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Original Research Article

A Cross-Sectional Analytical Evaluation of the Role of Fetal Epicardial Fat Thickness as a Marker and Use it in Pregnancies to Screen for Gestational Diabetes Mellitus

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Abstract

Aim: The aim of the present study was to evaluate the role of fetal epicardial fat thickness as a marker and use it in pregnancies to screen for gestational diabetes mellitus.

Methods: A cross-sectional analytical study was conducted at Department of Radiology Katihar Medical College and Hospital, Katihar, Bihar, India. Pregnant patients at 24 + 0/6 to 28 + 0/6 weeks of gestation who were scheduled for a 75 g oral glucose tolerance test (OGTT) according to the American Diabetes Association criteria (fasting ≥ 92 mg/dL, 1 hour ≥ 180 mg/dL, or 2 hours ≥ 153 mg/dL) were included in the study. During the study period, 50 cases of GDM and 50 non-GDM patients were identified after the application of inclusion and exclusion criteria.

Results: The mean gestational age of cases (26.24 ±1.32 weeks) were matched with that of controls (26.56 ±1.28 weeks). The mean fetal EFT in mothers with GDM was significantly higher, i.e., 0.16 ±0.03 cm than in mothers without GDM, i.e., 0.13 ±0.02 cm ($p < 0.001$). The 2 hours OGTT results of cases had an average value of 180.22 ±9.81 mg/dL and controls had an average 2 hours OGTT value of 128.72 ±16.32 mg/dL. The receiver operating characteristic (ROC) curve plotted from values calculated from our results showed high sensitivity (i.e., 95.65% and specificity (i.e., 90%) of fetal EFT as a predictor for GDM.

Conclusion: In conclusion, EFT is a reliable marker for GDM. Measure- ment of EFT is reproducible, does not require any additional training, and does not adds to scan time.

Keywords: fetal, epicardial fat thickness, marker, gestational diabetes mellitus

Introduction

Gestational diabetes mellitus (GDM) is defined as the new onset of various degrees of glucose intolerance during pregnancy. This definition applies to whether insulin or only diet modification is used for treatment and whether the condition persists after pregnancy. It is diagnosed following a population screening for hyperglycemia in pregnant women. [1,2]

In India, the prevalence rate of GDM is 10–14.3% which is much higher than in the western population. The incidence of GDM follows the incidence of insulin resistance and type 2 diabetes mellitus in each country's population. [3] Hence, the incidence of GDM in India is expected to increase to 20%, i.e., one in every 5 pregnant women will have GDM. With this increase in the incidence of GDM, the various complications, i.e., maternal (postpartum hemorrhage, need for cesarean section, birth trauma, prolonged and obstructed labor, infection) as well as fetal (congenital anomalies, stillbirths, intrauterine death, birth injuries, neonatal hypoglycemia, respiratory distress), will become even more dreadful for the entire health system. Also, children of mothers with uncontrolled diabetes are four times more likely to develop diabetes in adulthood leading to worse long-term outcomes. [4]

The timing and severity of maternal diabetes play a critical role in determining the effects on fetal metabolic state and fetal cardiovascular development. In pre-gestational diabetes, there is first-trimester hyperglycemia leading to adverse effects on fetal organogenesis and neural crest migration resulting in typical conotruncal cardiac defects. However, GDM in the 2nd and 3rd trimesters put the fetus at risk for myocardial hypertrophy and diastolic impairments with increased fetal cardiac interventricular septal thickness, which is the most common structural abnormality in GDM. [5] Also, 40% of the infants born to such diabetic mothers develop hypertrophic cardiomyopathy out of which 5% become symptomatic. [6] It may occur due to worsened metabolic state or due to neonatal hyperinsulinemia with increased expression and affinity of insulin receptors leading to the proliferation of cardiac myocytes.

The aim of the present study was to evaluate the role of fetal epicardial fat thickness as a marker and use it in pregnancies to screen for gestational diabetes mellitus.

Materials and Methods

A cross-sectional analytical study was conducted at Department of Radiology, Katihar Medical College and Hospital, Katihar, Bihar, India for one year Pregnant patients at 24 + 0/6 to 28 + 0/6 weeks of gestation who were scheduled for a 75 g oral glucose tolerance test (OGTT) according to the American Diabetes Association criteria (fasting ≥ 92 mg/dL, 1 hour ≥ 180 mg/dL, or 2 hours ≥ 153 mg/dL) were included in the study. During the study period, 50 cases of GDM and 50 non-GDM patients were identified after the application of inclusion and exclusion criteria.

