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  The Discussion section should mainly rely on the results derived from the study, with relevant citations from the most recent literature.

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6. Main text (subtitles)
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The impacts of amniotic fluid index, placental localization and fetal sex on the estimation of fetal weight

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Department of Obstetrics and Gynecology, Faculty of Medicine, Selçuk University, Konya, Turkey
Gynecology and Obstetrics Clinic, Konya Training and Research Hospital, Konya, Turkey

Abstract

Objective: In our study, we aimed to investigate the impacts of amniotic fluid index, placental localization and fetal sex on the estimation of fetal weight by ultrasonographic method.

Methods: The medical files of the patients who delivered between September 1 and December 31, 2016 in the Department of Obstetrics and Gynecology, Faculty of Medicine, Selçuk University were reviewed retrospectively after obtaining the approval of ethics committee. The patients with birth weight less than 2500 g and higher than 4500 g, patients with fetal intrauterine development, diabetes and additional diseases, multiple pregnancies, the deliveries with intrauterine death or fetuses with anomalies, the patients whose cervical dilatation was ≥ 4 cm during admission, and the patients with maternal body mass index (BMI) ≥ 25 were excluded from the study. The maximum duration from the ultrasonographic examination up to delivery of the patients was determined 72 hours, and the patients who delivered more than this duration were also excluded from the study. The data were compared according to fetal sex, anterior, posterior and lateral placental localizations, and oligohydramnios, polyhydramnios and normal values in the amniotic fluid index. The statistical analysis was carried out by SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Kruskal-Wallis H and Student t-tests were used for the data analysis.

Results: We evaluated a total of 387 patients. The mean age was 28, the cesarean section rate was 39.8%, normal delivery rate was 60.2%, mean ultrasonographic birth weight was 3319 g (±413 g), and mean birth weight was 3330 g (±376 g). Weight deficit was calculated as 7.2% in all patients. No statistically significant difference was observed between the groups in terms of fetal sex, placental localization and amniotic fluid index.

Conclusion: We found in our study that the amniotic fluid index, placental localization and fetal sex do not have a determining role on the estimation of fetal weight.

Keywords: Estimated fetal weight, placenta, sex, amniotic fluid index.

Özet: Amniyotik sıvı indeksi, plasenta lokalizasyonu ve fetal cinsiyetin fetal ağırlık tahminine üzerine etkisi

Amaç: Çalışmamızda amniyotik sıvı miktarı, plasenta lokalizasyonu ve fetal cinsiyetin ultrasonografik yöntemle fetal ağırlık tahminine etkisi incelenmektedir.


Bulgular: Toplam 387 hasta çalışmaya dahildi. Ortalama yaş 28 olup, hastalarda sezaryen oranı %39.8, normal doğum oranı ise %60.2, ortalamada ultrasonografik doğum ağırlığı 3319 g (±413 g), ortalama doğum ağırlığı 3330 g (±376 g) olarak bulundu. Tüm hastalarda kilo defisiti %7.2 olarak hesaplandı. Fetal cinsiyet, plasenta lokalizasyonu ve amniyotik sıvı indeksine göre gruplar arasında istatistiksel olarak anlamlı bir fark izlenmedi.

Sonuç: Çalışmamızda amniyotik sıvı indeksi, plasenta lokalizasyonu ve fetal cinsiyetin tahmini fetal ağırlık üzerinde belirleyici olmadığını bulunmuştur.

Anahtar sözcükler: Tahmini fetal ağırlık, plasenta, cinsiyet, amniyotik sıvı indeksi.

The impacts of amniotic fluid index, placental localization and fetal sex on the estimation of fetal weight.
Introduction
The follow-up of the fetal growth is a standard element of antenatal care. Many formulas have been developed to estimate fetal weight especially at the end of second trimester and at the third trimester. In these formulas, biometric measurements obtained by fetal ultrasonography are used. The fetal weight estimated by these biometric measurements is compared to the estimated weight which needs to be in the regarding week of baby. The follow-up of intrauterine fetal growth has reached a significant position in the obstetric follow-up today. In the formulas used for estimating fetal weight, biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) measurements are used frequently. While Warsof, Shepard and Hadlock formulas are the most common ones, more than 30 formulas have been reported. Most of them are preset formulas in the ultrasonography devices today. There are many studies on the formulas and each formula has a different margin of error. In addition to the difference among the formulas, there are also various factors affecting the estimation of fetal weight. Ethnicity, operator's experience, conditions affecting image quality (oligohydramnios, multiple pregnancy, maternal obesity, and fetal position etc.), changes in fetal body composition, gestational age, fetal anomaly, growth retardation, macrosomia and fetal sex are among these factors.

In our study, we aimed to assess the impacts of amniotic fluid amount and fetal sex, the activities of which are controversial, and placental localization, the activity of which is unknown, on the estimation of fetal weight by ultrasonographic methods.

Methods
The medical files of the patients who delivered between September 1 and December 31, 2016 in Department of Obstetrics and Gynecology, Faculty of Medicine, Selçuk University were reviewed retrospectively after obtaining the approval of ethics committee. The patients with birth weight less than 2500 g and higher than 4500 g, patients with intrauterine development, diabetes and additional diseases, multiple pregnancies, the deliveries with intrauterine death or fetuses with anomalies, the patients whose cervical dilation was ≥4 cm during admission, and the patients with maternal body mass index (BMI) ≥25 were excluded from the study. The maximum duration from the ultrasonographic examination up to delivery of the patients was determined 72 hours, and the patients who delivered more than this duration were also excluded from the study.

The ultrasonographic examinations of the patients were performed by senior physician assistant or senior physician using the same ultrasonography device (GE Medical Systems, Zipf, Austria). In the biometric measurements, BPD, HC, ACL and FL were checked as a standard procedure. The calculation was done by using Hadlock (BPD, HC, AC, FL) formula recorded in the ultrasonography device. Amniotic fluid index (AFI) was measured on four quadrants through maximum vertical pocket which is not extremity and cord. In our study, 50–240 mm was considered the normal limits for AFI. It was considered oligohydramnios when AFI was measured 49 mm and below, and polyhydramnios when AFI was measured 240 mm and above. We established three groups in our study, which were oligohydramnios, normal AFI and polyhydramnios. We calculated percent error of ultrasonography when estimating birth weight, and defined it as deficit percentage. The weight deficit percentage was equal to (birth weight - ultrasonographic weight estimation) / birth weight × 100. According to the placental localization where placenta adheres to internal wall of uterine, we established three groups, which were anterior, lateral and posterior localizations. We defined the anterior localization as placenta which adheres to internal surface of anterior uterine, the lateral localization as placenta which adheres to fundal, cervical and right and left lateral internal wall of uterine, and posterior localization as placenta which adheres to posterior wall of uterine. We compared the results of weight deficit percentage in fetal sex placental localization and amniotic fluid index groups. The statistical analysis was carried out by SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Kruskal-Wallis H and Student’s t-tests were used for the data analysis.

Results
We evaluated a total of 387 patients. Mean age was 28, and it ranged between 16 and 42 years. Gravida median value was found 2, parity median value was found 1 and gestational week was calculated 38 weeks. In the patients, the cesarean section rate was 39.8%, normal delivery rate was 60.2%, mean ultrasonographic birth
weight was 3319 g (±413 g), and mean birth weight was 3330 g (±376 g). The demographic and clinical data of the patients are shown in the Table 1.

Oligohydramnios group included 29 patients, normal AFI group included 343 patients and polyhydramnios group included 15 patients. The highest weight deficit percentage was observed in the polyhydramnios group, but there was no statistically significant difference among the groups. Total weight deficit in all patients was 7.2%. While the deficit was 6.75% in females, it was 7.59% in males. In terms of deficit percentages, we observed no significant difference between two sex groups. Considering the weight deficit according to the placental localization, there was no significant difference between the groups. The comparison of weight deficit percentages according to amniotic fluid index, sex and placental localization is shown in Table 2.

Table 1. Demographic and clinical data of the patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>28 (16–42)</td>
</tr>
<tr>
<td>Gravida†</td>
<td>2 (1–8)</td>
</tr>
<tr>
<td>Parity†</td>
<td>1 (0–5)</td>
</tr>
<tr>
<td>Week of gestation*</td>
<td>38 (33–42)</td>
</tr>
<tr>
<td>Cesarean section‡</td>
<td>154 (39.8%)</td>
</tr>
<tr>
<td>Normal delivery‡</td>
<td>233 (60.2%)</td>
</tr>
<tr>
<td>Ultrasonographic estimated weight§</td>
<td>3319 g (±413 g)</td>
</tr>
<tr>
<td>Birth weight§</td>
<td>3330 g (±376 g)</td>
</tr>
</tbody>
</table>

*mean (minimum–maximum), †median (minimum–maximum), ‡n (%), §mean (standard deviation).

Table 2. Comparison of weight deficit percentage according to amniotic fluid index, fetal sex and placental localization.

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (Weight deficit percentage)*</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amniotic fluid index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>29 (5.8)</td>
<td>0.225</td>
</tr>
<tr>
<td>Normal AFI</td>
<td>343 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>15 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>171 (6.75)</td>
<td>0.646</td>
</tr>
<tr>
<td>Male</td>
<td>216 (7.59)</td>
<td></td>
</tr>
<tr>
<td>Placental localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior placental localization</td>
<td>254 (7.3)</td>
<td>0.635</td>
</tr>
<tr>
<td>Lateral placental localization</td>
<td>75 (6.8)</td>
<td></td>
</tr>
<tr>
<td>Posterior placental localization</td>
<td>58 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>387 (7/2)</td>
<td></td>
</tr>
</tbody>
</table>

*n: Patient number in the group, the weight deficit percentage was equal to (birth weight - ultrasonographic weight estimation) / birth weight x 100.

Discussion

Estimating the fetal weight accurately during intrauterine period is important for antenatal care and follow-up. Knowing the growth during intrauterine period helps to manage many matters from intrauterine follow-up method up to delivery type. The problems about fetal growth are usually associated with increased morbidity. Estimating the birth weight of underweight (<1000 g) babies is important for intrauterine fetal follow-up and deciding delivery, and estimating the birth weight of overweight babies is important for deciding delivery type.\(^5,13\) The margin of error has been reported less than 7% in very few of these formulas.\(^7\) In our study, we found total margin of error as 7.2%.

In their prospective study, Scioscia et al. compared the estimated and actual birth weights of 441 patients from almost same ethnicity who delivered within 48 hours after ultrasonography by using 35 different formulas. While 29 formulas had 10% or less margin of error, 69.2% of actual weight was estimated when margin of error was considered 10% in all formulas, and 86.5% of actual weight was estimated when the margin of error was considered ±15%. High accuracy rate and low variability was found in 20 formulas. They found low margin of error (about 8%) in methods using fetal head, femur and abdominal circumferences.\(^15\) In a retrospective analysis performed by Sabbagha et al., 23 different models were compared in the estimation of fetal weight, and Hadlock formula using fetal head, abdominal and femur was found as the formula which had the lowest margin of error.\(^6\) We used Hadlock formula in our study.

Seimer et al. carried out a study for the impact of fetal sex on the estimation of birth weight and investigated 3254 singleton pregnancies with weights between 2501 and 3999 g, and they found that performing sex-based investigation for the accurate estimation had the most accurate result compared to all society screening.\(^9\) In the retrospective study of Melamed et al., the authors found more accurate sex-based weight estimations in male fetuses. In our study, we observed no statistical difference between the sexes in terms of weight deficit; however, we calculated lower margin of error in female babies (6.75 vs. 7.59).
Amniotic fluid is especially necessary for fetal anatomic evaluation during ultrasonographic examination. The impact of amniotic fluid on fetal weight estimation ultrasonographically is controversial. While it was found in some studies that amniotic fluid amount has no impact on the estimation of fetal weight, some studies found that oligohydramnios has an adverse effect on the estimation of fetal weight.\[16\–19\] We found in our study that amniotic fluid measurements had no impact on estimated fetal weight.

Although there are studies in the literature on the estimated birth weight according to the placenta volume, there is no study in the literature investigating the impact of placental localization on estimated fetal weight.\[20\] It has been considered theoretically that placental localization may be determinant in the weight estimation, but we found no impact of placental localization on the estimation of weight in our study.

Our study being retrospective, performance of ultrasonographic examinations by different individuals, and low number of patients are the limitations of our study.

**Conclusion**

Estimated fetal weight is an active parameter used in all stages of pregnancy from intrauterine follow-up to delivery. We found in our study that the amniotic fluid index, placental localization and fetal sex do not have a determining role on the estimation of weight.

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

**References**

Plasma selenium levels in pregnant women with preeclampsia

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Abstract

Objective: In this study we aimed to compare selenium (Se) levels in preeclamptic women to healthy pregnant women.

Methods: The study included 84 pregnant women: 39 women with preeclampsia (Group 1), and 45 maternal age, gestational age, and body mass index (BMI) matched healthy pregnant women (Group 2). The maternal levels of plasma Se were analyzed in flame photometer of atomic absorption spectrophotometer.

Results: Plasma Se levels in preeclamptic group were significantly lower than those in the healthy control group (p<0.05). There was no significant correlation between Se levels and BMI, gestational week at sampling, birth weight, triglycerides, cholesterol, the homeostasis model assessment of insulin resistance, and systolic and diastolic blood pressures in preeclamptic and healthy pregnant women (p>0.05).

