was recorded as a pass. In this study, babies who had risk factors that would cause hearing loss (hearing loss in the family and consanguineous marriage, birth defects, infections such as toxoplasmosis, measles, or herpes, etc.) were excluded.

The ABR test was administered using an auditory evoked potential analyzer (EP25, Interacoustics, Middelfart, Denmark) in a soundproof room. When the subjects were in natural sleep or hypnosis after being given 10% chloral hydrate, the reference electrode and recording electrode were placed onto the ipsilateral mastoid and forehead, and alternating click stimuli was administered with an interelectrode resistance of ≤5KΩ and a filtering bandwidth of 100–3000 Hz. The scan was performed for a duration of 10 ms. The results of the hearing screening analyses of the newborns performed using the TEOAE and ABR tests were achieved with archive scan.

It was determined by the covariance analysis if the confounding factors such as maternal and paternal age; age of the father; weight gained by the mother during pregnancy; number of doctor visits during pregnancy; phone SAR value; type of birth; fetal distress; presence of meconium; toxoplasmosis; rubella; cytomegalovirus; presence of herpes simplex and HIV; placental disease; systemic diseases; condition of the amniotic fluid; multiple pregnancies; stillbirth; gestational vitamin usage comprising ferritin, vitamin D, and folic acid; exposure to radiation; urinary tract infections; vaginitis; chorioamnionitis; smoking and alcohol consumption; amount of daily cigarettes smoked; presence of a base station in the neighborhood, etc. had any impact or not. It was found that the confounding factors had no impact on the groups as p value was >0.05.

Descriptive statistics for the continuous variables were presented as the mean, standard deviation, and minimum and maximum values, while count and percentages were used for the categorical variables. For determination of linear relationships between the categorical variables, the chi square test was performed. Statistical significance was accepted as p<0.05 and the Statistical Package for the Social Sciences (SPSS) v.13 (SPSS Inc., Chicago, IL, USA) software was used for all of the statistical computations. Moreover, due to the fact that the rate of success in hearing tests (p) ranged from 75% to 95% in the results of a previous study by Yorgancilar et al.,[14] the success rate was accepted as 85% in the current study. Furthermore, for the 0.05 type I error rate, the Z value and the effect size were assumed as 1.96 and 6%, respectively. Based on this information, the necessary sample size was determined as a minimum of 136 individuals according to the equation for sample size calculation [n=Z2 (pxq)/d2]. In other words, the statistical power (sample size) of the current study was appropriate.

Results
Herein, 91.9% of the newborns in the control group, 89.7% of those in Group 1, 97.3% of those in Group 2, and 80.6% of those in Group 3 passed the TEOAE1 test (Table 1). Since p>0.05, the results of the TEOAE1 test were not statistically associated with speech groups. Herein, 80.0% of the newborns in the control group,
50.0% of those in Group 1, 100.0% of those in Group 2, and 65.0% of those in Group 3 passed the TEOAE2 test (Table 2). No significant difference was found when the groups were compared in terms of the results of TEOAE2 test (p=0.280). Only 58 of the babies included in the study were administered the ABR test because they had passed the 2 earlier tests (TEOAE1 and TEOAE2) and they eventually passed all of the tests.

**Discussion**

The newborns successfully passed the TEOAE and ABR tests. Mobile phones used by the pregnant mothers emitted between 900 and 1800 MHz RFR according to the information that was received from the GSM service providers. No statistically significant differences were found among the speech groups according to the results of the hearing tests. The results showed that exposure to between 900 and 1800 MHz RFR during the intrauterine period did not affect the hearing status of the newborns. Moreover, exposure durations of the infants to RFR during the prenatal period were also found to not have any effect.

The effects of RFR exposure on fetuses and newborns are still not well known. Several studies have reported that even RFR exposure below the safety standards of the International Commission on Non-Ionizing Radiation Protection have caused harmful effects on human health.[23]

Fetuses have a high number of stem cells, which are responsible for the formation of the fetal neural system.[24] Stem cells are very susceptible to toxins and RFR. Thus, exposure of the fetus to EMFs can increase the risk of adverse health outcomes.[25] Several studies have reported harmful effects related to RFR exposure in human stem cells.[26,27] A study carried out on the Danish National Birth Cohort indicated a positive and dose-dependent relationship between the use of the mobile phones by mothers during pregnancy and the behavioral problems of their offspring.[28–30] Moreover, brain development is quite responsive to RFR exposure during the prenatal period.[23] Hardell and Sage[31] noted that RFR exposure could induce some changes in the brain and neural system functions, and children should be warned about the unknown biological complications of prolonged RFR exposure. Furthermore, it was stat-

<table>
<thead>
<tr>
<th>Talking</th>
<th>Passed</th>
<th>Failed (bilateral)</th>
<th>Failed (unilateral)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>34</td>
<td>2</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>% while talking</td>
<td>91.9%</td>
<td>5.4%</td>
<td>2.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE1</td>
<td>25.4%</td>
<td>20.0%</td>
<td>20.0%</td>
<td>24.8%</td>
</tr>
<tr>
<td>% of total</td>
<td>22.8%</td>
<td>1.3%</td>
<td>0.7%</td>
<td>24.8%</td>
</tr>
<tr>
<td>2–15 min/day (Group 1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>35</td>
<td>3</td>
<td>1</td>
<td>39</td>
</tr>
<tr>
<td>% while talking</td>
<td>89.7%</td>
<td>7.7%</td>
<td>2.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE1</td>
<td>26.1%</td>
<td>30.0%</td>
<td>20.0%</td>
<td>26.2%</td>
</tr>
<tr>
<td>% of total</td>
<td>23.5%</td>
<td>2.0%</td>
<td>0.7%</td>
<td>26.2%</td>
</tr>
<tr>
<td>15–60 min/day (Group 2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>36</td>
<td>0</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>% while talking</td>
<td>97.3%</td>
<td>0.0%</td>
<td>2.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE1</td>
<td>26.9%</td>
<td>0.0%</td>
<td>20.0%</td>
<td>24.8%</td>
</tr>
<tr>
<td>% of total</td>
<td>24.2%</td>
<td>0.0%</td>
<td>0.7%</td>
<td>24.8%</td>
</tr>
<tr>
<td>&gt;60 min/day (Group 3)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Count</td>
<td>29</td>
<td>5</td>
<td>2</td>
<td>36</td>
</tr>
<tr>
<td>% while talking</td>
<td>80.6%</td>
<td>13.9%</td>
<td>5.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE1</td>
<td>21.6%</td>
<td>50.0%</td>
<td>40.0%</td>
<td>24.2%</td>
</tr>
<tr>
<td>% of total</td>
<td>19.5%</td>
<td>3.4%</td>
<td>1.3%</td>
<td>24.2%</td>
</tr>
<tr>
<td>Total</td>
<td>134</td>
<td>10</td>
<td>5</td>
<td>149</td>
</tr>
<tr>
<td>% while talking</td>
<td>89.9%</td>
<td>6.7%</td>
<td>3.4%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE1</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% of total</td>
<td>89.9%</td>
<td>6.7%</td>
<td>3.4%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi-square test= 6.674; p=0.352.
ed that RFR exposure during pregnancy could cause adverse health effects in the fetuses, even if the exposure levels were within the legal levels accepted by many countries. Some studies have reported that exposure to RFR could change gene expression during gestation. However, the few epidemiologic studies that have been conducted were insufficient to exhibit a potential association between developmental conclusions and prenatal RFR exposure.

Many studies have researched the effects of RFR on the central or peripheral auditory system. Some researchers have investigated the effects of exposure to RFR on the central auditory system using the ABR test or potentially related auditory incidents; however, no effects were determined. Similarly, several studies have been performed using otoacoustic emissions; however, it was reported that RFR exposure did not cause any effects on the inner ear. When the effects of mobile phone-like 900 MHz RFR on the cochlear function of rats was investigated, no variations in the DPOAE values were determined. Similarly, in another study, it was reported that 10 min RFR exposure at maximum power (2 W at 900 MHz or 1 W at 1800 MHz) did not cause any alterations in the DPOAE values. On the other hand, it was reported that 24 h/day long-term exposure (1 year) to 2.4 GHz RFR significantly affected DPOAE values and could cause impairment the hearing of adult Wistar rats. In a recent study of mice during the postnatal period, following exposure to 1850 MHz RFR, no significant changes were observed in the hearing threshold of the ABR test. It was reported that RFR might directly affect brainstem auditory circuits, but did not change the general sound perception. In another study, no significant effects were observed in the TEOAE results of 30 cases after exposure to between 900 and 1800 MHz RFR emitted from mobile phones. These contradictory results may have been due to the dissimilar designs of the RFR sources. In a study of the cochlear functions of infant rabbits exposed to RFR during the intrauterine and extrauterine periods, it was reported that GSM-like RFR during the intrauterine period was less harmful when compared to that in the extrauterine period. This was due to the fact that the water content of the middle and inner ear, and the amniotic fluid during the intrauterine period, have a protective role.

Table 2. Results of the TEOAE2 test.

<table>
<thead>
<tr>
<th>Talking</th>
<th>Count</th>
<th>Passed</th>
<th>Failed (bilateral)</th>
<th>Failed (unilateral)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% while talking</td>
<td>80.0%</td>
<td>13.3%</td>
<td>6.7%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE2</td>
<td>30.0%</td>
<td>20.0%</td>
<td>25.0%</td>
<td></td>
<td>27.8%</td>
</tr>
<tr>
<td>% of total</td>
<td>22.2%</td>
<td>3.7%</td>
<td>1.9%</td>
<td></td>
<td>27.8%</td>
</tr>
<tr>
<td>2–15 min/day (Group 1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% while talking</td>
<td>50.0%</td>
<td>37.5%</td>
<td>12.5%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE2</td>
<td>10.0%</td>
<td>30.0%</td>
<td>25.0%</td>
<td></td>
<td>14.8%</td>
</tr>
<tr>
<td>% of total</td>
<td>7.4%</td>
<td>5.6%</td>
<td>1.9%</td>
<td></td>
<td>14.8%</td>
</tr>
<tr>
<td>15–60 min/day (Group 2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% while talking</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE2</td>
<td>27.5%</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
<td>20.4%</td>
</tr>
<tr>
<td>% of total</td>
<td>20.4%</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
<td>20.4%</td>
</tr>
<tr>
<td>&gt;60 min/day (Group 3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% while talking</td>
<td>65.0%</td>
<td>25.0%</td>
<td>10.0%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE2</td>
<td>32.5%</td>
<td>50.0%</td>
<td>50.0%</td>
<td></td>
<td>37.0%</td>
</tr>
<tr>
<td>% of total</td>
<td>24.1%</td>
<td>9.3%</td>
<td>3.7%</td>
<td></td>
<td>37.0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% while talking</td>
<td>74.1%</td>
<td>18.5%</td>
<td>7.4%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% within TEOAE2</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
<td>100.0%</td>
</tr>
<tr>
<td>% of total</td>
<td>74.1%</td>
<td>18.5%</td>
<td>7.4%</td>
<td></td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Pearson’s chi-square test= 7.470, p=0.280.
A possible explanation for the results of the current study may be the protective effects of maternal estrogen and corticosteroids. It is well-known that maternal estrogen increases during pregnancy. The estrogen receptor, which has β-mediated neuroprotective efficacy involving the brain-derived neurotrophic factor in the auditory system, protects the functions of the inner ear. Moreover, maternal corticosteroids, which increase during the prenatal period, develop the hearing system and protect the ear from the detrimental effects of the RFR emitted by mobile phones.

Conclusion
Consequently, the data herein showed that the hearing sensitivity and peripheral sound perception of newborns were not affected by RFR exposure emitted by mobile phones during the intrauterine period. However, it should be stated that RFR exposure during the prenatal period could cause circuit alterations in the auditory nervous system, without influencing the functions of sound perception. To our knowledge, this study was the first human study to investigate the effects of mobile phone use by mothers during the prenatal period on the sense of hearing of newborns. To date, among the studies carried out on this subject, there has not been any consistency in terms of experimental parameters and the results of the investigations. Thus, characterization of the exposure to RFR may be significant to further research the mechanisms of the action EMFs.

Conflicts of Interest: No conflicts declared.

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Comparison of the levels of antenatal anxiety in pregnant women admitted for delivery before and after COVID-19 outbreak in Turkey

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Abstract

Objective: This study aimed to compare the level of anxiety in pregnant women who were admitted to our institute before and after confirmation of COVID-19 outbreak have reached Turkey.

Methods: One-hundred and fifty consecutive pregnant women admitted to our institute following the emergence of the global COVID-19 outbreak (Group 1) and 150 age-matched pregnant women who were admitted to our institute for delivery following the confirmation of COVID-19 outbreak have reached Turkey (Group 2) were enrolled in this study. All patients were asked to fill out the State and Trait Anxiety Inventory (STAI).

Results: STAI-Trait scores, which reflect long term anxiety levels were similar in subjects admitted to our institute for delivery before the COVID-19 outbreak in Turkey compared to those admitted after COVID-19 outbreak (42.5±5.8 vs. 42.2±3.2, respectively; p=0.487). However, there was a significant difference in STAI-State scores, indicating state anxiety, between subjects admitted to our institute for delivery before and after confirmation of COVID-19 outbreak in Turkey (44.6±5.3 vs. 42.9±5.1, respectively; p=0.05).

Conclusion: Pregnant women admitted to our institute for delivery subsequent to the announcement of first COVID-19 case and declaration of the state of alarm have higher levels of state anxiety compared to those admitted before the establishment of first COVID-19 cases and containment measures.

Keywords: COVID-19, antenatal anxiety, pregnant.

Introduction

Several cases of pneumonia with unknown etiology have emerged in Wuhan, Hubei Province, China towards the end of the 2019. Fewer and cough, which were prior to an acute respiratory distress syndrome were the most prominent initial symptoms. Following the identification of a novel coronavirus in the throat swab sample of one patient by the Chinese Center for Disease Control...
and Prevention (CDC), World Health Organization (WHO) named the novel coronavirus as 2019nCoV.[9] The rapid spread of the pneumonia to other regions of China and overseas led World Health Organization (WHO) declare this outbreak as the public health emergency of international concern (PHEIC). In February 2020, the virus was renamed as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses.[4] Epidemic disease caused by SARS-CoV-2 was further announced by the WHO as coronavirus disease 2019 (COVID-19).

