Effectiveness of first trimester maternal fat tissue measurement in prediction of gestational diabetes: a prospective cohort study

Çağdaş Nurettin Emeklioğlu[1], Hicran Acar Şirinoğlu[2], Miraç Özalp[2], Melike Eren[3], Elif Akkoç Demirel[4], Simten Genç[4], Veli Mihmanlı[4]

[1]Clinic of Obstetrics and Gynecology, Karabük University Training and Research Hospital, Karabük, Turkey

[2]Clinic of Obstetrics and Gynecology, Unit of Perinatology, University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, İstanbul, Turkey

[3]Clinic of Obstetrics and Gynecology, Ahlat State Hospital, Bitlis, Turkey

[4]Clinic of Obstetrics and Gynecology, University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, İstanbul, Turkey

Abstract

Objective: The aim was to find a cost-effective, more practical method to be used in the early gestational weeks as an alternative to the oral glucose tolerance test (OGTT) for predicting gestational diabetes mellitus (GDM). The method selected was adipose tissue measurements made in the first trimester.

Material and Methods: The study was designed as a prospective, cohort study. Ultrasound images were used to calculate abdominal visceral (VAT) and subcutaneous adipose tissue (SAT) thicknesses of the first trimester pregnant women. Two groups were formed: those who were diagnosed with GDM and those who were not, based on the results of the OGTT performed in the same patients at 24th-28th weeks of gestation. Ultrasonographic records were examined and compared between these two groups using received operator characteristic curves and logistic regression analyses.

Results: A total of 292 pregnant women were included, of whom 21.2% were diagnosed with GDM. In the group diagnosed with GDM, SAT, VAT and total adipose tissue (TAT) values were significantly higher than the women who did not have GDM. Threshold values for SAT, VAT and TAT were 18 mm, 55 mm and 55 mm.

Conclusion: First trimester SAT, VAT and TAT measurements of pregnant women with GDM were significantly higher than those without GDM diagnosis. Although our results showed that adipose measurements cannot be an alternative to OGTT; they may be a powerful aid in identify at-risk pregnant women, suggesting to perform an early OGTT in the first trimester. (J Turk Ger Gynecol Assoc. 2024; 25: 224-30)

Keywords: Gestational diabetes, subcutaneous adipose tissue, visceral adipose tissue, first trimester screening

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Introduction

Gestational diabetes mellitus (GDM) is a serious public health problem that can cause adverse perinatal complications (1,2). Therefore, standardized screening, diagnosis and treatment for GDM are also important. Classically, screening has been performed between the 24th and 28th weeks in pregnant women who showed no evidence of glucose intolerance in the early pregnancy period. However, there is no consensus on the optimal approach among national and international organizations, and the choice often depends on local choices.

Address for Correspondence: *Elif Akkoç Demirel*
e.mail: akkocelif@hotmail.com ORCID: orcid.org/0000-0003-1910-9113
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Maternal obesity has been reported to negatively affect the early and late prognosis of mother and fetus (3). The World Health Organization (WHO) classification defines a body mass index (BMI) above 30 as obesity (4). However, maternal obesity does not affect every mother and fetus to the same extent. Furthermore, it is thought that the distribution of fat around the body may be more important than the total fat mass in terms of risk factors associated with obesity. Abdominal fat storage is more strongly linked to metabolic diseases (5,6).

Studies have found that central fat storage was more closely correlated with perinatal diseases, such as preeclampsia, GDM, and preterm birth, compared to peripheral lipidosis (7-10). In non-pregnant women, increased abdominal adipose tissue was associated with an increased risk of diabetes, atherosclerosis, dyslipidemia, and metabolic syndrome (11,12).

Abdominal adipose tissue has two compartments, namely visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). Some previous studies have shown that visceral and subcutaneous fat tissue measurements can provide early predictions regarding glucose intolerance, metabolic syndrome and insulin resistance (13-15). However, it is not yet clear which fat compartment increase is associated with the development of GDM in pregnant women.

