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Measurement of Fetal Abdominal and Subscapular Subcutaneous Soft Tissue Thickness to Predict Macrosomia in Pregnancies Affected By Gestational Diabetes

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Abstract:
Background*: Gestational diabetes mellitus (GDM) is the most common metabolic complication leading to macrosomia. This study was aimed to evaluate accuracy of fetal subcutaneous soft tissue thickness in predicting macrosomia among neonates delivered by the women with GDM.*
Materials and Methods *This hospital based prospective study was carried out in a tertiary care teaching hospital of Karnataka. A total of 50 women with GDM referred for routine ultrasound scan during the period from August 2019 to November 2019 were subjected to estimation of fetal abdominal soft tissue thickness (FASTT) and sub scapular soft tissue thickness (SSSTT) by ultrasound.*
Results*: Most of the women were aged < 30 years (72%). Normal vaginal delivery was noted in 52% of the women and 48% of the women underwent LSCS. Macrosimia was noted in 6% of the babies. There was significant strong positive correlation between birth weight and SSSTT (r=0.645;R^2=0.4431;p<0.001) as well as FASTT (r=0.666;R^2=0.4154;p<0.001). The receiver operating characteristics (ROC) curve for SSSTT showed a cut off value of 5.45 cm in predicting macrosomia with area under the curve (AUC) being 0.982 (Standard error[SE]=0.021 95% confidence interval[CI]= 0.942-1.000;p=0.005) and showed diagnostic accuracy of 92% with sensitivity of 100%, specificity of 91.49%, positive predictive value (PPV) of 42.86% and negative predictive value (NPV) of 100% (p=0.002). The ROC curve for FASTT showed a cut off value of 5.15 cm in predicting macrosomia with AUC being 0.982 (SE=0.038;95%;CI=0.887-1.000; p=0.008) and showed diagnostic accuracy of 88% with sensitivity of 100%, specificity of 87.23%, PPV of 33.33% and NPV of 100% (p=0.004).*
Conclusion: *Sonographically determined SSSTT and FASTT significantly and strongly correlate with birth and a cut of value of 5.45 and 5.15 cms respectively are highly accurate in predicting macrosomia among the neonates delivered by women with GDM.*
Key Word*: Abdominal soft tissue thickness; Gestational diabetes mellitus; Macrosomia; Subcutaneous soft tissue thickness;*

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I. Introduction

Gestational diabetes mellitus (GDM) is glucose intolerance of variable degrees with an onset, or first recognized, during pregnancy.[1] It is estimated that GDM affects around 7–10% of all pregnancies worldwide;[2] The prevalence of GDM has tremendously increased in the past few years, especially in the developing countries like India. It is reported that, Indian women have 11 times more risk of developing GDM as compared to women in other parts of the world. The prevalence of GDM in India varies in different regions with a reported prevalence of 3.8% in Kashmir, 9.5% in Western India, 6.2% in Mysore and 22% in Tamil Nadu.[3] Using different criteria, prevalence rates as high as 35% from Punjab and 41% from Lucknow have been reported. It is estimated that about 4 million women are affected by GDM in India, at any given time point.[4]

Gestational diabetes mellitus has implications for the both mother as well as the foetus. Maternal complications include pre-eclampsia, stillbirths, macrosomia and need for caesarean section and neonatal outcomes such as hypoglycaemia and respiratory distress are few to name.[3] Data from the Diabetes in Early Pregnancy Study indicate that fetal birth weight correlates best with second- and third-trimester postprandial blood sugar levels and not with fasting or mean glucose levels.[1] When postprandial glucose values average 120 mg/dl or less, approximately 20% of infants can be expected to be macrosomic, and if the glucose values are as high as 160 mg/dl, the rate of macrosomia can reach up to 35%. Macrosomic fetuses in diabetic pregnancies develop a unique pattern of overgrowth, involving the central deposition of subcutaneous fat in the abdominal and interscapular areas.[1] They have larger shoulder and extremity circumferences, a decreased head-to-shoulder ratio, significantly higher body fat and thicker upper-extremity skinfolds. Because fetal head size is not increased, but shoulder and abdominal girth can be markedly augmented, the risk of Erb's palsy, shoulder dystocia and brachial plexus trauma is more common.[1] Hence for many aspects of perinatology, it is important to ensure that the fetal growth rate is appropriate for the age of the fetus. Abnormal fetal growth can cause prenatal and postnatal complications, and is associated with increased neonatal morbidity and mortality.[5]

