ORIGINAL RESEARCH

Prediction of gestational diabetes mellitus by first trimester abdominal adipose tissue thickness

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ABSTRACT

Gestational Diabetes Mellitus (GDM) is a common medical disorder with adverse maternal and perinatal outcomes, affectingup to 10-14.3% of pregnant women in India¹. These outcomes can be improved by early detection of GDM, especially insulin requiring GDM. It has been found that body fat distribution is important in determining the risk for GDM, this is assessed by traditional conventional methods likeBMI andWaist circumference (WC). USG is a reliable and safe method for the assessment of abdominal adiposity in pregnancy.

The present study was prospective cohortstudy done on 105 pregnant women visitedthe department of OBGVydehi Institute of Medical Sciences, Bangalore, Karnataka, India. Routine NT scan which is done at 11-14 weeks, is performed in antenatal mothers, weutilized this opportunity for screening of GDM by USG based abdominal adipose tissue thickness. Patients were followed up and 75 gram GTT was done at 24-28 weeks of gestation to diagnose GDM. Evaluated the association of abdominal adipose tissue thickness in prediction of GDM. In our study total of 105 pregnant women were included,out of which 17 developed GDM and 88 were non-GDM.Abdominal adipose tissue thickness measured in first trimester, analysis done by ROC area under the curve SAT (AUC 0.694,95% CI 0.571-0.817),VAT(AUC 0.959 95% CI 0.914-1.00),TAT(AUC 0.945 95% CI 0.897-0.992) all were associated with GDM development. However VAThad higher significant correlation in developing GDM especially Insulin dependent GDM when compared to TAT and SAT. BMI >26 kg/m² with sensitivity of 88.24 and specificity of 72.73 and WC >77cm with sensitivity of 88 and specificity of 72.7. Were significant.VAT,TAT had higher correlation of GDM than BMI and WC. SAT had leastsignificance when compared to VAT, TAT,BMIand WC. GDM is a leading complication seen in pregnancy which has adverse effect on both mother and fetus, so early detection of GDM isimportant.

Key words:GDM,SAT,VAT,TAT,BMI,WC,USG

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INTRODUCTION

Gestational Diabetes Mellitus (GDM) is glucose intolerance, resulting in new onset in pregnancy. It has become a global public health concern.

GDM is associated with adverse maternal and perinatal outcomes, affectingup to 10-14.3% of pregnant women in India¹.These outcomes can be improved by early detection of GDM, especially insulin requiring GDM.

According to World health organization (WHO), the prevalence of GDM is raising mainly due to worldwide epidemicityof obesity. Obesity is associated with production of increased inflammation and cytokines causing metabolic dysfunction i.e.; insulin resistance which accounts to major risk factor for diabetes mellitus. When determining metabolic risk factors, it is thought that body fat distribution is more important than the overall body fatty mass.

Regional abdominal adipose tissue has emerged as a critical pathogenesis mediator especially visceral compartment.

Studies have shown that prepregnancy high BMI(Body Mass Index) and excessive gestational weight gain particularly in early and midtrimester has arisk of developing GDM compared to lean or normal BMI².

It has been found that body fat distribution is important in determining the risk for GDM, this is assessed by BMI and Waist circumference (WC), of these WC is a good marker of fat distribution. But USG (Ultrasonography)measurement of fat distributionis a better tool³.

Conventionally traditional methods BMI, waist circumference and hip circumference are used to predict GDM however there is need for newer more reliable methods like USG guided measurement ofadipose tissue thickness in first trimester as conventional methods have limitations. BMI doesn't reflect the metabolically active adipose tissue, also BMI cannot differentiate between muscle mass/bone mass/fat thickness to corelate with risk of insulin resistance leading to GDM.

USG is a reliable and safe method for the assessment of abdominal adiposity (fat distribution) in $pregnancy^4$.

The storage of adipose tissue occurs in two distinct compartment of body assubcutaneous adipose tissue and visceral adipose tissue. Total Abdominal adipose tissue thickness (TAT) is sum of SAT and VAT.

Study has showed that SAT of pregnant women secretes inflammatory mediators like leptin, adiponectin, retinol binding protein 4 more compared to visceral adipose tissue, which cause insulin resistance leading to GDM. Study showed that SAT may be helpful in predicting the risk of development of GDM⁵.