The aim of this study was to examine the effectiveness of first trimester maternal SAT, VAT and total adipose tissue (TAT) measurements and the ratios of these measurements, in predicting GDM in the early period, and whether they can be used as an alternative to oral glucose tolerance test (OGTT).

Material and Methods

This was designed as a prospective cohort study. Ethics committee approval was obtained from the Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital (approval number: 14, date: 31.01.2022). Based on the prevalence of GDM in society, the sample size required to investigate the role of adipose tissue thickness in predicting GDM was calculated to be 225 pregnant women (two sided α=0.05, power=95%). Women who attended the University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital Perinatology Outpatient Clinic between 07.02.2022 and 07.08.2022 for 11th-14th weeks screening, were 18 years of age and older, had a single pregnancy, did not have any known systemic or chronic disease, were otherwise healthy and did not have a pre-existing diagnosis of diabetes mellitus (DM) or a history of drug use related to it, and who did not have any scarring in the area to be measured, were included in the study. Pregnant women were excluded from the study in the presence of any structural anomaly of the fetus or in the absence of fetal heartbeat. Written informed consent was obtained from all participants.

Demographic information of all participants was recorded, including age, gravida, parity, and weight and height before conception. Maternal SAT thickness and VAT thickness were measured ultrasonographically, and these measurements, the sum of these measurements and their ratio to each other were noted. All fetal and maternal measurements were made by the same perinatologist (H.A.Ş.) with the same ultrasonography device (Mindray Resona 7, 1.2-6 MHz convex abdominal probe). Maternal VAT and SAT measurements were made as described by Armellini et al. (16) and shown in Figure 1 and noted.

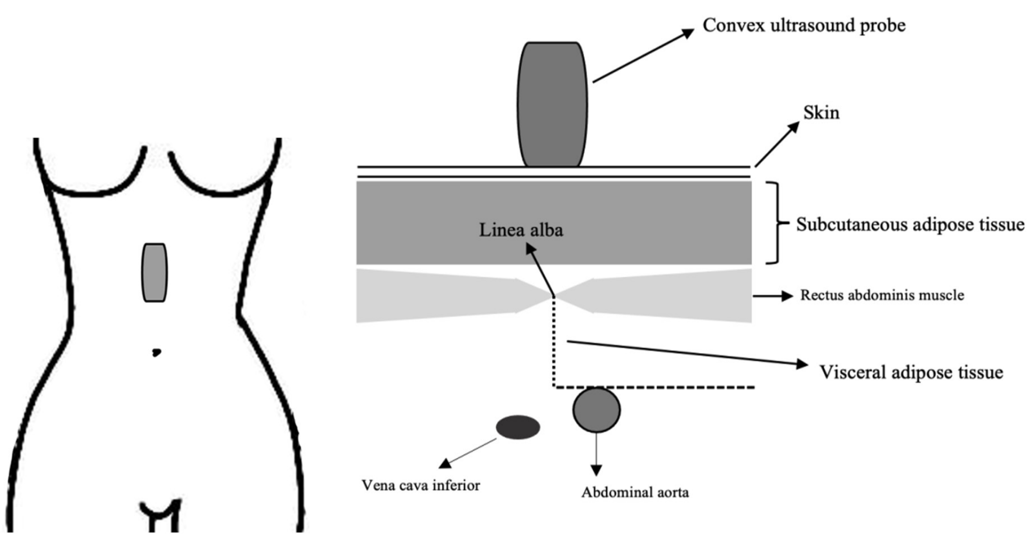

Figure 1. Ultrasonographic measurement of maternal subcutaneous and visceral fat tissue thickness

The measurement was made with a convex ultrasonography probe placed on the xipho-umbilical axis at the end of expiration while the mother was lying in a rested, supine position. The distance from the probe to the rectus abdominis muscle was measured as SAT, and the vertical distance from the linea alba to the abdominal aorta was measured as VAT. The maximum measurable values were obtained after repeated measurements. All pregnant women included in the study underwent 75-gram OGTT as a direct diagnostic test between 24th and 28th weeks for GDM screening. The test was performed after at least eight hours of fasting. The criteria suggested by the International Association of the Diabetes and Pregnancy Study Groups, which are fasting plasma glucose <92 mg/dL, <180 mg/dL at 1 hour, and <153 mg/dL at the second hour, were used as diagnostic criteria (17). GDM was diagnosed if at least one of these values was at the threshold value or above. Pregnant women who were not diagnosed with GDM constituted the control group.