Conclusion: Our results show that there are decreased levels of Se in plasma of preeclamptic subjects and this may indicate that Se could play a role in the pathogenesis of preeclampsia. However, further experiments are needed to clarify this role.

Keywords: Preeclampsia, selenium.

Introduction

Preeclampsia is a human pregnancy specific multisystem disorder in which hypertension arises after 20 weeks of gestation and is accompanied by either proteinuria or thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms.¹² It is the most common medical complication of pregnancy, occurring in 5–7% of all pregnancies, and is a leading cause of both maternal-fetal morbidity and mortality.¹³ Although the mechanisms involved in the etiology of this disorder have not been clearly identified, it is thought to include two components of the placenta: (i) insufficient trophoblast invasion and (ii) insufficient spiral artery with endothelial dysfunction.¹⁻⁴

Previous studies have demonstrated that diminished placental perfusion and vascular endothelial dysfunction

Abstract

Özett: Preeklampsili gebelerde plazma selenyum düzeyleri

Amaç: Bu çalışmada, sağlıklı gebe kadınlara preeklampsili kadınlardaki selenyum (Se) düzeylerini karşılaştırmayı amaçladık.

Yöntem: Preeklampsili 39 kadın (Grup 1) ve maternal yaş, gestasyonel yaş ve vücut kitle indeksi (VKI) benzer olan 45 sağlıklı gebe (Grup 2) olmak üzere çalışmaya toplam 84 gebe dahil edildi. Maternal plazma Se düzeylerinin ölçümlü atomik absorbsiyon spektrofotometri cihaz kullanlarak yapıldı.

Bulgular: Preeklampisli gruptaki plazma Se düzeyleri, sağlıklı kontrol grubuna kıyaslala anlamlı derecede daha düğüktü (p<0.05). Preeklampsili ve sağlıklı gebe kadınlarda Se düzeyleri ile VKI, _örnek alma tarihindeki gebelik haftası, doğum ağırlığı_, triglisiterler, kolesterol, _insülin direnci_, _sistolik ve diastolik kan basınciasi_ arasında anlamlı bir ilişki saptanmadı (p>0.05).

Sonuç: Elde ettğımız sonuçlar, preeklampisli olguların plazma Se düzeylerinin azalığını göstermektedir ve bu durum, Se’nin preeklampsi patogenezinde bir rol oynamayacağını belirtmektedir. Ancak bu rolü netleştirmek için daha fazla araştırma ihtiyaç vardır.

Anahtar sözcükler: Preeklampsi, selenyum.
result in placental ischemia, oxidative stress, apoptosis, and necrosis. These cellular changes further result in increased trophoblast shedding into the maternal circulation, which leads to the clinical manifestations of preeclampsia.\textsuperscript{6–10}

Selenium (Se) is an essential trace element that has importance for human health and plays a vital role by incorporating selenoproteins into thyroid hormone metabolism, antioxidant defense systems, and immune function.\textsuperscript{11} It is incorporated as selenocysteine (SeCys) at the active site of antioxidant enzymes. In the human body, more than 25 selenoproteins have been identified that play significant roles in the cellular redox system.\textsuperscript{12} Glutathione peroxidases (GPx), thioredoxin reductases (Thx-R), and iodothyronine deiodinases are the main Se containing enzymes involved in redox reactions.\textsuperscript{13} Human placentas produce important antioxidant proteins, which support placentation and reduce inflammation and certain forms of oxidative stress, such as superoxide dismutase (SOD), GPx, Thx, and Thx-R.\textsuperscript{10}

Several studies have found depleted Se levels in preeclamptic women and shown a correlation with the activity of plasma GPx levels.\textsuperscript{14,15} Rayman et al. notably showed that preeclamptic mothers have a lower Se status prior to diagnosis of the syndrome.\textsuperscript{15} Similarly, many additional studies have reported Se deficiency in the development of preeclampsia.\textsuperscript{11–24} By contrast, other studies have found either similar or higher plasma Se levels in preeclamptic pregnant women.\textsuperscript{25–30}

As seen from the studies mentioned, there is considerable inconsistency in the literature regarding the relation between plasma Se levels and preeclampsia. In this study, we aimed to accomplish the following: (1) evaluate plasma Se concentrations in preeclamptic, normotensive pregnant women and (2) investigate the association between maternal plasma Se concentrations and body mass index (BMI), triglycerides (TG), cholesterol, insulin resistance (IR), and a variety of other parameters.

Methods

A total of 84 pregnant women who were recruited from the antenatal clinics of the Department of Gynecology and Obstetrics of the Faculty of Medicine, Kahramanmaraş Sütçüimam University (Kahramanmaraş, Turkey) were included in the study. Research ethics approval was obtained from the Ethics Committee of Kahramanmaraş Sütçüimam University before the initiation of the study and signed informed consent was obtained from all patients and volunteers. The study population consisted of 2 groups; the Group 1 included 39 women with preeclampsia and the Group 2 consisted of 45 normotensive healthy pregnant women.

The diagnosis of preeclampsia was made according to the guidelines of the American College of Obstetricians and Gynecologists\textsuperscript{31} and to the criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP).\textsuperscript{31} Preeclampsia was diagnosed in the presence of hypertension (blood pressure of 140/90 mmHg or higher, on at least two occasions, at least 6 h apart, after the 20th week of gestation) and proteinuria (>300 mg in a 24-h urine collection or ≥1+ by dipstick and more) or other maternal organ dysfunction (thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms) or uteroplacental dysfunction (fetal growth restriction). Preeclamptic women and normal controls were carefully matched for maternal age, gestational age, and body mass index (BMI). Gestational age was calculated based on menstrual history or, in the case of irregular cycles, from ultrasound data obtained during the first or second trimester of pregnancy. The BMI was calculated as weight (kg) / height squared (m\(^2\)). All participants were non-smokers, had not received any medication before becoming pregnant, and had no clinical evidence of cardiovascular, metabolic, or inflammatory diseases. Exclusion criteria were multiple gestation, confirmed diabetes mellitus, chronic hypertension, connective tissue disease, inflammatory or infective disorders and heart disease, as well as treatment with aspirin, warfarin, lipid-lowering drugs, nonsteroidal anti-inflammatory drugs, or antibiotics. Other exclusion criteria were ruptured fetal membranes, active labor, and polyhydramnios. The normotensive pregnant women selected as controls had no signs of gestational complications or fetal distress.

Blood sampling

A blood sample was taken from each participant before administration of any medication and before any medical or surgical intervention. None of them were in active labor before or at the time of blood collection. The blood samples, which were obtained from the antecubital area, were collected between the hours of 08:00...
and 09:00 following 10–12 h of fasting. Fasting venous blood specimens were drawn from the antecubital vein and collected in no additive vacutainer (Becton-Dickinson, Franklin Lakes, NJ, USA) blood-collecting tubes according to standard hospital guidelines for venipuncture and sample collection. The serum separator tube specimens were allowed to clot and then centrifuged for 10 minutes at 3000 g to separate the serum. Serum glucose, TG, cholesterol and insulin levels were measured the same day using a Dade Behring RXL calibrated autoanalyzer (Dade Behring Inc., Newark, DE, USA) and Immulite 2000 instrument (Siemens, Flanders, NJ, USA). Plasma samples were separated and stored at -70°C until the analysis of Se levels.

**Measurement of serum Se levels**

Selenium measurement was performed in a graphite furnace atomic absorption spectrophotometer (Analyst 800; Perkin Elmer, Waltham, MA, USA) using Zeeman background correction. Matrix modifiers were palladium (4 mg in a 20-mL sample) and magnesium sulfate (3 mg in a 20-mL sample). Samples and calibration standards were diluted 1:3 with 0.05% Triton X-100 to improve the sample viscosity and the reproducibility of the results. Selenium levels in all groups were evaluated according to a standard curve as μg/L, and Se calibration standards were prepared from the commercial Se standard (1000 mg/L) by serial dilutions. According to the Se tests of the control and patient groups, a sensitivity of 72% and a specificity of 55.5% were found.

IR was assessed by Homeostasis Model Assessment (HOMA), HOMA-IR = [fasting insulin (U/ml)] × [fasting glucose (mg/dl)] / 405.

**Statistical analyses**

All data were analyzed using the Statistical Package for the Social Sciences for Windows version 17.0 (SPSS, Chicago, IL, USA). The data were initially tested for normal distribution by Kolmogorov-Smirnov test and found abnormal (p<0.05). The Mann-Whitney U test was used to test the significance of differences in variables among groups. A correlation analysis by the Spearman’s rho test was used to test the relationship between levels of Se and variables. Data are presented as mean±SD. Statistical significance was defined as p<0.05.

**Results**

The clinical characteristics of the groups are reported in [Table 1](#). Demographic features (median maternal age, gestational age at sampling, and BMI) in all groups were similar (p>0.05). Gestational age at delivery and birth weight were significantly lower in the preeclamptic group than in the healthy control group (p<0.05). When compared to Group 2, significant increases in both the systolic and diastolic blood pressures were found in Group 1 (p<0.05).

The plasma Se levels and other laboratory findings of the groups are shown in [Table 2](#). Plasma Se levels were significantly lower in Group 1 when compared to Group 2 (46.81±15.35 vs. 61.77±14.49, respectively) (p<0.05). Fasting serum TG and cholesterol levels were similar in...

**Table 1. The clinical characteristics of groups.*

<table>
<thead>
<tr>
<th></th>
<th>Preeclamptic pregnant women</th>
<th>Healthy pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Group 1) (n=39)</td>
<td>(Group 2) (n=45)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>29.36±6.45</td>
<td>27.89±7.06</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.57±4.42</td>
<td>28.86±3.88</td>
</tr>
<tr>
<td>Gestational age at sampling (week)</td>
<td>34.90±2.01</td>
<td>34.02±1.67</td>
</tr>
<tr>
<td>Gestational age at delivery (week)</td>
<td>34.74±1.45</td>
<td>39.11±1.56</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2233.64±712.79</td>
<td>3224.67±334.51</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>158.21±11.89</td>
<td>106.22±10.72</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>99.23±8.07</td>
<td>65.78±8.39</td>
</tr>
</tbody>
</table>

*All parameters are given mean±standard deviation. BMI: body mass index; n: subject number.

**Table 2. Laboratory results of groups.*

<table>
<thead>
<tr>
<th></th>
<th>Preeclamptic pregnant women</th>
<th>Healthy pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Group 1) (n=39)</td>
<td>(Group 2) (n=45)</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>294.30±133.83</td>
<td>256.64±82.18</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>232.62±79.79</td>
<td>265.76±185.49</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.09±2.09</td>
<td>1.61±1.74</td>
</tr>
<tr>
<td>Selenium (μg/L)</td>
<td>46.81±15.35</td>
<td>61.77±14.49</td>
</tr>
</tbody>
</table>

*All parameters are given mean±standard deviation. HOMA-IR: homeostasis model assessment of insulin resistance; n: subject number. p>0.05 insignificant, p<0.05 significant.
both groups (p>0.05). The HOMA-IR was significantly higher in Group 1 than in Group 2 (p<0.05).

There was no significant correlation between Se levels and BMI, gestational week at sampling, birth weight, TG, cholesterol, HOMA-IR, and systolic and diastolic blood pressures in preeclamptic and healthy pregnant women (Table 3) (p>0.05).

Discussion

The present study has shown that serum Se levels were significantly lower in patients with preeclampsia than in maternal age, BMI, and gestational age matched control subjects. Relatively few investigators have assessed the extent to which levels of Se in maternal blood are altered in preeclamptic vs. normotensive pregnancies. Our findings of decreased plasma Se levels in women with preeclampsia were consistent with those of Maleki et al., who found reduced Se plasma levels in preeclamptic women in Iran.[22]

Previous studies of maternal Se level status in preeclamptic and normotensive pregnancies have been inconsistent. Several investigations, which were consistent with our results, have found low Se concentrations in women with preeclampsia compared to normotensive pregnant women.[15–24] However, not all prior studies were consistent with our results, and some failed to find any correlation between Se status and hypertensive disorders in pregnant women.[25–30]

Mistry et al.[27] found no differences in selenoproteins in preeclamptic and normotensive pregnant women who were matched by gestational age, parity, and age; however, serum Se concentrations were 15% higher for the preeclampsia cases, as compared to the controls (55.6 vs. 48.5 ng/cm³). In a recent study, da Silva et al. found similar Se levels in preeclamptic and normotensive pregnant women.[24] Gromadzinska et al.[31] (in a study with 49 pregnant women) reported higher maternal plasma Se concentration, and Mahomed et al.[32] found an elevation in median leucocyte Se concentrations in preeclampsia cases, as compared to the controls.

An imbalance of decreased expression and activity of antioxidants and a concomitant increase in lipid peroxides in human placenta play major roles in the etiology of preeclampsia.[6,34] Selenium eliminates lipid peroxides through its incorporation into GPx. In order to protect the fetus from damage caused by oxygen radicals, the human body consumes excessive Se to eliminate oxidative production, which could decrease the Se concentration in preeclamptic women. However, it is still unclear whether the role of oxidative stress in the mechanism of preeclampsia is either the primary event or merely plays a major role in the pathophysiology of the disease. Selenoproteins are major antioxidants that protect endothelium by down-regulating cytokine-induced adhesion molecule expression and reduce inflammation.[22]

Elevating blood Se concentrations with Se supplementation during pregnancy may be beneficial in pregnant women who have a high risk for preeclampsia due to low Se status.[23] However, previous studies on the role of antioxidants in reducing the rate of preeclampsia are limited, and the results remain controversial. Several studies have shown beneficial effects in only a small number of cases.[25,37] Cochrane’s review of the supplementation of antioxidants, such as vitamin C, vitamin E, lycopene, and Se, reported no impact on the prevention of preeclampsia.[36] Another area that requires further investigation is determining the most beneficial times and doses of Se for pregnant women.

