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The Role of Fetal Epicardial Fat Thickness and Truncus Pulmonalis Diameter in Prediction of Perinatal Outcomes in Diabetic Pregnancies

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ABSTRACT

Background: Maternal diabetes continues to be a global health concern, with long-term effects on offspring that include metabolic syndrome, obesity, and cardiovascular illness, in addition to immediate neonatal morbidity. Finding early indicators of cardiometabolic risk in babies exposed to maternal diabetes mellitus, such as fetal epicardial fat thickness (fEFT) and main pulmonary artery diameter (MPAD), has become more popular as a result.

Objective: To investigate the relationship between the major pulmonary artery diameter and the thickness of the fetal epicardial fat and the perinatal outcomes in pregnancies with and without diabetes.

Patients and Methods: 81 pregnant females who were admitted to Menoufia University's Obstetrics and Gynecology Department between August 2022 and November 2024 were the subjects of this case-control study, which involved three case cohorts; 27 healthy, non-diabetic females made up **Cohort A**; 27 females with gestational DM were in **Cohort B**; and 27 females with pre-gestational (preexisting) diabetes mellitus, including type 1 and type 2, were in **Cohort C**.

Results: While main pulmonary artery diameter lacks the sensitivity and specificity of fEFT, did not differ significantly across cohorts, and only demonstrated a weak predictive ability for neonatal respiratory distress or NICU admission, our findings show that fEFT is significantly increased in fetuses of diabetic mothers (in pregestational DM more than gestational DM), and is clearly correlated with adverse neonatal outcomes.

Conclusion: According to our research, adding fEFT measurement to third-trimester ultrasound evaluations may help identify fetuses at risk in diabetes pregnancies early on, enabling improved surveillance and focused perinatal care.

Keywords: fEFT, MPAD, Gestational DM, Diabetic Pregnancies.

INTRODUCTION

Significant maternal and fetal morbidity as well as unfavorable perinatal outcomes, including fetal macrosomia, birth trauma, polyhydramnios, respiratory distress syndrome, hypoglycemia, and surgical delivery, are caused by diabetes during pregnancy [(1)]. Modified adiposity, elevated insulin resistance, inflammation, and hematologic alterations indicative of chronic hypoxia are all present in fetuses of diabetic moms [(2)].

Because of this, there is increasing interest in finding early indicators of cardiometabolic risk in fetuses exposed to maternal diabetes mellitus [(3)]. Measured by ultrasound, fetal epicardial fat thickness (fEFT), a metabolically active visceral fat depot around the heart and coronary arteries, may be a sign of cardiometabolic risk [(4)].

A poor prognostic indicator, the significant dilatation of the fetal main pulmonary artery in the latter part of the third trimester prior to delivery indicated improper lung development during pregnancy [(5)].

Aim of the work was to investigate the relationship between the main pulmonary artery diameter and the thickness of the fetal epicardial fat and the perinatal outcomes in pregnancies with and without diabetes.

PATIENTS AND METHODS

81 pregnant females who were admitted to Menoufia University's Obstetrics and Gynecology Department participated in this observational study. The range of their gestational ages was 34–39 weeks + 6 days.

The trial, which involved three case cohorts in the study design, took place between August 2022 and November 2024.

81 females were divided into three cohorts: 27 healthy, non-diabetic females made up Cohort A; 27 females with gestational DM were in Cohort B; and 27 females with pre-gestational (preexisting) diabetes mellitus, including type 1 and type 2, were in Cohort C.

Inclusion criteria:

Unbroken fetal membranes, a singleton pregnancy, and no signs of an impending delivery from either the mother or the fetus.

Cohort B (gestational diabetes mellitus) (GDM) cases were diagnosed upon recommendation of American diabetic association 2022.

Cohort C (preexisting diabetes mellitus) cases were diagnosed also upon recommendations of American diabetic association (ADA) 2022.

Exclusion criteria:

Premature membrane rupture, abruptio placentae, significant obstetric hemorrhage, preeclampsia, eclampsia, cardiac illnesses, chorioamnionitis, intrauterine growth restriction, intrauterine fetal death, and fetal distress all require immediate delivery.

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Every case underwent an ultrasound examination, confirmatory diabetes panel, clinical evaluation, and complete history taking.

Fetal echocardiogram was performed using a non-blind sonographer to determine the main pulmonary artery diameter and the thickness of the fetal epicardial fat at gestational age 35 weeks (0/ 6) days.