Statistical analysis

Statistical analyzes were performed with Number Cruncher Statistical System (NCSS) 2007 Statistical Software (NCSS, Utah, USA). In addition to descriptive statistical methods including (mean ± standard deviation and median with interquartile range), the distribution of variables was examined with the Shapiro-Wilk normality test. Data were compared using the independent t-test for the comparison of normally distributed variables between paired groups, and the Mann-Whitney U test was used for comparison of non-normally distributed variables between the paired groups. The chi-square test was used to compare qualitative data. Since the group of patients with a history of GDM was a small group, Fisher's exact test was used for this group to compare the qualitative data. Univariate and multivariate logistic regression analysis was performed to separate the influential factors in the patient group with GDM. The areas under the received operator characteristic (ROC) curve were calculated for differential diagnosis of GDM, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), logistic regression (+) values, and cut-off values of the variables were determined. The results were evaluated at the significance level of $p<0.05$.

Results

Maternal SAT and VAT were measured in the first trimester in a total of 369 pregnant women. However, 77 were excluded from the study for reasons including withdrawal from the study, refusing the OGTT, not tolerating the OGTT, moving out of the city, diagnosis of fetal anomaly in the late period, abortion, and loss of communication with the patient. Thus the study cohort numbered 292 pregnant women. Of these, 62 (21.2%) were diagnosed with GDM, and 230 did not have a diagnosis of GDM. The comparison of the demographic characteristics of these two groups is shown in Table 1. There was no significant

Table 1. Demographic characteristics of the groups

		GDM (-) (n=230)	GDM (+) (n=62)	p
Age (years)	Mean ± SD	30.64±4.94	31.49±5.24	0.233
Gravida	Mean ± SD	2.3±1.24	2.32±1.44	0.825
	Median (IQR)	2 (1-3)	2 (1-3)	
Parity	Mean ± SD	0.96±0.88	1±0.99	0.937
	Median (IQR)	1 (0-2)	1 (0-2)	
Abortus	Mean ± SD	0.33±0.68	0.29±0.64	0.864
	Median (IQR)	0 (0-0)	0 (0-0)	
BMI (kg/m^2)	Mean ± SD	25.43±4.85	27.84±3.91	<0.001*
BMI (kg/m^2)	<30	196 (85.23%)	42 (67.74%)	0.002
	>30	34 (14.78%)	20 (32.26%)	
Family history of DM	(-)	166 (72.17%)	40 (64.52%)	0.24
	(+)	64 (27.83%)	22 (35.48%)	
GDM in previous pregnancy	(-)	228 (99.13%)	60 (96.77%)	0.199
	(+)	2 (0.87%)	2 (3.23%)	
SAT† (mm)	Mean ± SD	18.7±9.55	22.51±7.66	0.004*
VAT‡ (mm)	Mean ± SD	35.37±14.89	43.72±17.38	<0.001*
VAT/SAT	Mean ± SD	2.19±1.03	2.15±1.13	0.798
TAT§ (mm)	Mean ± SD	54.06±18.76	66.23±19.45	<0.001*

*Statistically significant, SAT†: Subcutaneous adipose tissue, VAT‡: Visceral adipose tissue, TAT§: Total adipose tissue, GDM: Gestational diabetes mellitus, SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index, DM: Diabetes mellitus difference between the two groups in terms of age, gravida, parity, abortion, family history of DM, history of GDM in previous pregnancy, and VAT/SAT ratios. However, the BMI of the pregnant women in the GDM (+) group was significantly higher than the pregnant women in the GDM (-) group ($p<0.001$). Mean SAT, VAT and TAT measurements in the GDM (+) group were significantly larger than the means in the GDM (-) group ($p=0.004$, $p<0.001$ and $p<0.001$, respectively).