Therefore, evaluation of fetal intrauterine growth by ultrasound measurements is advisable. A range of ultrasound (US) anthropometric parameters are used to determine normal fetal growth. Of these, fetal abdominal circumference or fetal weight calculated using a combination of ultrasound-derived parameters, is commonly used. However, both of these measures have a limited sensitivity and specificity. As Cetin et al.[6] reported, the percentage error of these methods of fetal weight estimation could be as high as 25% due to technical measurement errors and erroneous assumptions of fetal density. Additionally, the fetal abdominal circumference measurement only predicts 78% of macrosomic foetuses. Therefore, researchers have been investigating the usefulness of another sonographic measurement, subcutaneous tissue thickness (SCTT), taken at a range of locations on the fetal anatomy.[5]

Fetal abdominal subcutaneous tissue thickness (FASTT) is one such ultrasound parameter which is an independent factor in predicting big babies and when substantiated with other ultrasound parameters can predict fetal weight for large for gestational age babies. Number of studies done in Asian population is few; the fetuses are likely to have less subcutaneous fat compared to developed countries. The cut off value obtained for western population may not be applicable to Asian population.[7] The present study was aimed to evaluate the measurement of fetal subcutaneous soft tissue thickness (FSSTT) in third trimester as a predictor of macrosomia at birth in fetuses of women with gestational diabetes which may provide a window in reduction of perinatal and postnatal complications by early identification of fetal macrosomia among the women with pregnancies affected by GDM.

II. Material And Methods

Study Design: A hospital based cohort study

Study Location: This was a tertiary care teaching hospital based study done in Department of Radiology of a tertiary care teaching hospital attached to Yenepoya Medical College, Mangalore, Karnataka, India

Study Duration: August 2019 to November 2019.

Sample size: 50 patients.

Sample size calculation: The sample size was estimated on the basis of a single proportion design. Assuming confidence level of 95%, power of the study as 85%, prevalence of macrosomia as 12% and sensitivity of 79% based on the study by Bhat RG et al.[7] (2014), the minimum sample requireted determine the objective was 50 women with GDM

Subjects & selection method: A total of 50 women with GDM, with gestational age between 31-37 weeks having singleton pregnancy referred for routine scanning in the department of Radio-diagnosis, were enrolled based on convenient sampling method. Pregnant women with chromosomal anomalies, autoimmune disorders, pregnancy induced hypertension and ucooperative patients were excluded from the study.

Inclusion criteria:

1. Women with GDM, with gestational age between 31-37 weeks having singleton pregnancy referred for routine scanning

Exclusion criteria:

1. Pregnant women with chromosomal anomalies, autoimmune disorders, pregnancy induced hypertension and un-cooperative patients.

Procedure methodology

The study was conducted in accordance with the ethical norms as laid down in declaration of Helsinki. Prior to the commencement, ethical clearance was obtained from Ethics and Research Committee. Women were screened for the eligibility and those fulfilling the selection criteria were briefed about the nature of the study. The women expressing their willingness to participate in the study were enrolled after obtaining a written informed consent.

The selected women were interviewed and demographic data like age, obstetric history that is parity and gravida were obtained and noted. Women were also History of other complications like pregnancy induced hypertension (PIH) co-morbid conditions such as, hypertension. The gestational age was confirmed by an ultrasound scan performed no latter than 22 weeks. A thorough physical examination was conducted followed by systemic examination. Further these women underwent investigations for fasting blood sugar (FBS), post prandial blood sugar (PPBS) at one and two hours, and glycosylated haemoglobin (HbA1c). All these parameters were recorded on a predesigned and pretested proforma.

