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Sonographic Assessment of fetal subcutaneous Fat thickness as an indicator of gestational diabetes

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Abstract

Background: Gestational diabetes is the most common metabolic complication affecting women during pregnancy. It is a critical issue during pregnancy, due to possible maternal and fetal complications. The most common consequence to the fetus is macrosomia, which has an incidence rate of 26% among diabetic pregnancies. It is well known that adipose tissue thickness and skin fold thickness are greater in newborns of mothers with gestational diabetes than in the offspring of mothers with normal glucose metabolism Fetal adiposity is known to be a consequence of maternal diabetes. Recently, ultrasound had been used as a non invasive and well-tolerated method to compare the measurements of subcutaneous fetal fat tissue in pregnancies with normal and abnormal GTT as an additional tool in predicting gestational diabetes. **Aim of the work:** The present study was designed to investigate the use of ultrasound to compare the measurements of subcutaneous fetal fat in pregnancies with normal and abnormal GTT, as an additional tool in predicting gestational diabetes. **Patients and methods:** It was performed at Al-Azhar university hospital, New Damietta, Obstetrics and Gynecology Department. Fifty women with singleton pregnancies between 24 and 26 weeks' gestation were participate in our study. We measured fetal subcutaneous fat tissue thickness and fetal weight in 25 women with abnormal GTT (Group A, study group) and 25 women with normal GTT (Group B, control group). Each patient was underwent two-dimensional (2D) ultrasound evaluation between 24, 26 weeks. At least two measurements were taken for each parameter. **Results** of the present study revealed that: There was statistically non-significant difference between the study and the control group as regard BMI; Fetuses of mothers in the study group showed statistically significant increase of fetal tissue thickness in all measures areas in comparison to the control group; The study group showed statistically significant increase of cesarean delivery in comparison to the control group; Fetuses of mothers in the study group showed statistically significant increase of fetal birth weight in comparison to control group. **Conclusion:** The results of the present study suggest the possibility of using sonographically determined fetal subcutaneous fat measurements as a criterion to distinguish women at high risk for gestational diabetes. Assessing these parameters is easily reproducible, noninvasive and could enable real-time detection of fetal overgrowth and disproportion, potentially resulting in early detection and reducing fetal morbidity. In addition, a sonographic evaluation of fetal fat body mass, however, can be considered as an effective, noninvasive and cost-effective method that can prove useful for evaluating the fetal consequences of maternal hyperglycemia.

Keywords: fetal subcutaneous fat, gestational diabetes.

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Approximately 7% of all pregnancies are complicated by GDM **(Karagiannis et al., 2010).** During pregnancy, increase in insulin resistance occurs. Euglycemia is maintained through a compensatory insulin secretion.

The key factor which results in the development of gestation diabetes appears to be a failure to compensate with increased insulin secretion. As the increase in insulin resistance is greatest in the third trimester, GDM usually develops going into this period. Therefore, screening for GDM usually occurs around 24 – 28 weeks into the pregnancy **(Cheung, 2009).** ‘

The most important risk factors of GDM are high maternal age, family history of type 2 diabetes and overweight before pregnancy and GDM or glucose intolerance in previous pregnancies. There is also some evidence that excessive gestational weight gain, high intake of saturated fat and low intake of poly-unsaturated fat may increase the risk of GDM on the other hand, physical activity improves glucose tolerance and insulin sensitivity in pregnant women. Physical activity before or during pregnancy is also associated with reduced risk of GDM **(Luoto et al., 2010).** Diabetes during pregnancy increases fetal and maternal morbidity and mortality. Neonates are at risk of respiratory distress, hypoglycemia, hypocalcemia, hyper-bilirubinemia, polycythemia and hyperviscosity. Poor control of gestational diabetes during organogenesis (up to about 10 week's gestation) increases risk of major congenital malformations and spontaneous abortion. Poor control of diabetes later in pregnancy increases risk of fetal macrosomia (usually defined as fetal weight > 4000 or >4000g at birth), preeclampsia and spontaneous abortion. However, gestational diabetes can result in fetal macrosomia even if plasma glucose is kept nearly normal **(Sean, 2009).**

The oral glucose Tolerance test is the most frequently used diagnostic test for gestational diabetes; however, it is time consuming and less tolerated and is usually performed between 24 and 28 weeks of gestation. It is well known that adipose tissue thickness and skin fold thickness are greater in newborns of mothers with gestational diabetes than in the offspring of mothers with normal glucose metabolism Fetal adiposity is known to be a consequence of maternal diabetes. Recently, ultrasound had been used as a non invasive and well-tolerated method to compare the measurements of subcutaneous fetal fat tissue in pregnancies with normal and abnormal GTT as an additional tool in predicting gestational diabetes **(Tantanasis et al., 2010).**

Aim of the work

The aim of this study is to use ultrasound to compare the measurements of subcutaneous fetal fat in pregnancies with normal and abnormal GTT, as an additional tool in predicting gestational diabetes.