Conclusion

In conclusion, we demonstrated that circulating concentrations of Se were significantly decreased in women with established preeclampsia. Further investigations with larger numbers of preeclamptic women
are necessary to determine the role of Se in the etiopathogenesis of preeclampsia and to assess maternal endogenous antioxidant status.

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

**References**


Thicknss measurement of fetal epicardial adipose tissue in structurally normal fetuses between 24 and 28 weeks of gestation

And Yavuz¹, Mekin Sezik¹, Mehmet Özugr Akkurt¹, Serenat Eriş Yakçin¹, Gökhan Karakoç²

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²Perinatology Clinic, Edik Zübeyde Hanım Gynecology Training and Research Hospital, Ankara, Turkey

Introduction

The heart is surrounded by parietal and visceral (serous) pericardium. Visceral pericardium is of mesothelial origin and named as epicardium. Epicardial adipose tissue (EAT) is the region between myocardium and visceral pericardium, and it directly contacts with myocardium.¹² As there is no fascia which separates EAT from myocardium, they share the same micro-circulation.¹ It is originated from brown adipose tissue during embryogenesis.¹ Since it originates from brown adipose tissue,
it is thought that it has a protective effect on heart against hypothermia.\(^4\) Also, EAT absorbs free fatty acids and protect heart in this environment when it is of high amount during circulation, it also may function as energy source in cases when energy need increases.\(^5\) EAT contains more proteins than other adipose tissues and it has a faster fatty acid synthesis and degradation.\(^6\) It is metabolically very active tissue. It secretes many proinflammatory, proatherogenic cytokines and vasoactive peptide associated with obesity, hypertension and coronary heart disease such as interleukin 6, tumor necrotizing factor alpha, angiotensin 2, plasminogen activator, omentin and neuronal growth factor.\(^7,8\) It also secretes anti-inflammatory and antiatherogenic adipokines such as adiponectin and adrenomedullin.\(^9\)

EAT measurement was first done by Iacobellis.\(^10\) The thickest location of EAT is the perpendicular wall of right ventricle. Therefore, the measurement is done on this location.\(^11\) EAT thickness varies between 1 and 23 mm in adults.\(^12\) EAT thickness can be decreased by weight loss in obese individuals.\(^13\)

Since EAT measurement is not affected by the differences in skin and muscle tissue layers, it shows visceral adiposity more precisely than abdominal circumference measurement. In the studies performed, EAT was measured by echocardiogram and a close correlation was found with abdominal adipose tissue measured by MRI and CT.\(^16\) It was reported that EAT increases in insulin resistance and diabetes mellitus.\(^14\) There are studies reporting that EAT thickness is correlated with the presence and severity of coronary artery disease.\(^15\)

EAT is still a popular measurement which is frequently carried out in adults and inspires many researches. However, fetal data on this measurement is very limited. In our study, we aimed to find normal fetal EAT thicknesses by measuring fetal EAT thickness according to the weeks of gestation for the first time in a Turkish population as far as we know.

**Methods**

A total of 39 pregnant women, who had no anomaly according to fetal anatomy screening and fetal echocardiogram performed in our clinic previously and were between 24 and 28 weeks of gestation according to their last menstrual period, were included in our study. Pregnant women who were taking drugs other than multivitamins, who did not know their last menstrual date, who had concomitant disease(s) and macrosomic or fetal growth retardation were excluded from the study. Body mass index (BMI) values of all pregnant women were calculated by measuring their heights and weights. Pregnant women whose BMI values and ages were similar were included in the study.

Fetal ultrasonographic measurements were carried out with Voluson E6 (General Electric, Tiefenbach, Austria) ultrasonography device and 2–7 MHz convex abdominal probe by a single perinatologist. Fetal EAT measurement was performed through perpendicular wall of right ventricle at 3rd cardiac cycle at the end of diastole perpendicular to the positions of aortic valves, as described by Iacobellis for adults previously\(^10\) (Fig. 1).

Pregnant women at each week of gestation were separated into different groups and their data were recorded. The data were represented by median and interquartile range. Kruskal-Wallis and Mann-Whitney U tests were used for comparison. Analyses were done on SPSS 22.0 (SPSS Inc., Chicago, IL, USA). In all analyses, p<0.05 was considered statistically significant.

**Results**

There were 10, 10, 10 and 9 pregnant women on 24+, 25+, 26+ and 27+ weeks of gestation, respectively. There was no statistical difference between weeks of gestation and BMI and maternal age (p=0.88 and 0.33, respectively). Fetal EAT thicknesses at 24+, 25+, 26+ and 27+ weeks of gestation were 1.29 mm [1.267–1.320], 1.295 mm [1.275–1.305], 1.325 mm [1.297–1.355] and 1.34 mm [1.330–1.355], respectively (Table 1). It was seen that EAT thickness increased as week of gestation advanced. While no significant difference was found among median values at 24–25 and 26–27 weeks of gestation (p=0.87 and 0.231, respectively), there was significant increase between 25 and 26 weeks of gestation (p=0.048) (Fig. 2).

**Discussion**

EAT thickness measurement in adults by transthoracic echocardiogram has become a popular research topic recently. Jeong et al. found mean EAT thickness in Caucasian race as 7 mm in males and 6.3 mm in females.\(^14\) In our study, we measured mean EAT thickness in structurally normal fetuses as 1.29, 1.295, 1.32
and 1.34 mm in 24, 25, 26 and 27 weeks of gestation, respectively. The reason for choosing these weeks is to ensure the most appropriate measurement. Carrying out the measurement at early or late weeks is technically difficult and decreases the precision of the measurement.

A correlation was found between epicardial adipose and hypertension in adults, and increased EAT thickness was reported in hypertensive individuals.\[17,18\] In the measurements done in pregnant women in recent years, similar relationship was found between gestational hypertensive diseases and maternal EAT. Can et al. measured maternal EAT thickness, total cholesterol level, left ventricular end systole and diastole volumes in 40 preeclamptic and 38 normal pregnant women. In the study, EAT value was found thicker in preeclamptic pregnant women (7.2 mm) than normal pregnant women (5.6 mm).\[19\] Total cholesterol and left ventricular end systole and diastole volumes were found similar. In the same study, preeclampsia group were divided into two sub-groups (severe and mild). EAT thickness value was found significantly thicker in severe preeclamptic group (7 mm) than the mild preeclamptic group (6.6 mm).\[19\] In a similar study, Oylumlu et al. found that EAT thickness was higher, which was statistically significant, in preeclamptic pregnant women (6.9 mm) than normal pregnant women (5.6 mm).\[20\]

In many studies, EAT increase was associated with metabolic syndrome and coronary heart diseases.\[14,15,21\] A connection was found between EAT and fasting blood glucose and diabetes mellitus (DM) in previous studies.\[22\] Çalışkan et al. found EAT thickness significantly increased in women with previous history of gestational diabetes mellitus (GDM) compared to the control group.\[23\] According to a study conducted on pregnant women, mean EAT value was measured 7.2 mm in pregnant women with GDM, it was 5.6 mm in the control group (p<0.001). In the same study, a correlation was found between EAT and postprandial glucose level.\[24\] In our study, we found that fetal EAT thickness measurements increased in proportion to the

<table>
<thead>
<tr>
<th>Weeks of gestation</th>
<th>24th week (n=10)</th>
<th>25th week (n=10)</th>
<th>26th week (n=10)</th>
<th>26th week (n=9)</th>
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<tbody>
<tr>
<td>BMI</td>
<td>27.7±3.6</td>
<td>26.8±3.6</td>
<td>27.9±1.4</td>
<td>27.5±1.2</td>
</tr>
<tr>
<td>Maternal age</td>
<td>25.2±7.3</td>
<td>29.3±7</td>
<td>27.8±5</td>
<td>28.1±5.3</td>
</tr>
<tr>
<td>Fetal EAT</td>
<td>1.292±0.031</td>
<td>1.296±0.036</td>
<td>1.326±0.032</td>
<td>1.340±0.017</td>
</tr>
<tr>
<td>25th percentile</td>
<td>1.267</td>
<td>1.275</td>
<td>1.297</td>
<td>1.330</td>
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<tr>
<td>50th percentile</td>
<td>1.290</td>
<td>1.295</td>
<td>1.325</td>
<td>1.340</td>
</tr>
<tr>
<td>75th percentile</td>
<td>1.320</td>
<td>1.305</td>
<td>1.355</td>
<td>1.355</td>
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</tbody>
</table>

*The data have been given as median±standard deviation.
week of gestation. We detected that the only statistically significant increase was between 25 and 26 weeks of gestation. This increase may arise from the increase of diabetogenic hormones at second trimester of pregnancy or secondary to the thickening in the parallel tissue upon the growth of fetus.

Jackson et al. performed fetal EAT measurement for the first time during the pregnancies of diabetic women.\[^{25}\] In this study, EAT thicknesses of fetuses of 28 diabetic and 28 non-diabetic pregnant women between 20 and 28 weeks of gestation were measured retrospectively. While EAT thickness was 1.43 mm in the diabetic group, it was 1.11 mm in the non-diabetic group and it was found statistically different (p=0.02). There was no significant difference between two groups in terms of age, BMI, hemoglobin A1C, week of gestation, estimated fetal weight, fetal abdominal circumference and subcutaneous adipose thickness. Although the first fetal EAT measurement was carried out by Jackson et al., it is not possible to take the mean values by measuring through 3rd cardiac cycle at diastole end as described by Iacobellis since it was a retrospective study. In a study we performed previously, we performed fetal EAT thickness measurement prospectively for the first time. In this study, we made maternal and fetal EAT measurements in pregnant women with GDM and normal pregnant women. While maternal EAT thickness was 6.9 mm in the GDM group, it was 5.3 mm in the control group (p<0.001). We found statistically significant increase in the fetal EAT thickness in GDM group (1.34 mm) compared to normal pregnant women (1.31 mm) (p=0.004). While there was no difference in EAT thickness in terms of fetal sex, maternal and fetal EAT thicknesses had a correlation.\[^{26}\] In our study, consistent with the data of these two studies, fetal EAT thickness was between 1,267 and 1,355 mm in non-complicated pregnancies at 24–27 weeks of gestation.

Conclusion

As far as we know, this is the first study on fetal EAT thickness in non-complicated pregnancies in our society. However, low number of cases is the limitation of our study. Fetal EAT measurement is a very new parameter which is non-invasive and painless, does not need any preparation in advance and does not take time. On the other hand, it is a test which needs high-resolution ultrasound device and personnel specialized on fetal echocardiogram and quite difficult to measure when heart is posterior position and patient is on early weeks of gestation. Therefore, measurement is not considered in routine pregnancy follow-ups. However, these measurements can be performed in perinatology centers on selected patient groups. Further wide prospective studies are needed to create a nomogram according to the weeks of gestation and to identify if pregnancy is complicated in abnormal measurements and to understand the importance of this measurement by following up newborns after their births.

Conflicts of Interest: No conflicts declared.

References


Assessment of the training on placenta and umbilical cord given to midwives

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Abstract

Objective: The aim of this study was to assess the interactive training on placenta and umbilical cord given to midwives who provide care for pregnant women and newborns.

Methods: The midwives accepted the invitation for interactive presentation before the training. The introductory information of participants was collected by a questionnaire form prepared by researchers. Assessment of the knowledge of the participants on placenta and umbilical cord was performed by using a 24-question questionnaire form prepared by the researchers in accordance with the literature. A pre-test was conducted before the training. The participants were not informed whether the test would be repeated at first and third months after the training or not. The test was repeated 1 and 3 months later. Friedman test was used in the comparison of the mean values of more than two dependent groups as the data did not provide parametric characteristics, and Kruskall-Wallis test was used for the comparison of two groups. Statistically significant level was considered p<0.05 for all the data.

Results: The mean age of midwives included in the study was 37.23±6.19 (range: 25 to 51) years, 52.9% of them had bachelor’s degree, 88.2% of them were married, their total experience in their profession was 15.88±6.90 years and they were working in the same unit for 7.5 (range: 1 to 26) years. Of the participants, the mean pre-test score was 12.88±2.15, and mean final test scores 1 month and 3 months later were 21.61±1.75 and 23.23±0.85, respectively.

Conclusion: Interactive training given on placenta and umbilical cord provides a positive contribution to increase the knowledge score of midwives. It may be suggested to repeat in-service trainings in the organization regularly.

Keywords: Placenta, umbilical cord, midwife, interactive training.

Özet: Plasenta ve umbilikal kordon hakkında ebelere verilen eğitim değerlendirilmesi

Amaç: Bu çalışma gebelere ve yenidoğana bakım veren ebelere, plasenta ve umbilikal kordon hakkında verilen interaktif eğitimdeki değerlendirme amacıyla yapılmıştır.