Measurement of fetal epicardial fat thickness (Figure 1): The best view to see the hypoechoic space between the epicardial surface and parietal pericardium at the right ventricle is the apical five chamber view of the fetal heart, which is obtained in a transverse plane through the fetal thorax and left ventricular outflow tract (LVOT). fEFT was measured on the free wall of the right ventricle. A reference line was created as an anatomic landmark that extends from the descending aorta through the aortic valve's annulus and then upward to a location on the right ventricle's free wall during end systole in order to increase repeatability and standardize data.

Measurement of fetal truncus pulmonalis / main pulmonary artery (MPA) diameter (Figure 2):
MPA diameter was taken at the level of three vessel trachea view (3VT view).

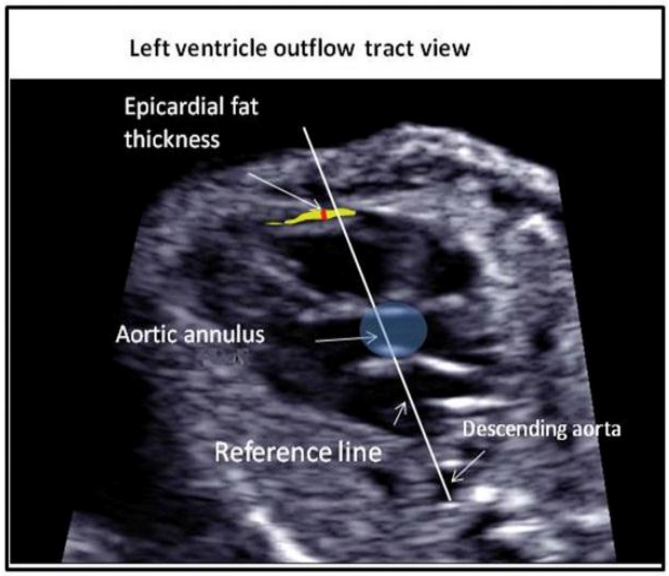

Figure (1): This figure shows standardized measurement of the epicardial fat thickness. The epicardial fat tissue (yellow shaded area) was measured at the largest point (red line) closest to the reference line running through descending aorta to aortic annulus (white line) [(6)].

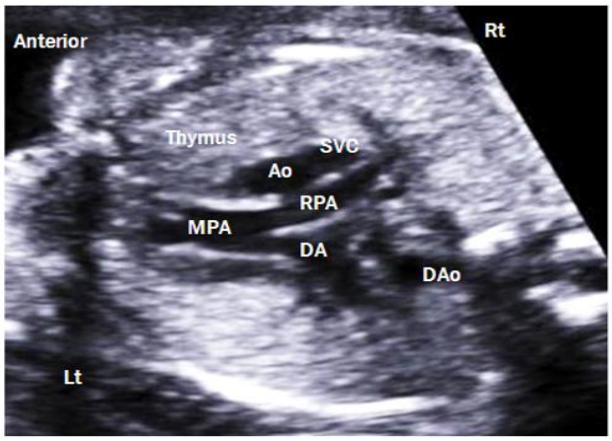

Figure (2): Measurement of main pulmonary artery diameter [(7)].

Study Outcomes: 1[ry] outcome: to investigate the relationship between the incidence of neonatal hypoglycemia and respiratory distress in both diabetes and non-diabetic pregnancies and changes in the fetal epicardial fat thickness and main pulmonary artery diameter. **2[ry] outcome:** to investigate the relationship between the incidence of neonatal hypoglycemia and respiratory distress in both diabetes and non-diabetic pregnancies and changes in the fetal epicardial fat thickness and main pulmonary artery diameter.

Ethical approval:
Following each participant's given informed permission and approval by the hospital's Research Ethics Committee under code number: (8/2022OBSG29). The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

The collected data were tabulated and analysed by SPSS statistical package version 26 on IBM compatible computer. Quantitative data were presented as mean, standard deviation (SD), range, median, and interquartile range (IQR). Qualitative data were presented as frequency and percentage. The following tests were used: Pearson Chi-squared test, Fisher exact test, one-way ANOVA test, Kruskal Wallis test, post hoc test, Pearson correlation, Receiver operating characteristic (ROC) curve, and logistic regression. P value <0.05 was set to be statistically significant.