Coronavirus disease 2019 was the third coronavirus disease within the last two decades following severe acute respiratory syndrome coronavirus (SARS-CoV) which resulted in more than 8000 infections and 774 deaths in 37 countries, and Middle East respiratory syndrome coronavirus (MERS-CoV) which resulted in 2494 infections 858 deaths.[3,4] As of May 25, 2020, COVID-19 has been reported to affect about 5.5 million individuals and caused over 340,000 fatalities globally.[5] The high virulence, rapid spread and related mortality alerted healthcare authorities and many of the countries announced containment measures to slow down the spread of the COVID-19. Accumulating data indicate that declaration of the state of alarm by many countries and related containment measures along with the public-health messages not only raised public’s knowledge concerning the COVID-19 but also led to global anxiety resulting from the fear of being infected by the SARS-CoV-2.[5–10] A number of studies have shown that antenatal anxiety could result in adverse perinatal outcomes.[11] Given that COVID-19 may trigger excessive anxiety, we hypothesized that the announcement of containment measures as a consequence of the arrival of COVID-19 in our country would trigger anxiety in pregnant women.

This study aimed to compare the level of anxiety in pregnant women who were admitted to our institute before and after confirmation of COVID-19 outbreak have reached Turkey.

Methods
One-hundred and fifty consecutive pregnant women aged between 18 and 35 years who were admitted to the our hospital following the emergence of the global COVID-19 outbreak (Group 1) and 150 age-matched pregnant women who were admitted to our institute for delivery following the confirmation of COVID-19 outbreak have reached Turkey (Group 2, before March 11, 2020) were enrolled in this study. Women with previous anxiety disorders or mental syndromes, high blood pressure, lung, kidney, or heart problems, diabetes, autoimmune disease, sexually transmitted diseases, preeclampsia, multiple pregnancies, placenta previa were excluded. Written informed consent was obtained from all subjects included in the study. The study was approved by the Institutional Ethical Committee and was performed in accordance with the recent version of the Helsinki Declaration. The power calculation was based on our pilot study with the first 15 patients. We used “priori t-tests; the difference between two independent means” for post-information State and Trait Anxiety Inventory-State (STAI-S) measurements in the two groups (Group 2 patients: 45.3±4.6, STAI-S score of Group 1 patients: 42.4±4.2, alpha error: 0.05, power: 0.95, effect size: 0.65).[12] Results showed that at least 102 patients were required for an adequate sample size.

All patients were asked to fill out the STAI, which is a validated and widely used self-report questionnaire assessing both state and trait anxiety.[13,14] STAI includes two questionnaires with 20 questions in each; STAI-S, which intends to evaluate the current state of anxiety, and trait anxiety (STAI-T) that measures long term anxiety levels. Responses for the STAI-S scale evaluate the intensity of current feelings “right now”: (1) not at all, (2) somewhat, (3) moderately so, and (4) very much so. Responses for the STAI-T scale evaluate the frequency of feelings “in general”: (1) almost never, (2) sometimes, (3) often, and (4) almost always. Item scores are added to obtain subtest total scores. Each answer was scored on a scale of 1–4 and was added to reach a final score. The overall score ranges between 20 and 80, the higher score indicating greater anxiety.

The difference between the anxiety levels of subjects in Group1 and Group 2 was the primary outcome measure of this study. Statistical analyses were carried out using SPSS for Windows, version 17 (SPSS, Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation (mean±SD) and categorical variables as frequency (n) and percentage (%). Kolmogorov-Smirnov test was used to determine the normal distribution of the data. The comparison of the two groups was
performed with Student’s t-test, Mann-Whitney U test, \( \chi^2 \)-test or Fisher’s exact test, where appropriate. Two-sided p-value \( \leq 0.05 \) was interpreted as statistically significant.

**Results**

The mean age and the mean week of gestation of the study subjects were 28.6\( \pm \)4.7 years and 35.5\( \pm \)2.1 weeks, respectively. The two groups were similar with respect to age, week of gestation, body mass index, gravidity, and parity. STAI-T scores, which reflect long term anxiety levels were similar in subjects admitted to our institute for delivery before the confirmation of COVID-19 outbreak have reached our country compared to those admitted after COVID-19 outbreak have reached our country (42.5\( \pm \)5.8 vs. 42.2\( \pm \)3.2, respectively; p=0.487). However, there was a significant difference in STAI-State scores, indicating state anxiety, between the subjects admitted to our institute for delivery before and after confirmation of COVID-19 outbreak have reached our country (44.6\( \pm \)5.3 vs. 42.9\( \pm \)5.1, respectively; p=0.005) (Table 1).

**Discussion**

Despite similar long-term anxiety scores between the two groups, our findings show that subjects admitted to our institute for delivery following the confirmation of COVID-19 outbreak have reached our country had higher levels of state anxiety compared to subjects admitted before the confirmation of COVID-19 outbreak have reached our country.

Antenatal anxiety, which is shown to affect about 20% of pregnant women, has been reported to be associated with adverse outcomes for both mother and baby following delivery.\[^{[15]}\] While postpartum hemorrhage, and postpartum depression are more frequent in pregnant with antenatal anxiety, preterm birth, low mean birth weight, and small head circumference might be observed in infants born to mothers with antenatal anxiety.\[^{[16–20]}\] Moreover, measures aiming to relieve anxiety have been shown to improve pregnancy outcomes in women with antenatal anxiety.\[^{[21,22]}\]

Turkish Ministry of Health announced the first COVID-19 case in Turkey on March 11, 2020. A state of alarm, including several containment measures such as school closures, transport bans and workplace shutdowns has been established following this first case. Individuals <20 years and >65 years were obliged to stay at home since this population may either be vulnerable to complications of COVID-19 or may facilitate the spreading of the COVID-19. Elective interventional and surgical procedures were also postponed due to the heavy burden on the healthcare systems loaded by COVID-19 cases. Television programs started to broadcast certain public messages regarding the virulence and rapid spread of SARS-CoV-2 and global mortality from COVID-19. Following the establishment of containment measures by governments, many of the individuals are observed to hesitate seeking medical help even for emergency situations.\[^{[23]}\] There are several recent reports demonstrating a dramatic decline in hospital admissions even from life-threatening conditions such as acute myocardial infarction or acute heart failure after containment measures.\[^{[24–26]}\] It simply appears that declaration of the state of alarm by many countries and related containment measures along with the public-health messages have created a global anxiety among individuals requiring healthcare for causes other than COVID-19 and led

<table>
<thead>
<tr>
<th></th>
<th>Group 1 n=150</th>
<th>Group 2 n=150</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>29.1( \pm )5.1</td>
<td>28.2( \pm )4.3</td>
<td>0.141</td>
</tr>
<tr>
<td>Week of gestation, n</td>
<td>39.6( \pm )2.1</td>
<td>39.3( \pm )1.4</td>
<td>0.211</td>
</tr>
<tr>
<td>Body mass index, kg/m(^2)</td>
<td>28.2( \pm )3.3</td>
<td>28.5( \pm )2.8</td>
<td>0.198</td>
</tr>
<tr>
<td>Gravidity, n</td>
<td>1.84( \pm )0.43</td>
<td>1.85( \pm )0.58</td>
<td>0.903</td>
</tr>
<tr>
<td>Parity, n</td>
<td>0.69( \pm )0.07</td>
<td>0.78( \pm )0.07</td>
<td>0.239</td>
</tr>
<tr>
<td>STAI-State</td>
<td>44.6( \pm )5.3</td>
<td>42.9( \pm )5.1</td>
<td>0.005</td>
</tr>
<tr>
<td>STAI-Trait</td>
<td>42.5( \pm )5.8</td>
<td>42.2( \pm )3.2</td>
<td>0.487</td>
</tr>
</tbody>
</table>

Data are presented as mean \( \pm \) standard deviation. STAI: State and Trait Anxiety Inventory.
to a self-censorship resulting from the possible contamination in hospitals. A recent study from China has shown that initial phase of the COVID-19 outbreak triggered extensive anxiety among general population.\[7\] Another study among active Weibo users has reported short-term individual changes in psychological conditions after the outbreak.\[27\]

Currently, there are only a few studies investigated the role of COVID-19 outbreak on antenatal anxiety. The study of Durankus et al., which included an online questionnaire consisting of depression and anxiety inventories, has shown that COVID-19 pandemic had critical impact on the depression and anxiety levels of pregnant women.\[28\] A multi-center cross-sectional study from China, which compared the mental status of pregnant women before and after the announcement of the COVID-19 epidemic has reported that pregnant women assessed after the declaration of COVID-19 epidemic had significantly higher levels of anxiety and higher rates of depressive symptoms compared to women assessed prior to announcement of the COVID-19 epidemic.\[29\] However, there is still gap in data regarding the role of COVID-19 outbreak on antenatal anxiety.

This study shows that pregnant women admitted after announcement of the first COVID-19 case and containment measures in Turkey had higher levels of anxiety compared to women admitted before containment measures. Our findings confirm the results of the previous two studies indicating higher levels of anxiety in pregnant women following the COVID-19 outbreak. The lack of a significant difference in STAI-T scores between subjects admitted before and after COVID-19 outbreak indicates that psychological impact of the outbreak is short-term and is associated with either the COVID-19 outbreak itself or with the containment measures established to prevent the spread of the disease. Strategies targeting to relieve maternal stress should be provided by all decision-makers, health authorities, and health care professionals to prevent potential adverse pregnancy outcomes which are closely linked with antenatal anxiety.

**Conclusion**

Results of this study clearly shows that pregnant women admitted to our institute for delivery subsequent to the announcement of first COVID-19 case and declaration of the state of alarm have higher levels of state anxiety compared to those admitted before the establishment of first COVID-19 cases and containment measures. Given the negative impact of antenatal anxiety on pregnancy outcomes, we consider that health authorities should provide strategies targeting to relieve maternal stress on pregnant women.

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

**References**


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Does fetal MR alter the management of pregnancy in the diagnosis of isolated corpus callosum agenesis?

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Abstract

Objective: To determine if fetal MR alters the management of pregnancy and family decisions in the isolated corpus callosum agenesis (CCA) cases or not.

Methods: Fetal MR was carried out in the cases diagnosed with CCA in the Perinatology Unit of our hospital between 2013 and 2019 after they were differentiated as complex and isolated CCA cases. The impact of MR results on the family decisions and their approaches towards termination were assessed.

Results: A total of 109 out 139 cases were evaluated as isolated CCA. While 93 (85.32%) of them were diagnosed with the complete CCA, 16 (14.68%) cases were diagnosed with the partial CCA. When the period after 2017 during which fetal MR was recommended to all patients was reviewed, it was seen that 7 (23.3%) of 30 cases who underwent fetal MR and 2 (20%) of 10 cases who did not undergo fetal MR terminated their pregnancies. There was no statistical difference between two groups in terms of the decisions of the patients for gestational termination who did and did not undergo fetal MR.

Conclusion: Fetal MR imaging in the isolated CCA does not change the decisions of the families for the gestational termination. In terms of the termination decision, week of gestation and socio-cultural factors may have more impacts.

Keywords: Isolated corpus callosum agenesis, complete/partial, fetal MR, gestational termination.

Introduction

Corpus callosum (CC), originating from white matter, is the greatest interhemispheric connection between the hemispheres.1,2 These connections play a significant role in the integration of sensational, motor and cognitive functions.2 Complete agenesis, partial agenesis, hypoplasia and hyperplasia are among the developmental anomalies of CC during fetal process, and the prevalence of CC anomalies vary according to the population, which is 1.8/1000 birth in the general population and increases up to 3% in the societies displaying developmental disabili-
bral and extra-cerebral malformations, are associated with the chromosomal pathologies and genetic syndromes. Therefore, the general prognosis of CA is controversial, and neurodevelopmental delay is seen frequently in the presence of additional anomaly. The etiology of corpus callosum agenesis (CCA) is heterogeneous in this regard; it may exist as a component of Aicardi syndrome, and it may coexist with CNS malformations such as Dandy-Walker or Arnold-Chiari malformation. Besides, CCA may also be associated with holoprosencephaly, schizencephaly, TORCH or Zika virus infections. Genetic interaction may occur depending on autosomal dominant, autosomal recessive or X. While 30–35% of the genetic reasons can be identified depending on the syndromes, 20–35% of them are under the influence of monogene. Major chromosomal anomalies such as trisomy 18, trisomy 13 or mosaic trisomy 8 were found in 18% of CCA cases.

Fetal ultrasonography and neurosonography are the basic / primary imaging methods, and they can be used after 18 weeks of gestation. Normal CC development may also be imaged indirectly by revealing pericallosal artery before 18 weeks of gestation, but this practice is not recommended in the routine evaluation for the final diagnosis. It has been found out in the recent years that fetal MR imaging can be used to confirm the diagnosis and it may provide information about the related fetal central nervous system anomalies including cortical development disorders in particular, and that it can change the prognosis and clinical management with the help of additional fetal clinical findings in 20% of the cases after 24 weeks of gestation.

The aim of our study is to evaluate the impact of additional fetal MR practice on the decisions of families for gestational termination (GT) in the patients diagnosed with isolated CCA.

**Methods**

The fetuses diagnosed with CCA in the Perinatology Unit of Istanbul Kanuni Sultan Suleyman Training and Research Hospital between 2013 and 2019 were included in this retrospective study. All fetuses with CCA pre-diagnosis/diagnosis were evaluated by detailed sonographic and neurosonographic (GE Healthcare Ultrasound E6; RAB 6D [2-7 MHz] probe; Milwaukee, WI, USA) examinations in terms of additional anomalies. The patients were assessed in two groups as the fetuses with isolated and non-isolated/complicated CCA diagnosis.

The fetal neurosonography for the pregnant women was conducted transabdominally on axial, sagittal and coronal planes in accordance with the guidelines published by ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) in 2007. The anatomic parts (rostrum, genu, truncus and splenium) of CC were evaluated in all fetuses and the total lengths and thicknesses of CCs were measured. In addition, all cases underwent detailed anomaly examination and fetal echocardiography screening. The transvaginal fetal examination was carried out in the cases which were not on cephalic position in accordance with the recommendations of Timor-Trisch and Monteagudo. The diagnosed cases were recommended karyotype analysis after they were provided genetic consultation. Fetal MR imaging was done by using 1.5% system (General Electric Healthcare, Explorer 1.5T; Milwaukee, WI, USA) without sedation. Ultra T2 weighted single-shot fast spin echo imaging was used for axial, coronal and sagittal planes with 2–3 mm section thickness, and it was for the detection of early myelination. In addition, T1 radiofrequency sections were taken on axial planes, and these sections were applied for fat tissue to reveal myelin structure in the developed brain and bleeding.