Yöntem: Eğitim faaliyeti öncesinde ebel interaktif sunum davet ettiler. Çalışmada katılımcıların tanıtıceği özellikleri içeren bilgiler araştırmacılar tarafından hazırlanan anket formu ile toplandı. Katılımcıların konu ile ilgili bilgilerinin değerlendirilmesi araştırıcılar tarafından literatür doğrultusunda hazırlanan 24 soruluk soru formu kullanarak yapıldı. Eğitim on test uygulandı. Eğitimden 1 ve 3 ay sonra tekrar edilip tekrarlama yaradığı konusunda katılımcılara bilgi verilmedi. Son test 1 ve 3 ay sonra tekrarlandı. İkiden çok bağımlı grupların ortalama ar的各项ları veriler parametrik özelliklere sahip olmadığından Friedman testi, ikili grup karşılaştırılmada Kruskall-Wallis testi kullanıldı. Tüm veriler için istatistiksel anlamlılık düzeyi p<0.05 olarak alındı.

Bulgular: Çalışmaya dahil edilen ebelin yaş ortalaması 37.23±6.19 (dağılım: 25–51), %52.9’u lisans mezunu, %88.2’şi evli, toplam mesleği deneysel süresi 15.88±6.90 ve birim time ortalaması 7.5 (dağılım: 1–26) yıl göre yapıtı safeguard. Katılımcıların ön test puanı ortalaması 12.88±2.15, 1 ay sonra son test puanı ortalaması 21.61±1.75 ve 3 ay sonra son test puanı ortalaması 23.23±0.85 olarak bulundu.

Sonuç: Plasenta ve umbilikal kordon hakkında verilen interaktif educação bilgi düzeyi puanı yükselmesi ile ilgili tekrar edilmiş. Çalışma sonucunda, işverenlerin eğitim veren ebelin bu konuda verilen eğitimdeki rolünün önemini vurgulayarak tekrar edilmesi önerildi.

Anahtar sözcükler: Plasenta, umbilikal kordon, ebe, interaktif eğitim.
Introduction

Placenta starts to develop 13–15 days after the ovulation. Normal implantation of the placenta is necessary for the success of pregnancy. Cytokines, steroid hormones, immunological factors, prostaglandins and some other mediators are necessary for a successful placentation.[1] Placenta is the greatest endocrine organ in human body responsible for the intrauterine development of fetus.[2] The delivery of placenta occurs at the third phase of labor.[3]

All placentas should be examined by clinician. In the examination, the integrity of maternal surface of membranes, presence of retroplacental hematoma, and the presence of hematoma on the cord and rupture on membranous vessels should be checked. In placenta, the presence of 15–40 cotyledons and lobules up to 200 is reported.[4]

Umbilical cord, which carries out the duties of transferring all substances necessary for fetal development from placenta to fetus and carrying waste materials back to placenta,[5] consists of two arteries (two similar vessels with thick wall and narrow internal orifice) and one vein (with thin wall and wide internal orifice). In a non-twisted umbilicus, the arteries are seen on 4 and 7 o’clock positions, and the vein is seen on 12 o’clock position.[6]

During delivery, placenta should be evaluated generally by observation. Midwives and nurses should inform physician immediately when they observe any abnormality in placenta and cord. Therefore, the awareness of midwives and nurses should be raised for adopting evidence-based practices.[3,4] To that end, we planned the study in order to determine the current knowledge level of midwives on placenta and umbilical cord, who work in delivery room and maternity emergency room, and the contribution of training provided for this purpose on the knowledge level.

Methods

The study was planned between September 31 and December 31, 2016 in prospective and definitive correlational type with the design of single group pre-test and repeating final test in order to assess the knowledge of midwives on placenta and umbilical cord who work in the delivery room and maternity emergency room of a training and research hospital.

Following questions were answered in the research:

- What level of knowledge do midwives have on placenta and umbilical cord?
- Does the knowledge level of midwives differ at first and third months after the training provided?

The population and sample of the study

All midwives in 2 campuses of a university training and research hospital in the city center of Sakarya were the population of the study (n=34), and 34 volunteer midwives who were informed orally were the study sample (100% participation).

Exercising the research

We started to collect the data after obtaining necessary institutional and ethics committee approvals. A pre-test was applied to the midwives included in the research in groups of 10, 11 and 13 individuals in 3 sessions without informing in advance about the training and Powerpoint presentation including the answers of the questions was made. The same individuals were contacted 1 and 3 months after the study and final test with questions used in the pre-test was carried out. The study was conducted with 100% (n=34) participation of the volunteer participants. The questionnaire form consisting of 24 questions and definitive demographic characteristics based on literature were prepared by the researchers. Right answers were scored “1” while wrong answers were scored “0”. Mean scores were obtained according to the answers given to the questions. Increase of the scores showed that knowledge level increased and it was evaluated as a positive condition.

Data collection tools

The data was collected by applying face-to-face interview technique through “Information Form” and “Question Form on Placenta and Umbilical Cord Knowledge” (Appendix).

The Information Form has been developed according to the related literature by researchers and it includes the questions for age, gender, marital status, educational status and year in profession of the midwives.

Question Form on Placenta and Umbilical Cord Knowledge includes the questions such as placental abnormalities, placenta delivery maneuvers during term, structure and anomalies of umbilical cord and approach to umbilical cord in term and preterm infants.

The analysis of data

The analysis of the data was done by SPSS 20.0 (SPSS Inc., Chicago, IL, USA). While mean value and standard deviation (mean±SD) and lowest and highest values were expressed in the numeric data, numbers and percentages were used in categorical data. Normal distribution of the
data was checked by Kolmogorov-Smirnov test, it was seen that there was no normal distribution. Friedman test was used in the comparison of the mean values of more than two dependent groups as the data did not provide parametric characteristics, and Kruskall-Wallis test was used for the comparison of two groups. Statistically significant level was considered p<0.05 for all the data.

Limitations of the research
The research population consisted of only the midwives working in 2 hospitals in the city center of Sakarya. Therefore, we believe that research results cannot be generalized.

Results
The mean age of nurses included in the study was 37.23±6.19 (range: 25 to 51) years, 52.9% of them had bachelor’s degree, 88.2% of them were married, their total experience in their profession was 15.88±6.90 years and they were working in the same unit for 7.5 (range: 1 to 26) years (Table 1).

For the questions to assess the knowledge of midwives on placenta, it was found that 70.6% of them provided wrong answer for the question that delivery of placenta occurs at fourth phase, 26.5% of them for the question that closure of cervical opening by placenta is called ablatio placentae, %73.5% of them for the question that it is called placenta increta if villi enter into myometrium, and 52.9% of them for the question that remaining placenta pieces accelerate uterine involution by increasing uterine contractions.

It was found that 74.9% of the participants provided wrong answer for the knowledge that umbilical cord has both maternal and fetal surfaces, 55.9% of them for the knowledge that there are two arteries and one vein, 38.2% of them for the interpretation that the presence of one artery and one vein is not a problem, 35.3% of them for the knowledge that meconium staining umbilical cord is an indicator of fetal distress, 20.6% of them for the knowledge that newborn blood transfusion is carried out through the umbilicus, 52.9% of them for the definition of omphalocele, and 55.9% of them for the definition of gastroschisis.

It was seen that 35.3% of the participants provided correct answer for the knowledge that umbilicus should be clamped at pelvis level, 35.3% of them for the knowledge that clamping duration should be approximately 30–60 seconds, 14.7% of them for the knowledge that umbilical cord should not be stroked towards baby in problem-free term deliveries, 64.7% of them for the knowledge that umbilical cord should be stroked towards baby in premature deliveries, 91.2% of them for the knowledge that the average period for dropping of umbilical cord after delivery was 7–10 days, 35.3% of them for the knowledge that there is a difference between term and premature infants in terms of the period for dropping of umbilical cord, and 35.3% of them for the knowledge that sterile approach is required for cord prolapse. It was found that 44.1% of the midwives provided correct answer for the fact that pregnant women with pregestational diabetes may have small for gestational age (SGA) babies, and 91.2% of them for the fact that pregnant women with gestational diabetes may have large for gestational age (LGA) babies.

There was a significant increase in pre-test, and 1-month and 3-month final test scores of the participants (Fig. 1).

Table 1. Demographic data of the participants.

<table>
<thead>
<tr>
<th></th>
<th>n=34</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>37.23±6.1</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>4</td>
<td>11.8</td>
</tr>
<tr>
<td>Married</td>
<td>30</td>
<td>88.2</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school/Associate’s degree</td>
<td>11</td>
<td>32.4</td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>18</td>
<td>52.9</td>
</tr>
<tr>
<td>Master’s degree</td>
<td>5</td>
<td>14.7</td>
</tr>
<tr>
<td>Years in profession</td>
<td>15.88</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Mean knowledge score at three different periods.
It was assessed by Friedman test whether there is any difference among the knowledge levels of midwives evaluated in 3 different time period as shown in Table 2, and it was found that there was a statistically significant difference among the groups ($c^2=65.786$, $p=0.000$).

Wilcoxon test with Bonferroni correction was used to see which groups have significant difference. As the study had 3 comparisons, the value $0.05/3=0.017$ was considered significance level with 95% confidence in paired comparisons.

According to the Table 3, mean score of the participants before the training (12.88±2.15) was lower than the mean score 1 month later (21.61±1.75), and the difference of mean knowledge scores before and after the training was statistically significant ($p<0.001$). Mean score of the participants included in the study before the training (12.88±2.15) was lower than the mean score 3 months after the training (23.61±1.75), and the difference of mean knowledge scores before and after the training was statistically significant ($p<0.001$). Similarly, mean score 1 month before the training (21.61±1.75) was lower than the mean score 3 months after the training (23.23±0.85), and the difference of mean knowledge scores before and after the training was statistically significant ($p<0.001$).

The interquartile range data were presented in Table 4 to determine the direction of differences, and it can be seen in the table that knowledge score value increases as the assessments advance.

### Discussion

The structure and function of placenta is important for mother and fetus during pregnancy and in future life of newborn.[7] The transfer of blood from placenta to baby during the period between the delivery of baby and clamping of umbilical cord is defined as “placental transfusion”. There are two placental transfusion methods defined to prevent prematurity anemia. These methods are the delayed cord clamping (DCC) and umbilical cord milking (UCM). Although transfusion volumes by DCC after delivery differ greatly and significantly higher hemoglobin values cannot be reached in many studies, it is recommended to refer DCC method for placental transfusion in premature babies. It was shown that DCC method is applicable, provides improvement in blood pressure at early period and protects against intraventricular hemorrhage and late-onset sepsis at further periods although it does not make a significant hemoglobin or hematocrit difference in premature babies between 24 and 32 weeks.[8]

American Pediatric Association (APA) recommends DCC method during delivery[9] but it reported that DCC method should not be used in all deliveries. If clinical condition of newborn is not appropriate or if urgent resuscitation is needed, UCM is recommended instead of DCC.[10] In recent years, it has been reported by various studies that delaying umbilical cord clamping for 30–45 seconds compared to 2–3 minutes may yield better results. In cases requiring urgent resuscitation, milking the cord towards the baby was tested and found effective.[11] Oliveira et al. highlighted in their study performed with premature babies born less than 2500 g and under 37 weeks (n=555) that umbilical cord clamping at 60th second decreases anemia risk.[12]

The presence of single artery may coexist with some anomalies such as Potter syndrome.[13] Knowing

### Table 2. Knowledge comparison of midwives in 3 different time periods (Friedman test).

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean±SS</th>
<th>$p; \chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge before training</td>
<td>12.88±2.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knowledge 1 month after training</td>
<td>34</td>
<td>21.61±1.75</td>
<td>$&lt;0.001; 65.786$</td>
</tr>
<tr>
<td>Knowledge 3 months after training</td>
<td>23.23±0.85</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Knowledge comparison of midwives in 3 different time periods (Wilcoxon test with Bonferroni correction).

<table>
<thead>
<tr>
<th></th>
<th>Mean±SS</th>
<th>$p; Z$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge before training</td>
<td>12.88±2.15</td>
<td></td>
</tr>
<tr>
<td>Knowledge 1 month after training</td>
<td>21.61±1.75</td>
<td>$&lt;0.001; -5.098$</td>
</tr>
<tr>
<td>Knowledge 3 months after training</td>
<td>23.23±0.85</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4. Interquartile range of midwives’ knowledge in 3 different time periods.

<table>
<thead>
<tr>
<th>Assessments</th>
<th>Median</th>
<th>Interquartile range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-test</td>
<td>13.000</td>
<td>3.25</td>
</tr>
<tr>
<td>Repeating test 1 month later</td>
<td>22.000</td>
<td>2.25</td>
</tr>
<tr>
<td>Repeating test 3 months later</td>
<td>23.000</td>
<td>1</td>
</tr>
</tbody>
</table>
the number of vein and artery in umbilical cord by midwife managing the delivery, establishing early diagnosis on a newborn with single artery and directing to a podiatrist for necessary examinations are very important in terms of baby.

Those who are diagnosed with diabetes during pregestational period are defined as pregestational diabetes mellitus and diabetes developing during pregnancy for the first time is defined as gestational diabetes mellitus. In pregestational diabetes, there is the risk of premature and SGA baby delivery. In gestational diabetes, the number of LGA baby is three times more. Knowing the characteristics of baby to be delivered during pregestational and gestational diabetes is significant to identify newborns with risk.