Ultrasound scan was done using GE-VOLUSON E8 US machine with a 3.15-MHz probe. The scan was done by the principal investigator. In addition to regular Hadlock method which includes abdominal circumference, head circumference, femur length and biparietal diameter, two additional measurements- Abdominal and subscapular soft tissue thickness was added to the normal examination which requires no more than 2 minutes to the duration of scan. During the evaluation, two qualified radiologists, recorded routine fetal ultrasonographic biometric parameters, including biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), and humerus length (HUM), at each selected GA. Two fetal fat mass indices, FASTT and SSSTT, were assessed using the technique of Rigano et al.[8] Briefly, FASTT was evaluated by measuring the thickness of the anterior abdominal subcutaneous tissue on the same axial image as that used for abdominal circumference measurement. To measure SSSTT, the fetus was imaged in a naturally prone or lateral posture, as far as possible, so the entire scapula was seen. The caliper was positioned between the skin surface and the subcutaneous tissue at the interface, perpendicular to the lowest end of the scapula. All measurements were performed by two trained observers. To test the intra- and inter-observer reproducibility, the FASTT and SSSTT parameters were assessed in 25 different images. The coefficients of variation for each parameter were calculated as 7.5% and 8.9% for FASTT and 8.4% and 9.1% for SSTT, respectively. The selected women were followed up till the delivery and these women were evaluated for pregnancy outcome like mode of delivery, indication for LSCS, birth weight of the neonate which was obtained from the department of obstetric and gynecology.

