The Value of First-trimester Maternal Abdominal Visceral Adipose Tissue Thickness in Predicting the Subsequent Development of Gestational Diabetes Mellitus

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ABSTRACT

Objective: To examine the performance of first-trimester visceral (pre-peritoneal), subcutaneous, and total adipose tissue thickness (ATT) to predict the patients with subsequently developing gestational Diabetes mellitus (GDM).

Study Design: Observational study.

Place and Duration of Study: Department of Obstetrics and Gynecology, Diyarbakır Gazi Yaşargil Training and Research Hospital from January 2021 to July 2021.

Methodology: A total of 100 pregnant women underwent sonographic measurement of subcutaneous and visceral ATT at 11-14 weeks' gestation. A 75-g oral glucose tolerance test (OGTT) was conducted between 24-28 weeks of pregnancy for the diagnosis of GDM.

Results: The mean visceral, subcutaneous, and total ATT were significantly higher in the GDM group (24.75 ± 10.34 mm, 26.33 ± 5.33 mm, 51.08 ± 14.4 mm) than in the group without a GDM diagnosis (16.68 ± 6.73 mm, 17.68 ± 4.86 mm, 34.25 ± 11.04, respectively, $p<0.001$). A pre-gestational BMI >30 kg/m^2 (Odds ratio [OR]=10.20, 95% CI=2.519-41.302, p=0.001), visceral ATT (OR=33.2, 95% CI=7.395-149.046, $p<0.001$), subcutaneous ATT (OR=4.543, 95% CI=1.149-17.960, p=0.031), and total ATT (OR=10.895, 95% CI=2.682-44.262, p=0.001) were the factors that were found to be significantly associated with the subsequent development of GDM after adjusting for potential confounders (maternal age, and parity). The most significant risk factor for the prediction of GDM is visceral ATT with an OR of 33.2.

Conclusion: US measurement of maternal visceral ATT during first-trimester fetal aneuploidy screening is a reliable, reproducible, cost-effective, and safe method to identify pregnant women at high risk for GDM.

Key Words: *Gestational diabetes mellitus, Visceral adipose tissue thickness, Subcutaneous adipose tissue thickness.*

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INTRODUCTION

Gestational Diabetes mellitus (GDM) is the most prevalent metabolic disorder during pregnancy and is defined as glucose intolerance first identified during the second or third trimester of pregnancy that is not preexisting overt diabetes before pregnancy.[1] Uncontrolled hyperglycemia is related to an increased risk for adverse pregnancy outcomes for both mother and fetus.[2-4]

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Current guidelines suggest performing GDM screening at 24 to 28 weeks of gestation.[5,6] However, this approach can substantially postpone the diagnosis of GDM from its beginning. The decision to initiate dietary or insulin treatment after 24 weeks' gestation might be extremely late to positively influence placental integrity or fetal growth.[7] Therefore, the prediction of the future onset of GDM in early pregnancy could potentially improve pregnancy outcomes because of appropriate dietary advice and pharmacological interventions.[8]

Maternal obesity during pregnancy is a well-documented predictor variable for numerous fetal and maternal complications, including metabolic syndrome, insulin resistance, and GDM.[9] However, the frequency of GDM and metabolic disorders differ among the overweight pregnant population. It was considered that body fat distribution is more crucial than the

total amount of adipose tissue in determining the risk of metabolic diseases and GDM.[10] The total body adipose tissue is distributed into two compartments as subcutaneous adipose tissue, which represents 85% of the total, and visceral adipose tissue, which accounts for the remaining 15%.[11] An excessive accumulation of adipose tissue in the central (abdominal) zone and especially in the visceral compartment is significantly correlated with an increased risk for metabolic disorders and diabetes mellitus when compared to peripheral fat storage.[5,11] Routinely, body mass index (BMI) is utilised to assess the risk status of obesity-associated adverse pregnancy outcomes in obstetric units.[9] However, BMI is a formula that regards total body weight rather than central obesity or body fat, and can not provide sufficient information on fat distribution or the proportion of adipose to nonadipose tissue.[12] Ultrasonography (US) is a simple, cost-effective, safe, and reliable method for the evaluation of maternal central obesity during pregnancy.[10] Maternal central obesity is crucial and may indicate the proportion of adipose to nonadipose tissue or fat distribution.[13] An increased accumulation of fat tissue into the visceral compartment in the first trimester of pregnancy was found to be strongly correlated with the subsequent development of the metabolic syndrome and GDM.[7,10]