RESULTS

Table (1) shows that there was a statistically significant difference between study cohorts regarding their age, BMI, gravidity (P value < 0.05).

Table (1): Maternal demographic and obstetric history among studied cohorts (No=81)

Variable	Cohort A (No=27)	Cohort B (No=27)	Cohort C (No=27)	Test of significance P value	Post Hoc test
Maternal age (Years) Mean ±SD Range	27.22 ±5.67 20-40	30.46 ±5.07 20-41	32.30 ±6.84 20-44	F=5.02 **P=0.008***	P1=0.199 **P2=0.007*** P3=0.605
BMI (Kg/m^2) Mean ±SD Range	24.41 ±3.35 19-32	26.17 ±3.98 19-33	29.33 ±4.46 19-35	F=10.89 **P<0.001***	P1=0.338 **P2<0.001*** **P3=0.011***
Gravidity Median (IQR) Range	2 (1-4) 1-8	3 (2.75-4.25) 1-7	4 (2-4) 1-8	H=6.47 **P=0.039***	P1=0.069 **P2=0.014*** P3=0.548
Parity Median (IQR) Range	1 (0-2) 0-4	2 (1-2.25) 0-5	1 (1-3) 0-5	H=4.36 P=0.113	

Cohort A: Healthy non-diabetic females. Cohort B: Females diagnosed with gestational diabetes mellitus. Cohort C: Females diagnosed with pre-gestational (preexisting) DM including both type 1 and type 2. *: significant.
P1: P value between Cohort A and Cohort B. P2: P value between Cohort A and Cohort C. P3: P value between Cohort B and Cohort C.

Table (2) shows that there was a statistically significant difference between study cohorts regarding abdominal circumference, estimated fetal weight, AFI, EFT and HbA1c (P value < 0.05).

Table (2): Fetal data among studied cohorts (No=81)

Variable	Cohort A (No=27)	Cohort B (No=27)	Cohort C (No=27)	Test of significance P value	Post Hoc test
Abdominal circumference (mm) Mean ±SD Range	328.78 ±22.86 280-365	334.26 ±23.69 285-370	349.44 ±28.77 280-390	F=4.86 **P=0.010***	P1=0.706 **P2=0.011*** P3=0.090
Estimated weight (gm) Mean ±SD Range	3175.93 ±327.98 2400-3700	3338.89 ±268.30 2900-3800	3501.85 ±507.73 1950-4500	F=4.92 **P=0.010***	P1=0.363 **P2=0.007*** P3=0.363
UAPI Normal Abnormal	26 (96.3) 1 (3.7)	26 (96.3) 1 (3.7)	27 (100.0) 0 (0.00)	χ^2=1.03 P=1.000	
UARI Normal Abnormal	26 (96.3) 1 (3.7)	26 (96.3) 1 (3.7)	27 (100.0) 0 (0.00)	χ^2=1.03 P=1.000	
AFI Normal Polyhydramnios Oligohydramnios	26 (96.3) 0 (.00) 1 (3.7)	14 (51.9) 13 (48.1) 0 (0.00)	6 (22.2) 21 (77.8) 0 (0.00)	χ^2=35.04 **P<0.001***	**P1<0.001*** **P2<0.001*** **P3=0.024***
fEFT Mean ±SD Range	1.24 ±0.12 1.1-1.5	1.45± 0.07 1.3-1.6	1.62 ±0.11 1.2-1.75	F=88.14 **P<0.001***	**P1<0.001*** **P2<0.001*** **P3<0.001***
MPAD Mean ±SD Range	6.53 ±0.82 5.5-8.5	7.08 ±0.57 5.9-8.1	6.63 ±0.57 5.9-8.1	F=5.26 **P=0.007***	**P1=0.009*** **P2=0.845** **P3=0.039***
HbA1c Mean ±SD Range	5.07 ±0.55 4-6	7.13 ±0.77 6.1-8.9	8.69 ±1.61 6-12.3	F=76.61 **P<0.001***	**P1<0.001*** **P2<0.001*** **P3<0.001***

*: significant. P1: P value between Cohort A and Cohort B. P2: P value between Cohort A and Cohort C. P3: P value between Cohort B and Cohort C.

Table (3) shows that there was a statistically significant difference between study cohorts regarding fetal outcome including delivery time, neonatal birth weight, APGAR (degree of RD), NICU admission and neonatal hypoglycemia (P value < 0.05).