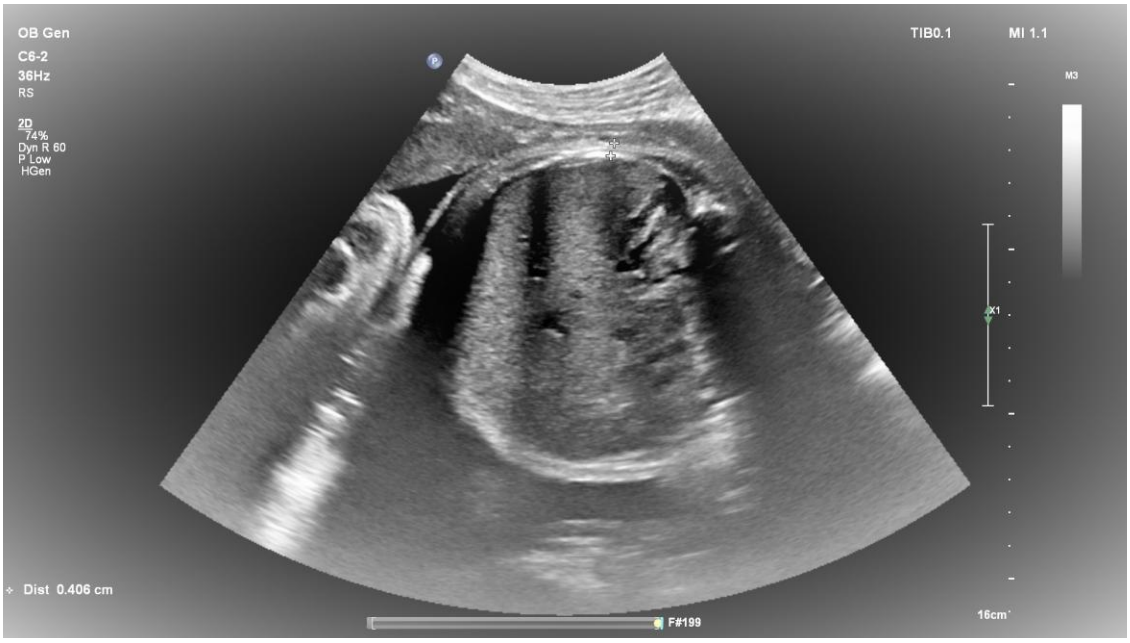


Illustration 1. Measurement of abdominal soft tissue thickness

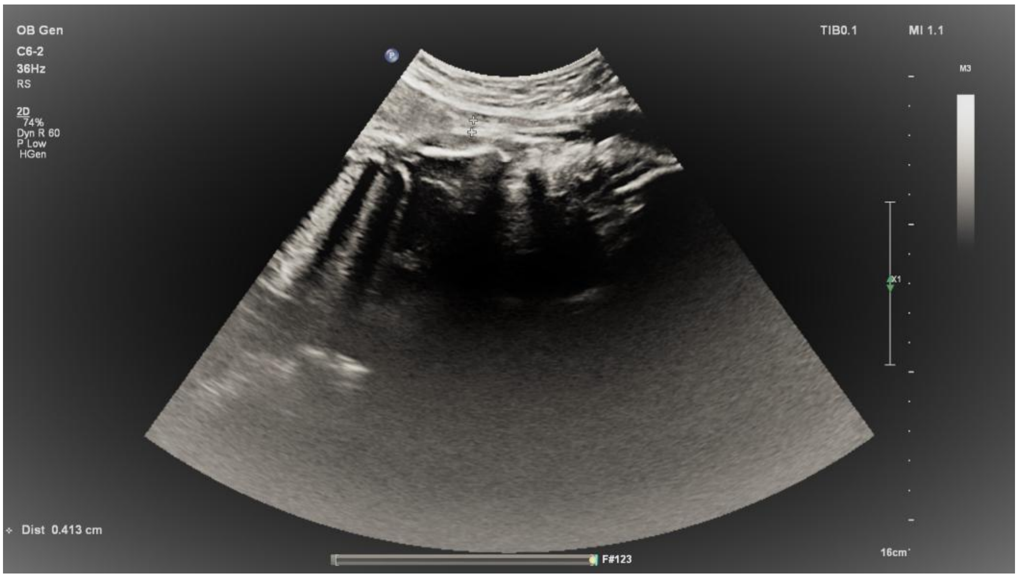


Illustration 2. Measurement of subscapular soft tissue thickness

Statistical analysis

The data obtained was coded and entered into Microsoft Excel Worksheet. The data was analysed using statistical software SPSS version 20.0. Continuous variables were presented as mean±standard deviation (SD) and analyzed for normality by the Shapiro-Wilk test. Categorical variables were compared using the Chi-square or Fisher's exact. Pearson correlation coefficient (r) was used to study the correlation between FASTT and birth weight, Cut-off value for FASTT AND SSSTT were obtained using ROC curve analysis with area under the curve (AUC) to determine the prognostic accuracy of FASTT and SSSTT in predicting Macrosomia. The accuracy of fetal FASTT and SSSTT in predicting macrosomia was determined in terms of diagnostic accuracy (DA), sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV). All tests were two-tailed and a p-value of less than 0.05 was considered significant.

III. Result

The maternal, neonatal, blood sugar and USG parameters of the study population are as depicted in table 1. It was observed that most of the women were aged <30 years (72%). The mean FBS levels were 108.24±8.59 mg/dL and the mean HbA1c levels were 5.69±0.28. most of the women belonged to gravida 2 and 3 (42% each). The mean gestational age at scan was 35.68±1.46 weeks and most of the women had gestational age of <37 weeks. The mean BMI was 30.52±1.75 Kg/m^2 and most of the women had BMI of >30 Kg/m^2 (Table 1 and 2) The SSTT in the population studied ranged between 2.90 to 5.90 mm and the mean and median SSTT were noted as 4.52±0.86 and 4.70 mm. Similarly the FASTT ranged between 2.70 to 5.80 mm and the mean FASTT was 4.28±0.89 and 4.40 mm (Table 1). Term delivery was noted in 94% of the women and 52% of the women had normal vaginal delivery while 48% of the women underwent LSCS and Cephalopelvic disproportion was the common indication for LSCS (50%). The birth weight ranged between 3.00 to 4.20 kg and the mean and median birth weight were noted as 3.46±0.25 and 3.40 Kg. Most of the newborns (54%) had normal birth weight while macrosomia was evident in 6% of the neonates (Table 1 and 2).

Table 1. Maternal, neonatal, blood sugar and USG parameters of the population studied