Patients and Methods

The present study was performed at Al-Azhar university hospital, New Damietta (Obstetrics & Gynecology Department). Fifty women with singleton pregnant women between 24 and 26 weeks of gestation participated in our study. The study was approved by the Ethical Committee of our institution and all participants provided informed consent, 25 women with abnormal GTT (Group A, study group) and 25 women with normal GTT (Group B, control group). Women were selected for this study should have all the following criteria: no past medical history of diabetes; non-smokers; BMI less than 30 kg/m^2; and no obvious fetal anomalies during ultrasound examination.

All women selected for this study were subjected to: history taking; estimation of gestational age (estimation on the basis of the last menstrual period that confirmed by ultrasound biometry 22 weeks of gestation; the oral glucose screening test was performed at 24 weeks of gestation and Ultrasound detection of maximum subcutaneous fat tissue thickness.

The oral glucose screening test that we used consisted of oral administration of 75 g of sugar diluted in water and serial measurements every 30 min up to 2 h from initiation of the test. According to the **World Health Organization (WHO) criteria (1999),** fasting plasma glucose ≥7.0 mmol/l (126 mg/dl) or plasma glucose ≥11.1 mmol/l (200mg/dl) at 2 h after the GTT is considered as indicative of diabetes mellitus.

Ultrasound detection of maximum sub-cutaneous fat tissue thickness:

It was carried out at 24-26 weeks of gestation. At least two measurements were taken for each parameter and performed at three different levels of the fetal body from the inner to the outer aspect of the echogenic subcutaneous fat. One measurement was performed at the level of the biparietal diameter (BPD), measuring the parietal subcutis, labeled as head circumference (HC); a second measurement was at the level of the abdominal circumference (AC) with the fetal abdomen free from contact with arms or legs and with amniotic fluid between the fetal trunk and the uterine wall and the third measurement was performed sagittally at the level of the thoracic spine (TS). The sonographers were unaware of which group women belonged to. The scans were performed by two experienced operators with Voluson 730 (Germany) with transabdominal 3.5 mHz curved transducers.

Follow up: every 2 weeks by post-prandial blood glucose and measurements with ultrasound up to delivery.

The outcomes: All results were estimated to the significance of the different measurements among both groups as regard the relations between fetal subcutaneous fat tissue thicknesses, fetal birth weights and blood glucose levels.

Statistical analysis of data: the collected data were organized, tabulated and statistically analyzed using SPSS, version 16, running on IBM compatible computer. Quantitative data were represented as mean ± standard deviation (SD) while qualitative data were represented and frequency (n) and percentage (%) and for comparison between two groups, the student (t) test was used for quantitative data, and Chi square test used for qualitative data. P value set at < 0.05 was considered significant.

Results

As regard patient BMI, it ranged from 23.81 to 28.04 kg/m^2 with a mean of 26.23±1.20 kg/m^2 and there was statistically insignificant difference between study and control groups as regard BMI (26.52±1.24 vs 25.95±1.12 kg/m^2 respectively). Gestational age at first examination ranged from 24 to 26 weeks with a mean of 24.92±0.63 and there was statistically insignificant decrease of GA at examination in the study group in comparison to control group (24.80±0.64 vs 25.04±0.61 respectively). At delivery, there was statistically significant decrease of GA at delivery in study group in comparison to control group (37.52±1.29 vs 38.04±1.01 respectively). Mode of delivery was normal vaginal delivery (NVD) in 74% of cases and Cesarean section (CS) in 26% of cases and there was statistically significant increase in CS delivery in study group in comparison to control group (40% vs 12% respectively). Fetal birth weight ranged from 2850 to 4100 g with a mean of 3487.8±362.53 g and there was statistically significant increase in fetal birth weight in the study group in comparison to control group (3784.4±187.99 vs 3191.2±222.97 respectively) (table 1).