There are many evaluation measures of maternal central obesity. However, the predictive value of these measures and which of them is more effective in predicting the subsequent development of GDM remains unclear. The aim of this study was to examine the performance of first-trimester visceral (pre-peritoneal), subcutaneous, and total adipose tissue thickness (ATT) to predict the patients with subsequently developing GDM.

METHODOLOGY

This observational study was carried out at Diyarbakır Gazi Yaşargil Training and Research Hospital, Turkey, from January 2021 to July 2021. In this study, we retrospectively analysed the data of 100 pregnant women. A total of 100 pregnant women aged 20 years and older with a viable singleton pregnancy were invited to participate in this study during their first-trimester screening for fetal aneuploidies between $11^{0/7}$ and $14^{0/7}$ weeks' gestation. The exclusion criteria were having a pre-gestational diabetes mellitus, a previous history of pregnancy affected by GDM, multiple pregnancies, chronic drug treatment with steroids, previous epigastric surgery, major fetal structural abnormalities, and pregnancies complicated by inflammatory diseases of pregnancy, including preeclampsia and preterm premature rupture of membranes.[14-18] Participants' fasting plasma glucose level was measured at the time of recruitment. Fasting plasma glucose level ≥92 mg/dL was described as first-trimester GDM and was not considered eligible for entry into the study.[19] All study participants provided written informed consent. The Ethics Committee of the hospital approved the research project.

All participants experienced sonographic measurement of subcutaneous and visceral ATT at 11-14 weeks' gestation by an experienced sonographer using a technique as previously described by Martin *et al.*[20] Transabdominal US was performed using a RAB4-8 curvilinear array probe with a frequency range of 4-8 MHz (Voluson P8 Ultrasound system, GE Healthcare Inc., Milwaukee, WI, USA). Sonographic assessments were done by the same sonographer to provide good reliability and reproducibility. To provide correct measurement, the sonographer reduced the image depth to decrease the error margin. For the evaluation of ATT, participants were positioned in a supine position and the measurements were conducted immediately at the end of the maternal expiration to avoid inspiration originated abdominal wall tension. The sonographer obtained a longitudinal scan, ensuring that the US transducer applied the minimum probable pressure on the abdomen to avoid the compression of the adipose tissue. The probe was always positioned perpendicular to the skin on the line alba. On every single image landmarks, including skin, linea alba, subcutaneous tissue, xiphoid process, and liver, were identified. The minimum subcutaneous ATT and the maximum preperitoneal ATT were measured from the area where the subcutaneous adipose tissue was minimal, which was determined by conducting a longitudinal scan along the linea alba from the xiphoid process to the umbilicus. The visceral ATT was defined as the vertical distance between the anterior liver surface and the posterior edge of the linea alba. The subcutaneous ATT was described as the vertical distance between the skin-fat interface and the anterior edge of the linea alba. The same sonographer performed three measurements of the visceral and subcutaneous ATT. The mean visceral and subcutaneous ATT values were calculated for each pregnant woman. Total ATT was calculated as the addition of visceral and subcutaneous ATT. The measurements of subcutaneous and visceral ATT were carried out three times by another experienced clinician to assess the accuracy and reproducibility (inter-observer agreement).

All pregnant women subsequently underwent a 75-g oral glucose tolerance test (OGTT) between 24-28 weeks of pregnancy for the diagnosis of GDM according to the 2010 International Association of Diabetes in Pregnancy Study Groups (IDPSG) criteria.[19] GDM was diagnosed based on at least one abnormal glucose value, as follows: a fasting plasma glucose ≥92 mg/dL, a 1-hour value of ≥180 mg/dL, or a 2-hour value of ≥153 mg/dL. All the pregnant women diagnosed with GDM were referred to a dietitian for nutrition counselling and an endocrinologist for the assessment of the requirement for insulin treatment.