As OGTT is performed as a routine test in every pregnancy between 24 weeks to 28 weeks of gestation, it did not add any extra cost to the patient. Proper prior informed consent was taken from the patient before performing the ultrasound. The ultrasound examination of these patients was performed before the results of the OGTT to eliminate the information bias to the sonographer. Out of 180 patients in this time frame, 30 patients with raised 75 g OGTT results (cases of GDM) and 30 patients with normal 75 g OGTT results were randomly included as a convenient sample size. Patients with pre- existing type 1 or type 2 diabetes, congenital fetal anomalies, and women on medications except for oral iron supplementation or multivitamins were excluded from this study because pre-existing diabetes mellitus, and medications act as confounding factors and congenital anomalies can also alter the results as these patients will have an already raised fetal EFT due to pre-existing diabetes, and effect of medications can also alter the metabolism. Gestational age was calculated from the last menstrual period confirmed by gestational age according to ultrasound well-being scan as gestational age according to ultrasound depicts more accu- rate growth and development of the fetus.

Ultrasound technique used: Ultrasound was performed on Voluson E8 Expert BT12 (Wipro GE) ultrasound machine transabdominally using a linear 5 to 10 MHZ probe and convex rab 6D (2–7) MHZ probe. Ultrasound was done by radiologists with more than 10 years of experience in fetal imaging.

The left ventricle outflow (LVOT) view is ideal to visualize the space between the myocardium and epicardium along the right ventricle. EFT represented by the hypoechogenic area between the visceral pericardium and myocardium was identified. A reference line passing through the right ventricular wall, aortic annulus, and descending aorta was drawn. EFT was measured at the end-diastole of the cardiac cycle. Dynamic and static images were stored due to a lack of control over the cardiac cycle. The calipers measured the inner-to-inner aspect of the hypoechoic area through the available wall of the right ventricle nearest to the reference line. The maximum EFT along the reference line passing through the aortic annulus and intersecting the right ventricular wall was measured at 90 degrees to the wall. A major prerequisite for this measurement included in this study was the anterior position of the fetal heart to minimize the limitations of reproducibility of previous studies.

The reproducibility of the technique has been investigated before the initiation of the study. A blinded investigator measured EFT in 20 randomly selected normal fetuses. The images were stored separately in the same ultrasound ma- chine, and EFT was remeasured from the stored images after 2 weeks by the same investigator. The mean of these two measurements performed by the same investigator was calculated. This mean EFT value was used for the final analysis of the results.[7]

The fetal EFT values obtained in patients with raised OGTT test results were compared with those patients having normal OGTT test results.

Data Entry and Statistical Analysis

The collected data were transformed into variables, coded, and entered in the Microsoft Excel. Data were analyzed and statistically evaluated using the SPSS-PC-25 version.

The normal distribution of different parameters was tested by the Shapiro–Wilk normality test.

Quantitative data are expressed as mean standard deviation or median with interquartile range and depends on the normality difference between the mean of two groups and were compared by student's t-test or Mann–Whiney U test. Qualitative data are expressed in frequency and percent- age, and statistical differences between the proportions were tested by the chi-square test or Fisher's exact test.

ROC curve was prepared using fetal EFT to differentiate between GDM and non-GDM and based on that, the cut-off value was calculated. Sensitivity, specificity, PPV, and NPV of fetal EFT were calculated. P-value less than 0.05 was considered statistically significant.

Results

Table 1: Comparison of mean gestational age between both groups

	GDM-nt (n =50)	GDM + nt (n=50)	p-Value
Mean gestational age in weeks	26.24 ±1.32	26.56 ±1.28	0.32

The mean gestational age of cases (26.24 ±1.32 weeks) were matched with that of controls (26.56 ±1.28 weeks).

Table 2: Comparison of mean fetal epicardial fat thickness between both groups

	GDM-nt (n = 50)	GDM + nt (n = 50)	p-Value
Mean fetal epicardial fat thickness (in cm)	0.13 ±0.02	0.16 ±0.03	<0.001
Median (IQR)	0.12 (0.11–0.13)	0.17 (0.16–0.19)	

The mean fetal EFT in mothers with GDM was significantly higher, i.e., 0.16 ±0.03 cm than in mothers without GDM, i.e., 0.13 ±0.02 cm ($p < 0.001$).