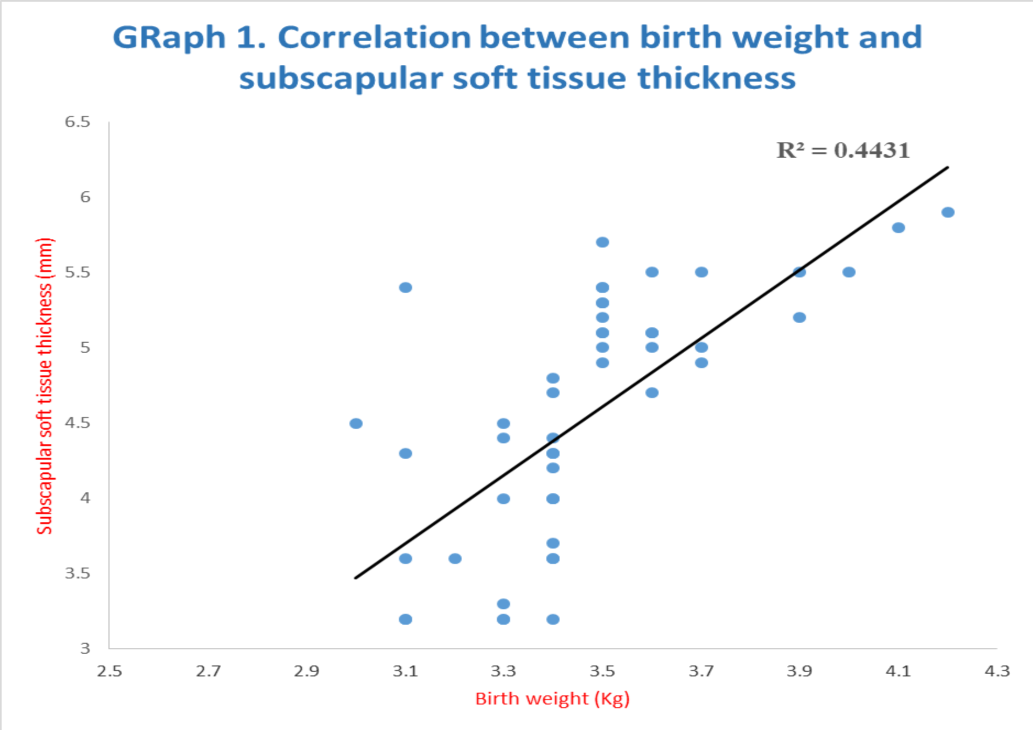
Parameters	Mean (n=952)		Median	Range	
	Mean	SD		Min	Max
Age (years)	28.50	2.23	29.00	25.00	34.00
Gestational age (weeks)	35.68	1.46	36.00	31.00	37.00
Height (Cms)	153.00	3.91	152.00	144.00	160.00
Weight (Kg)	71.54	5.37	71.50	60.00	85.00
Body mass index (Kg/m^2)	30.52	1.75	30.70	26.00	33.30
Birth weight (Kg)	3.46	0.25	3.40	3.00	4.20
FBS (mg/dL)	108.24	8.59	109.00	93.00	124.00

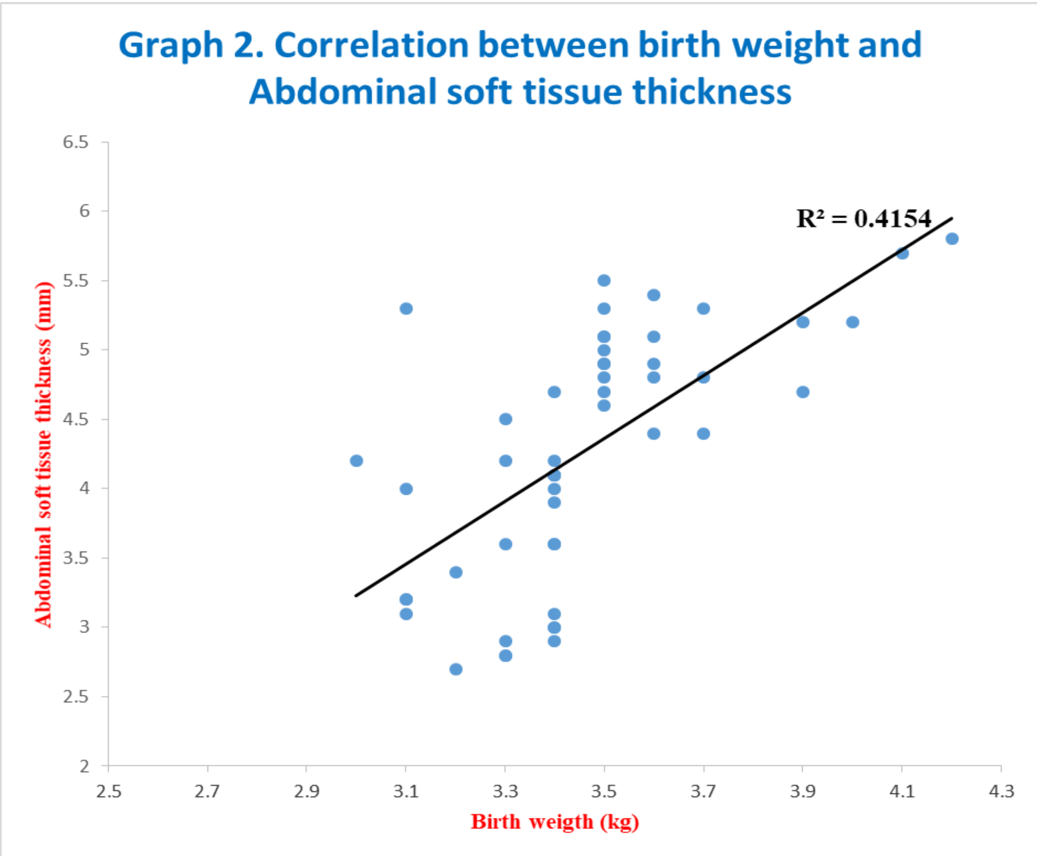
PPBS 1h (mg/dL)	200.72	11.33	199.00	180.00	227.00
PPBS 2h (mg/dL)	171.20	14.39	171.50	119.00	199.00
HbA1c (%)	5.69	0.28	5.70	5.00	6.20
Biparietal Diameter (mm)	92.10	2.92	92.80	84.20	98.00
Head circumference (mm)	329.35	9.07	330.60	303.90	349.80
Abdominal Circumference (mm)	337.51	14.02	338.60	303.10	370.00
Femoral Length (mm)	71.76	5.16	72.55	43.40	80.30
SSSTT(mm)	4.52	0.86	4.70	2.90	5.90
FASTT (mm)	4.28	0.89	4.40	2.70	5.80
Estimated Fetal Weight (USG) (gms)	3230.58	371.33	3270.50	2278.00	4078.00