Group sample sizes of 12 cases and 88 controls achieve 81% power to detect a difference of approximately 50% between the group means which are defined as GDM positive and negative. This power is been calculated for a significance level (alpha) of 0.05 using a two-sided, two independent sample t-test, by using PASS 11.

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the normality. Appropriate test methods were selected according to the results. Continuous variables that satisfy the assumption of normal distribution were compared using Student's t-test and the others by using the Mann-Whitney U-test. Mean ± standard deviation and median (Range) were given as descriptive statistics for these variables. The differences in proportions between groups were compared by using Chi-Square or Fisher's Exact Test and the categorical variables were expressed as counts and percentages. Receiver operating characteristic (ROC) curves were used to describe and compare the performance of diagnostics value of 4 variables, including BMI, visceral ATT, subcutaneous ATT, and total ATT. The area under the corresponding curves was calculated and compared. For the variables whose diagnostic powers were found to be statistically significant, the cut-off points were determined according to the Youden index. To define independent risk factors of outcome variables, we ran univariate logistic regression analyses which are adjusted for maternal age and parity, and odds ratios with their confidence intervals were calculated. To evaluate the diagnostic accuracy of BMI, visceral, subcutaneous, and total ATT in predicting GDM, separate ROC analyses were performed. Further, to assess these markers jointly, binary logistic regression models were fitted, taking GDM as a dependent variable and markers as independent variables, then probabilities calculated from these models were used as predictors in the ROC analyses. A p-value less than 0.05 was considered statistically significant. IBM SPSS Statistics for Windows, Version 26.0 package program was used for all statistical methods utilised.

We determined the intra- and inter-observer reliabilities using the intraclass correlation (ICC) coefficient with a 95% confidence interval (CI). According to the ICC estimate, values <0.5, between 0.5-0.75, between 0.75-0.90, and >0.90 are indicative of poor, moderate, good, and excellent reliability, respectively.[21]

RESULTS

Reliability analyses were based on all pregnant woman's measurements. ICC analysis demonstrated excellent intra-observer (0.946; 95% CI: 0.918-0.965) and inter-observer reliability (0.926; 95% CI: 0.908-0.947) of visceral ATT measurement. Also, the ICC for subcutaneous ATT measurement was 0.938 (95% CI: 0.914-0.964) for intraobserver agreement and 0.922 (95% CI: 0.906-0.937) for interobserver agreement, indicating excellent reliability.

Demographic features, biochemical values, and subcutaneous, visceral, and total ATT measurements of the study subjects are listed in Table I. A total of 100 patients were eligible for the study and presented in this cohort. Twelve (12%) of all participants developed GDM in the second trimester, of which 5 (5%) cases were insulin-requiring GDM. There was no significant difference in the GDM group concerning maternal age, parity, the gestational week at recruitment for the study, plasma fasting glucose, insulin, HOMA-IR, HDL, LDL, VLDL, and triglyceride levels when compared to the non-GDM group. The mean BMI at recruitment and pre-gestational body weight at 11-14 weeks' gestation were significantly higher in the GDM group (36.17 ± 5.36 Kg/m^2 and 85.5 ± 11.33 Kg, respectively) than in the group with normal glucose metabolism (26.97 ± 4.89 Kg/m^2 and 65.23 ± 12.31 Kg, respectively, p<0.001). However, weight gain during pregnancy was found to be similar between the groups (p=0.330). The mean visceral, subcutaneous, and total ATT were significantly higher in the GDM group (24.75 ± 10.34 mm, 26.33 ± 5.33 mm, 51.08 ± 14.4 mm) than in the group without a GDM diagnosis (16.68 ± 6.73 mm, 17.68 ± 4.86 mm, 34.25 ± 11.04, respectively, p<0.001).

Diagnostic performance of pre-gestational BMI, current BMI, visceral ATT, subcutaneous ATT, and total ATT were assessed (Table II). ROC curve analysis demonstrated that pre-gestational BMI >30 Kg/m^2 predicted subsequent GDM with a sensitivity of 75.0%, a specificity of 78.41%, BMI in the first trimester predicted with a sensitivity of 75.0%, a specificity of 54.55%. Visceral ATT >18 mm had a sensitivity of 75.0%, a specificity of 78.18%; subcutaneous ATT >25 mm had a sensitivity of 66.67%, a specificity of 85.45%; total ATT >44 mm had a sensitivity of 75.0%, and a specificity of 81.82% in predicting women with subsequent GDM.