Table (1): Comparison between study and control groups as regard BMI and GA at first examination and at delivery, mode of delivery and fetal birth weight

Variable	Study Group	Control Group	Test	P Value
BMI (kg/m^2) (mean±SD)	26.52±1.24	25.95±1.12	1.70	0.07(NS)
GA at first examination (weeks) (mean±SD)	24.80±0.64	25.04±0.61	1.34	0.18(NS)
GA at delivery	37.52±1.29	38.04±1.01	1.57	0.12(NS)
Mode of delivery (n,%)				
NVD	15 (60.0%)	22 (88.0%)		
CS	10 (40.0%)	3 (12.0%)	5.09	0.024*
Fetal birth weight (mean±SD	3784.4±187.99	3191.2±222.97	10.16	<0.001*

At the level of biparietal diameter, fat thickness (mm), ranged from 2 to 6.2 mm with a mean of 3.81±1.47 mm and there was statistically significant increase in fat thickness in the study group in comparison to control group (5.15±0.60 vs 2.46±0.55 mm respectively). At abdominal circumference, fat thickness (mm), ranged from 2.2 to 8.2 mm with a mean of 4.67±1.64 mm and there was statistically significant increase in fat thickness in the study group in comparison to control group (6.18±0.68 vs 3.15±0.53 mm respectively). Fat thickness at thoracic circumference (mm) ranged from 2.2 to 8.2 mm with a mean of 4.93±2.03 and there was statistically significant increase in fat thickness in the study group in comparison to control group (6.87±0.66 vs 2.99±0.41 mm respectively) (table 2).

Table (2): Comparison between study and control groups as regard subcutaneous tissue fat thickness at biparietal diameter, abdominal circumference and thoracic circumference

Variable	Study group	Control group	Test	P Value
Biparietal diameter (mean±SD)	5.15±0.60	2.46±0.55	16.33	<0.001*
Abdominal circumference (mean±SD)	6.18±0.68	3.15±0.53	17.43	<0.001*
Thoracic circumference (mean±SD)	6.87±0.66	2.99±0.41	24.79	<0.001*

The best cut off for subcutaneous fat tissue thickness at abdominal circumference was 4.55 mm with sensitivity of 100% and Specificity of 100%. The best cut off for subcutaneous fat tissue thickness at BPD was 3.90 mm with sensitivity of 100% and Specificity of 100%. The best cut off for subcutaneous fat tissue thickness at thoracic spine was 4.50 mm with sensitivity of 100% and Specificity of 100% (Table 3).

Table (3): cut off, Sensitivity and specificity of subcutaneous fat tissue thickness at abdominal circumference, biparietal diameter and thoracic circumference

	Positive if Greater Than or Equal To	Sensitivity	1- Specificity
Abdominal circumference	**4.55**	**1.0**	**0.000**
	5.10	0.96	0.000
	5.35	0.92	0.000
Biparietal diameter	3.65	1.000	0.080
	3.90	**1.000**	**0.000**
	4.10	0.92	0.000
Thoracic circumference	3.45	1.000	0.080
	4.50	**1.000**	**0.000**
	5.65	0.960	0.000

Figure (1): Ultrasound measurement of AC (abnormal glucose tolerance test); (6mm)

Figure (2): Ultrasound measurement of AC (normal glucose tolerance test); (4.2)

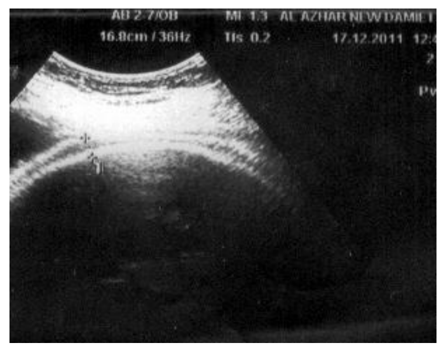

Figure (3):Ultrasound measurement of BPD (abnormal glucose tolerance test); 7.1mm