As the part of active management of third phase, two simple maneuvers are performed to help the birth of placenta. These maneuvers are fundal pressure (Crede) or controlled traction of cord (Brandt-Andrews). In Crede’s maneuver, one hand is placed on the fundus of uterus and fundus is pressed with thumb and other fingers to separate placenta and help the delivery. In Brandt-Andrews maneuver, one hand is placed on lower abdomen and umbilical cord is pulled upwards by maintaining opposite pressure or one hand applies a slight traction on the cord while other hand strokes uterus upwards through symphysis pubis. The midwives had difficulties when matching the definitions of maneuvers and only 41.2% of the midwives defined both maneuvers correctly.

In anomalies such as ablatio placentae, placenta previa and placental attachment, pregnancy process can be managed by antenatal care. Gastrochisis and omphalocle are the most common (3/10,000) fetal abdominal wall defects. In gastrochisis, intestines may extend outside of the body on the right of umbilical cord and other intraabdominal organs may extend outside of the body. In omphalocle, there is a herniated sac developing outwards within umbilical cord. Half of the participants could not define these anomalies properly. Midwives who have active roles during delivery should know these anomalies and be able to perform appropriate approach.

The first feces of newborn is called as meconium and defecation is expected within 24–48 hours after delivery. Intrauterine meconium outflow may occur in cases such as placental failure, preeclampsia, oligohydramnios and maternal drug use. Amniotic fluid stained by meconium is seen in 5–24% of normal pregnancies (mean: 13%) (5.1% in preterm, 16.5% in term and 27.1% in postterm), and it is a potential fetal distress indicator. Choi et al. found that the rate of babies born with meconium stain was 10.6% (71/671). Mechanical occlusion in the airways associated with meconium aspiration, surfactant inactivation and respiratory distress syndrome associated with pulmonary hypertenasion develop. One third of these babies need intubation. The midwives who have a key role in delivery should have sufficient knowledge on newborn resuscitation and first care of baby in delivery room, and should be able to initiate the process effectively and rapidly.

**Conclusion**

In our study shows that the knowledge of midwives on placenta and umbilical cord is insufficient, and therefore the knowledge of midwives who provide care for pregnant women and newborns should be reinforced. It is possible to reinforce their professional knowledge by in-service and on-the-job trainings after graduation. By the feedbacks received, the midwives stated that they carried out their routine duties by being more aware with the help of training and they updated their current knowledge. We concluded that such trainings can be used to remedy the professional deficiencies.

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

**References**

Appendix. Question and information forms

<table>
<thead>
<tr>
<th>Question Form</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dear participant, the questions below will set light to our practices in delivery rooms and will help us to see theoretical deficiencies in the practices. Thank you for contributing to the reliability and validity of the result obtained by providing individual answers.</strong></td>
</tr>
</tbody>
</table>

1. In term babies, how many days do approximately take for umbilical cord to dry and drop?
   - A) 1–2 days
   - B) 2–3 days
   - C) 7–10 days
   - D) 10–15 days

2. There is no difference in the duration of dropping of umbilical cord in term and preterm babies.
   - A) True
   - B) False

3. Umbilical cord has 2 arteries and one vein.
   - A) True
   - B) False

4. Umbilical cord has both maternal and fetal surfaces.
   - A) True
   - B) False

5. There is no problem usually in babies born with umbilical cord having 1 artery and 1 vein; what matters is that there should be at least one for each from two different structures (artery and vein).
   - A) True
   - B) False

6. What is the average duration of cord clamping in term baby?
   - A) 10–15 sec.
   - B) 15–30 sec.
   - C) 30–60 sec.
   - D) 90–120 sec.

7. When cord is being clamped in preterm babies, cord blood should be milked towards the baby.
   - A) True
   - B) False

---


8. When cord is being clamped in term babies, cord blood should be milked towards the baby.  
   A) True  
   B) False

9. Which of the following statements is a condition that should be done before clamping?  
   A) The baby is hold at maternal pelvis level, so anemia is prevented in baby.  
   B) The baby is hold above the maternal pelvis level, so anemia is prevented in mother.  
   C) The baby should be hold at the same level with pelvis.  
   D) Clamping should be performed when heartbeat is stopped in umbilical cord.

10. Umbilical cord stained by meconium is an indicator for fetal distress.  
    A) True  
    B) False

11. The birth of placenta occurs at the 4th phase of delivery.  
    A) True  
    B) False

12. Closure of cervical opening by placenta is called ablatio placentae.  
    A) True  
    B) False

13. It is called placenta increta if villi enter into myometrium.  
    A) True  
    B) False

14. Which of the following options is the herniation of intraabdominal organs associated with the extension of umbilical cord in fetal umbilicus on abdominal wall?  
   A) Omphalocele  
   B) Gastrochisis  
   C) Aged placenta  
   D) Short placenta

15. Which of the following options is the extension of intestines outside of the body from an opening on the side of baby’s cord?  
   A) Omphalocele  
   B) Gastrochisis  
   C) Aged placenta  
   D) Placenta accreta

16. Baby with omphalocele should be evaluated in terms of chromosomal anomaly.  
    A) True  
    B) False

17. Blood transfusion of a newborn is carried out through the umbilicus.  
    A) True  
    B) False

18. Select the wrong approach in cord prolapse.  
   A) Check cord pulsation  
   B) Determine the labor phase of pregnant woman  
   C) In the first labor phase of pregnant woman, the hand should be placed on vagina by wearing a non-sterile glove and those coming out should be pushed upwards and moved away from the pelvis in order to decrease the pressure on cord.  
   D) If pregnant woman is at the second phase of labor, the delivery should be accelerated by episiotomy, and, if possible, vacuum extraction or forceps.

19. If cord has no pulsation during cord prolapse, it means that the fetus is dead; the safest way for pregnant woman is to carry out delivery by section.  
    A) True  
    B) False

20. In order to ease the separation and birth of placenta, one hand pulls umbilical cord downward while the other hand on umbilicus is kept on fundus of uterus for the prevention of uterine inversion. Which of the following options is the definition of this maneuver?  
   A) Brandt-Andrews maneuver  
   B) Crede’s maneuver

21. In order to ease the separation and birth of placenta, upward traction is applied by hand on abdomen and uterus is protected and supported while the hand below fixes the cord. Which of the following options is the definition of this maneuver?  
   A) Brandt-Andrews maneuver  
   B) Crede’s maneuver

22. Remaining placenta pieces accelerate uterine involution by increasing uterine contractions.  
    A) Correct  
    B) False

23. Babies delivered by women with gestational diabetes are usually macrosomic and their umbilical cords are thick.  
    A) Correct  
    B) False

24. Babies delivered by women with pregestational diabetes are usually SGA (small gestational age) and their umbilical cords are thin.  
    A) Correct  
    B) False

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**Information Form**

1. Your age: 
2. Your educational status: [ ] High school / Associate’s degree  [ ] Bachelor’s degree  [ ] Master’s degree
3. Your title: [ ] Nurse  [ ] Midwife
4. Years in profession: 
5. The clinic you currently work: 
6. For how many years have you been working at this clinic? 
7. Your marital status: [ ] Single  [ ] Married
The effects of multivitamin use during pregnancy on birth weight

Sevcan Arzu Arıkan, Emin Erhan Dönmez, Zafer Bütün, Mehmet Teoman Bilgiç, Murat Muhcu
Zeynep Kamil Maternity and Pediatrics Training and Research Hospital, Istanbul, Turkey

Abstract

Objective: In Turkey, multivitamin supplements are prescribed to pregnant women from all socioeconomic levels. In our study, we aimed to determine the effects of multivitamin and antianemic use on birth weight.

Methods: A total of 595 pregnant women who were fulfilling inclusion criteria among those who delivered term single baby were included in our study. Types and period of use of multivitamins and period of antianemic use within first 24 hours after delivery by puerperant women included in the study were investigated. The demographics, delivery and newborn information of patients were accessed through patient files.

Results: In our study, the mean age of pregnant women was 26.9±5 and mean hematocrit value of all cases was 35.68±3.7. Mean periods of antianemic and multivitamin use were 16.45±10.5 and 14.18±10.8, respectively. Mean weight gained by cases during pregnancy was 12.9±5.3 kg and mean birth weight was 3400±440 g. There was a statistically significant difference between the mean birth weight (3435 g) of those who received multivitamin during pregnancy and the mean birth weight (3358 g) of those who did not receive. Also, no statistically significant difference was found between the mean birth weight (3418 g) of those who received antianemics and the mean birth weight (3338 g) of those who did not receive. Birth weight and period of multivitamin use, and the weight gained by mother during pregnancy and maternal BMI were associated with a positive correlation. No statistically significant correlation was found between birth weight and maternal hematocrit value before delivery and period of antianemic use.

Conclusion: In our study, fetal birth weight in pregnant women who used multivitamin during pregnancy is 77 g higher. Although this difference is statistically significant, the correlation is poor. However, we found no relationship between antianemic use and birth weight.

Keywords: Birth weight, multivitamin supplement, pregnancy.

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QR (Quick Response) Code:
**Introduction**

In general, nutritional status of women who eat three meals a day consuming vegetable, fruit, cereal products, foods low in fat and protein is considered sufficient. Additional daily calorie intake requirement during pregnancy is 340 kcal in second trimester and 452 kcal in third trimester. Pregestational weight and weight gain during pregnancy affect fetal weight and gestational period. Underweight women who cannot gain sufficient weight during pregnancy have the risks of delivering low-weight fetus and preterm labor. The supplementation on the diet and nutrition during pregnancy is considered beneficial for women with nutritional deficiency. In countries with low income levels, macronutrient and micronutrient supplements in pregnant women are considered to have a positive effect on gestational outcomes and early childhood outcomes. However, this relationship is complex and controversial. Multivitamin supplement is recommended for pregnant women who have high risk for nutritional deficiency, those with multiple pregnancy, heavy smokers, adolescents, full vegetarians, and those with lactase deficiency. In well-nourished pregnant women, micronutrient supplement is not considered to have a certain effect on gestational period and birth weight.\(^1\,^2\)

Periconceptional folic acid supplement is recommended to prevent neural tube defects. During preconceptional period and first trimester, daily intake of 0.4–0.8 mg folic acid is recommended. It is recommended for pregnant women in high-risk group to increase the dose and take 4 mg daily. Full calcium and iron stores are important for bones and erythrocyte development. Iron supplement during pregnancy decreases maternal anemia in delivery. However, the effects of iron supplement on the delivery outcomes of pregnant women, who are not anemic and nourished well, are unclear. Low or high levels of iodine may cause fetal goiter. High dose of vitamin A (10,000 IU) during pregnancy is teratogenic.\(^3\)

In Turkey, multivitamin supplements are prescribed to pregnant women from all socioeconomic levels. In our study, we aimed to determine the effects of multivitamin and antianemic use on birth weight.

**Methods**

A total of 595 pregnant women, who were fulfilling inclusion criteria among those who delivered term single baby at Zeynep Kamil Maternity and Pediatrics Training and Research Hospital, were included in the study. The cases with multiple pregnancies, those who have high-risk pregnancies such as chronic diseases, structural/chromosomal anomalies, intrauterine growth retardation, gestational diabetes and preeclampsia, and the cases smoking and consuming alcohol were excluded from the study.

Types and period of use of multivitamins and period of antianemic use within first 24 hours after delivery by puerperant women included in the study were investigated. The demographics, delivery and newborn information of patients were accessed through patient files.

SPSS 22.0 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. When evaluating the study data, Spearman correlation analysis, independent samples t test and Kolmogorov-Smirnov test as well as definitive statistical methods (mean, standard deviation) were used. Significance was considered at p<0.01 and p<0.05 levels.

**Results**

In our study, the mean age of pregnant women was 26.9±5 years, mean gravida was 2, the period between two pregnancies was 2.4±3 years and mean body mass index (BMI) was 29.29±4. Mean hematocrit value of all cases was 35.68±3.7 (Table 1). Mean periods of antianemic and multivitamin use were 16.45±10.5 and 14.18±10.8, respectively. The weight gained by the cases during pregnancy was found 12.9±5.3 kg.

Mean birth weight was 3400±440 g. The difference between the mean birth weight (3435±430 g) of those who received multivitamin during pregnancy (n=326) and the mean birth weight (3358±450 g) of those who did not receive (n=266) was 77 g and it was statistically sig-

**Table 1. Demographic variables.**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Minimum</th>
<th>Maximum</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>26.98</td>
<td>16.00</td>
<td>44.00</td>
<td>5.61</td>
</tr>
<tr>
<td>Gravida</td>
<td>2.16</td>
<td>1.00</td>
<td>9.00</td>
<td>1.38</td>
</tr>
<tr>
<td>Period between two pregnancies (year)</td>
<td>2.42</td>
<td>.00</td>
<td>19.00</td>
<td>3.36</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.29</td>
<td>17.60</td>
<td>52.40</td>
<td>4.45</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3400</td>
<td>2000</td>
<td>4720</td>
<td>440.62</td>
</tr>
<tr>
<td>Maternal Htc</td>
<td>34.68</td>
<td>21.00</td>
<td>45.70</td>
<td>3.79</td>
</tr>
<tr>
<td>Antianemic period (week)</td>
<td>16.45</td>
<td>.00</td>
<td>40.00</td>
<td>10.56</td>
</tr>
<tr>
<td>Multivitamin period (week)</td>
<td>14.18</td>
<td>.00</td>
<td>39.00</td>
<td>10.87</td>
</tr>
</tbody>
</table>

BMI: Body mass index, Htc: Hematocrit, SD: Standard deviation
significant (p=0.035). However, the correlation was poor. The difference between the mean birth weight (3418±435 g) of those who received antianemics during pregnancy (n=461) and the mean birth weight (3338±454 g) of those who did not receive (n=131) was 80 g and it was not statistically significant (p=0.066) (Table 2).