The effectiveness of the variables, which were found to be significant regarding their diagnostic power when taken individually and categorized with the cut-off points according to the Youden index, in predicting the development of GDM was analyzed with logistic regression analysis, and the odds ratios were presented with the relevant p-values and 95% confidence interval (CI) in Table III. Accordingly, the variable BMI in the first trimester >30 Kg/m^2 was found to be 3.49 times riskier to predict GDM, regardless of maternal age and parity, but this was not statistically significant (p=0.078). A pre-gestational BMI >30 Kg/m^2 (Odds ratio [OR]=10.20, 95% CI=2.519-41.302, p=0.001), visceral ATT (OR=33.2, 95% CI=7.395 - 149.046, p<0.001), subcutaneous ATT (OR=4.543, 95% CI=1.149 - 17.960, p=0.031), and total ATT (OR=10.895, 95% CI=2.682 - 44.262, p=0.001) were the factors that were found to be significantly associated with the subsequent development of GDM after adjusting for potential confounders (maternal age, and parity). The most significant risk factor for the prediction of GDM is visceral ATT with an OR of 33.2.

DISCUSSION

The current study intended to evaluate the value of first-trimester maternal visceral ATT to predict the subsequent development of GDM. These findings indicated that visceral ATT between 11-14 weeks' gestation was significantly higher in patients with subsequently developed GDM than the healthy pregnancies. It is probable to predict the second-trimester GDM in a pregnant woman with first-trimester visceral ATT >18.0 mm with a sensitivity of 75.0% and a specificity of 78.18%.

Table I: Demographic features, biochemical values, and subcutaneous, visceral, and total ATT measurements of the study subjects.

	Non-GDM group (n=88)		GDM group (n=12)		p-value
	Mean±S.Dev.	Median (Range)	Mean±S.Dev.	Median (Range)	
Maternal age, years	27.31 ± 5.38	27 (24)	29.5 ± 6.29	30.5 (19)	0.198*
Parity, n	2.69 ± 1.7	2 (9)	3.33 ± 1.23	3.5 (4)	0.072
Gestational week at recruitment	12.28 ± 0.97	12 (3)	12.75 ± 1.06	12.5 (3)	0.126*
Fasting plasma glucose, mg/dL	85.69 ± 14.61	83.5 (97)	99.08 ± 22.48	91 (82)	0.004
Plasma insulin, IU/mL	22.24 ± 19.07	18 (115.1)	23.41 ± 19.02	16.3 (55)	0.987
HOMA-IR	5.05 ± 5.58	3.64 (33.75)	6.13 ± 5.76	3.74 (17.66)	0.734
HDL, mg/dL	58.78 ± 15.84	59 (84.3)	62.33 ± 19.64	64 (67)	0.633
LDL, mg/dL	79.34 ± 22.73	78.5 (141)	79.08 ± 23.56	76 (80)	0.975
VLDL, mg/dL	23.68 ± 8.21	23 (44)	22.75 ± 6.94	21 (24)	0.742
Triglyceride, mg/dL	125.49 ± 53.44	115.5 (261)	134.92 ± 41.27	124 (138)	0.359
Systolic blood pressure	99.2 ± 12.06	100 (50)	108.33 ± 14.03	105 (40)	0.034
Diastolic blood pressure	61.5 ± 6.35	60 (40)	65.83 ± 9.0	60 (20)	0.053
Body mass index, kg/m^2	26.97 ± 4.89	27.15 (18.1)	36.17 ± 5.36	39.15 (13.5)	<0.001
Pre-gestational body mass index, kg/m^2	25.66 ± 4.67	25.40 (17.4)	34.18 ± 5.39	35.15 (14.6)	<0.001
Pre-gestational body weight, kg	65.23 ± 12.31	65 (43)	85.5 ± 11.33	86 (31)	<0.001*
Weight gain during pregnancy	4.41 ± 3.02	4 (12)	6.5 ± 4.85	5.5 (13)	0.330
Visceral adipose tissue thickness, mm	16.68 ± 6.73	16 (33)	24.75 ± 10.34	23.5 (34)	<0.001
Subcutaneous adipose tissue thickness, mm	17.68 ± 4.86	17 (19)	26.33 ± 5.33	29.5 (14)	<0.001
Total adipose tissue thickness, mm	34.25 ± 11.04	35(44)	51.08 ± 14.4	51 (44)	<0.001