Univariate logistic regression analysis was performed for the factors affecting the diagnosis of GDM (Table 2). The following factors were identified as significant: BMI >30 BMI odds ratio (OR): 0.36 (0.19-0.69) ($p=0.002$); SAT measurement (defined threshold value was 18 mm) OR: 1.04 (1.01-1.08) ($p=0.006$); VAT measurement (defined threshold value was 55 mm) OR: 1.03 (1.02-1.05) ($p<0.001$); and TAT measurement (defined threshold value was also 55 mm) OR: 1.03 (1.02-1.05) ($p<0.001$).

Multivariate logistic regression analysis was then performed to assess the strength of the relationship between outcome and predictor variables as well as the importance of each of the predictors to the relationship, for the factors affecting the diagnosis of GDM. Having a BMI >30 lost its significance but all the other factors identified by univariate regression analysis retained significance (Table 2).

Among the factors in the prediction of GDM positivity, the area under the ROC curve for BMI was 0.673 (0.616-0.726), the area under the curve for SAT was 0.723 (0.686-0.767), for VAT it was 0.738 (0.680-0.763) and for TAT it was 0.781 (0.684-0.797). In general, for the area under the ROC curve, 0.7 to 0.8 is considered acceptable and the higher this value, the more valuable the result is considered. The areas under the ROC curve of SAT, VAT and TAT variables all exceeded the 0.7 limit (Figure 2, Table 3).

Based on the ROC curves optimal threshold values were calculated to predict GDM. The optimal threshold value for SAT was >18 mm with a sensitivity of 67.74%, specificity of 60.87%, PPV of 41.8%, NPV of 87.5%, and a likelihood ratio (LR) of 1.73. Similarly, for VAT the threshold was 55 mm, with a sensitivity of 52.26%, specificity of 75.43%, PPV of 54.6%, NPV of 83.2%, and LR of 3.37 for VAT >55 mm. Thus, a pregnant woman with a VAT measurement >55 mm was found to be 3.37 times more likely to have GDM than a pregnant woman with a VAT measurement of <55 mm.

In addition, the same calculations were made for the sum of SAT and VAT. The optimal threshold value calculated for TAT thickness was also 55 mm, similar to that for VAT alone. Thus for a TAT thickness >55 mm, sensitivity was 77.42%, specificity was 56.52%, PPV was 42.4%, NPV was 90.3%, and the LR was 1.78 (Table 4).

Discussion

Our intention was to examine measurement of SAT and VAT as a cheap, practical and effortless method that would be useful for screening for GDM in pregnant women attending for first trimester screening. Our findings showed that the risk of