Table (3): Fetal outcomes among studied cohorts (No=81)

Variable	Cohort A (No=27)	Cohort B (No=27)	Cohort C (No=27)	Test of significance P value	Post Hoc test
Delivery time (Weeks)					**P1=0.003***
Mean ±SD	38.59 ±1.25	37.63 ±0.97	37.15 ±0.82	F=13.86	**P2<0.001***
Range	36-40	35-39	35-39	**P<0.001***	P3=0.267
Birth weight (gm)					**P1=0.002***
Mean ±SD	3266.67 ±270.68	3651.85 ±242.38	4112.96 ±576.06	F=31.35	**P2<0.001***
Range	2700-3700	3300-4200	3100-5500	**P<0.001***	**P3<0.001***
FHR pattern					
Normal	26 (96.3)	26 (96.3)	25 (92.6)	0.53	1.000
Abnormal	1 (3.7)	1 (3.7)	2 (7.4)		
Neonatal sex					P1=0.057
Male	18 (66.7)	16 (59.3)	9 (33.3)	χ^2=6.64	**P2=0.014***
Female	9 (33.3)	11 (40.7)	18 (66.7)	**P=0.036***	P3=0.056
APGAR (degree of RD)					
Normal	26 (96.3)	17 (63.0)	7 (25.9)	χ^2=33.27	
RD1	1 (3.7)	6 (22.2)	7 (25.9)	**P<0.001***	**P1=0.009***
RD2	0 (.00)	4 (14.8)	8 (29.6)		**P2<0.001***
RD3	0 (.00)	0 (.00)	5 (18.5)		**P3=0.014***
NICU admission					**P1<0.001***
Yes	1 (3.7)	13 (48.1)	24 (88.9)	χ^2=39.36	**P2<0.001***
No	26 (96.3)	14 (51.9)	3 (11.1)	**P<0.001***	**P3=0.001***
Neonatal hypoglycemia					**P1=0.019***
Present	0 (.00)	5 (18.5)	17 (63.0)	χ^2=28.58	**P2<0.001***
Absent	27 (100.0)	22 (81.5)	10 (37.0)	**P<0.001***	**P3<0.001***

*: significant. P1: P value between Cohort A and Cohort B. P2: P value between Cohort A and Cohort C. P3: P value between Cohort B and Cohort C.

Table (4) shows that there was a positive significant correlation between fEFT and maternal age, BMI, abdominal circumference, estimated fetal weight, birth weight and HbA1c but there was a negative significant correlation between fEFT and MPAD and delivery time (P value <0.05).

Table (4): Correlation between fetal epicardial fat thickness and other parameters among studied participants (No=81)

Parameter	fEFT	
	r	**P value**
Maternal age (Years)	0.330	**0.003***
BMI (Kg/m^2)	0.378	**<0.001***
Gravidity	0.236	**0.035***
Parity	0.177	0.114
Abdominal circumference (mm)	0.521	**<0.001***
Estimated weight (gm)	0.497	**<0.001***
Mean Pulmonary Artery Diameter (MPAD)	-0.066	0.561
HbA1c	0.759	**<0.001***
Delivery time (Weeks)	-0.428	**<0.001***
Birth weight (gm)	0.732	**<0.001***

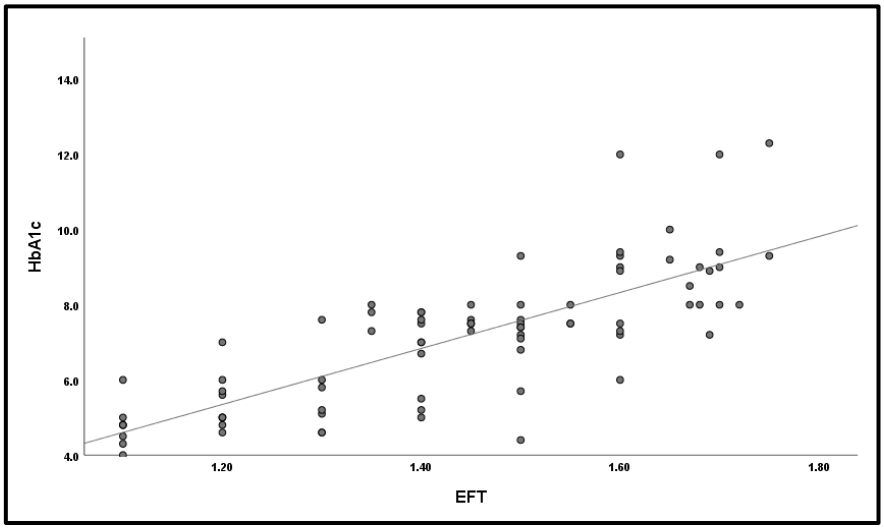

Figure (3): Scatter plot of fEFT in relation to HbA1c.