It was started to conduct fetal MR as a routine practice for the patients with isolated CCA diagnosis after 2017 in our institution. While fetal MR imaging was a partial practice before 2017 in accordance with the recommendations of the international guidelines, all cases admitted to our hospital as of this date were recommended and imaging was conducted in the cases whose families accepted. In our study, the sonography results of the patients diagnosed with isolated partial CCA (pCCA) and isolated complete CCA (cCCA) were checked with fetal MR and their diagnosis compatibilities were evaluated. After the families together with the diagnosed fetuses were re-examined in the multidisciplinary perinatology council of our family, they were informed about the postpartum outcomes, risks and prognosis of isolated pCCA and cCCA cases through the consultation of pediatric neurology unit, and the gestational termination was offered to the families as an option.

The variables evaluated in the study were the demographic data of the pregnant women, diagnosis age during pregnancy, week of gestation during fetal MR, additional cranial and extracranial malformations, karyotype results and the impacts of related results on the decision of families for the gestational termination.
SPSS 23.0 (Statistical Packages for Social Sciences; SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. The numerical data were presented as mean ± standard deviation and range (min–max), and the categorical data were represented as percentage (%) in the evaluation. TOP values of the cases who did and did not undergo MR were compared by using Kruskal-Wallis test (in 95% CI, p<0.05 is significant).

Results

Of 139 cases diagnosed with CCA in our hospital or admitted to our hospital through referral, 109 (78.4%) were evaluated as isolated CCA. Additional anomaly/anomalies were found in other 30 (21.6%), and they were evaluated as non-isolated/complicated cases (Fig. 1). The mean age of the pregnant women with isolated CCA diagnosis was 28.6±6.4, and their mean week of gestation during diagnosis was 28.6±4.8. The demographic characteristics of both groups are shown in Table 1. The mean age of the patients in the isolated CCA group was 28.6±6.43, and their mean week of gestation during diagnosis was 28.6±4.8. The demographic characteristics of both groups are shown in Table 1. The mean age of the patients in the isolated CCA group was 28.6±6.43, and their mean week of gestation during diagnosis was 28.6±4.8. The difference was significant in terms of age variable in the both groups (p=0.041). When mean gravida was compared between two groups, it was seen that the mean gravida of the patients in the isolated CCA group (2.42±1.43) was higher than the mean value of the patients in the non-isolated/complicated CCA group (1.13±2.59), but this difference was not significant. Similarly, the mean parity of the patients in the isolated CCA group (1.04±1.09) was slightly higher than the values of non-isolated/complicated CCA group (0.52±1.29), but it was not significant. The ultrasonographic diagnosis was established at 28.66±4.86 weeks in in the isolated CCA cases while the diagnosis was established at 26.57±3.45 weeks in the other group. The week of gestation during diagnosis was statistically significant for both groups (p= 0.028).

When all patients are considered, 93 (85.3%) of isolated CCA cases were evaluated as cCCA and 16 (14.7%) of them were evaluated as pCCA after the detailed assessment conducted in our clinic. Twenty-seven cases diagnosed with cCCA and 7 cases diagnosed with pCCA underwent fetal MR imaging. After fetal MR imaging, it was observed that MR diagnoses were fully compatible with cCCA diagnosis of the fetuses (US/MR diagnosis compatibility for cCCA diagnosis: 27/27 cases) and highly compatible with pCCA diagnosis of the fetuses (US/MR diagnosis compatibility for pCCA diagnosis: 5/7 cases) (Fig. 2). Accordingly, neurosonography and fetal MR were compatible for 94% of the cases. Of the two patients who were observed to have incompatible US/fetal MR results, inferior vermian hypoplasia was found in the first one as an additional anomaly.

Table 1. The demographic characteristics of the cases.

<table>
<thead>
<tr>
<th></th>
<th>Isolated CCA (n=109; 78.4%)</th>
<th>Non-isolated / complicated CCA (n=30; 21.6%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.63±6.43</td>
<td>22.67±3.50</td>
<td>0.041*</td>
</tr>
<tr>
<td>Gravida</td>
<td>2.42±1.43</td>
<td>1.13±2.59</td>
<td>0.234</td>
</tr>
<tr>
<td>Parity</td>
<td>1.04±1.09</td>
<td>0.52±1.29</td>
<td>0.325</td>
</tr>
<tr>
<td>Week of gestation during diagnosis</td>
<td>28.66±4.86</td>
<td>26.57±3.45</td>
<td>0.028*</td>
</tr>
</tbody>
</table>

*p<0.05.
second patient, a fetus diagnosed with cCCA by sonography during antenatal period was reported to have CC hypoplasia after fetal MR. It was seen that the last diagnosis of postnatal MR was also cCCA in this patient who was followed up during pregnancy.

Similarly, when the period after 2017 in which all patients were recommended fetal MR was reviewed, it was seen that 24 of 34 pregnant women who were established the preliminary diagnosis of cCCA accepted further investigation and underwent fetal MR, and US/MR compatibility was observed. Five of 6 patients who were recommended fetal MR due to the preliminary diagnosis of partial CCA accepted further investigation and US/MR compatibility was observed in these patients as well (Fig. 3).

The decisions of the families for the gestational termination, who did / did not undergo fetal MR during antenatal period, were assessed in the council and provided consultation by the pediatric neurology, were evaluated. When all patients were assessed, it was seen that gestational termination was preferred for 8 (23.5%) fetuses in the group (n=34) that underwent fetal MR imaging, and 16 families in the group (n=75) which did not undergo MR imaging. When diagnosis distribution was conducted for these 24 cases, it was seen that 20 (21.3%) of isolated CCA cases were cCCA and 4 (25%) of them were pCCA cases. There was no statistically significant difference between 34 cases who underwent fetal MR imaging and 75 cases who did not undergo fetal MR imaging (p=0.624). While 8 (23.5%) of the families accepted gestational termination according to the fetal MR result in isolated CCA anomaly cases, 16 (21.3%) of them did not accept it. There was no difference for the decisions of gestational diagnosis in terms of isolated CCA diagnosis (p=0.078).

When the period after 2017 during which all patients were recommended fetal MR was reviewed, it was seen that 7 (23.3%) of 30 cases who underwent fetal MR imaging and 2 (20%) of 10 cases who did not undergo fetal MR imaging preferred the gestational termination. During this period, 7 (23.3%) families in the isolated CCA anomaly cases accepted gestational termination according to the fetal MR results while 20% of the patients who did not undergo fetal MR imaging did not accept termination (p=0.212).

In our study, we used Kruskal-Wallis test to investigate the impact of fetal MR result on the termination decisions of families in isolated CCA anomaly cases statistically; no statistically significant difference was found between all patients during both periods and between the groups during the period after 2017 (p=0.098; 95% CI, p<0.05) (Table 2).

42 pregnant women diagnosed with cCCA and 7 pregnant women diagnosed with pCCA underwent invasive procedure for karyotype analysis in terms of genetic diagnosis during diagnosis and follow-up processes. The diagnosis was trisomy 21 only in one fetus diagnosed with cCCA, and it was seen that this fetus died at the 34 weeks of gestation during gestational follow-up.

In addition, intrauterine loss was observed for 3 other fetuses diagnosed with pCCA during antenatal follow-up after diagnosis. Only one of them underwent fetal MR imaging, and none of the cases accepted karyotype offer after diagnosis.

**Discussion**

The screening at axial and sagittal planes for the image sections of fetal anterior and mid-brain is done by imag-
ing cavum septum pellucidum (CSP) and ventricles in the head.\[10,11\] While cCCA diagnosis is established by the failure of imaging corpus callosum through direct imaging in the sagittal sections, incompatibilities related with the length or thickness of CC or malformations are considered among the findings of pCCA and CC hypoplasia.\[10\] On the other hand, the failure of imaging CSP in the standard cranial axial sections, CS width, length or the disproportions between them, interhemispheric fissure mark (three-line view consisting of the medial margins of falx and hemispheres), atrial width being > 10 mm and the presence of medium severity of ventriculomegaly, the colpocephaly view formed by the dilation of occipital horns related with the non-development of the posterior part of CC, the tear drop view of the lateral ventricles, and more separate view of lateral ventricles from each other are among the indirect findings in the sonography. The displacement of 3rd ventricle upwards in the coronal sections and delta-like view are considered among the findings of pCCA and CC hypoplasia.\[11\] Lastly, the pathological course of pericallosal arteries is also among the findings of CCA. While these sonographic findings can be seen in cCCA distinctly, they can be seen partially or nonspecifically in the cases diagnosed with pCCA. In this regard, CSP helps us more: although CSP development has a pathological view usually in cCCA cases, the posterior part of CC generally has a developmental disorder (not a rule) and CSP view is preserved in pCCA cases.\[12–14\]

In the literature, the incidence of chromosomal anomaly was reported as high as 17.8% in the cases diagnosed with CCA.\[16\] However, this rate is not only for isolated cases but applies for all patients diagnosed with CCA whereas our case included only the cases diagnosed with isolated CCA. We found Trisomy 21 (the incidence of aneuploidy was 2.2%) only in one of 49 fetuses after karyotype analysis in our series. As we excluded multiple anomalies from our study, we did not observe potentially higher aneuploidy rates in our study. However, as poor postnatal development possibility usually can be seen highly together with euploidy series in CCA cases even the isolated ones, microarray first and then exome sequencing, if necessary, as a two-step process in the prenatal genetic panel are the additional recommendations that can be done for the diagnostic test during antenatal process.\[19\] Sub-microscopic copy number variation (CNV) can be seen with a rate of 3.1–7.9% in the fetuses which are found to have limited anomaly by a single system in the sonography but found to be euploidy in the classic karyotyping, and it provides more detailed information about fetal prognosis together with phenotype.\[20\]

Paladini et al. evaluated different sonographic cranial findings in their study,\[13\] and they found ventriculomegaly in about 26% of the fetuses diagnosed before the 24 weeks of gestation and in 74% of the fetuses diagnosed after the 24 weeks of gestation. Similarly, they found colpocephaly finding in about 21% of the cases diagnosed before the 24 weeks of gestation and in 69% of the cases diagnosed after the 24 weeks of gestation. It is seen that the ventricles dilate by becoming clearer after the 24 weeks of gestation in fetuses diagnosed with both pCCA and cCCA. In another study assessing ventriculomegaly, 10 (13.5%) of 74 fetuses with lateral ventricle more than 10 mm were diagnosed with CCA.\[16\] This correlation shows both the importance and the difficulty of imaging CC in fetuses with ventriculomegaly. Similarly, Paladini et al.\[13\] showed that the colpocephaly finding which is an indirect indicator of CCA becomes clear as the weeks of gestation advance. Conversely, the failure of imaging CSP in the same study was assessed only for pCCA cases, and the failure of imaging CSP was observed in 35.3% of the cases younger than 24 weeks while the rate was 20% in cases above 24 weeks. Karl et al. reported that pCCA diagnosis can be established more easily through the differences between CSP shapes and rates.\[17\] Similarly, Shen et al. also presented the data showing that CSP deformities could be an indirect indicator for pCCA diagnosis.\[21\]

Although there is a general literature information stating that the fetal MR imaging for distinctive diagnosis after the preliminary diagnosis of ventriculomegaly may detect additional 15–20% pathologies, it is usually not specified whether the sonography procedure is carried out by experienced experts or not when comparing both methods.\[8,11–14\] However, fetal MR was highlighted more for the investigation of a general multi-etiological finding such as ventriculomegaly through partial bias in the early 2000s.\[22\] The arguments such as the exact number of intracranial pathologies which do not require MR and established the final diagnosis with the sonography and

Table 2. The impact of fetal MR results on the termination decision of families in isolated CCA anomaly cases (total and routine imaging procedures after 2017).

<table>
<thead>
<tr>
<th>Cases who underwent</th>
<th>Cases who did not undergo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n, %)</td>
<td>(n, %)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal MR imaging</td>
<td>34 (23.5%)</td>
<td>75</td>
</tr>
<tr>
<td>Gestational termination</td>
<td>8 (23.5%)</td>
<td>16 (21.3%)</td>
</tr>
<tr>
<td><strong>After 2017</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal MR imaging</td>
<td>30 (23.3%)</td>
<td>10</td>
</tr>
<tr>
<td>Gestational termination</td>
<td>7 (23.3%)</td>
<td>2 (20.0%)</td>
</tr>
</tbody>
</table>

Kruskal-Wallis test. *p<0.05.
the direct MR request instead of neurosonography and transvaginal sonography procedures, if necessary, after the preliminary diagnosis by transabdominal sonography were suggested among the primary topics as the reasons of bias.\(^\text{23}\) This argument started discussions among those working on radiology, fetal sonography and imaging fields in terms of developing algorithms.\(^\text{23}\) However, many studies reported that the diagnosis during prenatal period can be provided via sonography/neurosonography by the experts without fetal MR or independent from fetal MR in both isolated cCCA\(^\text{12,13,24,25}\) and isolated pCCA\(^\text{12,13,26,27}\) cases. Accordingly, Malinger et al. suggested in their editorial article for the evaluation of CCA diagnosis that the limitation of cranial evaluation only with the axial sections and the exclusion of sagittal and coronal sections from the examination are the most important issues missing in the sonographic examination.\(^\text{28}\) 

After the ventriculomegaly diagnosis published most recently on this topic, the rate of detecting additional anomaly after neurosonography was 5.0% while it was 16.8% after only standard axial sections for the anomalies in which the neurosonography was applied/not applied before fetal MR. The rate of detecting additional anomaly in the birth after prenatal MR was reported 0.9%. It was reported that maternal body mass index (BMI), the cases with medium-severe level ventriculomegaly more than mild ventriculomegaly and fetal MR conducted after 24 weeks of gestation were among the factors affecting the detection of additional anomaly.\(^\text{23,25}\) Although the fetal MR conducted before 24 weeks of gestation also performs well, the cortical and white matter anomalies and intracranial hemorrhage diagnoses were the diagnosis groups which made fetal MR superior at the third trimester.\(^\text{29,25}\)

According to the literature data, prognosis cannot be predicted in pCCA cases due to the uncertainty of antenatal, postnatal and newborn processes.\(^\text{18}\) In our clinic, we routinely recommend diagnosed families the gestational termination due to these unpredictable prognosis conditions. In this way, four pCCA cases decided to terminate pregnancy while three of them which rejected termination had intrauterine fetal loss after 32 weeks of gestation. Therefore, the families diagnosed with pCCA should also be informed the fact that they may encounter the risk of spontaneous intrauterine fetal death during pregnancy follow-up.