Study has shown that along with secreting inflammatory mediators causing insulin resistance VAT has role in insulin resistance by regulating the adipose derived exosomes miRNA-148 (Ribonucleic acid) family,which affect the development of GDM⁶.

Some other studies have suggested that VAT in early pregnancy is strongly associated with a positive glucose challenge test and is independent of BMI⁷.

However which compartment of adipose tissue causes insulin resistance is not clearly known. Also there is a paucity of literature in Indian studies. Hence this study was undertaken.

Routine NT scan which is done at 11-14 weeks, is performed in most of antenatal mothers, we aim to utilize this opportunity for screening of GDM by USG based abdominal adipose tissue thickness, weutilized this opportunity for screening of GDM by USG based abdominal adipose tissue thickness. Patients were followed up and 75 gram GTT was done to diagnose GDM. Evaluated the association of abdominal adipose tissue thickness in prediction of GDM.

METHODOLOGY PLACE OF STUDY

The present study was carried out in the Department of Obstetrics and Gynecology, Vydehi Institute of Medical Sciences, Bangalore, Karnataka, India

TYPE OF STUDY

The present study was a prospective cohort study.

DURATION OF STUDY

The study was carried out for a period of 18 months.

SAMPLE SIZE:

The study was conducted on 105 patients.

INCLUSION CRITERIA

Patients meeting the following criteria were enrolled into the study.

- 1. Patients with singleton pregnancy between 11-14 weeks of gestation.
- 2. Patients screened negative for diabetes.

EXCLUSION CRITERIA

Patients meeting the following criteria were excluded from the study.

1. Pregnant women with Type 2 or Type 1 Diabetes Mellitus.

EQUIPMENT NEEDED

Our study required the following equipment:

- Linear 5-12 MHz frequency probe.
- Curvilinear 2-6 MHzfrequency probe.
- Ultrasound Machine (Affinity 50 G, PHILIPS Device).

INFORMED CONSENT

All the patients fulfilling selection criteria were explained about the details and significance of study.Written informed consent was obtained before enrolment. They were informed of their right to withdraw from the study at any stage.

DATA COLLECTION

- All consecutive pregnant women visiting with period of gestation of 11-14 weeks, satisfying inclusion criteria were included in the study after obtaining an informed consent. Thorough history taking and clinical examination was done.
- They were advised to undergo abdominal adipose tissue measurement along with their scheduled Nuchal Thickness (NT) ultrasonography at our Radiology department. TAT, SAT, VAT were measured by a single radiologist to provide good reliability and reproducibility.
- Subcutaneous adipose tissue thickness was measured in supine position on expiration using linear 5-12 MHz frequency probe 2.5 cm above Umbilicus and Visceral adipose tissue thickness by Curvilinear 2-6 MHz frequency probe 6.5 cm above umbilicus (Affinity 50 G, PHILIPS Device). SAT was measured from skin to outer border of rectus abdominis muscle, VAT was measured from inner border of rectus abdominismuscle to abdominal aorta.
- BMI, WC and SAT, VAT were measured. They were subjected to the OGTT 75gm screening test for GDM at 24-28weeks.GDM in each were diagnosed by IADPSG criteria. Subcutaneous and visceral adipose tissue thickness were compared to predict GDM. Data was recorded on a proforma and it was analyzed.
- All women were followed up till delivery by standard ANC protocol and outcomes were noted.

 Data was analyzed to compare outcomes of mothers with no GDM, non-insulin requiring GDM and insulin requiring GDM by plotting ROC curve.

RESULTS

Table 1: Investigation Parameters

Variable	GI	DM	Non-GDM	
v al lable	Mean	SD	Mean	SD
FBS	85.41	6.529	83.81	6.049
PPBS	121.65	11.827	106.89	14.160
HbA1C	5.753	.2982	5.253	.2532
RBS	148.94	18.226	110.13	13.382
GTT FASTING	96.88	14.701	85.32	5.945
GTT SAMPLE 1	160.18	25.486	130.30	17.189
GTT SAMPLE 2	151.18	30.562	126.26	18.973

As shown in table above, FBS ≥ 85.41 (F) $\geq 96.8(S1) \geq 160, S2 \geq 151$ had positive correlation PPBS $\geq 121.65, HbA1c$ $\geq 5.75, RBS \geq 148$ GTT with GDM development.