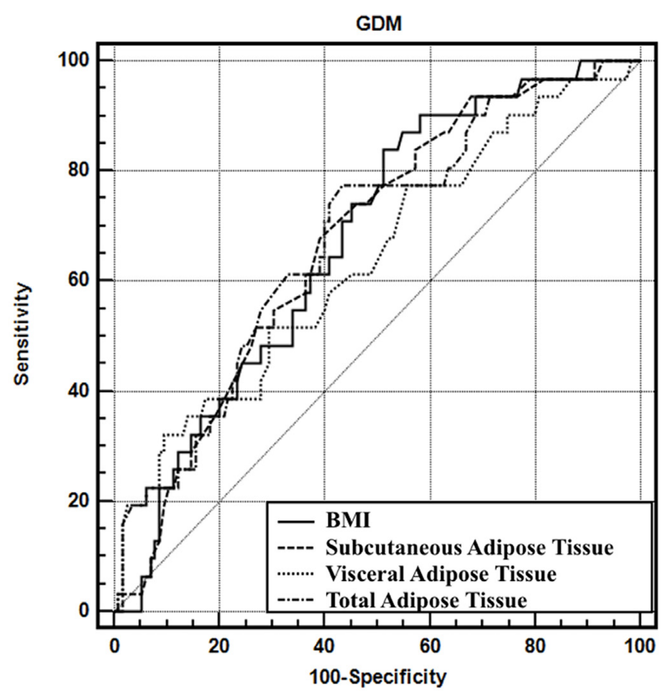

Figure 2. ROC curves for body mass index, subcutaneous adipose tissue, visceral adipose tissue, and total adipose tissue variables
ROC: Receiver operating characteristic, GDM: Gestational diabetes mellitus, BMI: Body mass index

Table 2. Logistic regression analysis for factors affecting gestational diabetes mellitus positivity

	Univariate		**Multivariate**	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
>30 BMI (kg/m^2)	0.36 (0.19-0.69)	0.002*	0.64 (0.31-1.34)	0.237
SAT (>18 mm)	1.04 (1.01-1.08)	0.006*	1.03 (1.00-1.06)	0.036*
VAT (>55 mm)	1.03 (1.02-1.05)	<0.001*	1.03 (1.01-1.02)	0.005*
TAT (>55 mm)	1.03 (1.02-1.05)	<0.001*	1.04 (1.00-1.06)	0.006*

*Statistically significant, OR: Odd ratio, BMI: Body mass index, SAT: Subcutaneous adipose tissue, VAT: Visceral adipose tissue, TAT: Total adipose tissue, CI: Confidence interval developing GDM was higher in pregnant women with a SAT thickness of over 18 mm in the first trimester compared to pregnant women with a thickness below 18 mm. It was also found that a cut-off value of 55 mm for VAT and TAT tissue measurements may be a valuable indicator that will warn of an increased risk of GDM. Although the areas under the curve for SAT, VAT and TAT measurements were above the 0.700 limit, these thresholds had relatively good NPVs but poor PPVs so these measurements will not replace OGTT screening. However, these results would be available earlier in pregnancy than the OGTT screening is usually performed, so it would be feasible to identify women at greater risk of GDM and perhaps bring forward the OGTT test in patients with SAT, VAT and TAT values above the thresholds identified.

Furthermore, our study suggests that VAT, SAT and TAT are related to GDM and these measurements, which are available from routine ultrasonographic pregnancy monitoring, may be a more valuable tool than BMI in predicting GDM. All three values remained significant in multivariate regression analysis. In contrast, BMI, specifically being obese with a BMI >30 kg/m^2, lost significance in multivariate regression analysis. TAT seems to be more valuable than the other two abdominal compartments in terms of predicting GDM by looking at the areas under the curve calculated after the ROC curves. In a large-scale study conducted by Bourdages et al. (18) with 1048 pregnant women, it was reported that SAT, VAT and total fat tissue thickness measurements in the first trimester could be used to predict GDM, and a significant relationship was found, especially with those with GDM who needed insulin.

Although there are various studies on the use of abdominal adipose tissue to predict GDM, there are differences and contradictions between studies regarding which compartment is useful. Gur et al. (13) measured visceral and subcutaneous fat tissues of 94 pregnant women and then the women were examined in two groups; those who were diagnosed with GDM and those who were not. While VAT thickness was found to be more valuable than BMI in predicting GDM, no significant difference was found in the two groups in terms of SAT thickness, which is inconsistent with our findings. Similar findings were reported by D'Ambrosi et al. (19), who looked at SAT and VAT thicknesses of 295 pregnant women. These authors also found VAT thickness to be significantly increased in those diagnosed with GDM, while SAT thickness did not differ significantly between the two groups. In contrast, the studies of Yang et al. (20) and Kansu-Celik et al. (21) examined the relationship between SAT and GDM, but did not examine the visceral component and its relationship with GDM. In these two studies, SAT thickness was found to be significantly higher in pregnant women diagnosed with GDM, and it was reported that measurement of SAT could be used to predict GDM.