**Student's t-test and all others from Mann whitney U-test.*

Table II: Area under curve statistics for parameters.

Test result variables	AUC	Std. error	p	Asymptotic 95% Conf. Int.	
				Lower bound	Upper bound
Pre-gestational body mass index >30 kg/m^2	0.870	0.060	<0.001	0.788	0.924
Body mass index in the first trimester >30 kg/m^2	0.866	0.061	<0.001	0.746	0.986
Visceral ATT >18 mm	0.745	0.076	0.006	0.597	0.893
Subcutaneous ATT >25 mm	0.860	0.060	<0.001	0.742	0.978
Total ATT >43 mm	0.822	0.066	<0.001	0.693	0.951

ATT: Adipose tissue thickness.

Table III: Adjusted logistic regression models as the predictors of GDM.

	B	S.E.	p	Exp (B)	95% C.I. for Exp (B)	
					Lower	Upper
Pre-gestational BMI >30 kg/m^2	2.322	0.714	0.001	10.20	2.519	41.302
BMI in the first-trimester >30 kg/m^2	1.235	0.700	0.078	3.439	0.872	13.563
Visseral ATT >18.0 mm	3.503	0.766	<0.001	33.200	7.395	149.046
Subcutaneous ATT >25.0 mm	1.514	0.701	0.031	4.543	1.149	17.960
Total ATT >44.0 mm	2.388	0.715	0.001	10.895	2.682	44.262

ATT: Adipose tissue thickness. All parameters were adjusted for maternal age and parity.

Few studies investigated the association between the sonographic thickness of maternal visceral adipose tissue in the first trimester of pregnancy and the subsequent development of GDM. Gur *et al.* found that visceral ATT was significantly correlated with insulin resistance and hyperglycemia, and has more sensitivity to indicate the metabolic risk than BMI.[10] Thaware *et al.* concluded that visceral ATT in early pregnancy was independently associated with a positive glucose challenge test between 24-32 weeks' gestation, which persisted after adjustment for maternal age, parity, and pre-pregnancy BMI. They also reported that there is no correlation was found between subcutaneous ATT and subsequent GDM after adjustment for confounders.[22] Recently, D'Amrosio *et al.* indicated that the first-trimester visceral adipose tissue appears to act a stronger and more relevant role than gestational weight gain, BMI, or subcutaneous adipose tissue in patients with a subsequent diagnosis of GDM and this association remains significant in the multivariate regression model after adjusting for the other possible confounders.[23] In this study, the sonographic thickness of maternal visceral ATT at 11-14 weeks of pregnancy was significantly higher in the second-trimester GDM group compared to the non-GDM group. Visceral ATT in early pregnancy significantly predicted the GDM risk in later pregnancy weeks with a sensitivity of 75.0% and a specificity of 78.18%. After adjustment for confounding variables associated with GDM, including maternal age and parity, visceral ATT was found to be independently associated with the subsequent development of GDM.

The measurement of visceral ATT in the early pregnancy may provide an additional contribution in the early identification of cases at risk of developing diabetes. Screening for

GDM in the first trimester has the major benefit of determining high-risk patients who may take advantage of initiating dietary, lifestyle modifications, or pharmacological interventions to reduce the GDM prevalence and its associated maternal and fetal complications.[11] Bourdages *et al.* reported that the sum of visceral and subcutaneous adipose tissue thickness in early pregnancy can predict the insulin-requiring GDM, particularly in combination with BMI and maternal age. They suggested that US measurement of ATT could improve the recognition of GDM patients without additional costs who should immediately initiate insulin treatment or those who might obtain dietary advice to curb their progression to the GDM development.[24] This study also demonstrated that increased visceral ATT (>18.0 mm) can be used as an independent and strong predictive factor for the subsequent GDM development.