Table 2. Maternal and neonatal characteristics of the study population

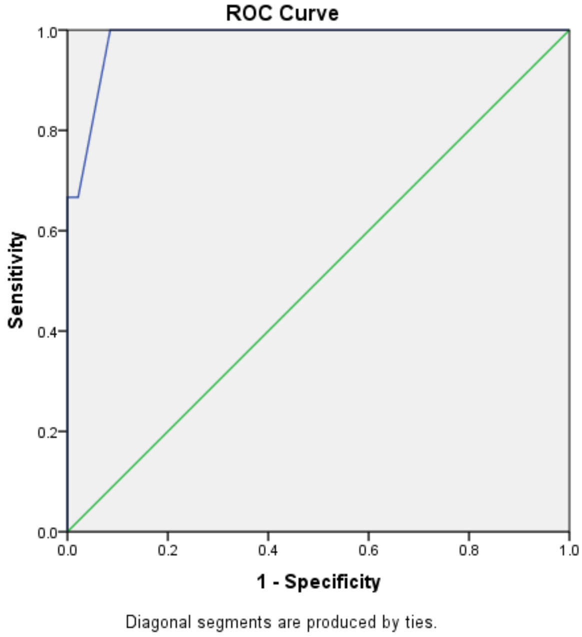
Parameters	**Subgroups**	**Distribution (n=40)**	
		Number	**Percentage**
Maternal age (Years)	< 30	36	72.00
	≥ 30	14	28.00
Gravida	1	2	4.00
	2	21	42.00
	3	21	42.00
	4	4	8.00
	5	2	4.00
Gestational age (weeks)	< 37	31	62.00
	≥ 37	19	38.00
Body mass index (Kg/m^2)	<19.8	0	0.00
	19.8 to 26.0	1	2.00
	26.10 to 29.99	16	32.00
	> 30	33	66.00
Gestational age at delivery	Term	47	94.00
	Preterm	3	6.00
Mode of delivery	Normal vaginal delivery	26	52.00
	LSCS	24	48.00
Indications for LSCS	Breech	5	20.83
(n=24)	Cephalopelvic Disproportion	12	50.00
	Fetal distress	3	12.50
	Placenta praevia	2	8.33
	Previous LSCS	2	8.33
Birth weight (Kg)	<2500	0	0.00
	2501 to 3499	27	54.00
	3500 to 3999	20	40.00
	4000 or more	3	6.00

Significant strong positive correlation was noted between birth weight with SSTT (r=0.645; R^2=0.4431; p<0.001), and FASTT (r=0.666; R^2=0.4154; p<0.001) (Graph 1 and 2).