There was a positive correlation between birth weight and the period of multivitamin use, and between weight gained by mother during pregnancy and maternal BMI (rs=0.108, p=0.029; rs=0.057, p=0.172; rs=0.223, p<0.01).

No statistically significant correlation was found between birth weight and maternal hematocrit value before delivery and period of antianemic use (rs=0.077, p=0.062; rs=0.310, p=0.533).

**Discussion**

While routine multivitamin supplement is not recommended generally, clinicians prescribe prenatal vitamin in order to compensate potential dietary deficiencies. The micronutrient need during pregnancy increases depending on the physiological changes. Common nutritional deficiency during pregnancy depends on various demographic characteristics such as young maternal age, low income and low educational level. Maternal nutritional status at pregestational and early gestational periods decreases poor gestational outcomes such as birth defects, premature labor and low birth weight. Improving pregestational nutritional status affects neonatal and pediatric outcomes positively.

Insufficient maternal micronutrient level is associated with premature labor, low-birth-weight delivery, increased perinatal mortality, small head circumference, neural tube defect and anemia in newborn. In order to prevent these conditions, World Health Organization recommends 60 mg elementary iron and 400 μg folic acid daily. Jabbari et al. showed in their study that iron supplement during pregnancy increased heights and weights of newborns and the birth weights and heights of newborns of mothers who received iron sulfate more than 120 mg daily were higher than those of the mothers who did not receive iron supplement. Also, they showed that multivitamin supplement had no effect on birth weight or height. In our study, however, we found that the birth weight in pregnant women who received multivitamin was 77 g higher and this difference is statistically significant. Also, we found 80 g difference in the mean birth weights of women who received antianemics during pregnancy compared to those who did not receive, but this difference was not statistically significant.

Preconceptional multivitamin supplement decreases the incidence of neural tube defect; however, no significant effect was observed on gestational outcomes. Andrew et al. showed in their study that periconceptional multivitamin supplement decreased the rate of neural tube defect, but had no significant effect on gestational outcomes. However, they reported that it may decrease monozygotic twin pregnancy, extremity anomaly, congenital pyloric stenosis and some heart diseases. Greenberg et al. reported in their study that folic acid use during conceptional period decreased neural tube defect as well as the risk for premature labor and congenital heart diseases.

Janet et al. found that regular multivitamin use just before conceptional period decreases premature labor risk in overweight pregnant women and similarly, it decreases low-birth-weight deliveries independent from BMI.

Multivitamin use 6 weeks before and after conception decreases preeclampsia incidence, growth retardation and premature labor incidence. However, it is considered that regular periconceptional multivitamin use slightly increases the risk of early fetal death (<20 weeks) but regular use after conception decreases late fetal loss risk.

<table>
<thead>
<tr>
<th>Table 2. Relationship between vitamin use and birth weight.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antianemic use</strong></td>
</tr>
<tr>
<td>Birth weight (g)</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Multivitamin use</strong></td>
</tr>
<tr>
<td>Birth weight (g)</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

*Independent samples t test. SD: Standard deviation
It is taught that regular multivitamin use by pregnant women in developed countries has no effect on birth weight and multivitamin use at third trimester increases premature labor risk. Yet, multivitamin supplement is recommended to women with pregnancy potential in some developed countries such as the USA. Alwan et al. showed in their study that daily intake of multivitamin-mineral during any period of pregnancy has no effect on low birth weight. On the other hand, they showed that multivitamin mineral supplement at third trimester is 3 times more associated with premature labor. It was also reported that the relationship is more distinct in primiparous women. Some studies reported that antioxidant vitamin supplements such as vitamins C and E may have a negative effect on the gestational outcomes of pregnant women who receive sufficient micronutrient in their diets. Smedts et al. showed in their study that periconceptional vitamin E supplement increases the risk of congenital heart diseases for 9 times in pregnant women who receive high amount of vitamin E with their diet. Another study reported that vitamins C and E supplement is associated with increased EMR risk. In the meta-analysis performed, vitamins C and E supplement has no positive effect on maternal and neonatal outcomes and increases gestational hypertension risk in pregnant with preeclampsia risk. In the study carried out, multivitamin and mineral supplement at third trimester is associated with premature labor risk but not associated with birth weight. In the light of these results, Alwan et al. at least recommends to prescribe multivitamin-mineral supplement carefully to pregnant women, who have no micronutrient deficiency, especially in the last periods of pregnancy.

It was shown that multivitamin supplement for HIV-negative pregnant women in Tanzania increased gestational weight gain and that the increased gestational weight gain increased the newborn birth weight.

Hashemipour et al. demonstrated in their study that vitamin D supplement in pregnant women with vitamin D deficiency increased the height, weight and head circumference of newborn.

In their study, Ozturk et al. reported that there was no statistically significant difference in terms of birth weight and obstetric outcomes between pregnant women who have and do not have B12 deficiency. They showed that maternal B12 deficiency had no effect on birth weight and week of gestation.

Conclusion
In our study, fetal birth weight in pregnant women who used multivitamin during pregnancy is 77 g higher. Although this difference is statistically significant, the correlation is poor. However, we found no relationship between antianemic use and birth weight. Birth weight and period of multivitamin use, and the weight gained by mother during pregnancy and maternal BMI were associated with a positive correlation. However, no statistically significant correlation was found between birth weight and maternal hematocrit value before delivery and period of antianemic use. Pregnant women without chronic disease who keep a balanced diet are not recommended using multivitamin supplement during pregnancy.

Conflicts of Interest: No conflicts declared.

References


Investigating the effects of progesterone-derived medication during first and second trimesters on the gestational diabetes development and gestational outcomes

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Abstract

Objective: We aimed to compare newborn outcomes and blood glucose values of 75-g oral glucose tolerance test (OGTT) in pregnant women who were diagnosed gestational diabetes mellitus and did not receive progesterone in 1st and 2nd trimesters and the pregnant women who received progesterone for at least 4 weeks.

Methods: This single-center, retrospective, cross-sectional case study was conducted on pregnant women who were admitted to our obstetrics polyclinic between January 2014 and June 2016. A total of 337 pregnant women who were established with the diagnosis of gestational diabetes mellitus during their pregnancies followed up and delivered at our clinic were included in the study. The patients were separated into two groups as those received progesterone during 1st or 2nd trimester of their pregnancies (n=59) and those did not receive progesterone (n=278). The data were analyzed by SPSS software.

Results: While there was no statistically significant difference between the group not receiving progesterone-derived medication and the group receiving progesterone-derived medication in terms of mean 0-hour and 2-hour blood glucose values of 75-g OGTT, 1-hour blood glucose values were significantly higher in the group receiving progesterone (p<0.05). This high value was observed in pregnant women who received 17-OH progesterone caproate, which is a weekly injection form of progesterone derivatives. There was no statistically significant difference between the groups in terms of birth weight, and 1-minute and 5-minute APGAR scores.

Conclusion: We found significant increase in 1-hour values of 75-g OGTT in pregnant women who received 17-OH progesterone caproate for at least four weeks during first and second trimesters of their pregnancies. Further studies are required to compare our results since our population is small.

Keywords: Diabetes mellitus, insulin, pregnancy, progesterone.

Özet: Birinci ve ikinci trimesterde progesteron türevi ilaç kullanımının gestasyonel diayabet oluşumu ve gebelek sonuçlarına etkisinin araştırılması

Amaç: Gestasyonel diabetes mellitus tanısal olup 1. ve 2. trimesterde progesteron kullanmamış gebeler ile en az 4 hafta progesteron kullanmış gebelerin 75 g oral glukoz tolerans testi (OGTT) kan şekeri değerleri ile yeni doğan sonuçların karşılaştırılmasını amaçlanmıştır.


Bulgular: 0. ve 2. saat ortalama kan şekeri değerleri açısından istatistiksel olarak anlamlı bir fark gözlenemezken; 1. saat kan şekeri değerleri progesteron kullanan grupta anlamlı yüksek bulundu (p<0.05). Bu yükseklik progesteron türevinden hafiflik enjeksiyon formu olan 17-OH progesteron kaproat kullanan gebellerde gözlandı. Gruplar arasında doğum ağırlığı, 1. dakika APGAR skor ve 5. dakika APGAR skor açısından da istatistiksel olarak anlamlı bir fark gözlememiş bulunmamaktadır.

Sonuç: Gebeliklerin birinci ve ikinci trimesterinde en az dört hafta, intramüsküler 17-OH progesteron kaproat kullanulan gebelerde 75 g OGTT 1. saat değerlerinde anlamlı yükselme tespit edilmiştir. Popülasyonumuzun kücük olması sebebiyle sonuçlarımızın karşılaştırılması labileceği yeni çalışmalara ihtiyaç duyulmaktadır.

Anahtar sözcükler: Diabetes mellitus, gebelek, insülin, progesteron.
**Introduction**

Gestational diabetes mellitus (GDM) is the glucose intolerance which appears during pregnancy for the first time or diagnosed during pregnancy for the first time.\(^1\) Although GDM can be seen in all periods of pregnancy, it is mostly diagnosed beginning from the 24 weeks of gestation. The reason is that the human placental lactogen (hPL), which is a placental hormone antagonizing the blood glucose-decreasing effect of insulin, reaches maximum level beginning from this period.\(^2,3\) Therefore, GDM is a metabolic disorder which should be taken under control as of 24 weeks of gestation.\(^4,5\)

In various societies, 1–14% of pregnancies are established with the diagnosis of gestational diabetes while 0.5% of all pregnancies are established with the diagnosis of pregestational diabetes.\(^6\)

Pregnancies complicated with diabetes have various maternal and fetal risks compared to healthy pregnancies. While pregnancies complicated with diabetes had high rates of maternal mortality (45%) and perinatal mortality (60%) in the early periods of previous century, these rates decreased significantly when insulin began to be used in treatments in 1920s.\(^2\)

Progesterone is a steroidal hormone which should be secreted sufficiently in order to provide embryonic implantation and maintain pregnancy and is produced in corpus luteum in the beginning, and placenta undertakes this duty as of the 9 weeks of gestation.\(^7,8\) Progesterone has a key role to maintain the atonicity of the uterus; however, its mechanism has not been fully understood.\(^9–11\) Although progesterone is prescribed widely for the treatment of imminent abortion in obstetric practice, the meta-analysis conducted by Wahabi et al. could not find any evidence showing that vaginal progesterone support is effective in the treatment of imminent abortion,\(^12\) and some studies showing the efficacy of progesterone support to decrease preterm labor risk were published.\(^13,14\)

On the other hand, some studies reported that the use of progesterone increases the risk of developing GDM.\(^13,16\)

In our study, we aimed to compare newborn outcomes and blood glucose values of 75-g oral glucose tolerance test (OGTT) in pregnant women who were diagnosed GDM in our clinic and did not receive progesterone in 1st or 2nd trimester and the pregnant women who received progesterone-derived medication for at least 4 weeks.

**Methods**

A total of 337 patients, who were admitted to our obstetrics polyclinic between January 2014 and June 2016, established with the diagnosis of GDM and delivered at our clinic, were included in this single-center, retrospective, cross-sectional case study.

The inclusion criteria were determined as being pregnant between 17- and 46-year-old, undergoing 75-g OGTT as GDM screening and diagnostic test between 24 and 29 weeks of gestation and being established with the diagnosis of GDM as a result, and receiving progesterone-derived medication for at least 4 weeks due to miscarriage risk or preterm labor threat.

The exclusion criteria were determined as having pregestational DM diagnosis, termination due to anomaly in pregnancy or intrauterine death of fetus, having any hepatic, renal or thyroid dysfunction during pregnancy which may affect glucose or protein metabolism, and discontinuing follow-up or control.

Age, gravida, parity, history of previous pregnancies, background, family history, history of current pregnancy, medication, and weight gained of pregnant women who included in the study were obtained through their medical records. Gestational ages of the patients were determined according to the first day of their last menstrual period and confirmed by CRL (crown-rump length) measurements established by first trimester ultrasonography. It was recorded whether each patient received progesterone during their pregnancies or not, and if they received, for how long did they receive progesterone-derived medication. Body mass index (BMI: weight [kg]/height\(^2\) [m\(^2\)]) of each patient was calculated by prenatal weight and height. The birth weights and 1-minute and 5-minute APGAR scores of newborns were reached by their records.

For pregnant women who underwent 75-g OGTT, the diagnosis was deemed positive when either 0-hour blood glucose level was \(\geq 92\) mg/dL, 1-hour blood glucose level was \(\geq 180\) mg/dL or 2-hour blood glucose level was \(\geq 153\) mg/dL according to the criteria of American Congress of Obstetricians and Gynecologists (ACOG Practice Bulletin 2008) and American Diabetes Association (2003).\(^11,17\)

The patients were separated into two groups as those receiving progesterone-derived medication during 1st or 2nd trimester of pregnancy and those not receiving
progesterone, and their OGTT values were compared. The pregnant women who were receiving progesterone-derived medication were also separated into 3 subgroups, which where oral progesterone (Progestan®, Koçak Farma, Istanbul, Turkey) (n=31), daily intramuscular progesterone (Progynex®, Farmako Eczacılık, Istanbul, Turkey) (n=16), and weekly intramuscular 17-OH progesterone caproate (Proluton®, Bayer, Istanbul, Turkey) (n=12).

SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. The data were presented as mean ± standard deviation. Independent two-sample t-test was used for comparisons between two groups, Kruskal-Wallis variance analysis was used for comparisons between more than two groups, and Mann-Whitney U test was used as post-hoc test to identifying the group causing the difference. Pearson correlation test was conducted to determine any relationship between newborn birth weight and APGAR scores and OGTT levels. In all comparisons, p<0.05 was considered statistically significant.

**Results**

Of 337 patients included in the study, 82.5% (n=278) did not receive any progesterone-derived medication during their pregnancies, and 17.5% (n=59) received any progesterone-derived medication for at least 4 weeks. The distribution of receiving progesterone-derived medication was 9.2% (n=31) for oral progesterone, 4.8% (n=16) for daily intramuscular progesterone, and 3.5% (n=12) for weekly intramuscular 17-OH progesterone caproate.

Of the patients not receiving progesterone-derived medication, the mean age was 30.8 years, mean weight was 80.2 kg and mean BMI was 30.6 kg/m². Of the patients receiving progesterone-derived medication, the mean age was 29.5 years, mean weight was 81.4 kg and mean BMI was 32.9 kg/m². There was no statistically significant difference between the groups in terms of age, gravida, parity, weight and BMI values (Table 1).

The groups receiving and not receiving progesterone-derived medication were compared in terms of 0-hour OGTT, 1-hour OGTT and 2-hour OGTT values. While no significant difference was observed between the groups in terms of 0-hour and 2-hour OGTT values, the values of 1-hour OGTT were significantly higher in the group receiving progesterone (p=0.045) (Table 2).

No difference was observed in 0-hour and 2-hour values when the patients receiving progesterone-derived medication were compared among themselves; however, 1-hour values of the group receiving 17-OH progesterone caproate were significantly higher the values of pregnant women receiving oral progesterone and daily intramuscular progesterone (p<0.05) (Table 3).

When 0-hour, 1-hour and 2-hour OGTT values of the patients not receiving progesterone-derived medication were compared with 0-hour, 1-hour and 2-hour OGTT values of the patients receiving oral progesterone and daily intramuscular progesterone (p<0.05).

**Table 1. The comparison of the demographic data of two groups.**

<table>
<thead>
<tr>
<th>Group 1 (n=278)</th>
<th>Group 2 (n=59)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>30.8±8.2</td>
<td>29.5±6.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.2±12.3</td>
<td>81.4±10.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.6±4.3</td>
<td>32.9±5.9</td>
</tr>
<tr>
<td>Gravida (number)</td>
<td>2 (1-6)</td>
<td>2 (0-6)</td>
</tr>
<tr>
<td>Parity (number)</td>
<td>2 (0-6)</td>
<td>1 (0-5)</td>
</tr>
</tbody>
</table>

*The data are presented as mean ± standard deviation and median (minimum–maximum). Group 1: The patient group not receiving progesterone-derived medication, Group 2: The patient group receiving progesterone-derived medication.

**Table 2. The comparison of 0-hour OGTT, 1-hour OGTT and 2-hour OGTT values of two groups.**

<table>
<thead>
<tr>
<th>Group 1 (n=278)</th>
<th>Group 2 (n=59)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OGTT 0 (mg/dL)</td>
<td>96.0±14.3</td>
<td>94.1±10.3</td>
</tr>
<tr>
<td>OGTT 1 (mg/dL)</td>
<td>160.2±45.2</td>
<td>170.6±52.1</td>
</tr>
<tr>
<td>OGTT 2 (mg/dL)</td>
<td>131.5±38.1</td>
<td>133.2±29.9</td>
</tr>
</tbody>
</table>

*The data are presented as mean ± standard deviation. Group 1: The patient group not receiving progesterone-derived medication, Group 2: The patient group receiving progesterone-derived medication.

**Table 3. The comparison of OGTT values of the pregnant women by progesterone derivation taken.**

<table>
<thead>
<tr>
<th>OP (n=31)</th>
<th>ImP (n=16)</th>
<th>17-OHP (n=12)</th>
<th>p-value (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OGTT 0 (mg/dL)</td>
<td>93.1±15.2</td>
<td>95.8±16.2</td>
<td>93.4±13.8</td>
</tr>
<tr>
<td>OGTT 1 (mg/dL)</td>
<td>161.9±37.2</td>
<td>169.9±42.7</td>
<td>189.7±56.7†</td>
</tr>
<tr>
<td>OGTT 2 (mg/dL)</td>
<td>131.2±39.9</td>
<td>132.3±42.9</td>
<td>136.9±33.1</td>
</tr>
</tbody>
</table>

*The data are presented as mean ± standard deviation. †Kruskal-Wallis variance analysis. The superscript numbers are presented to indicate the difference between the groups (Mann-Whitney U test, p=0.011). 17-OHP: Weekly intramuscular 17-OH progesterone caproate, ImP: Daily intramuscular progesterone, OGTT: 75-g oral glucose tolerance test; OP: Oral progesterone.
terone, intramuscular progesterone and weekly intramuscular 17-OH progesterone caproate, it was found that there was a significant difference between 1-hour values of the groups. In the inter-group sub-comparison, it was seen that the difference was caused by the patient group receiving intramuscular 17-OH progesterone caproate (p=0.011) (Table 3).

The newborn birth weights and 1-minute and 5-minute APGAR scores of the patients who were included in the study are presented in Table 4. No statistically significant difference was found between the groups in terms of birth weights and APGAR scores (p>0.05). No relationship was found in the correlation analysis conducted between 1-hour 75-g OGTT results and birth weight, and 1-minute and 5-minute APGAR scores.

**Discussion**

In our study, we found that 1-hour OGTT values of the patient group who were receiving intramuscular 17-OH progesterone caproate during 1st or 2nd trimester of pregnancy were significantly higher than those of the patients who did not receive progesterone-derived medication, but there was no significant difference in terms of 0-hour and 2-hour OGTT values. Also, there was no significant difference between the groups receiving oral progesterone and intramuscular progesterone and those not receiving progesterone-derived medication in terms of 0-hour, 1-hour and 2-hour OGTT values. In addition, we found no significant difference between the pregnant women with GDM who were receiving and not receiving in terms of birth weights and 1-minute and 5-minute APGAR scores.

Hormones synthesized during pregnancy such as estrogen, placental lactogen, human chorionic somatomammotropin and progesterone are responsible for the development of insulin resistance and hyperglycemia. It was shown that progesteron in particular decreased insulin sensitivity. In a study conducted on pregnant rats, progesteron was shown to cause decreased insulin sensitivity. In various studies, a relationship was also found between insulin resistance and oral contraceptives containing only progesterone. In a recent study performed on adolescents, Aldhoon-Hainerová et al. investigated the relationship between insulin resistance (HOMA-IR) value and endogenous hormone levels, and found that endogenous progesterone level was in direct proportion to HOMA-IR values in female adolescents. Nunes et al. showed in their cell culture study that progesterone caused apoptosis in the cells synthesizing insulin.

Progesterone support in the treatment of imminent abortion and recurrent pregnancy wastage has become a common treatment option. Also, the recent studies showing the efficacy of progesterone treatment for the prevention of preterm labor have drawn attention. Meis et al. initiated 17-OH progesteron treatment on 16–20 weeks of gestation on 310 pregnant women who had high risk for preterm labor below 37 weeks of gestation. This group was compared to 153 pregnant women who also had high risk for preterm labor but not administered progesterone treatment. After the comparison, it was shown that 17-OH progesterone treatment was efficient to prevent preterm labor and to decrease perinatal morbidity. In their study, Fonseca et al. compared a group consisting of 72 pregnant women who received vaginal progesterone to another group consisting of 70 pregnant women who received placebo and showed that vaginal progesterone is efficient in the prevention of preterm labor. In 2008 after these two randomized controlled studies, ACOG recommended progesterone support for preterm labor prophylaxis in singleton pregnancies with the history of preterm labor.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=278)</th>
<th>Group 2 (n=59)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (gram)</td>
<td>3201±584</td>
<td>3107±498</td>
<td>0.16</td>
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<tr>
<td>1-minute APGAR score</td>
<td>9.1±0.7</td>
<td>8.9±1.1</td>
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<td>5-minute APGAR score</td>
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With the increased practice of progesterone treatment during pregnancy, the investigation of potential fetal and maternal side effects of this treatment was brought to agenda. It was brought to agenda that progesterone in particular may affect insulin resistance and may cause the development of gestational diabetes. In their retrospective study, Egerman et al. compared 491 obese pregnant women with GDM diagnosis to 408 obese pregnant women without GDM diagnosis. It was found out in the history of pregnant women with GDM diagnosis that the frequency of 17-OH treatment initiated at 16–20 weeks of gestation was higher. In another retrospective study, 110 pregnant women who underwent weekly 17-OH progesterone treatment during their pregnancies were compared to the control group consisting of 330 pregnant women who did not receive progesterone during their pregnancies in terms of 1-hour 50-g OGTT blood values. In pregnant women who underwent progesterone treatment, 1-hour 50-g OGTT results were significantly higher than the control group. Unlike this study, we did not have any control group in our study, and we only compared pregnant women, who were established with GDM diagnosis, and received and did not receive progesterone during their pregnancies in terms of 1-hour 50-g OGTT values. We observed that 1-hour 75-g OGTT values were significantly higher in the group receiving progesterone-derived medication than those who did not receive. We found that this difference was caused by the group which underwent 17-OH progesterone treatment.

In the literature, there are studies with different results reporting that progesterone support increases GDM diagnosis frequency. In their prospective study, Rebarber et al. compared 557 pregnant women, who underwent weekly 17-OH progesterone treatment for the prevention of preterm labor, to 1524 healthy pregnant women who did not undergo progesterone treatment. In the group which underwent weekly 17-OH progesterone treatment, GDM incidence was significantly higher than the control group. In the prospective study of Wolfe et al., 67 pregnant women who underwent 17-OH progesterone treatment for the purpose of preterm labor prophylaxis were compared to 140 healthy pregnant women who did not undergo progesterone treatment in terms of 1-hour 50-g OGTT values and GDM frequency. They reported that there was no significant difference between the groups in terms of preprandial blood glucose levels, 1-hour OGTT values and GDM diagnosis frequency. Gyamfi et al. conducted a study to perform secondary analysis of two double-blind, randomized, controlled studies to investigate the effects of serial progesterone treatment on GDM risk on 1094 pregnant women. The population consisted of 441 singleton and 653 twin pregnancies. While 616 of the pregnant women underwent 17-OH progesterone treatment, 478 patients were in the placebo group. GDM incidence in singleton and twin pregnancies that underwent and did not undergo progesterone treatment was compared separately. While GDM incidence in singleton pregnancies receiving progesterone and placebo was 5.8% and 4.7%, respectively (p<0.05), it was 7.4% and 7.6% in twin pregnancies, respectively (p<0.05). Consequently, they reported that weekly progesterone treatment did not increase GDM rate in both singleton and twin pregnancies.

In our study, unlike the studies investigating the relationship between progesterone and GDM to the best of our knowledge, we compared GDM cases only through the progesterone use and investigated the effects of oral natural progesterone and daily intramuscular natural progesterone on 75-g OGTT values. Small patient group receiving progesterone-derived medication and the lack of healthy control group seem to be the limitations of our study.

**Conclusion**

In conclusion, our study shows that receiving intramuscular 17-OH progesterone caproate causes a significant increase in 1-hour 75-g OGTT values compared to other progesterone derivatives and not receiving progesterone. In the obstetric practice where progesterone use increases gradually with the indication of preterm labor prophylaxis, further wide prospective studies investigating the relationship between GDM and all progesterone-derived preparations are needed.

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

**References**


Round ligament varicosities mimicking inguinal hernia in pregnancy: a case report

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Introduction

Inguinal masses during pregnancy are not frequent conditions that we observe, and it is first suspected to be previously known or new inguinal hernia. Other differential diagnoses for inguinal mass lesions can be lymphadenopathy, cyst of the canal of Nuck, cystic lymphangioma, mesothelial cyst, round ligament varicosities, pseudoaneurysm, lipoma, endometriosis or abscess.10 We present our case with round ligament varicosity (RLV), which is one of the significant reasons of inguinal mass during pregnancy and reported in the literature rarely, in order to highlight that it can be easily diagnosed radiologically.

Case Report

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Case Report

Thirty-one-year-old female patient, who was referred to our clinic for ultrasonographic examination at 29 weeks of gestation with the clinical suspicion of inguinal hernia, had a mass complaint which started with inguinal pain at 27 week of gestation and increased gradually. There were visible mass which was about 1.5–2 cm on the right groin and a slight sensitivity with probe pressure in the case whose first pregnancy was terminated with twin abortion and other pregnancy was completed with a problem-free singleton and who had no such complaints in her previous pregnancies.