The main limitation of this study is the case-control design, and being a single-centre study. The main strength of this study is proposing an earlier screening method during first-trimester fetal aneuploidy screening that appears to be more predictive than BMI for evaluating the risk of GDM. A predictive method for GDM in the second trimester is not beneficial in suggesting an early diagnosis of GDM and it may not protect the fetus from dysglycemic changes. It also confirmed the excellent intra- and inter-observer reliability of these measurements.

CONCLUSION

US measurement of maternal visceral ATT during first-trimester fetal aneuploidy screening is a reliable, reproducible, cost-effective, and safe method to identify pregnant women at high risk for GDM and select patients who may take advantage of screening and adequate glycemic control a couple of weeks before the standard screening period of 24 to 28 weeks of gestation.

ETHICAL APPROVAL:

The Ethics Committee of Diyarbakır Gazi Yaşargil Training and Research Hospital approved the research project (Approval No. 2021/865).

PATIENTS' CONSENT:

All study participants provided written informed consent.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTIONS:

ST: Surgical and medical practices, concept, design, data collection/processing, analysis/ interpretation, literature search, and writing.
SCO: Surgical and medical practices, concept, design, data collection/processing, analysis/interpretation, writing, and critical review.
FO: Concept, design, analysis/interpretation, and literature search.
ZGO: Concept, design, analysis/interpretation, and literature search.
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REFERENCES

1. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2019. *Diabetes Care* 2019; **42(Suppl 1)**:S13-S28. doi: 10.2337/dc19-S002.
2. Oğlak SC, Bademkıran MH, Obut M. Predictor variables in the success of slow-release dinoprostone used for cervical ripening in intrauterine growth restriction pregnancies. *J Gynecol Obstet Hum Reprod* 2020; **49(6)**:101739. doi: 10.1016/j.jogoh.2020.101739.
3. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci* 2018; **19(11)**:3342. doi: 10.3390/ijms19113342.
4. Oğlak SC, Obut M. Expression of ADAMTS13 and PCNA in the placentas of gestational diabetic mothers. *Int J Morphol* 2021; **39(1)**:38-44. doi: 10.4067/S0717-95022021000100038.
5. Akgöl S, Budak MŞ, Oğlak SC, Ölmez F, Dilek ME, Kartal S. Can maternal abdominal fat thickness predict antenatal insulin therapy in patients with gestational diabetes mellitus? *J Obstet Gynaecol Res* 2021; **48(3)**:634-639. doi: 10.1111/jog.15128.
6. Paracha AI, Haroon ZH, Aamir M, Bibi A. Diagnostic accuracy of markers of ınsulin resistance (HOMA-IR) and ınsulin sensitivity (QUICKI) in gestational diabetes. *J Coll Physicians Surg Pak* 2021; **31(09)**:1015-1019. doi: 10.29271/jcpsp.2021.09.1015.
7. De Souza LR, Kogan E, Berger H, Alves JG, Lebovic G, Retnakaran R, *et al*. Abdominal adiposity and insulin resistance in early pregnancy. *J Obstet Gynaecol Can* 2014; **36(11)**:969-975. doi: 10.1016/S1701-2163(15)30409-6.
8. Plasencia W, Garcia R, Pereira S, Akolekar R, Nicolaides KH. Criteria for screening and diagnosis of gestational diabetes mellitus in the first trimester of pregnancy. *Fetal Diagn Ther* 2011; **30(2)**:108-15. doi: 10.1159/000324684.
9. Dolin CD, Kominiarek MA. Pregnancy in women with obesity. *Obstet Gynecol Clin North Am* 2018; **45(2)**: 217-232. doi: 10.1016/j.ogc.2018.01.005.
10. Gur EB, Ince O, Turan GA, Karadeniz M, Tatar S, Celik E, *et al*. Ultrasonographic visceral fat thickness in the first trimester can predict metabolic syndrome and gestational diabetes mellitus. *Endocrine* 2014; **47(2)**:478-84. doi: 10.1007/s12020-013-0154-1.
11. D'Ambrosi F, Crovetto F, Colosi E, Fabietti I, Carbone F, Tassis B, *et al*. Maternal subcutaneous and visceral adipose ultrasound thickness in women with gestational diabetes mellitus at 24-28 weeks' gestation. *Fetal Diagn Ther* 2018; **43(2)**:143-147. doi: 10.1159/000475988.
12. Nassr AA, Shazly SA, Trinidad MC, El-Nashar SA, Marroquin AM, Brost BC. Body fat index: A novel alternative to body mass index for prediction of gestational diabetes and hypertensive disorders in pregnancy. *Eur J Obstet Gynecol Reprod*