GRaph 1. Correlation between birth weight and subscapular soft tissue thickness
R² = 0.4431
Subscapular soft tissue thickness (mm)
Birth weight (Kg)
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2.7
2.9
3.1
3.3
3.5
3.7
3.9
4.1
4.3

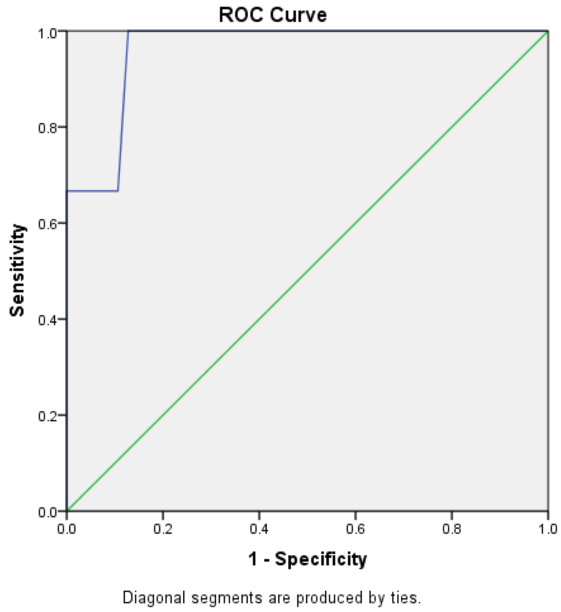

Graph 2. Correlation between birth weight and Abdominal soft tissue thickness
R² = 0.4154
Abdominal soft tissue thickness (mm)
Birth weigth (kg)
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
2.5
2.7
2.9
3.1
3.3
3.5
3.7
3.9
4.1
4.3

Graph 3. Receiver operating characteristics curve for SSSTT and birth weight



Cut-off value=5.45 mm;Cut-off=AUC=0.982;SE=0.021; 95% CI=0.942 to 1.000; p=0.005

Graph 4. Receiver operating characteristics curve for FASTT and birth weigth



Cut-off value=5.15 mm; AUC=0.961; SE=0.038; 95% CI=0.887 to 1.000; p=0.008

Table 3. Association and accuracy of SSSTT in predicting macrosomia

SSSTT (mm)	Macrosomia				Total	
	High (> 1059)		Low (≤1059)			
	No	%	No	%	No	%
> 5.45	3	100.00	4	8.51	7	14.00
≤5.45	0	0.00	43	91.49	43	86.00
Total	**3**	**6.00**	**47**	**94.00**	**50**	**100.00**

p=0.002; Sensitivity=100%; Specificity=91.49%; PPV=42.86%; NPV=100%; DA=92%;

Table 4. Association and accuracy of FASTT in predicting macrosomia

FASTT (mm)	Macrosomia				Total	
	High (> 1059)		Low (≤1059)			
	No	%	No	%	No	%
> 5.15	3	100.00	6	12.77	9	18.00
≤5.15	0	0.00	41	87.23	41	82.00
Total	**3**	**6.00**	**47**	**94.00**	**50**	**100.00**

p=0.004; Sensitivity=100%; Specificity=87.23%; PPV=33.33%; NPV=100%; DA=88%;

Based on the AUC determined by ROC a cut off value of 5.45 for SSSTT and 5.15 for FASTT were obtained in discriminating macrosomia and showed diagnostic accuracy of 92% with sensitivity of 100%, specificity of 91.49%, positive predictive value (PPV) of 42.86% and negative predictive value (NPV) of 100% (p=0.002) for SSSTT. The ROC curve for FASTT showed a cut off value of 5.15 cm in predicting macrosomia with diagnostic accuracy of 88% with sensitivity of 100%, specificity of 87.23%, PPV of 33.33% and NPV of 100% (p=0.004) (Graph 3, 4 and Table 3,4).