In the superficial gray scale ultrasonography, a great number of anechoic structures were seen which had tubular and round shapes reaching up to 5.1 mm diameter on right inguinal area and which could be compressed with probe pressure (Fig. 1). In the colored Doppler ultrasonographic examination, venous drainage samples were collected and it was understood that they were dilated venous vascular structures (Fig. 2). Inguinal canal dilated to a diameter of 8.4 mm (Fig. 3). No other mass lesion or herniated bowel loop was observed during the examination.

Upon this diagnosis, the patient was taken to untreated follow-up during her pregnancy. On second-month ultrasonographic examination after the delivery, it was seen that the varicosities were regressed completely.

Discussion

Round ligament (ligamentum teres uteri), is the ligament that provides the uterine anteversion. Beside the pregnancy, cardinal ligament supports the uterine angle.

Round ligament starts from the lateral side of uterine, passes through inguinal canal and ends on labium majus. RLV, on the other hand, stems from round ligament veins and the inguinal canal which drains into inferior epigastric vein. Actual incidence of RLV is unknown, because there is limited number of cases reported in the literature. Although it is unavailable during the first pregnancy, it may appear in the following pregnancies of multiparous cases.

Round ligament varicosities are rarely seen at times other than during pregnancy. Pelvic veins dilate during pregnancy and they sometimes reach up to round
ligament veins which pass through inguinal canal. The pressure of growing uterus on pelvic veins and the increase of cardiac output - venous return have an influential function.\(^{[3-5]}\) Also, progesterone receptors are within the round ligament veins and increasing progesterone level during pregnancy leads to the relaxation and dilatation of smooth muscles in these veins.\(^{[6]}\) In addition, inguinal hernia may also develop as a result of increased intraabdominal pressure during pregnancy. Both entities appear at second trimester or at the early phases of third trimester.\(^{[2]}\)

When round ligament enters into inguinal canal, it also brings along some periton and if this structure encysts during maturation phase, the cyst of the canal of Nuck, which engages in the differential diagnosis with inguinal cystic masses, is formed.\(^{[7]}\)

In our case, wider varicose structures become more evident with Valsalva maneuver. Particularly, ambulatory examination or Valsalva maneuver has critical significance for not overlooking the diagnosis in mild cases.

The treatment of round ligament varicosities is conservative, because it regresses spontaneously during postpartum period.\(^{[4]}\) The treatment of symptomatic inguinal hernias can be surgical at second trimester. Differential diagnosis is very important at this point.

When thrombosis develops as a complication, it may mimic strangulated inguinal hernia. In our case, there was no intraluminal echogenicity which made us suspect thrombus.

**Conclusion**

In order to avoid unnecessary operation, superficial tissue ultrasonography and Doppler ultrasonography are recommended for pregnant cases who apply with the complaint of inguinal mass. Ultrasonographic examination is not only important for diagnosis but also for the follow-up in terms of the development of thrombosis or rupture.

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

**References**

Rusty pipe syndrome

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Department of Gynecology and Obstetrics, Faculty of Medicine, Selçuk University, Konya, Turkey

Introduction

Bloody discharge from nipples during lactation can create anxiety in both mother and her doctors, but it is usually harmless and self-limited condition. Bleeding from nipples can be caused by various conditions such as cracked nipples, mastitis, trauma, ductal papilloma and physiological conditions. Rusty pipe syndrome is a benign physiological condition which can also cause bilateral bloody discharge in lactating mothers. It is defined for those who have bloody nipple discharge during the first days of lactation at first week. In this case report, we aim to present a case of rusty pipe syndrome in a woman who delivered twin babies.

Case Report

A 28-year-old primigravida with a 33-week twin pregnancy delivered with a cesarean section in our hospital.

Abstract

Objective: Rusty pipe syndrome is a physiological condition which can cause bilateral bloody discharge in lactating mothers. In this report, we aim to present a case of rusty pipe syndrome in a woman who delivered twin babies.

Case: A 28-year-old primigravida patient delivered twin babies prematurely with a cesarean section in our hospital. Both infants were admitted to the pediatric intensive care unit due to prematurity. The mother was milking with breast pump at the first postoperative hour. She had bilateral painless bloody milk discharge from the breasts. Examination of the breasts did not reveal any tenderness, engorgement, mass lesion, cracks or fissures. The ultrasound scan did not find any pathology such as breast mass or dilated ducts. Cytological examination of the discharge was negative for neoplasm. She was advised to continue milking by pump, and the bloody discharge resolved spontaneously 7 days and did not recur. Thereafter, the patient breastfed properly.

Conclusion: Rusty pipe syndrome is a benign physiological condition despite its dramatic symptoms, therefore awareness of medical personnel dealing with lactating mothers is very important for proper management of this condition, and also to avoid unnecessary investigations and to reduce anxiety in the mothers.

Keywords: Rusty pipe syndrome, bloody discharge, lactating.
The babies’ weights were 1600 and 2060 g. Both infants were admitted to the neonatal intensive care unit due to prematurity. The mother was milking with breast pump at the first postoperative hour. She had bloody milk discharge from breasts (Fig. 1). The discharge was bilateral and painless. Examination of the breasts did not reveal any tenderness, engorgement, mass lesion, cracks or fissures. The ultrasound examination did not find any pathology such as breast mass or dilated ducts. Cytological examination of the discharge was negative for neoplasm. She was advised to continue milking by pump and the bloody discharge resolved spontaneously 7 days and did not recur. Breastfeeding was then started.

**Discussion**

Rusty pipe syndrome is a breastfeeding condition that the color of the breast milk looks pink, orange, brown, or rust-colored, almost like the dirty water from an old rusty pipe. The rusty color usually comes from a small amount of blood that mixes with the colostrum or first breast milk. This rusty colored milk usually appears during the first few days of breastfeeding, and this condition is commonly seen at first pregnancy. Rusty pipe syndrome is a physiological condition, and it causes transient painless bloody discharge from breasts. It occurs because of the increased vascularization of rapidly developing alveoli which have a delicate network of capillaries. These capillaries get traumatized easily and result in bleeding from nipples. This delicate network may be injured during pregnancy but commonly in early lactation. Breastfeeding should not be discontinued but encouraged. If baby tolerates bloody milk, breastfeeding can be continued during this period. Bloody and serous nipple discharge may also be a sign of serious illness. This discharge is usually unilateral, localized to a single duct, persistent, and spontaneous. It can be serous (clear or yellow), sanguineous (bloody), or serosanguineous (blood-tinged). The most common cause of pathologic nipple discharge is ductal papilloma. Malignancy is found in 5 to 15 percent of cases of pathologic nipple discharge. Bloody nipple discharge during pregnancy and lactation usually resolves within 3–7 days after delivery, and there are no contraindications for breastfeeding. If discharge persists for more than a week, it should be evaluated further.

**Conclusion**

Rusty pipe syndrome is a benign physiologic condition although its dramatical symptoms, therefore awareness of medical personnel dealing with lactating mothers is important for proper management of this condition, and also to avoid unnecessary investigations and to reduce anxiety in the mothers.

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

**References**

HELLP syndrome complicated by hepatic rupture

Şerife Özlem Genç¹, Yasemin Albak¹, Gamze Sönmez¹, Tahsin Taç⁵, Savaş Karakuş¹, Ali Yanık¹, Hüsnü Çağrı Genç², Sinan Soylu²

¹Department of Obstetrics and Gynecology Faculty of Medicine, Cumhuriyet University, Sivas, Turkey
²Department of General Surgery Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

Abstract

Objective: Although spontaneous hepatic rupture associated with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome is rare, it is a life-threatening complication of pregnancy. The cornerstone of prognosis for successful outcome is its prompt diagnosis.

Case: We report a case of 34-year-old female at 29 weeks of gestation with spontaneous hepatic rupture caused by HELLP syndrome as a presenting symptom of weakness without right upper quadrant abdominal pain.

Conclusion: If there is a pregnant woman who is complaining of weakness accompanying with hypotension, obstetrician should check the patient for the presence of hepatic rupture. Hepatic rupture in HELLP syndrome should be considered as a differential diagnosis in pregnant patients with the complaint of weakness. It usually causes sudden onset of abdominal pain and accompanying hypotension. But as in this case, it may present without abdominal pain. An interdisciplinary surgical approach including supportive measures with the use of temporary packing of the liver to control the bleeding can result in successful outcome.

Keywords: Atypical presentation, HELLP syndrome, hepatic rupture.

We report a patient with spontaneous hepatic rupture without a history of sudden-onset upper abdominal pain.

Case Report

A 34-year-old woman, gravida 2, para 1, was admitted to our emergency room at 29 weeks of gestation. She had history of gestational diabetes in current pregnancy and...
mild preeclampsia in her previous pregnancy, and vaginal delivery at term. She denied any history of trauma. When she admitted to the hospital, she was acutely ill with a pale face developed within an hour. Her arterial blood pressure was 50/35 mmHg with a pulse rate of 144 beats/min, and her body temperature was 36.4 °C. The clinical examination on admission revealed no abdominal pain, no tenderness or rigidity. Her laboratory findings revealed that white blood cell count (WBC) was 16,010/mm$^3$, hemoglobin was 12.3 g/dL, thrombocytes was 46,000/μL, aspartate aminotransferase (AST) was 419 U/L, alanine aminotransferase (ALT) was 321 U/L, and lactate dehydrogenase (LDH) was 688 U/L. Other laboratory values were unremarkable. On ultrasonography, the liver showed heterogeneous echogenicity, and a hyperechogenic material was noted in the perihepatic space, suggesting the possibility of perihepatic hematoma and fetal heart beats could not be found. We established the clinical diagnosis for suspected hemorrhage or rupture of liver with a circulatory collapse. Therefore, emergency cesarean section was performed.

On opening the peritoneum, we encountered a massive intraperitoneal hemorrhage from a large ruptured subcapsular hepatic hematoma (Fig. 1). The color of the amniotic fluid was clear. After performing the quick delivery of the fetus with no life sign, uterine incision was promptly closed and, we examined solid abdominal organs as a potential source of bleeding. At the same time, general surgery was called for an intraoperative consultation. Due to the actively bleeding large liver hematoma, direct pressurization was applied for five minutes with cotton gauze tampons to the perihepatic region after the aspiration of free blood from peritoneal cavity. The operation was terminated when the evident bleeding stopped. The patient received intravenous fluid resuscitation with two units of packed red blood cells, three units of fresh frozen plasma, and was admitted to the intensive care unit for additional support. Postoperatively, the blood pressure increased to 170/115 mmHg. Postoperative intravenous magnesium sulfate was given to the patient for eclampsia prophylaxis. On the first postoperative day, WBC was 9310/mm$^3$, hemoglobin was 7.8 g/dL, thrombocytes was 87,000/μL, serum creatinine was 0.47 mg/dL, serum AST level was 411 U/L, serum ALT level was 373 U/L, and LDH was 493 U/L. Urine output was adequate. By the 7th postoperative day, ALT and AST levels declined to 49 and 25 U/L, respectively. It was confirmed by clinical signs and serial ultrasound examinations that the patient had no other complications and no evidence of further intra-abdominal bleeding. She was transferred from intensive care unit to normal service floor on postoperative 5th day and discharged from the hospital on the 23rd postoperative day with scheduled outpatient follow-up.

**Discussion**

The clinician should keep in mind the spontaneous hepatic rupture as a rare complication of HELLP, which results in fetal and maternal mortality. The incidence of this complication is estimated to be about 1 case in 45,000–220,000 births.$^{[4,5]}$ Hepatic rupture associated with pregnancy is accompanied by preeclampsia in 80% of the cases.$^{[6]}$ Rupture of hepatic hematoma should be suspected in HELLP syndrome in the presence of sudden hypotension, tachycardia, abdominal pain and pain on the right shoulder.$^{[7]}$ Haram et al. reviewed the complications of HELLP syndrome, and reported that symptoms of spontaneous rupture of subcapsular liver hematoma are sudden-onset severe pain in the epigastric and right upper abdominal quadrant radiating to the back, right shoulder pain, anemia and hypotension.$^{[2]}$ Mascarenhas et al. reported a series of five pregnant women with spontaneous hepatic rup-
ture, and found that pregnant women with HELLP syndrome are more prone to hepatic rupture, but it can also occur with other liver pathology such as hepatic adenomas, primary and secondary malignancies and hemangiomas. In their case reports, all patients had history of sudden-onset upper abdominal pain.\(^{[1]}\) It should not be forgotten that although hepatic rupture with pregnancy is accompanying with severe abdominal pain, it is possible to present without pain complaint as in our case.

Although there is still not an agreement on the best approach to treat hepatic rupture, in any case, when it is suspected of hepatic rupture, exploratory laparotomy should be performed.\(^{[8]}\) Hepatic packing has the lowest mortality (25–30%) and that is why it is used as a first option surgical treatment. Other treatment options, such as hepatic lobectomy, hepatic artery ligation, and hepatic embolization, have high mortality of 75%, 40%, and 35%, respectively, can be used if packing does not work.\(^{[8]}\)

**Conclusion**
Consequently, early surgical intervention plays a crucial role in HELLP with hepatic rupture. Furthermore, we indicate that hepatic rupture in pregnancy requires a multidisciplinary teamwork including supportive measures with the use of temporary packing of the liver to control the bleeding to obtain a successful outcome. Additionally, it should be realized that, pregnant women with complaints of weakness accompanying with hypotension may be considered to have HELLP syndrome with hepatic rupture even if there is no abdominal pain.

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

**References**
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