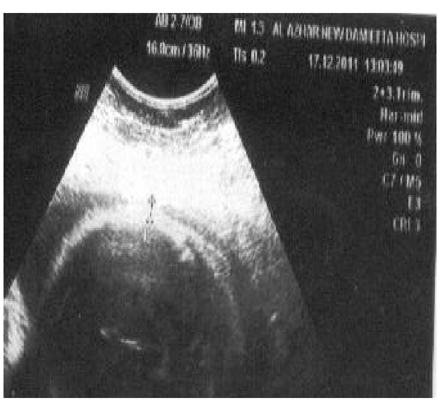

Figure (4):Ultrasound measurement of BPD (normal glucose tolerance test); 3.5mm

Figure (5):Ultrasound measurement of TS (abnormal glucose tolerance test); 6.3mm

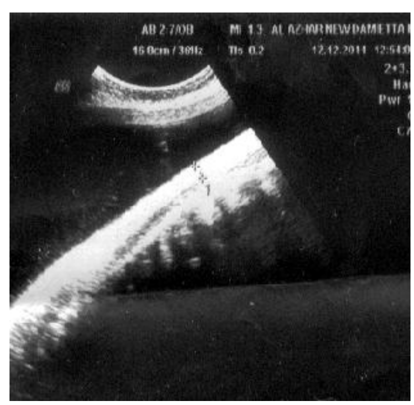

Figure (6): Ultrasound measurement of TS (normal glucose tolerance test); 3.8mm

Discussion

The present study was designed to investigate the use of ultrasound to compare the measurements of subcutaneous fetal fat in pregnancies with normal and abnormal GTT, as an additional tool in predicting gestational diabetes. It was performed at Al-Azhar university hospital, New Damietta, Obstetrics and Gynecology Department. Fifty women with singleton pregnancies between 24 and 26 weeks' gestation were participate in our study. We measured fetal subcutaneous fat tissue thickness and fetal birth weight in 25 women with abnormal GTT (Group A, study group) and 25 women with normal GTT (Group B, control group). Each patient was underwent two-dimensional (2D) ultrasound evaluation between 24, 26 weeks. At least two measurements were taken for each parameter.

As regard patient BMI it ranged from 23.81 to 28.04 kg/m^2 with a mean of 26.23±1.20 kg/m^2 and there was statistically insignificant difference between study and control groups as regard BMI. These results are in agreement with that reported by **Gruendhammer et al. (2003)** who reported that, patients and controls were matched for BMI and thus there was statistically insignificant difference between groups.

As regard gestational age at ultrasonic examination, it ranged from 24 to 26 weeks with a mean of 24.92±0.63 and there was statistically insignificant decrease of GA at examination in the study group in comparison to control group (24.80±0.64 vs 25.04±0.61 respectively). At delivery, there was statistically insignificant decrease of GA at delivery in study group in comparison to control group (37.52±1.29 vs 38.04±1.01 respectively). In their work, **Larciprete et al. (2003)** reported that, gestational age at delivery in the study group was 38.6 ± 2.6 weeks, while it was 39.0±3.0 weeks in control group with statistically insignificant difference between groups. These results are in agreement with that of the present study. In addition, **Parretti et al. (2003)** reported that, gestation age at delivery of the study group was 39.2±1.6 weeks, while in control group; it was 39.8±1.4 weeks with statistically insignificant difference between groups. Again, these results are in disagreement with that of the present study.

As regard fat thickness at the level of biparietal diameter (mm), it ranged from 2 to 6.2 mm with a mean of 3.81±1.47 mm and there was statistically significant increase of fat thickness in the study group in comparison to control group (5.15±0.60 vs 2.46±0.55 mm respectively). As regard to fat thickness at abdominal circumference (mm), it ranged from 2.2 to 8.2 mm with a mean of 4.67±1.64 mm and there was statistically significant increase of fat thickness in the study group in comparison to control group (6.18±0.68 vs 3.15±0.53 mm respectively). In the present study, fat thickness at thoracic circumference (mm) ranged from 2.2 to 8.2 mm with a mean of 4.93±2.03 and there was statistically significant increase of fat thickness in the study group in comparison to control group (6.87±0.66 vs 2.99±0.41 mm respectively).

In agreement with the results of the present work, it was reported that, it is well known that adipose tissue thickness and skin fold thickness are greater in the newborns of mothers with gestational diabetes than in the offspring of mothers with normal maternal glucose metabolism **(Greco et al., 2003).** In their evaluation of the subcutaneous fat tissue thickness and the significance of the different measurements among pregnant women with normal and abnormal GTT, **Tantanasis, et al. (2010)** reported a close correlation between GTT and subcutaneous fat tissue thickness. In fact, there was a significant difference between the study group and the control group regarding the fetal fat thickness in all three parameters examined.