Table 2: SAT(SubcutaneousAdipose Tissue Thickness)

Variable	GDM		Non-	D Value	
variable	Mean	SD	Mean	SD	P value
SAT	2.2447	.92976	1.7699	.47329	0.002

In the present study SAT of ≥ 2.24 cm had significant correlation in developing GDM. ≤ 1.76 cm had no significance of developing GDM.

Table 3: VAT(Visceral Adipose Tissue Thickness)

Variable	GDM		Non-	D Value	
variable	Mean	SD	Mean	SD	r value
VAT	5.4782	1.39395	3.0647	.76867	0.001

In the present study VAT of \geq 5.47 cmhad significant correlation in developing GDM with P value 0.001.

Table 4:TAT(Total Adipose Tissue Thickness)

Variable	GDM		Non	D Value	
variable	Mean	SD	Mean	SD	r value
TAT	7.7200	2.22410	4.8278	1.17096	0.001

In the present study TAT of \geq 7.72 cmhad significant corelation in developing GDM with P value 0.001

Table 5: GDM on MNT in Correlation with Abdominal Adipose Tissue Thickness

Variable	GDMN=8		Non	D Voluo	
variable	Mean	SD	Mean	SD	r value
SAT	1.9238	.37614	1.8404	.60802	0.704
VAT	4.6088	.73647	3.3603	1.25073	0.007
TAT	6.5250	.83109	5.1947	1.76688	0.038

As shown in table above out of 17 GDM cases,8 of them developed GDM on MNT.When compared with

SA,VAT and TAT.VAT and TAT had significance in developing GDM,but not SAT.

Table 6: GDM on OHAin Correlation with Abdominal Adipose Tissue Thickness

Variable	GDM(N=2)		Nor	D Voluo	
variable	Mean	SD	Mean	SD	r value
SAT	2.0100	.41012	1.8436	.59664	0.696
VAT	5.5900	.15556	3.4140	1.23740	0.015
TAT	7.6000	.56569	5.2514	1.73338	0.059

In the above table its shown positive correlation of developing GDM with VAT \geq 5.59 cm and TAT \geq 7.6cm with P value 0.015 and 0.05 respectively.SAT did not have significant correlationin development GDM on OHA.

Table 7: GDM on Insulin in Correlation with Abdominal Adipose Tissue Thick	ness
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Variabla	GDM(N=7)		Non	D Walwa	
variable	Mean	SD	Mean	SD	rvalue
SAT	2.6786	1.31787	1.7873	.46442	0.124
VAT	6.4400	1.56635	3.2422	.93037	0.001
TAT	9.1200	2.85243	5.0230	1.28081	0.001

In the above table its shown positive correlation of developing GDM with VAT 6.44 cm and TAT \geq 9.12cm with P value 0.001 and 0.001 respectively.SAT did not have significant correlationin development GDM on OHA with P value0.124.



Table 8	8:	Area	under	the	Curve

Variable		Std Ennon	D Voluo	95% Confidence Interval		
variable	Area	Stu. Error	r value	Lower Bound	Upper Bound	
BMI	.848	.057	.001	.737	.959	
WC	.832	.062	.001	.710	.953	
SAT	.694	.063	.012	.571	.817	
VAT	.959	.023	.001	.914	1.000	
TAT	.945	.024	.001	.897	.992	

Arear under curve analysis showed VAT had 0.959 higher significance in developing GDM when compared to TAT and SAT.Abdominal adipose tissue

thickness (SAT, VAT, TAT) had more significant correlation in developing GDM when compared to BMI and WC.

Variable	Cut Off	Sensitivity	Specificity
BMI	>26	88.24	72.73
WC	>77	88.24	72.73
SAT	>1.7	82.35	50.00
VAT	>4	94.12	92.05
TAT	>6.35	88.24	93.18

 $BMI \ge 26 \text{kg/m2}, WC \ge 77 \text{cm}, SAT \ge 1.7 \text{ cm} VAT \ge 4 \text{cm}, TAT \ge 6.35 \text{cm}$ these are the cutoff shown in study.

DISCUSSION

	VAT(CM)			
	GDM Non GDM P Value			
Present Study	5.47	3.06	0.001	
Joao G Alves <i>et al.</i> ⁸	5.1	2.92	< 0.001	

In the present study, VAT cut off of >3.06 cm developed GDM with P value 0.001 which is statistically significant. Using ROC, VAT had area under the curve of 0.959 with CI of 95% (0.912-1) with sensitivity 64% of and specificity of 84%. Joao G

Alves *et al.* showed a cut off of >5.1cm with CI of 95%(5.3-5.5),16.8% pregnant women developed GDM.Both studies have similar results,VAT has significant risk fordeveloping GDM.