There is a limited number of publications on the contribution of fetal MR to the gestational termination. In the review of Di Mascio et al.,\(^\text{10}\) the rate of gestational termination request after standard sonography was 5.1% while it was 2.9% after the fetal MR which was added later. Similar to our study, it can be concluded that we need to investigate other factors rather than the diagnosis type in terms of convincing patients. A study investigating gestational termination in our society reported that newborn being incompatible with life after pregnancy, multiple anomalies and pathologies such as chromosomal/genetic anomalies are more prominent reasons than mental retardation.\(^\text{10}\) Similarly, another study reported that the early diagnosis of anomaly was one of the leading reasons for preferring termination in the conservative societies.\(^\text{11}\)

### Conclusion

In relation to our study, we found similar diagnostic accuracies in the fetal MR and regular multi-sectional prenatal sonographic examinations for the prenatal diagnosis of CCA. On the other hand, we concluded that conducting fetal MR imaging for the decision of gestational termination and/or the confirmation of diagnosis does not change the decision of parents for the gestational termination. Further studies are required on the gestational termination, and the impacts of multifactorial topics such as socio-cultural and religious perspective of families/mothers, week of gestation during diagnosis and additional methods should be investigated.

### Conflicts of Interest: No conflicts declared.

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All we know about COVID-19 in pregnancy: from perinatal to ethical and psychological perspective

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Introduction

In December 2019, a novel Coronavirus (COV), labelled as Wuhan coronavirus, causes the 2019-nCoV acute respiratory disease or COVID-19. While coronavirus infection is a common and usually self-limiting infection, in a specific population like pregnant women, complications of the disease appear to be more relevant, and pregnant women are particularly susceptible to morbidity and mortality, especially in case of high pathogenicity virus. Most common complications associated with COVID-19 in pregnancy include preterm birth, cesarean delivery, and perinatal deaths. The risk of vertical transmission seems to be negligible.

Keywords: COVID-19, pregnancy, maternal mortality, perinatal outcomes.

Abstract

The Novel Coronavirus (SARS-CoV-2), also known as Wuhan coronavirus, causes the 2019-nCoV acute respiratory disease or COVID-19. While coronavirus infection is a common and usually self-limiting infection, in a specific population like pregnant women, complications of the disease appear to be more relevant, and pregnant women are particularly susceptible to morbidity and mortality, especially in case of high pathogenicity virus. Most common complications associated with COVID-19 in pregnancy include preterm birth, cesarean delivery, and perinatal deaths. The risk of vertical transmission seems to be negligible.

Keywords: COVID-19, pregnancy, maternal mortality, perinatal outcomes.
The homology between the SARS-CoV-2 and SARS-CoV-1 genomes has been reported to be about 82%, and while the overall mortality rate appears to be lower than previous epidemics caused by two other Coronaviruses, also known as SARS and MERS, a higher rate of patients require admission to the intensive care unit (ICU).

The main concern when focusing on COVID-19 and pregnancy is that physiological adaptations occurring during pregnancy might predispose women to a more severe respiratory disease, thus leading to higher rates of maternal and fetal complications. Due the limited information currently available, there are still several outstanding issues that need to be highlighted to guide the antenatal counselling and management of women with COVID-19 during pregnancy.

The aim of this study is to review what is known so far about COVID-19 infection during pregnancy.

**Diagnosis**

COVID-19 is diagnosed on the basis of guidance of World Health Organization (WHO). A confirmed case of COVID-19 is defined as a positive result on reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasal and/or pharyngeal swab specimens. The rate of asymptomatic pregnant women tested positive to COVID-19 at RT-PCR nasal and pharyngeal swab ranges from about 25% in referral centers where suspected women are evaluated due to symptoms or exposure and then consequently tested for COVID-19, up to 88% in cohort of women receiving universal screening for SARS-CoV-2.

Antibody response generally needs several days to develop. In a study of 173 patients with COVID-19, the median time from symptom onset to antibody response was 12 days for IgM and 14 days for IgG. In the first week since symptom onset, less than 40 percent had detectable antibodies; after 15 days, IgM and IgG were detectable in 94% and 80%, respectively.

Several serological blood tests have reported, but the diagnostic accuracy of blood antibodies is still unclear. The three most common methods are IgM and IgG title measured by either chemiluminescence immunoassay analysis or enzyme-linked immunosorbent assay (ELISA) and a rapid IgM-IgG combined antibody test. Chemiluminescence has a higher detection rate compared to ELISA in detecting COVID-19, with a sensitivity of IgM and IgG of 48.1% and 88.9%, and a specificity of 100% and 90.9%, respectively.

The rapid combined antibody test is a simple test that can simultaneously detect IgM and IgG antibodies against SARS-CoV-2 virus in human blood within 15 minutes. The overall testing sensitivity is 88.66% and specificity is 90.63%.

**Clinical Features and Maternal Course of COVID-19 in Pregnant Women**

There is still a limited evidence about the clinical course of COVID-19 in pregnant women. Generally, there is a particularly high risk for pregnant women because they are in a special state of immune suppression and they have physiological adaptations occurring during pregnancy, including increase in tidal volume, diaphragm elevation, increased oxygen consumption, reduced buffering capacity to acidosis and decreased functional residual capacity, that make them intolerant to hypoxia and might predispose pregnant women to a more severe course of pneumonia, that is one of the main concern when managing respiratory disorders during pregnancy. In prior pandemics such as SARS and H1N1, pregnant women were indeed more susceptible to severe illness and had greater mortality than general population. Moreover, COVID-19 may predispose the general population to a thrombotic condition, mostly due to inflammation, platelet activation, endothelial dysfunction, and stasis and this hypercoagulability state might intuitively assume an important role in pregnancy due to its inherent prothrombotic state. However, current literature has not elucidated yet the strength of this association in pregnant women affected by COVID-19.

According to the National Institute of Health, the severity of COVID-19 can be classified as: (i) asymptomatic (positive test, no symptoms), (ii) mild (any signs and symptoms without shortness of breath, dyspnea, or abnormal chest imaging), (iii) moderate (lower respiratory disease by clinical assessment or imaging and a saturation of oxygen >93% on room air at sea level), (iv) severe (respiratory frequency >30 breaths per minute, a saturation of oxygen ≤93% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen <300, or lung infiltrates >50%), (v) critical (respi-
Conversely, another classification adopted at the beginning of the pandemic divided COVID-19 clinical course into three stages of disease (the so called Wu’s criteria): (i) mild (no or mild symptoms), (ii) severe (tachypnea, hypoxia, or >50% lung involvement on imaging), (iii) critical (respiratory failure, shock, multiorgan dysfunction). Most of these patients had mild disease and only 1.3% were critically ill.\[^{14}\]

To date, universal screening for SARS-CoV-2 is performed in almost every institution at admission. There are no specific clinical features that can distinguish COVID-19 from other viral respiratory infections, neither in pregnancy nor in non-pregnant women and currently there.

Fever, cough and dyspnea are the most frequent symptoms of COVID-19 during pregnancy, but also upper respiratory tract symptoms, myalgias, diarrhea, and smell or taste disorders are quite common, as well as in the general population. Pneumonia is the most frequent serious manifestation of infection, mostly characterized by bilateral infiltrates on chest imaging.\[^{3,15}\] Laboratory findings usually involve lymphopenia, thrombocytopenia, and abnormal liver enzymes.

When considering severe sequelae of maternal infection, the actual rate of pregnant women admitted to intensive care unit (ICU) ranges from 3% to 5%, with <2% requiring mechanical ventilation.\[^{14}\]

Of note, the incidence of adverse events caused by COVID-19 infection during pregnancy appears to be lower than what previously reported for MERS and SARS infections also in terms of maternal mortality: while the mortality rate in pregnant women affected by SARS and MERS ranged from 25% to 30%\[^{1,4}\] the actual rate of maternal mortality associated with COVID-19 is very low.\[^{16}\]

The largest multicenter study (the WAPM study)\[^{16}\] published in this topic and including 388 pregnant women from 73 different hospitals in 22 countries in Europe, Asia, America and Oceania, showed that in pregnancies complicated by COVID-19 infection, the risk of maternal mortality was 0.8%. Only few other cases published so far reported the occurrence maternal deaths in women generally healthy before the infection.

**Obstetrical and Perinatal Outcomes**

One of the first metanalyses published\[^{17}\] included 19 studies and 79 pregnant women and aimed to explore pregnancy and perinatal outcomes of Coronavirus spectrum infections (defined as either SARS, MERS or COVID-19) occurring during pregnancy. Authors found that hospitalized mothers infected with COVID-19 infection were at higher risk of preterm birth, preeclampsia, cesarean delivery, and perinatal death.

Since then, many other reviews analyzing the association between COVID-19 and obstetrical and perinatal outcomes in larger populations have been published, and results are pretty concordant with these data.

Few data are available for the outcomes of pregnancy when the infection is acquired early in pregnancy. However, the rate of spontaneous miscarriage does not seem to be increased.

Preterm birth (PTB) is one of most frequent complications occurring in pregnancies affected by COVID-19 with an incidence ranging from 15–25%; of note, the majority of the studies does not specify whether PTB was spontaneous or iatrogenic, and it is entirely possible that a considerable part of PTB should be attributed solely to the infection, mostly at the beginning of the pandemic.\[^{17}\]

Furthermore, the incidence of other pregnancy complications, such as preeclampsia, IUGR, SGA and fetal distress was low in the majority of the studies published so far. Certainly, the main concern when managing pregnant women affected by COVID-19 is the risk of adverse perinatal outcomes, and in particular perinatal deaths.

The WAPM study\[^{16}\] reported that the rate of perinatal mortality was 4.2%, with stillbirth occurring in 2.7% (6/265) and neonatal death in 2.0% (5/250) of cases. These data are higher than what previously reported in other reviews, with both stillbirth and neonatal death occurring in less than 1% of cases, and the WAPM study authors acknowledge that, although large, the incidence of the adverse perinatal outcome in the overall population is low, thus making the sample size potentially underpowered to draw any convincing evidence.

When exploring maternal and pregnancy characteristics, authors found that early gestational age at infection, maternal ventilatory supports including either need
for oxygen or CPAP, and low birthweight were the main determinants of adverse perinatal outcomes in fetuses with maternal COVID-19 infection.

Finally, all the studies published so far are concordant about the negligible risk of vertical transmission. Vertical transmission of infection usually occurs during intrauterine life via the placenta, or during delivery via ingestion or aspiration of cervico-vaginal secretions, and in the post-partum period through breastfeeding. The risk of ingestion or aspiration of cervico-vaginal secretions or contact with perineal infected tissue is higher with vaginal delivery. Mother-to-child transmission is one of the main concerns in any case of maternal infection.

No case of clinical evidence of vertical transmission has been reported in a systematic review including 435 newborns from China, United States and Italy. In the WAPM study, only one out of 250 newborns had suspected vertical transmission (vertical transmission rate 0.4%). Amniotic fluid was not tested, and specimens from placenta were not obtained, and the newborn was asymptomatic, with a negative RT-PCR test after 14 days of life, thus leading the authors to question whether the infection occurred in utero or immediately prior or after birth.

Evidence for vertical transmission based on elevated IgM antibody values in blood drawn from the neonates following birth has been reported in two small reports, with no positive RT-PCR, and therefore no clear virologic evidence for congenital infection.

Recently, SARS-CoV-2 RNA on the fetal side of the placenta has been described in two mothers infected with COVID-19 and with neonates also positive for the virus at birth, thus revealing the concrete possibility of a mother-to-child transmission.

The lack of data during first and second trimester allow neither to evaluate whether the infection acquired early in pregnancy is associated with a higher risk of vertical transmission, nor to ascertain whether invasive prenatal diagnosis like amniocentesis, might determinate if fetus is infected.

Mode of Delivery

The rate of cesarean delivery in women affected by COVID-19 has been described to be very high, both in systematic reviews and cohort studies, ranging from 50 to 85%. However, indications for the majority of these deliveries were not available, and it is likely that many cesarean sections have been performed for COVID-19 infection alone.

Based on the limited information from the literature, COVID-19 cannot be considered as an indication for delivery and the timing and mode of delivery should be individualized according to maternal clinical conditions or obstetric factors (and not COVID-19 status alone). The decision should involve a multidisciplinary team including maternal fetal doctors, neonatologists, anesthesiologists and infective disease specialists.

Breastfeeding

The risk of transmission during breastfeeding is largely unknown. Very few reported cases provided information on the risk of newborn infection during breastfeeding. Preliminary data suggest that the virus is not detectable in milk, but different vision remain about breastfeeding and mother-baby contact after delivery.

Elements to consider include clinical conditions of the mother and child, test result of the mother (confirmed or suspected) and mother’s desire to breastfeed. Not least, the negative effects of the separation between mother and child should also be considered.

A mother with suspected, probable, or confirmed COVID-19 should be counseled to take all possible precautions to avoid spreading the virus to her infant, such as wearing a mask and washing her hands.

Moreover, symptomatic mothers who must be separated from their newborns might use pumps to express breast milk.

Management and Therapy

In the absence of obstetric problems, pregnant women with COVID-19 infection and mild disease do not require hospital treatment and they should perform self-isolation at home, similarly to non-pregnant patients. Conversely, pregnant patients with suspected or confirmed COVID-19 infection and more severe symptoms or obstetrical complications need hospital care.

Compared to nonpregnant women, in pregnancy there are some additional issues to consider, such as
fetal monitoring and the maintenance of a good mater-
nal oxygenation level, that COVID-19 infection can compromise, to warrant fetal well-being.\cite{20}

In view of the potential higher risk of thrombotic adverse events, pregnant and postpartum women with COVID-19 admitted to the hospital are frequently treated with low molecular weight heparin (LMWH) for thromboembolism prophylaxis.\cite{20}

Both hydroxychloroquine and chloroquine have been reported to inhibit SARS-CoV-2 in vitro, but their role in treatment of COVID-19 is under investigation.\cite{22}

Data from early randomized trials are mixed and do not suggest a clear benefit. Hydroxychloroquine crosses the placenta. Accumulation in fetal ocular tissues has been observed in animal studies, but fetal ocular toxicity has not been observed in humans, which is reassuring given that the drug has been widely used by pregnant women for treatment of systemic lupus erythematosus or for malaria.\cite{22}

Regarding antiviral drug therapy several agents are being evaluated for treatment of COVID-19, such as Kaletra (Lopinavir/Ritonavir), Darunavir/Cobicistat, Arbidol (Umifenovir), Remdesivir, or Favipiravir.\cite{22}

Some of these agents are clinically available for other indications their use for COVID-19 is still a subject of debate.