Biol 2018; **228**:243-248. doi: 10.1016/j.ejogrb. 2018.07.001.

13. Yao D, Chang Q, Wu QJ, Gao SY, Zhao H, Liu YS, *et al*. Relationship between maternal central obesity and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of cohort studies. *J Diabetes Res* 2020; **2020**:6303820. doi: 10.1155/2020/6303820.
14. Behram M, Oğlak SC, Başkıran Y, Süzen Çaypınar S, Akgöl S, Tunç Ş, *et al*. Maternal serum IL-22 concentrations are significantly upregulated in patients with preterm premature rupture of membranes. *Ginekol Pol* 2021; **92(9)**: 631-636. doi: 10.5603/GP.a2021.0036.
15. Oglak SC, Tunç S, Olmez F. First trimester mean platelet volume, neutrophil to lymphocyte ratio, and platelet to lymphocyte ratio values are useful markers for predicting preeclampsia. *Ochsner J* 2021; **21(4)**:364-370. doi: 10.31486/toj.21.0026.
16. Behram M, Oğlak SC. The expression of angiogenic protein Cyr61 significantly increases in the urine of early-onset preeclampsia patients. *J Contemp Med* 2021; **11(5)**: 605-609. doi: 10.16899/jcm.945345.
17. Behram M, Oğlak SC, Doğan Y. Evaluation of BRD4 levels in patients with early-onset preeclampsia. *J Gynecol Obstet Hum Reprod* 2021; **50(2)**:101963. doi: 10.1016/j.jogoh.2020.101963.
18. Olmez F, Oglak SC, Gedik Ozkose Z. Increased maternal serum aquaporin-9 expression in pregnancies complicated with early-onset preeclampsia. *J Obstet Gynaecol Res* 2021; **48(3)**:647-53. doi: 10.1111/jog.15129.
19. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, *et al*. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010; **33(3)**:676-82.
20. Martin AM, Berger H, Nisenbaum R, Lausman AY, MacGarvie S, Crerar C, *et al*. Abdominal visceral adiposity in the first trimester predicts glucose intolerance in later pregnancy. *Diabetes Care* 2009; **32(7)**:1308-10. doi: 10.2337/dc09-1848.
21. Koo TK, Li MY. A Guideline of selecting and reporting ıntraclass correlation coefficients for reliability research. *J Chiropr Med* 2016; **15(2)**:155-63. doi: 10.1016/j.jcm.2016.02.012.
22. Thaware PK, Patterson CC, Young IS, Casey C, McCance DR. Clinical utility of ultrasonography-measured visceral adipose tissue depth as a tool in early pregnancy screening for gestational diabetes: A proof-of-concept study. *Diabet Med* 2019; **36(7)**:898-901. doi: 10.1111/dme.13906.
23. D'Ambrosi F, Rossi G, Soldavini CM, Di Maso M, Carbone IF, Cetera GE, *et al*. Ultrasound assessment of maternal adipose tissue during 1st trimester screening for aneuploidies and risk of developing gestational diabetes. *Acta Obstet Gynecol Scand* 2020; **99(5)**:644-650. doi: 10.1111/aogs.13800.
24. Bourdages M, Demers MÉ, Dubé S, Gasse C, Girard M, Boutin A, *et al*. First-trimester abdominal adipose tissue thickness to predict gestational diabetes. *J Obstet Gynaecol Can* 2018; **40(7)**:883-7. doi: 10.1016/j.jogc.2017.09.026.