IV. Discussion

In view of the high morbidity and mortality in neonates with macrosomia born to the mothers having GDM this study was aimed to determine the measurement of FSSTT in third trimester as a predictor of macrosomia so as to reduce the perinatal and postnatal complications by early identification of fetal macrosomia.[9] This study showed not only strong correlation between birth weight with SSSTT as well as FASTT but also a cut-off value of 5.45 mm for SSSTT and 5.15 mm for FASTT strongly predict macrosomia in neonates delivered by women with GDM. A recent study by Kuttan KK et al.[10] (2019) also found that there is strong statistical correlation between the soft tissue measurements by ultrasound like ASTT (abdominal subcutaneous tissue thickness) and SSTT (subscapular subcutaneous tissue thickness) with the birth weight of the baby.

In the present study, SSSTT with a cut off value of 5.45 mm showed DA of 92% with sensitivity of 100%, specificity of 91.49%, positive predictive value (PPV) of 42.86% and negative predictive value (NPV) of 100% (p=0.002). Similarly FASTT with cut-off value of 5.15 mm was highly accurate in predicting macrosomia with DA of 88% with sensitivity of 100%, specificity of 87.23%, PPV of 33.33% and NPV of 100% (p=0.004). However the DA of SSSTT (92%) was slightly higher compared to FASTT (88%).

Garbedian C. et al.[11] (2013) found a cut off value of 5.15 for SSSTT with AUC of 0.736 was 73.3% sensitive and 69.2% specific in predicting large for gestational age neonates. A finding strongly in agreement with the present study. Several studies have been conducted to find the correlation between subcutaneous tissue thickness and birth weight. The observations noted in the present study were consistent with several other studies by Petrikovsky BM et al.[9] (1997), Foromouzmehr A et al.[12] (2004), Bhat RG et al.[7] (2014) and more recently by Khalifa EA et al.[13] (2019).

Bhat RG et al.[7] (2014) in a study to correlate FASTT measured by ultrasound at term and birth weight and to obtain a cut-off value of FASTT to predict large and small for gestational age reported that positive correlation between FASTT and birth weight. Mean FASTT increased as the birth weight increases with significance between FASTT and birth weight was obtained by r was 0.418. A finding sharply in agreement with the present study however the r value noted in the present study that is 0.666 (p<0.001) which was much stronger than the study by Bhat RG et al.6 (2014). In the present study the ROC curve for FASTT showed a cut off value of 5.15 mm in predicting macrosomia with diagnostic accuracy of 88% with sensitivity of 100%, specificity of 87.23%, PPV of 33.33% and NPV of 100% (p=0.004). Bhat RG et al.[7] (2014) reported the cut-off value of FASTT as 6.25 mm with sensitivity of 79% and specificity is 70% with a Positive Predictive Value (PPV) is 24.4% and Negative Predictive Value (NPV) is 96.4% which was comparable with the present study. The slight disparity in the cut-off value of FASTT as well as the sensitivity, specificity, PPV and NPV noted in the present study and the study by Bhat RG et al.[7] (2014) can be explained by the larger sample in the latter study (n=350). Similarly, Grace et al.[14] demonstrated that FASTT may be useful in the assessment of fetal nutritional risk as they showed a significant correlation between subcutaneous tissue thickness, estimated fetal weight, and actual BW. The findings of the present study were also in agreement with another recent study by Khalifa EA et al.[13] (2019) where FASTT showed a high significant statistical correlation with fetal birth weight (r=0.94, P=0.00); it showed higher sensitivity for large for gestational age (LGA) than small for gestational age (SGA) (90.9% and 86.9%, respectively). The best cutoff value for the detection of LGA was ≥ 9.2 mm and the accuracy of FASTT was 92%.

Overall the present study provides preliminary thresholds of FASTT and SSSTT measurements performed in third trimester in predicting macrosomia and show strong correlation between birth weight with SSSTT as well as FASTT. Further a cut-off value of 5.45 mm for SSSTT and 5.15 mm for FASTT strongly predict macrosomia in neonates delivered by women with GDM. However these finding require further validation due to potential limitations of the study that is relatively smaller sample size and single centre study also, the other complications of GDM were not considered which limit the study from generalizing the findings to entire population. Hence further multicentric studies involving large sample size documenting other complications of GDM may provide the precise cut-off values of FASTT and SSSTT in predicting macrosomia among the women with GDM.

V. Conclusion

Sonographically determined SSSTT and FASTT significantly and strongly correlate with birth and a cut of value of 5.45 and 5.15 cms respectively are highly accurate in predicting macrosomia among the neonates delivered by women with GDM.

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