Remdesivir is a novel nucleotide analogue that has activity against SARS-CoV-2 in vitro and related coronaviruses included SARS and MERS both in vitro and in animal studies.\cite{21}

A double-blind, randomized, placebo-controlled trial of intravenous Remdesivir in adults hospitalized with COVID-19 with evidence of lower respiratory tract involvement showed that Remdesivir was superi-
or to placebo in shortening the time to recovery.\cite{22}

In the WAPM study pharmacological treatment with LMWH and antiviral drugs was associated with a significantly lower rate of composite maternal outcome, while no difference was found among different therapies when assessing adverse composite perinatal outcomes. In this scenario, the authors conclude that in the absence of proven therapy, currently the care of patients with SARS-CoV-2 should be mostly based on supportive care, and further evidence is needed before drawing any robust conclusion.

### Psychological Impact of COVID-19 in Pregnant Women

The COVID-19 outbreak poses significant risk to public health, including mental health. During pregnancy, women experience elevated levels of stress and anxiety associated with potential adverse obstetrical outcomes such as intrauterine fetal death or fetal abnormalities. Stress and anxiety may also increase during infectious disease outbreaks. A recent cross-sectional survey study aimed to evaluate psychological impact and anxiety in pregnant women during the COVID-19 outbreak in Italy using validated questionnaires.\cite{24}

The study showed that the COVID-19 outbreak had a moderate-to-severe psychological impact on pregnant women. More than two third of the women also reported anxiety higher than the normal. Almost half of the women (46%) reported high anxiety regarding the vertical transmission of the disease.

### Ethical Perspective

The COVID-19 epidemic is necessitating a global bioethics reflection and response. A bioethics and ethics of science and technology perspective, rooted in human rights, should play a key role in the context of this challenging pandemic. On both national and international levels, health and social policies should be based on solid evidence, taking into account the uncertainties that exist during epidemic, especially in case of a novel pathogen. Epidemics clearly expose the strength and weaknesses of the healthcare systems in different countries, as well as the obstacles and inequities of access to healthcare. In summary, from an ethical point of view, there is an urgent need for coordination of international efforts and the formulation of common understanding of ethical review processes.\cite{25}

### Conclusion

The lack of data during the first and early second trimester does not allow to ascertain whether a sero-
conversion during early pregnancy may increase the risk of adverse perinatal outcomes and how it should be treated and monitored once the infection has passed. Another peculiar issue is whether infection before term is associated with a higher severity of pulmonary disease, due to the progressive lung adaptation occurring in the first trimester. However, at the moment there is
no univocal indication for the initiation of intensive maternal surveillance and no defined criteria to identify pregnant women who need mechanical ventilation. Importantly, there is no reported evidence on the type and frequency of fetal monitoring in critically-ill women and if increasing fetal surveillance may reduce fetal morbidities. Future studies should aim at reporting the actual risk of severe disease when infection is contracted in early pregnancy, the most appropriate type and frequency of fetal monitoring and the optimal timing of delivery.

Conflicts of Interest: No conflicts declared.

References


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COVID-19 during pregnancy and its impacts on perinatal health

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Abstract

In this review, we reviewed current literature on COVID-19 infection during pregnancy and provided up-to-date information and community/society recommendations. Although it has previous examples such as SARS and MERS and the infection findings appeared at an earlier period and have become known in China, the infection could not be limited and spread worldwide. Until June 8, 2020, a total of 6.8 million cases were reported and 397,000 cases died. As of the same date, the total case number in Turkey is 171,000 and total number of death is 4711. COVID-19 virus spread by droplets and its incubation period varies between 2 and 14 days. The rate of asymptomatic cases is 42% in non-pregnant patients while it is 44–89% in pregnant women. The disease progresses with mild-medium severity in about 80% of the patients, and it recovers by itself. A total of 17 maternal death cases has been reported. Although vertical transmission risk is very low according to a study investigating 265 pregnant women, there are cases showing fetal vertical transmission and we reviewed such cases in detail in this review.

Keywords: COVID-19, SARS, MERS, pregnancy.

Introduction

The mysterious pneumonia cases appeared in December 2019 attracted the attention of the world to China, and when it became a pandemic, each country started to monitor their situation and case numbers. While the first source of the new member of Coronavirus family, which is later called COVID-19 virus or SARS-Cov-2 or 2019-cCoV, is not known clearly, it was claimed that it is associated with a seafood market in Wuhan, the capital city of China’s Hubei province.1 The case numbers increased gradually, and the new cases were seen in Thailand, Japan, Hong Kong, Taiwan, South Korea and England at the end of January 2020.

COVID-19 virus show similarities with SARS (severe acute respiratory syndrome) and MERS (Middle
East respiratory syndrome) viruses, which are the other members of Coronavirus family. While there were 6 known types of Coronavirus until December 2019, this number reached 7 with the appearance of COVID-19. Non-SARS and non-MERS 4 members (HKU1, OC43, 229E, NL63) are associated with seasonal common cold, and they are responsible for 10% of non-influenza seasonal airway disease. MERS appeared in Saudi Arabia in 2012, and its R0 rate is less than 1 with a case-fatality rate of 34.4% (CFR) (858/2494).\(^2,^3\) R0 is an index showing how contagious is an infection and the average number of people who will contract an infection from one person. SARS pandemic was seen in 2002–2003, and its R0 rate was 2–4 with a case-fatality rate of 10.5% (774/8098).\(^4,^5\) While case-fatality rate is usually 0.5% in the seasonal flu, its R0 rate is 1.2–1.6.\(^6–^8\) The general characteristics of Coronavirus types and influenza H1N1 are shown in the Table 1.

The mortality rate of COVID-19 is associated with the age of patient and coexisting diseases, and it varies across countries. The overall mortality rate in China was reported 2.3% in the beginning, but it may increase up to 14.8% in cases over 80 years old. The mortality rates may increase up to 6% with coexisting hypertension, 7.3% with coexisting diabetes and 6.3% with coexisting chronic respiratory pathologies.\(^9\) However, it is accepted that the mortality rate of COVID-19 is higher than influenza.

Although it has previous examples such as SARS and MERS and the infection findings appeared at an earlier period and have become known in China, the infection could not be limited and spread worldwide. World Health Organization (WHO) held a meeting on January 22, 2020 and the Organization did not accept that COVID-19 infection was an international public health emergency, and the pandemic decision could only be made on March 11 by WHO. While the data of WHO on February 3 showed that there were 17,238 cases and 361 deaths in China, the number of diagnosed cases exceeded 3 million and 208,000 cases died as of April 27. In June 8, 2020, a total of 6.8 million cases were reported in the world and 397,000 cases died. As of the same date, total case number was 171,000 and death number was 4711 in Turkey.

COVID-19 virus spread by droplets.\(^10\) Its incubation period varies between 2 and 14 days (the mean period is 5.2 days).\(^11,^12\) It is known that the course of disease can be asymptomatic. While asymptomatic infection rate is about 42% in non-pregnant patients,\(^12\) it was reported between 44% and 89% in pregnant women.\(^13–^15\) The disease progresses with mild-medium severity in about 80% of the patients, and it recovers by itself. It is severe in 13.8% of the patients, and at a critical level in 6.8% of the patients.\(^16\) In this review, we reviewed current literature on COVID-19 infection during pregnancy and provided up-to-date information and community/society recommendations.

### Pregnancy and Pneumonia

Independently of COVID-19, pneumonia is one of the most important reasons of morbidity and mortality in pregnant women and the most common non-obstetric infection reason during pregnancy.\(^16\) Intensive care treatment may be required in 25% of patients due to the pneumonia.\(^17\) When compared to bacterial pneumonia cases, morbidity and mortality rates are higher in viral pneumonia cases.\(^18\) Premature rupture of membranes (PRM), preterm labor, stillbirth, fetal growth restriction and neonatal death are the most important complications of pneumonia during pregnancy.\(^17,^19,^20\)

### The Relationship Between Pregnancy and SARS, MERS and Influenza

Before investigating the relationship between pregnancy and COVID-19, it would be better to assess the relationship between pregnancy and other Coronavirus types and influenza virus, because the lessons that can be taken from these viruses may guide us with the fight with this new and young member of the family.

In terms of the course of other Coronavirus types during pregnancy, which cause significant pandemic, except COVID-19 infection (Table 2), it was reported that the rate of hospitalization in the intensive care unit due to SARS-CoV infection in pregnant women during SARS pandemic was 50%.\(^3\) It was observed that SARS-

### Table 1. Coronavirus types and the general characteristics of influenza H1N1.

<table>
<thead>
<tr>
<th></th>
<th>Genome</th>
<th>Case-fatality rate</th>
<th>R0</th>
</tr>
</thead>
<tbody>
<tr>
<td>MERS</td>
<td>RNA</td>
<td>2.7–34.4%(^{12,18})</td>
<td>&lt;1(^9)</td>
</tr>
<tr>
<td>SARS-CoV</td>
<td>RNA</td>
<td>10.5–25%(^{4,21})</td>
<td>2–4(^5)</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>RNA</td>
<td>1.3–3.85%(^{10,11})</td>
<td>2–2.5%(^{11})</td>
</tr>
<tr>
<td>Influenza H1N1</td>
<td>RNA</td>
<td>0.5%</td>
<td>1.2–1.6(^{14})</td>
</tr>
</tbody>
</table>
CoV infection during pregnancy has negative impacts on gestational outcomes. Abortion was reported in 57% of the women who had SARS-CoV infection during the first trimester, and fetal growth restriction in 40% of them and preterm labor in 80% of them during the second trimester.[21]

In MERS pandemic, the rate of hospitalization in the intensive care unit due to MERS-CoV infection in the pregnant women was reported 63.6%. It was seen that the poor gestational outcomes increased in MERS infection during pregnancy (91%) similar to SARS-CoV infection, and 55% of the newborns required hospitalization in the newborn intensive care unit.[22] No maternal-fetal vertical transmission was observed in SARS and MERS pandemics.[23]

When it comes to influenza which is another factor for respiratory tract infection, 1918 Spanish flu, 1956 Asian flu and 2009–2010 influenza pandemics are the significant ones. In the influenza pandemic called Spanish flu which occurred in the winter of 1918–1919 causing 500 million people to contract the disease and 40–70 million people to die, the mortality rate is 27% in the pregnant women and this rate reached 50% when the disease was complicated with pneumonia.[24]

In the pandemic that appeared in Asia in 1957 due to influenza A (H2N2) and caused 1.1 million people to die of which 116,000 were in the United States of America (USA), 50% of the death cases among women in reproductive period were pregnant.[25] In the spring of 2009, the pandemic which appeared due to influenza H1N1 which was also called swine flu was first seen in the USA and spread worldwide rapidly. According to the data of CDC, it is estimated that 151,700 – 575,400 people died in the year that H1N1 pandemic appeared. Similar to other flu viruses, the complication rates in this virus were also higher in pregnant women. Although only 1% of the US population consists of pregnant women, H1N1 virus infection during pregnancy is responsible for 6.3% of pandemic-related hospitalization rates, 5.9% of hospitalization in the intensive care unit and 5.7% of death cases.[26,27] The severity of disease increased with the progress of the week of gestation. The most severe cases were in the third trimester of gestation.[27] The death rate of H1N1 pandemic during pregnancy is between 8.2% and 9% and the rate decreases when the antiviral treatment is initiated within the first 3 days of infection.[28]

It was found in significant studies including broad patient groups that the influenza infection during pregnancy had a severe course also during non-pandemic periods compared to non-pregnant population and required more hospitalization.[28] In coexisting morbidity cases such as chronic heart and lung disease, diabetes, chronic kidney, cancer and suppressed immunization during pregnancy, this risk increases at least 3 times. The severity of H1N1 virus infection in pregnancy during non-pandemic periods also increases as the week of gestation proceeds and the most severe cases are seen during the third trimester of gestation.[27]

### COVID-19 and Pregnancy

When it comes to COVID-19 infection during pregnancy, COVID-19 was first reported in China as it appeared in this country first. The first study included the pregnant women population in Wuhan and 9 pregnant women who were diagnosed between January 20, 2020 and January 31, 2020 were reported.[10] The second manuscript is on “pregnant patient population in Hubei” and it reported the results of 9 patients and 10 newborns.[11] The clinical courses of these 19 pregnant women in total in these first 2 studies are similar to the non-pregnant patients; all pregnant women had pneumonia and there were typical infiltrates in their lung CTs. None of the

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**Table 2. Coronavirus types and gestational complications.**

<table>
<thead>
<tr>
<th></th>
<th>Case-fatality rate</th>
<th>Rate of hospitalization at intensive care</th>
<th>Preterm labor before 37 weeks</th>
<th>Preterm labor before 34 weeks</th>
<th>Preeclampsia</th>
<th>Preterm rupture of membranes</th>
<th>Intrauterine growth restriction (IUGR)</th>
<th>Delivery by cesarean section</th>
</tr>
</thead>
</table>
pregnant women needed mechanical ventilation and no death was reported. A total of 5 patients had PRM. Seventeen of the patients in these 2 studies delivered by cesarean section while 2 of them delivered vaginally. No infection was found in the newborns and placentas of these patients. While elevated cardiac enzymes were detected in a newborn in a Wuhan group, DIC-related death occurred in a baby born at 34.5 weeks of gestation. In the review of 6 studies conducted by Della Gatta et al. in April 2020, the authors reviewed 51 pregnant patients. The diagnosis was established by qRT-PCT in 50 of these 51 patients, one patient could be diagnosed as it was consistent with clinical COVID-19 and other potential factors were ruled out. In this review, the median maternal age was 30, median week of gestation during diagnosis was 36, median week of labor was 36.5, and 39% of the patients underwent preterm labor. The median of the period from the development of symptoms up to labor is 2 days. The symptoms developed after labor in 3 patients. During admission, 48% of the patients had fever and 46% of them had dry cough. Other rare symptoms are sore throat, dyspnea, fatigue, malaise, myalgia, diarrhea, and cholecystitis. Pregestational comorbidities such as hypertension, diabetes or cardiovascular diseases were not reported. Gestational hypertension was seen in one patient, preeclampsia in patient and influenza infection coexisting with COVID-19 in one patient. Two of the pregnant women were at the second trimester and 49 of them were at the third trimester during the diagnosis. The cesarean section was performed in 46 of 48 patients whose pregnancy were terminated. PRM developed in 26% of the pregnant women. Severe pneumonia requiring the use of ECMO developed in one of the pregnant women and stillbirth occurred. While there were typical findings in the lung tomography scan in 22 patients, lung tomography results of one patient were normal. Of the newborns, 48 had good health, but one newborn was stillbirth as stated above. In addition, one baby which was born at 34.5 weeks of gestation died on 9th day, but the test result of COVID-19 was negative. No fetal vertical transmission was observed in this review.