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	TAT (cm)				
	GDM Non GDM P Value				
Present Study	7.72	4.8	0.01		
Cremona A et al. ⁹	2.23	1.64	0.031		

In the present study, TAT cut off of >6.35 cm developed GDM with P value 0.001 which is statistically significant. Using ROC, TAT had area under the curve of 0.944 with CI of 95% (0.896-

0.992) with sensitivity of 88.24% and specificity of 93.10%. Cremona A *et al.*showed a cut off of >2.23 cmdeveloped GDM.Both studies have similar results,VAT has significant risk fordeveloping GDM.

Comparing BMI,WC,SAT,VAT and TAT in Present Study

Test Result Variables	Area under curve	CI 95%	P value
BMI	0.848	0.737-0.959	0.01
WC	0.832	0.710-0.953	0.01
SAT	0.694	0.571-0.817	O.12
VAT	0.959	0.914-1	0.01
TAT	0.945	0.897-0.992	0.01

To determine an effective cut off value for predicting GDM,ROC analysis was conducted using AUC of independent variables as accuracy criteria.ROC analysis showed AUCas shown above.

GDM prediction is more with VATwhen compared to BMI and WC and least with SAT.

VAT >TAT>BMI>WC>SAT with CI of 95% and hence showed significant association with GDM prediction.

Comparing BMI,WC,SAT and Vat in Present Study vs.Other Study

Parameters	Present study			Gur EB et al. ¹⁰		
	Cutoff	AUC	P value	Cutoff	AUC	P-value
BMI(kg/m ²⁾	>26	0.848	0.01	34.5	0.64	0.069
WC(cm)	>77	0.830	0.01	103.5	0.64	0.079
SAT(cm)	>1.7	0.694	0.02	1.23	0.63	0.04
VAT(cm)	>4	0.959	0.01	1.95	0.66	0.043

In our present study VAT of \geq 4cm thicknesshas higher risk of developing GDM (AUC-0.959 P value-0.01) when compared to SAT,BMI and WC.Similarly Study done by Gur EB *et al.* showed VAT of>1.95cm had higher corelation of developing GDM (AUC-0.66 P value-0.004)compared to BMI,SAT and WC.

In our study BMI has more risk of developing GDM with cutoff >26kg/m².

When compared to WCand SAT.In Gur EB *et al.* study BMI and WC(AUC-0.64) had similar risk of developing GDM and more significant than SAT.

In present study and Gur EB *et al.* study when compared to VAT,BMI and WC,SAT alone appeared less important to predict GDM.

Comparing BMI,WC,SAT,Vat and Tat in Present Study vs. Other Study

	Present study			Cremona A <i>et al.</i> ⁹		
	GDM	AUC	Pvalue	GDM	AUC	Pvalue
BMI	29.71	0.848	0.01	29.85	0.607	0.022

WC	90.17	0.830	0.01	90.3	0.705	0.006
SAT	>1.7	0.694	0.02	1.99	0.713	0.027
VAT	>4	0.959	0.01	0.78	0.743	0.002
TAT	>6.35	0.944	0.01	2.23	0.722	0.031

InOur study abdominal adipose tisuue thickness,BMI,WC all showed significant corelation with GDM. Cremona A *et al.* showed similar results of corelation with GDM.

In our present study VAT, TAT had a better predictive capacity than BMI and WC and SAT had least prediction when compared between these 5 elements. Cremona A *et al.* showed VAT had higher significance as similar to our study. Adipose tissue thicknessand WC had better significance compared to BMI.

CONCLUSION

In conclusion,our comprehensive findings suggest the potential important clinical utility of adipose tissue thickness measurement by USG in first trimester to predict GDM.

In our study, adipose tissue thickness measurement by USG had significant correlation with development of GDM and can be used as early predictor.

It can be used as a screening test with acceptable sensitivity and Negative P value.

As early detection of GDMhelps to prevent adverse outcomes on mother and fetus,first trimester screen by USG becomes one of the important parameter.

We consider Adipose tissue measurement is helpful as compared to conventional traditional methods to predict GDM.

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