Table 3: Comparison of OGTT test results between both groups

	GDM - nt (n = 50)	GDM + nt (n = 50)	p-Value
OGTT test result (mg/dL)	128.72 ±16.32	180.22 ±9.81	<0.001

The 2 hours OGTT results of cases had an average value of 180.22 ±9.81 mg/dL and controls had an average 2 hours OGTT value of 128.72 ±16.32 mg/dL.

Table 4: Diagnostic accuracy of fetal epicardial fat thickness for predicting GDM

	Fetal epicardial fat thickness
Area under curve	0.94
95% Confidence interval	0.94–1.0
Cut off value	0.148
Sensitivity (95% CI)	95.65% (82.78–99.92)
Specificity (95% CI)	90.0% (73.47–97.89)
PPV (95% CI)	90.64 (76.73–96.59)
NPV (95% CI)	97.43 (79.66–99.47)
Accuracy (95% CI)	94.33 (83.80–98.15)

The receiver operating characteristic (ROC) curve plotted from values calculated from our results showed high sensitivity (i.e., 95.65% and specificity (i.e., 90%) of fetal EFT as a predictor for GDM.

Discussion

Epicardial fat is located between the visceral pericardium and myocardium, mostly distributed adjacent to the right ventricle and adds significantly to myocardial energy production. [8,9] It is an active and complex endocrine organ that secretes multiple anti-inflammatory and proinflammatory molecules. [10,11] Gestational diabetes mellitus (GDM) is a disorder of metabolism that results in resistance to insulin during pregnancy. [12] Its diagnosis is necessary, as it results in fetal, neonatal, and maternal problems. [13-15] The resistance to insulin precedes the detection of an increase in glucose levels in the blood. [16,17] There have been studies on the association of epicardial fat thickness (EFT) measured on ultrasonography and insulin resistance in the adult population; however, there are limited data on EFT in fetuses and GDM.

The mean gestational age of cases (26.24 ±1.32 weeks) were matched with that of controls (26.56 ±1.28 weeks). The mean fetal EFT in mothers with GDM was significantly higher, i.e., 0.16 ±0.03 cm than in mothers without GDM, i.e., 0.13 ±0.02 cm ($p < 0.001$). The 2 hours OGTT results of cases had an average value of 180.22 ±9.81 mg/dL and controls had an average 2 hours OGTT value of 128.72 ±16.32 mg/dL. The receiver operating characteristic (ROC) curve plotted from values calculated from our results showed high sensitivity (i.e., 95.65% and specificity (i.e., 90%) of fetal EFT as a predictor for GDM. In the present study, it was seen that fetal EFT increased with advancing gestational age. Similar findings have been documented in studies in past by Aydin et al. [18] Yavuz et al, in their study, found similar findings of significantly increased epicardial fat thickness in fetuses of diabetic mothers. However, their measurement method was not standardized and they did not consider contributing factors such as the gestational age of the fetus. [19]

After controlling for gestational age, the present study demonstrated that EFT can be an individual marker for gestational diabetes. The pathophysiology of the regulation of insulin is same as in PDM (pre-gestational diabetes mellitus) and GDM, manifestations of insulin resistance occur in the later stages of gestation in GDM. [20] This is why an increase in EFT in GDM is more evident in the third trimester. Epicardial fat is involved in energy production for the myocardium and has increased fatty acid synthesis and lipogenesis due to insulin as compared with other types of fat. In cases with raised insulin, epicardial fat serves as a buffer to scavenge the extra toxic fatty acids. Therefore, in cases with raised fetal glucose levels, EFT will be increased long before other fat deposition occurs. [18,21] Insulin resistance occurs before increased glucose levels induce lipogenesis. [18] An increase in abdominal circumference and thickness of subcutaneous fat act as an indicator for more glycogen and fat deposition in the liver and subcutaneous tissue; however, the use of these markers in the second trimester is limited due to the incapacity of the fetus to store fat in mid-trimester. Increased fetal EFT can be a potential early marker and can be measured as early as 24 weeks of gestation to timely detect early altered fetal metabolism as a result of raised glucose before complications are apparent.

Conclusion

In conclusion, EFT is a reliable marker for GDM. Measurement of EFT is reproducible, does not require any additional training, and does not add to scan time.

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