The review in which 108 COVID-19 positive pregnant women were reviewed was published by Zaigham and Andersson. Of the patients, 68% had fever and 34% had fever. Lymphocytopenia was found in 59% of the patients, and elevated CRP in 59% of the patients. 91% of the pregnant women delivered by the cesarean section and three pregnant women required intensive care, but maternal mortality was not observed. Stillbirth was observed in one baby and neonatal death in one baby.

Afterwards, one of the biggest series was published in China. In the study evaluating 116 pregnant women with COVID-19 infection, the authors found severe pneumonia in 8 patients, but did not observe any maternal death. Eight of 116 pregnant women were detected in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5%). Preterm labor before 37 weeks of gestation was observed in 6 patients (6.1%), negative result was obtained in 86 newborns who underwent PCR test.

A total of 324 patients were evaluated in the systematic review of 9 case series and 15 case reports in May 2020. Of these patients, 211 (71.5%) were diagnosed by laboratory findings and 84 (28.5%) by clinical findings. The most common symptoms during the admission of pregnant patients were fever, cough, respiratory distress, fatigue and myalgia. Severe pneumonia was found in 0–14% of the patients who required intensive care. PCR tests were conducted on the vaginal secretion of 6 patients and on breast milk of 22 patients, and all results were reported negative. Spontaneous abortion was reported in 4 patients. The weeks of labor were 28–41 and 74.2% of them underwent the cesarean section. The authors reported that the preeclampsia risk did not increase in the pregnant women with COVID-19. One third of the newborns were followed up in the postpartum period was found higher than the non-pregnant women who are at similar ages.

COVID-19 binds to cells via ACE-2 receptor. ACE2 RNA expression is very low in the placenta during 6–14 weeks of gestation, and therefore it was asserted that the risk of placental transmission during first trimester is low. However, it was reported that pregnancy loss may be observed due to maternal respiratory distress and hypoxemia. Some inconsistencies were observed between the first manuscripts in the literature related with COVID-19 infection in pregnant women and abort-
tion risk. The first study on this topic is a review published in Iran.\[39\] This manuscript attributed the increase of abortion risk in COVID-19 to another manuscript,\[40\] but when that manuscript was reviewed, it was seen that SARS virus was reported as the virus increasing abortion risk but it did not mention COVID-19 infection and abortion risk. The second manuscript was published in Am J Obstet Gynecol, but the reference was not cited.\[41\] Again, although it was reported in another manuscript that the abortion risk increased in coronavirus infections, the increased rates were shown for MERS and SARS infections but not COVID-19.\[42\] According to the review published on April 17, 2020, COVID-19 infection has not been reported yet in the first trimester.\[43\] According to another review published in China, 8 of 116 COVID-19 positive pregnant women were detected in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5\%).\[14\] In another review evaluating the results of 324 pregnant women, pregnancy loss in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5\%).\[14\] Again, although it was reported in another manuscript that the abortion risk increased in coronavirus infections, the increased rates were shown for MERS and SARS infections but not COVID-19.\[42\] According to the review published on April 17, 2020, COVID-19 infection has not been reported yet in the first trimester.\[43\] According to another review published in China, 8 of 116 COVID-19 positive pregnant women were detected in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5\%).\[14\] In another review evaluating the results of 324 pregnant women, pregnancy loss in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5\%).\[14\] Again, although it was reported in another manuscript that the abortion risk increased in coronavirus infections, the increased rates were shown for MERS and SARS infections but not COVID-19.\[42\] According to the review published on April 17, 2020, COVID-19 infection has not been reported yet in the first trimester.\[43\] According to another review published in China, 8 of 116 COVID-19 positive pregnant women were detected in the first trimester or early second trimester and abortion was observed in one of these pregnant women (1/8; 12.5\%).\[14\]

The cases which have COVID-19 infection during pregnancy do not have more risk than non-pregnant women, and COVID-19 infection does not cause more severe infections in pregnant-women unlike other respiratory tract infections.\[41\] According to the review conducted on 147 pregnant patients in China by the World Health Organization in February 16–24, 2020, severe infection risk does not increase in pregnant women by COVID-19 infection unlike influenza.\[2\]

COVID-19 infection may also affect the conception plan of individuals. In an Italian study evaluating 1482 individuals, 37.3% of individuals with previous conception plan abandoned their conception plan.\[46\] According to a study published in Turkey, sexual desire and the frequency of sexual intercourse increased in women while desire for pregnancy decreased.\[47\]

Maternal mortality after COVID-19 infection during pregnancy was not reported in the first periods of pandemic, and it was asserted that the morbidity did not increase during pregnancy.\[48–51\] This was considered suspicious as maternal mortality cases were reported with MERS and SARS in the previous Coronavirus pandemics. However, a total of 17 maternal death cases consisting of 1 case from Iran,\[52\] 7 cases from Iran,\[53\] 1 case from Iran\[54\] and again 2 cases from Iran,\[55\] 1 case from England,\[56\] 1 case from the USA,\[57\] 1 case from Sweden\[58\] and 3 cases in the study of the World Association of Perinatal Medicine which is in publication process\[59\] were reported afterwards. It is impossible to calculate mortality rate during pregnancy in COVID-19 infection as the reports are currently in the form of case reports. It was also claimed that the increased rate of maternal mortality may not be associated with infection only, it may occur due to the use of uterotonic, antiepileptic and antibiotic drugs less than normal due to the decreased rates of admission to hospital and the low number of clean delivery units as a result, and 12,000 additional maternal mortality cases may be added within 6 months to the annual worldwide mortality rate even in the lowest severe scenario according to the modelling created.\[59\]

Covid-19 and Vertical Fetal Transmission

The most feared impact of maternal infection is the fetal exposure associated with vertical transmission. When any infection is transmitted to fetus from mother, the fetal exposure level may change depending on the variables such as the infection agent type, week of gestation and delivery type. The evidences showing the existence of fetal infection are the typical morphological changes and pathological and laboratory tests shown in baby. Congenital Zika virus infection can be given as an example for morphological exposure. In this infection, microcephaly was found in the newborns and this was shown as the evidence of Zika viral infection.\[60\] Fetal infection diagnosis can be established specifically by pathological and laboratory tests. However, it is important to conduct these tests properly and on time, and by the nature of the tests, it should be noted that false positive and negative results may be obtained. It is very important to show viral agent pathologically in the fetal organ systems or to produce culture in the samples collected; however, it is not possible in most of the viral agents. Finding COVID-19 viral nucleic acid in adults by using RT-PCR is reference standard diagnostic test. Viral agent can also be found by serological tests. In terms of infection diagnosis, it is significant to detect IgM in cord blood or fetal circulation because maternal IgG may pass through placenta but IgM cannot. The sensitivity and specificity of anti-SARS-CoV-2 IgM are 70.2–88.2%
and 96.2–99%, respectively, and therefore further studies are needed for COVID-19 diagnostic performance.\[37,61\] According to the recommendation of Turkish Neonatal Society, positive respiratory tract or blood test is needed for proven neonatal COVID-19 diagnosis.\[62\]

Although it was claimed that possibility of detecting the virus in placenta is low as the viremia in the symptomatic COVID-19 patients is 1% and temporary, SARS-CoV-2 positivity in the placenta was shown in the following studies.\[5\] In a study conducted in New York, USA, 32 SARS-CoV-2 positive pregnant women were evaluated, swab samples were collected from the amnionic surface of placenta and from the surfaces between amnion and chorion in 11 of these patients, and SARS-CoV-2 positivity was found in 3 of these 11 patients.\[63\] In the study evaluating the placentas of 16 COVID-19 positive pregnant women, the authors reported that maternal vascular malperfusion, abnormal or damaged maternal vessels and intervillous thrombus were observed more in these placentas than the control placentas, but acute and chronic inflammation did not increase.\[64\] Similar placental findings were also reported from the USA.\[65\] In the placental examination performed after the pregnancy was terminated due to preeclampsia and placent detachment in a 22-week pregnant woman, SARS-CoV-2 positivity and intense macrophage accumulation in syncytiotrophoblasts were reported.\[66\]

The study which evaluated 47 pregnancies and 46 neonatal outcomes has been the one of the greatest reviews on fetal transmission so far, and it provides evidences for and against fetal transmission.\[57\] According to the study evaluating 265 pregnant women who gave birth, vertical transmission risk was quite low.\[69\] In a case report published in April 2020, it was claimed that fetal vertical transmission is possible.\[69\] In this report, it was seen that the baby of the pregnant woman, who needed mechanical ventilation on the fifth day of the disease and delivered by the cesarean section, had COVID-19 PCR positivity, tested at 16th hour and confirmed at 48th hour, and intrauterine transmission was considered as the reason. However, amniotic fluid, cord blood and placental infection were not examined in this case. In the case report from China published in the March issue of JAMA, Dong et al. found ground-glass opacities consisted with viral pneumonia in the thorax CT scan performed in the clinic in a 29-year-old and 34-week and 2-day pregnant woman who applied for fever (37.9°C) and nasal congestion complaints on 28/01/2020, and the swab sample collected from the nasopharynx showed SARS-CoV-2 PCR positivity.\[68\] The pregnant woman was hospitalized and medical treatment was initiated, and consecutive 4 PCR tests also yielded positive results. In the blood antibody test performed on 21/02/2020, the IgG value of the patient was 107.89 AU/mL and IgM value was 279.72 AU/mL, and the pregnant woman delivered by the cesarean section by using N-95 mask in negative isolation room on 22/02/2020. The baby which was born 3120g was quarantined in the newborn intensive care unit without any contact with the mother. In the blood sample taken 2 hours after birth of the baby which showed no symptom, SARS-CoV-2 IgG and IgM levels were found 140.32 AU/mL and 45.83 AU/mL, respectively. It was also found that the cytokine levels (IL-6: 28.26 pg/mL; IL-10: 153.60 pg/mL) and leucocyte count (18.08×10^9/L) of the newborn were elevated. The thorax CT scan was evaluated normal. Swab samples were collected 5 times from the nasopharynx between the postnatal 2nd hour and 16th day, and all SARS-CoV-2 PCR tests yielded negative results. In the SARS-CoV-2 test performed on the newborn on 07/03/2020, IgG level was 69.94 AU/mL and IgM level was 11.75 AU/mL, which were still high. The newborn was discharged on 18/03/2020. The RT-PCR test yielded negative result on the breast milk sample collected from the mother on 28/03/2020, mother’s SARS-CoV-2 IgG and IgM levels were found 116.30 AU/mL and 112.66 AU/mL, respectively, and medium level resolution was observed in the ground-glass opacities in thorax CT scan. Although RT-PCR was not tested on placenta and amniotic fluid in this case report, the study provides valuable data in terms of showing IgM antibodies in the newborn just two hours after the birth. Considering that IgM antibodies does not exhibit transplacental transmission and IgM antibodies are not produced until 3–7 days after the acute infection, this publication is a significant case report in terms of presenting a case which suggests that a fetus exposed to maternal infection for 23 days during intrauterine period may contract COVID-19 infection through vertical transmission.\[68\] Some other studies were also published showing vertical transmission after these studies. The summaries of the studies suggesting fetal vertical SARS-CoV-2 transmission are presented in the Table 3.
Table 3. The summaries of the studies asserting fetal vertical SARS-CoV-2 transmission.