Some studies examining maternal adipose tissue to predict GDM have also proposed threshold values and suggested that pregnant women with measurements above the determined thresholds should be followed more closely. Thaware et al. (22) investigated 80 pregnant women and a threshold value of 42.7 mm was reported for VAT and it was suggested that this value may be used as a tool to predict GDM with high sensitivity and specificity. Similarly, threshold cut-off values were reported in the studies of Kansu-Celik et al. (21) (SAT thickness 16.75 mm), Yang et al. (20) (SAT thickness 24 mm), and Bourdages et al. (18) (TAT 61 mm).

The meta-analysis of Rahnemaei et al. (23) included 56,438 pregnant women from 29 studies and evaluated the relationship of various body compartments of the mother with GDM. VAT and SAT thickness emerged as parameters with utility in identifying women at risk of GDM and it was suggested that these measurements could help in managing GDM with low cost.

Our study, including 292 pregnant women is one of the largest patient populations published to date. In terms of measurement standardization, all measurements were made using the measurement method described by Armellini et al. (16), by the same perinatologist (H.A.Ş.) and using the same ultrasonography device.

Table 3. ROC curves and areas under the curve

	AUC	S.E.	95% CI
BMI (kg/m^2)	0.673	0.041	0.616-0.726
Subcutaneous adipose tissue (18 mm)	0.723	0.041	0.686-0.767
Visceral adipose tissue (55 mm)	0.738	0.042	0.680-0.763
Total adipose tissue (55 mm)	0.781	0.041	0.684-0.797

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, BMI: Body mass index

Table 4. Optimal threshold values and analysis results at 95% confidence interval to predict gestational diabetes mellitus in the first trimester

	Cut-off value (mm)	Sensitivity (%)	Specificity (%)	PPV* (%)	NPV† (%)	LR‡ (+)
SAT	>18	67.74 (54-79)	60.87 (54-67)	41.8 (39-43)	87.5 (81-92)	1.73
VAT	>55	52.26 (47-59)	75.43 (65-83)	54.6 (48-63)	83.2 (83-88)	3.37
TAT	>55	77.42 (65-87)	56.52 (50-63)	42.4 (37-54)	90.3 (84-94)	1.78

*PPV: Positive predictive value, †NPV: Negative predictive value, ‡LR: Likelihood ratio

Study limitations

This study has several limitations. It was single center and the patient population consisted of pregnant women living in the same region, with similar characteristics in terms of race and ethnicity, thus limiting the generalizability of the findings. The other major limitation was that pregnant women were not classified according to their insulin needs after the diagnosis of GDM. The final limitation was that the measurements made were only made at a single time point.

Conclusion

Maternal central obesity appears to be associated with an increased risk of GDM, as evidenced by several studies, including the findings of the present study. As we lacked a sufficiently diverse patient group to generalize to all populations, these results suggest that measurements of SAT, VAT and TAT have low sensitivity and specificity in predicting GDM and are not an alternative to OGTT. However, for early identification of pregnant women at increased risk for GDM, and these measurements may be useful in determining who should have an early OGTT in the first trimester.

Ethics Committee Approval: *This was designed as a prospective cohort study. Ethics committee approval was obtained from the Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital (approval number: 14, date: 31.01.2022).*

Informed Consent: *Written informed consent was obtained from all participants.*

Author Contributions: *Surgical and Medical Practices: C.N.E., H.A.Ş., H.A.Ş.; Concept: C.N.E., H.A.Ş., M.Ö., M.E.; Design: C.N.E., H.A.Ş., M.E., V.M.; Data Collection or Processing: C.N.E., H.A.Ş., M.Ö., E.A.D.; Analysis or Interpretation: H.A.Ş., M.Ö., V.M.; Literature Search: C.N.E., M.E., E.A.D.; Writing: C.N.E., H.A.Ş., M.Ö., E.A.D., V.M.*

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