Ultrasound measurement of soft tissue thickness is gaining popularity due to improvement in accuracy of fetal weight determination **(McNamara and Odibo, 2011).**

Gardeil et al. (1999) reported The value of the abdominal subcutaneous tissue thickness in predicting FGR was studied. Ultrasound scans were carried out at 20, 26, 31 and 38 weeks on 137 patients. The abdominal subcutaneous tissue thickness was measured on the anterior abdominal wall in millimeters (mm) anterior to the margins of the ribs, using magnification at the level of the AC. An abdominal subcutaneous tissue thickness measurement less than 5 mm at 38 weeks' gestation detected 76.2% of infants who weighed less than the 10^{th} centile at birth. The incidence of neonatal morbidity was significantly higher in infants with a subcutaneous fat of less than 5 mm at 38 weeks, compared with infants with a subcutaneous fat of 5 mm or more. The sensitivity of the abdominal subcutaneous tissue thickness measurements compared favorably with the other conventional biometry, however, the specificity and predictive values were low. In another study, it was set out to determine how measurements of the abdominal subcutaneous tissue thickness compared with established indices of growth restriction. A total of 100 women attending for fetal assessment between 40 and 42 weeks' gestation were studied. Infants with an abdominal subcutaneous tissue thickness of 5 mm were more likely to have an amniotic fluid index of 58 cm and to have an AC less than the 10th centile. A decreased abdominal subcutaneous tissue thickness measurement was also associated post-natally with a lower mean ponderal index and lower triceps and subscapular skinfold thickness **(Skinner et al., 2001).**

Higgins et al. (2008) described significantly higher anterior abdominal wall (AAW) thickness in insulin-treated diabetic pregnancies with macrosomic babies. By formulating cut-offs of AAW for gestational age, they showed that an AAW above the cut-off or an abdominal circumference greater than 90% increased prediction of LGA to 88%.

Gestational alterations in maternal metabolism provide nutrients in excess of those required for fetal growth and for maternal requirements. The presence of any degree of abnormal glucose tolerance, even if less than that required for the diagnosis of gestational diabetes, represents an altered intrauterine environment for the growth of the fetus. Although there is consensus that strict blood glucose control during pregnancy reduces the prevalence of macrosomia, recommendations for target blood glucose concentration differ and are based on maternal rather than fetal considerations. Optimal metabolic control in the mother does not seem to be sufficient to avoid fetal macrosomia **(Farah et al., 2009).** In a randomized study, the AC measurement was better than maternal glucose plasma concentrations in determining the need for a combined diet and insulin treatment in mothers with gestational diabetes **(Raychaudhuri and Maresh, 2000).**

It was reported that, subcutaneous fat appears to be a stronger index of maternal glucose control than does the ambulatory glycemic profile **(Bernstein and Catalano, 1994).**

As regard mode of delivery, it was normal vaginal delivery (NVD) in 74% of cases and Cesarean section (CS) in 26% of cases and there was statistically significant increase in CS delivery in study group in comparison to control group (40% vs 12% respectively). These results are in agreement with **Bernstein and Catalano (1994)** who reported that increased neonatal fat is associated with an increased risk of Cesarean delivery in infants born to mothers with GD.

Regarding fetal birth weight, it ranged from 2850 to 4100 g with a mean of 3487.8±362.53 g and there was statistically significant increase in fetal birth weight in the study group in comparison to control group (3784.4±187.99 vs 3191.2±222.97 respectively). In agreement with results of the present work, **Larciprete et al. (2003)** reported that fetal birth weight in study group was 3481±416 g while in control groups it was 3283±395 g with statistically significant increase in study group in comparison to control group. In their work, **Parretti et al. (2003)** reported that, there was statistically significant increase of fetus that was large for gestational age in study group in comparison to control group. These results agreed with that of the present study. In addition, it was reported that, fetal body was closely associated with maternal glucose control than birth weight. In adults there is a direct correlation between fat mass and energy stores. In newborns, although only 14% of birth weight composed of stored fat, 46% of variance in birth weight can be explained by fat body mass **(Rigano et al., 2000).** Even a small degree of abnormality in GTT could represent an altered metabolic environment for fetal growth **(Tantanasis et al., 2010).** Finally, **McNamara and Odibo (2011)** stated that, utilization of first trimester ultrasound for patients with diabetes greatly impacts pregnancy management.

In short, the results of the present study suggest the possibility of using sonographically determined fetal subcutaneous fat measurements as a criterion to distinguish women at high risk for gestational diabetes. Assessing these parameters is easily reproducible, noninvasive and could enable real-time detection of fetal overgrowth and disproportion, potentially resulting in early detection and reducing fetal morbidity. In addition, a sonographic evaluation of fetal fat body mass, however, can be considered as an effective, noninvasive and cost-effective method that can prove useful for evaluating the fetal consequences of maternal hyperglycemia.

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