<table>
<thead>
<tr>
<th>Study</th>
<th>Newborn characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patane et al. (Italy)</td>
<td>In 22 mothers with positive SARS-CoV-2 PCR result: the nasopharyngeal swabs of 2 newborns were positive for SARS-CoV-2. 1st newborn: Vaginal birth, 37.6 weeks, 2660g, 9–10 Apgar, cord pH: 7.28, staying in the same room with mother, and being breastfed. The nasopharyngeal swab right after birth, positive at 24th hour and 7th day, the newborn was asymptomatic and discharged on 10th day. Chronic intervillitis of the placenta, there were macrophages and syncytiotrophoblasts were positive for SARS-CoV-2 RNA. 2nd newborn: Cesarean section (unreliable NST), 35.1 weeks, 2668g, 9–10 Apgar, cord pH: 7.32. The newborn was taken to the follow-up in the newborn intensive care unit. The nasopharyngeal swab right after birth was negative, but positive at 7th day. The asymptomatic newborn was discharged on 20th day. Chronic intervillitis of the placenta, there were macrophages and syncytiotrophoblasts were positive for SARS-CoV-2 RNA.</td>
</tr>
<tr>
<td>Zamaniyan et al. (Iran)</td>
<td>The nasopharyngeal swab of 1 newborn was negative for SARS-CoV-2 but IgG and IgM were positive in 1 mother</td>
</tr>
<tr>
<td>Yang et al. (China)</td>
<td>The nasopharyngeal swab of 1 newborn was negative for SARS-CoV-2 but IgG and IgM were positive in 7 mothers with positive SARS-CoV-2 PCR result. 37 weeks, vaginal birth, 3120g, 9–10 Apgar, cord pH: 7.18, staying in the same room with mother, and being breastfed. The nasopharyngeal swab of the asymptomatic newborn was positive at 37th hour. The newborn was in good health.</td>
</tr>
<tr>
<td>Dong et al. (China)</td>
<td>The nasopharyngeal swab of 1 newborn was negative for SARS-CoV-2 in 1 mother with positive SARS-CoV-2 PCR result. 40 weeks, C/S labor, 3205g, 8–9 Apgar, follow-up in the newborn intensive care. Lymphopenia, impaired LFT, and elevated creatinine kinase were detected in the newborn. Nasopharyngeal swab at 36th hour is SARS-CoV-2 positive. Cord blood, placenta and breast milk were negative for SARS-CoV-2. The nasopharyngeal and anal swabs at 16th day were negative, discharged at 17th day.</td>
</tr>
<tr>
<td>Zeng L et al. (China)</td>
<td>Nasopharyngeal swabs of 3 newborns were positive for SARS-CoV-2 in 33 mothers with positive SARS-CoV-2 PCR result. 1st newborn: 40 weeks, CS birth (amniotic fluid with meconium and COVID-19 pneumonia in mother). Lethargy and fever in the newborn on postnatal 2nd day and the pneumonia in the chest radiography. The laboratory tests were normal. The nasopharyngeal and anal swabs were negative on the 2nd and 4th day, and negative on the 6th day. 2nd newborn: 40.4 weeks, CS birth (COVID-19 pneumonia in the mother). Lethargy, vomiting and fever in the newborn after birth and the pneumonia in the chest radiography. Leukocytosis, lymphopenia and elevated creatine kinase in the laboratory tests. The nasopharyngeal and anal swabs were positive on the 2nd and 4th days, and negative on the 6th day. 3rd newborn: 31.2 weeks, CS birth (fetal distress and COVID-19 pneumonia in the mother). Resuscitation needed, and Apgar scores were 3, 4 and 5. Postnatal RDS and pneumonia. Additionally, sepis, leukocytosis, thrombocytopenia and coagulopathy. The nasopharyngeal and anal swabs were positive on the 2nd and 4th days, and negative on the 7th day.</td>
</tr>
<tr>
<td>Alzamora et al. (Peru)</td>
<td>The nasopharyngeal swab of 1 newborn was positive for SARS-CoV-2 in 1 mother who was positive for SARS-CoV-2 PCR. 33 weeks, CS birth, 2970g, 6–8 Apgar, the newborn was intubated as mother’s sedation level was high. Separated from the mother, followed up in the newborn intensive care unit and not provided breast milk. IgG and IgM values of the newborn were negative. The nasopharyngeal swab was negative at 16th and 48th hours. On 6th day, the newborn had mild dyspnea and needed oxygen.</td>
</tr>
<tr>
<td>Dong et al. (China)</td>
<td>1 newborn of 1 mother with positive SARS-CoV-2 PCR result was evaluated. 37.6 weeks, CS birth, 3120g, 9–10 Apgar. Separated from the mother, followed up in the newborn intensive care unit. SARS-CoV-2 IgG and IgM were positive at 2 hour. IL-6 elevated and leucocytosis was present. 5 nasopharyngeal swabs from 2nd hour to 16th day were negative. The newborn was discharged on 25th day. The breast milk was PCR negative.</td>
</tr>
<tr>
<td>Ferrazzi et al. (Italy)</td>
<td>The nasopharyngeal swabs of 3 newborns were positive for SARS-CoV-2 in 42 mothers with positive SARS-CoV-2 PCR result. 2 postpartum mothers were diagnosed with COVID-19, and they breastfed their babies during this period without wearing mask, and the newborns were found to be positive for SARS-CoV-2. Third newborn was separated due to postpartum bleeding, and the mother was diagnosed with COVID-19 in the following days, and the test result of the newborn was also positive.</td>
</tr>
<tr>
<td>Yu et al. (China)</td>
<td>The nasopharyngeal swab of 1 newborn was positive for SARS-CoV-2 in 7 mothers with positive SARS-CoV-2 PCR result. The newborn was found to be positive for SARS-CoV-2 at postnatal 36th hour. Following 2 tests of the newborn whose mild respiratory distress improved were negative, and the newborn was discharged in 2 weeks. It was reported that the intrauterine transmission may not be the case in this pregnancy as placenta and cord blood were negative for SARS-CoV-2.</td>
</tr>
<tr>
<td>Yang et al. (China)</td>
<td>The nasopharyngeal swab of 1 newborn was negative for SARS-CoV-2 but IgG and IgM were positive in 7 mothers with positive SARS-CoV-2 PCR result. In the rapid test of the baby born by cesarean section due to PRM at 30.6 weeks of gestation, SARS-CoV-2 IgG and IgM were found positive, 2 PCR tests resulted negative. The newborn was discharged at 29th day.</td>
</tr>
<tr>
<td>Zamanian et al. (Iran)</td>
<td>The nasopharyngeal swab of 1 newborn was negative for SARS-CoV-2 but IgG and IgM were positive in 1 mother with positive SARS-CoV-2 PCR result. 32 weeks, SARS-CoV-2 pneumonia in mother, sample was collected from the amniotic fluid during labor by CS. The newborn was 2350g, 8-9 Apgar. The first nasal and throat swabs of the newborn were negative, but amniotic fluid was positive for SARS-CoV-2. The newborn swab at 24th hour was positive. The mother died, but the newborn is in good health.</td>
</tr>
<tr>
<td>WAPM study</td>
<td>The nasopharyngeal swab of 1 newborn was positive for SARS-CoV-2. In the asymptomatic newborn with positive nasopharyngeal swab right after the birth, PCR was negative on 14th day. Amniotic and placental samples were not tested.</td>
</tr>
<tr>
<td>Caroso et al. (Italy)</td>
<td>The nasopharyngeal swab of 1 newborn was positive for SARS-CoV-2. 37 weeks, vaginal birth, 3120g, 9–10 Apgar, the nasopharyngeal swab of the asymptomatic newborn was positive. The nasopharyngeal swab at 37th hour was negative, placental swab was negative, SARS-CoV-2 IgG was positive and IgM was negative in the cord blood.</td>
</tr>
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</table>
COVID-19 and Breastfeeding Period

Breastfeeding after delivery in patients who have COVID-19 infection is discussed by neonatology societies, and the policies vary in each country. According to the recommendation of Public Health General Directorate of the Turkish Ministry of Health, breastfeeding can be done by taking measures after advising mother and providing necessary information. Accordingly, if mother wants to breastfeed her baby, it can be done by wearing medical/surgical mask after ensuring hand hygiene. If mother wants to extract breast milk, it can be done by ensuring hand hygiene, cleaning nipple and wearing medical/surgical mask.

Management of COVID-19 Infection in Pregnant Women

As asymptomatic virus spread is possible, it is recommended to do COVID-19 test to all pregnant women who apply to some centers for labor; however, most of the centers cannot do these tests. According to a study conducted in New York, USA, 33 (15.4%) of 215 pregnant women who applied to hospital for labor between March 22 and April 4 were found SARS-CoV-2 positive, and 29 (88%) of these 33 patients were asymptomatic. In another study conducted in England and it was found that 8 (88.9%) of 9 patients with positive results were asymptomatic. In a similar study, 8 (88.9%) of 9 pregnant women who applied for labor were found SARS-CoV-2 positive, and 29 (88%) of these 33 patients were asymptomatic. Therefore, the perception that the pregnant women without symptom do not have the disease should be changed, and personal protection and hygiene rules should be followed assuming that each visiting individual is a potential patient.

During the pandemic, it was made compulsory to wear mask for healthcare professionals in most of the hospitals who are in contact with patients. Healthcare professionals, who contact with pregnant women that are diagnosed with COVID-19 infection or suspected to have infection due to contact, should use personal protective equipment. Visiting policies should be reviewed in order to decrease the infection risk of patients and visitors. The patients applied for labor should stay in the same room as much as possible, and it should be avoided to change rooms.

Various societies have different algorithms in the presence of suspected COVID-19 infection in a pregnant patient. As the patient number increases, algorithms also become diversified. The algorithm of the American College of Obstetricians and Gynecologists (ACOG) has been updated on May 19, 2020. The algorithms of the International Federation of Gynecology and Obstetrics (FIGO) on COVID-19 during pregnancy and at labor were prepared by Poon et al. The consensus report containing the experience of China in which the infection appeared first has a pregnancy follow-up algorithm. There is an opinion manuscript about “New Coronavirus Infection 2019” during pregnancy, labor and postpartum period published by Turkish Perinatology Society.

Under today’s conditions, the best precaution method is to protect ourselves as there is no primary treatment and vaccination for COVID-19 infection. Social isolation should certainly be practiced in regions with intense infection. It is recommended to keep at least 1.5 m distance among individuals in crowded areas where contact potential increases. It was shown that social isolation decreases the rate of pandemic. Hygiene rules should be followed, hands should be washed by soap for at least 20 seconds after contacting with objects such as computers, mobile phones, door handles etc. which are used commonly, and face, eyes, mouth and nose should not be touched by hands after any contact. Cleaning shared areas is also important. Pregnant women should be careful in the waiting rooms of healthcare centers. Pregnant women with high risk, who are diagnosed with COVID-19 infection and whose examinations still continue, should be isolated and these patients should stay away from general pregnant women population. It is important to establish centers that only the pregnant women in the same categories can apply in order to enable these pregnant women to apply under emergency conditions.

It is unknown how much routine follow-up frequencies of pregnant women will change or have to change due to COVID-19 infection. In order to decrease the contagion risk, the follow-up frequency in physical examination form at hospitals can be decreased in pregnant women with low risk in particular, and the remaining follow-ups can be maintained as tele-healthcare services via phone/Internet. Although it is not certainly known which patients have less risk, Dotters et al. reported that risky pregnancies are under lower risk in cases such as hypothyroidism, smoking, absence of medical complication, previous cesarean section, advanced maternal age (<40 years), IVF pregnancies, obesity class...
respectively. The radiological findings in pregnant women with COVID-19 positivity are similar to the findings of non-pregnant patients.\(^{44}\)

Maternal lung ultrasound scan can be used for the diagnosis of COVID-19 infection. Thickened pleural line and “white lung” exhibiting distribution in patched form together with generalized hyperechoic vertical artifacts in the lung ultrasound scan are the typical ultrasound findings.\(^{80}\)

Pregnant women with mild COVID-19 infection without any coexisting morbidity can be followed at home by resting, hydration and symptomatic treatments. Gestational follow-ups of these pregnant women can be done by phone.\(^{89}\) Fetal growth should be followed up closely in pregnant women who recover from COVID-19 infection but not give birth yet, because it is known that fetal growth is slowed down in other respiratory viruses causing severe infection.\(^{80}\) The use of non-steroidal anti-inflammatory drugs during COVID-19 infection is controversial. However, as there is no data confirming it, ACOG recommends pregnant women with preeclampsia risk using aspirin.\(^{81}\) On the other hand, it was also recommended discontinuing aspirin and not taking again until full recovery if a patient using prophylactic aspirin is diagnosed with SARS-CoV-2 as aspirin may cause severe bleeding in pregnant women who particularly contract COVID-19 infection at the 3rd trimester and are thrombocytopenic.\(^{82-84}\) If there is no medical indication in COVID-19 positive pregnant women who undergo ambulatory follow-up and are on 3rd trimester, 14-day quarantine should be waited to end before labor induction or planned cesarean section or negative test result should be waited.\(^{81}\)

If week of gestation is below 34 weeks in a pregnant woman who applies for preterm labor and has COVID-19 infection, corticosteroid use should be customized for lung maturation. If it is above 34 weeks, corticosteroids should not be used even though preterm labor risk is high, because it was asserted that steroids may exacerbate the prognosis in non-gestational COVID-19 infections.\(^{86}\) Acute progressive coagulopathy may develop in pregnant women contracting COVID-19 infection during third trimester. Therefore, the predisposition towards bleeding during prenatal and postnatal periods should be taken into consideration in the patients.\(^{86}\)

**Treatment in Pregnant Women with Suspected/Potential COVID-19 Infection**

The pregnant women with suspected, potential or confirmed COVID-19 infection should be followed up ideally in tertiary centers which are capable of providing isolation and taking protective measures. The pregnant women with suspected or potential COVID-19 infection should be isolated, and the pregnant women with confirmed COVID-19 infection should be followed up in negative-pressure rooms.\(^{87}\) In its management, fluid and electrolyte balance is paid attention and symptomatic treatment is administered by antipyretic and antidiarrheic agents. Ibuprofen can be used when necessary.\(^{85}\) Vital findings and oxygen saturation level should be monitored closely to keep maternal hypoxia at minimum level, arterial blood gas should be checked, lung imaging should be repeated when necessary, and full blood count, kidney and liver function tests and bleeding parameters should be measured regularly. Cardiotocography should be used for fetal heart beats after 23–28 weeks of gestation and gestational follow-up should be done according to clinical condition. The appointments should be delayed during isolation or until positive result or 2 negative results are obtained.
Treatment in Pregnant Women with Confirmed COVID-19 Infection

Mild disease: Fluid and electrolyte balance is paid attention, and symptomatic treatment is administered by antipyretic and antidiarrheic agents. Although there are drawbacks about the use of ibuprofen, WHO does not state that it should not be used.

There is no special antiviral treatment for COVID-19 infection. The antiretroviral drugs are used in the patients with severe symptoms. Currently, remdesivir and chloroquine are the strongest candidates for the use in this infection. While the use of remdesivir, of which in vitro effect was shown for COVID-19, seems safe in pregnant women, its Phase 3 studies have been conducted. A case on remdesivir use during pregnancy and the use of plasma obtained from a recovered patient was also reported. Chloroquine phosphate which is an antimalarial drug has antiviral and immunomodulator effects, and it causes COVID-19 to regress clinically, radiologically and serologically. There are evidences showing that lopinavir-ritonavir (LPV/r) may help in the treatment of COVID-19. Although there is no evidence for its safety in pregnant women with COVID-19, it was shown in the studies conducted on the pregnant women with HIV that it did not increase the risks for fetal anomaly, preterm labor and low birth weight. Ribavirin and baricitinib should not be used as they are fetotoxic. For now, the directives of the healthcare institutions of the countries should be followed for drug use, and the consents of patients should be obtained for the drugs to be used in pregnant women. Bacterial infections should be monitored by blood and urine culture tests, necessary treatments should be provided in case of any secondary bacterial infection. Cardiotocography should be used for fetal heart beats after 23–28 weeks of gestation and gestational follow-up should be done according to clinical condition.

Severe and critical disease: While high SOFA (sequential organ failure assessment) score and >1 mg/mL D-dimer level is associated with increased COVID-19 mortality in non-pregnant patients, its use is difficult in pregnant patients. As D-dimer level increases during pregnancy, its use is limited. The use of SOFA score is more appropriate by adjusting creatinine level for pregnant patients. According to the study evaluating 46 pregnant women with positive SARS-CoV-2 result, severe disease developed in 15% of the patients, and it was reported that these patients were overweight or obese with underlying diseases and therefore it should be paid attention in this group of patients.

The severity of COVID-19 pneumonia should be graded according to the guidelines of American Thoracic Society. Morbidity and mortality rates increase in pregnant women with severe COVID-19 pneumonia, and therefore an aggressive treatment is required. The mortality of a pregnant woman due to COVID-19 was first reported in Iran. These patients should be monitored preferably in a negative-pressure room in intensive care and by lying on their left sides, they should be supported with oxygen and hydration, and followed up by a multidisciplinary team. Any secondary bacterial infection should be treated accordingly, and their blood pressure and fluid balance should be monitored closely.

When evaluating pregnant women for COVID-19 infection, it should be kept in mind that their vital findings and acid/base parameters are different than non-pregnant patients. The oxygen saturation should be kept at 95% and above in pregnant patients with positive COVID-19 result. Ventilation type should be decided by intensive care specialists. The use of low-molecular-weight heparin (LMWH) is on the agenda as macroscopic bleeding areas and microthromboses can be observed in the lungs. Cardiotocography should be used for fetal heart beats after 23–28 weeks of gestation and gestational follow-up should be done according to clinical condition. The need for preterm labor with medical indication should be decided by a multidisciplinary team led by Perinatology department by evaluating the condition of patient.

Even though the infection is severe, it is not a labor induction. If pregnant woman is at term, there is no cesarean indication except obstetric indications. In the assessment of 13 patients who had COVID-19 infection, vaginal secretion samples showed negative results. In rare cases where patients are at critical condition, labor

<table>
<thead>
<tr>
<th>Arterial blood gas measurement</th>
<th>1st trimester</th>
<th>3rd trimester</th>
<th>Non-pregnant patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.42–7.46</td>
<td>7.43</td>
<td>7.4</td>
</tr>
<tr>
<td>PaO2 (mmHg)</td>
<td>105–106</td>
<td>101–106</td>
<td>93</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>28–29</td>
<td>26–20</td>
<td>37</td>
</tr>
<tr>
<td>Serum HCO3 (mEq/L)</td>
<td>18</td>
<td>17</td>
<td>23</td>
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</table>
may be needed to improve respiratory functions. When emergency cesarean section was performed in a patient with severe hypoxemia, hemodynamic collapse and COVID-19 positive twin pregnancy, it was reported that hemodynamic condition and respiratory function were improved quickly.\(^{[90]}\) It was reported in England that 2 preterm patients’ condition improved quickly by emergency cesarean section, and that it was highlighted that this is different than pregnant women with influenza.\(^{[97]}\)

In infection with mild or medium severity, it is not necessary to make 2nd stage of labor passive except obstetric indications, but operative labor can be performed in an intubated patient. The opinion of Turkish Neonatal Society regarding the perinatal and labor periods of a patient with COVID-19 infection can be accessed via its website.\(^{[62]}\)

The World Association of Perinatal Medicine (WAPM) initiated a multi-centered joint database globally to present the problems related with COVID-19 pandemic and pregnancy, and to help pregnant women and their families. It is expected that the first of this joint database will be completed by May 1, the second part by August 1, and the third part by November 1, 2020. Those who would like to participate in this initiative may visit http://www.worldperinatal.org/covid-19/.

**Conclusion**

In our review, we aimed to present the relationship between pregnancy and COVID-19 under the light of the up-to-date data. The data in this review will be updated as new data are reported. The last update is on June 8, 2020.

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

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“Near miss” maternal morbidity following repeat rescue cerclage for twin pregnancy

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Abstract

Objective: Repeat cervical cerclage is one of the treatment options described in the literature for when the primary cerclage suture fails. However, infectious complications of cerclage placement may be encountered which are more obvious for the newborn. In our presented case, severe acute maternal morbidity was encountered for the sake of prolonging pregnancy.

Case: Twenty-seven year old nullipar patient at 23+5 gestational weeks with dichorionic diamniotic pregnancy was admitted to our emergency clinic with complaints of “pain” and “vaginal bleeding”. At 18 weeks of pregnancy she had a Shirodkar cerclage procedure indicated by a short cervical length (14 mm) at our hospital. She presented with “bulging of membranes” to a different institution and underwent a repeat cerclage at 23+3 weeks. Chorioamnionitis was suspected and the patient was counselled for a pregnancy termination. After termination of pregnancy, “cardiac arrest” developed. After 2 minutes of resuscitation sinus rhythm was obtained. The patient was admitted to the ICU.

Conclusion: The role of repeat cerclage is controversial. Efforts should be maximized to rule out underlying intrauterine infection prior to placement of a cerclage suture for there to be a therapeutic benefit of prolonging the pregnancy.

Keywords: Cervical cerclage, repeat cerclage, preterm birth, chorioamnionitis, maternal morbidity.

Introduction

Twin pregnancies have a 50% rate of preterm birth (PTB) and 5 times higher risk of neonatal death compared to singleton pregnancies. Various treatment modalities have been attempted to delay the time of delivery to prevent PTBs in twin gestation. Cervical cerclage for twin pregnancy is not routinely indicated but appears beneficial for patients with a history of PTB or very short and/or dilated cervix.[1] Second trimester cervical length in twin pregnancies is similar to that of singletons, but a higher ratio of twins have cervical length <15 mm (4.5% versus 1.5%). Cervical length <15 mm is associated with 30% risk for PTB.[2] Cervical cerclage placement inherently beholds complications. The most common; preterm premature rupture of membranes (PPROM), chorioamnionitis, preterm labor, cervical trauma, suture displacement, and bleeding. Maternal mortality is rare.

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We hereby present a case of twin pregnancy where a repeat cerclage placement endangered the life of the mother.

**Case Report**

Twenty-seven year old nullipar patient at 23+5 gestational weeks with dichorionic diamniotic pregnancy was admitted to our emergency clinic with complaints of “pain” and “vaginal bleeding”. Her vitals were stable and she did not have a fever; however, she had moderate abdominal tenderness. Her medical history revealed that she had a uterine septum resection followed by repeated IVF treatments for infertility two years ago. At 18 weeks of pregnancy she had a Shirodkar cerclage procedure indicated by a short cervical length (14 mm) on ultrasonography at our hospital. She presented with “bulging of membranes” to a different institution and underwent a repeat cerclage at 23+3 weeks. Her primary cerclage (Braun, Aesculap, Tutlingen, Germany) was removed and replaced with a prolene stitch. Upon her presentation to our institution at 23+5 gestational week, her obstetric ultrasound verified fetal cardiac activity and normal amniotic fluid volume in the non-presenting twin. The presenting fetus had decreased amniotic fluid and a fetal heart beat was not present. The cervical length was: 18 mm. The speculum examination yielded no vaginal bleeding and her cerclage suture appeared intact with a closed cervical os. Her blood analysis revealed that she had mild leucocytosis (white blood cell count: 10,300/μL), thrombocytopenia (platelets: 11,000/μL) and an elevated C-reactive protein (81 mg/L) level. Chorioamnionitis was suspected and the patient was counselled for a pregnancy termination. An adequate supply of blood products were prepared in consultation with the blood bank and the intensive care unit (ICU) with the anticipation of imminent bleeding. The cerclage suture was removed and after oxytocin augmentation the pregnancy was terminated within hours. The cervical os contractions after the first placenta was delivered. In order to remove the second placenta the patient was given anesthesia. A Bakri balloon was inserted into the uterine cavity post-procedure because of postpartum hemorrhage. During awakening from anesthesia, the patient developed “cardiac arrest”. After 2 minutes of resuscitation sinus rythm was obtained. The patient was admitted to the ICU. In the ICU she developed new-onset fever, tachycardia and hypotension. Multi-organ dysfunction and critical sepsis developed (INR: 2.95, procalcitonin 166 ng/mL). Multidrug resistant *Escherichia coli* grew in blood cultures. After 7 days of meticulous and supportive antibiotic treatment she was discharged with no sequelae.

**Discussion**

Cervical cerclage in twin pregnancies remains controversial. Although there are some favorable results, a meta-analysis published in 2015 concludes that “cerclage cannot currently be recommended for clinical use in twin pregnancies with a maternal short cervical length in the second trimester”.[^5] Large trials are still necessary.

Commonly reported complications of cervical cerclage include PPROM, chorioamnionitis, preterm labor, cervical trauma, suture displacement, bleeding and cerclage failure. Cerclage failure can occur following primary cerclage. Frequently no further intervention is performed. However, one possible treatment modality that can be considered (if the diagnosis of PPROM/chorioamnionitis is ruled out in the beginning) is the placement of a “repeat cerclage” suture such as the occasion in our case. However, the patient in our report went on to develop chorioamnionitis and maternal sepsis. This was possibly because of a subclinical infection. The management in this case involved the cutting of the cerclage suture and induction of prompt delivery. The incidence of subclinical intra-amniotic infection in patients with mid-trimester cervical dilatation which was demonstrated by amniotic fluid cultures has been reported as high as 51%.[^6] On the other hand, performing a cervical cerclage in patients without intraamniotic infection increases the possibility of achieving a favorable pregnancy outcome.

In the study by Song et al. 22 patients with prolapsed membranes after cerclage placement were evaluated.[^5] The median gestational age at delivery, birthweight and survival rates were significantly higher in the repeat cerclage group compared to the bed rest group.[^5] However, there was an increase in the incidence of PPROM associated with emergency cerclage placement[^5] and chorioamnionitis was described in 12.5–50% of cases by Namouz et al.[^7]

It is apparent that the incidence of “neonatal” complications following emergency cervical cerclage are high. This is notably important where some associated co-factors could be aggravated in the presence of infection which in turn worsens the risk of long-term handicap in preterm neonates. One of the largest studies
which reports infectious complications of cervical cerclage placement concludes that “when the cerclage procedure is performed after the twentieth week of gestation, there is a higher incidence of chorioamnionitis, and intrauterine infection”. In our case the repeat cerclage was performed at 23 weeks of gestation which we believe caused the incidence of septic maternal outcome.

In our presented case “maternal sepsis” and severe acute maternal morbidity was encountered for the sake of prolonging pregnancy. This scenario was preceded by a subclinical intrauterine infection which rapidly developed into a full blown infectious state. The World Health Organization describes severe acute maternal morbidity (SAMM), also known as “near miss”, as “a very ill pregnant or recently delivered woman who would have died had it not been that luck and good care was on her side”. When we searched the literature for complications following cerclage procedure, we came across exclusively “neonatal outcomes”. No maternal morbidity or mortality was reported in the last 5 years. There are randomized controlled trials and 3 Cochrane systematic review articles and various meta-analysis evaluating the role of cerclage, often with conflicting results.

The value of repeat rescue cerclage is controversial and we wanted to contribute to the literature in reporting this case and help create vigilance in underlining that obstetrics is the science which takes care of both the mother and her future babies.

Conclusion
The role of repeat cerclage is controversial. Efforts should be maximized to rule out underlying intrauterine infection prior to placement of a cerclage suture for there to be a therapeutic benefit of prolonging the pregnancy.

Conflicts of Interest: No conflicts declared

References
Letter to the Editor: Extraperitoneal cesarean section and transperitoneal cesarean section: does extraperitoneal technique shorten the duration of surgical operation?

Dear Editor,

Recently, an article of Yeflilbafl and Erener published in your journal attracted our attention.\(^1\) I would like to congratulate the authors for their study comparing their case series consisting of 34 cases with the control group that they carried out through an unusual technique. We also have the opinion that conducting this technique on selected cases may contribute to the post-operative outcomes and in particular analgesic need as shown by Tappauf et al. in their randomized controlled study.\(^2\) However, we have concerns that the outcomes may not be as positive as reported by Yeflilbafl et al. when it is carried out in another center. The technique is unusual as reported, and requires clinical experience. It has not been indicated the level of experience of the operator on this technique in the publication. In addition, we have some questions regarding the article published: How did they decide extraperitoneal cesarean section? Did the patient prefer, and if so, how were the patients informed? Also, considering the study period stated, we believe that the number of cesarean section meeting the criteria in the stated center is more than the reported in a 1-year period. It was not clear which patients were included in the study as study group. In terms of the methods, the insertion site for uterine was not defined clearly, stating how the region without peritoneum is determined more clearly would help us and other researchers in their studies. Based on our clinical experience, we think that the undesired peritoneum perforation is the actual technical problem. In another study in which 105 cases underwent extraperitoneal cesarean section, 6 cases had peritoneum perforation.\(^3\) The last and really important issue is that the duration of the cesarean section was reported significantly shorter in the extraperitoneal group in the conclusion part. We did not understand the basis of this advantage. Apart from that, no significant change was observed from skin incision up to delivery. If no change was observed until the birth of the baby, what is the reason for not including the patients who are in need of emergency cesarean section in the study?

Kind regards,

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Conflicts of Interest: No conflicts declared

References

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Dear Editor,

We would like to thank Dr. Sargun, the author of Letter to the Editor,\(^1\) for her interest in our extraperitoneal cesarean section. We would to explain following matters for the clarification of the topic and the related cesarean section procedure.

The operator, in the said publication, gained the experience in the institution first that he specialized, and the other institutions that he has worked so far. He has an experience of a 20-case series. One of these 20 cases had peritoneum perforation.

The patient decided for the technique to be applied. The patient was informed about the anatomy of anterior abdominal wall, the definition of peritoneum and the possible advantages on intraoperative nausea-vomiting and postoperative pain by not entering into abdominal cavity.\(^2\) Although the number of cesarean section procedures is high in the stated center, most of them were not the cases of which records were kept completely.

The cases with the history of cephalopelvic disproportion, breech presentation and previous cesarean section which are the cesarean section and labor indications were included in the study. The cases with the history of abdominal surgery except cesarean section, multiple pregnancy, preterm labor before 34 weeks of gestation, placenta previa, the need for emergency cesarean section, transverse presentation, macrosomic fetus, the suspicion of placental attachment anomalies and body mass index above 35 were excluded from the study. The same criteria were used for the control group as well. In the technique, the region between rectus muscle and parietal peritoneum is dissected, and then the bladder is reached. The bladder is eliminated laterally by a blunt dissection and it is entered into the vesico-uterine area, and then uterus is reached through lower segment transverse incision. We used the technique described by Tappauf et al. in their study.\(^2\) Shorter surgery duration in the extraperitoneal group is consistent with the current literature.\(^2\,^4\) We believe that the shorter surgery duration in the extraperitoneal cesarean section group may be associated with the potential reasons such as the absence of peritoneal cleaning, intestines not blocking surgical area due to spinal anesthesia, and not closing visceral and parietal peritoneum. The reason for not including the cases which underwent emergency cesarean section is the failure of providing appropriate conditions to inform the emergency cases about the technique.

We would like to thank the author of the Letter to the Editor for this opportunity to make a detailed explanation about our study.

Kind regards,

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Conflicts of Interest: No conflicts declared
References


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