Table (5) shows that at cut off value ≥ 1.325, fEFT had sensitivity of 96% and specificity of 81% in diagnosis of gestational DM, while MPAD at cut off value ≥ 6.95 had sensitivity of 59% and specificity of 48% in diagnosis of gestational DM.

Table (5): Diagnostic accuracy of fEFT and MPAD for diagnosis of gestational DM (Cohort A Vs Cohort B)

Parameter	fEFT	MPAD
AUC	0.912	0.585
95% CI	0.829-0.994	0.432-0.738
P value	**<0.001***	0.283
Cut off value	≥ 1.325	≥ 6.95
Sensitivity	96%	59%
Specificity	81%	48%

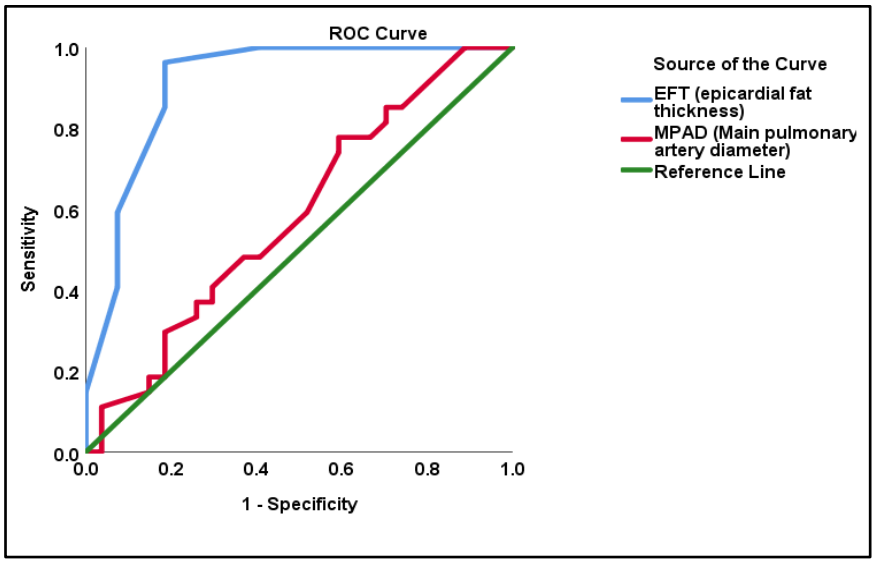

Figure (4): ROC curve fEFT and MPAD for diagnosis of gestational diabetes mellitus.

Table (6) shows that at cut off value ≥ 1.425, fEFT had sensitivity of 56% and specificity of 53% in prediction of C.S mode of delivery, sensitivity of 75% and specificity of 47% in prediction of abnormal FHR. At cut off value ≥ 1.695, fEFT had sensitivity of 67% and specificity of 94% in prediction of maternal hypoglycemia, and at cut off value ≥ 1.475 it had sensitivity of 81% and specificity of 74% in prediction of abnormal APGAR score, sensitivity of 74% and specificity of 77% in prediction of NICU admission and sensitivity of 77% and specificity of 74% in prediction of neonatal hypoglycaemia.

Table (6): Diagnostic accuracy of fEFT in prediction of perinatal outcomes

Parameter	AUC	95% CI	P value	Cut off value	Sensitivity	Specificity
Mode of delivery (CS)	0.585	0.439-0.731	0.307	≥ 1.425	56%	53%
Abnormal FHR	0.500	0.305-0.695	1.000	≥ 1.425	75%	47%
Maternal hypoglycemia	0.838	0.648-1.000	**0.048***	≥1.695	67%	94%
Male sex	0.627	0.504-0.750	0.050	≤ 1.475	61%	55%
Abnormal APGAR	0.869	0.791-0.947	**<0.001***	≥1.475	81%	74%
NICU admission	0.862	0.783-0.941	**<0.001***	≥ 1.475	74%	77%
Fetal hypoglycemia	0.807	0.704-0.911	**<0.001***	≥1.475	77%	74%

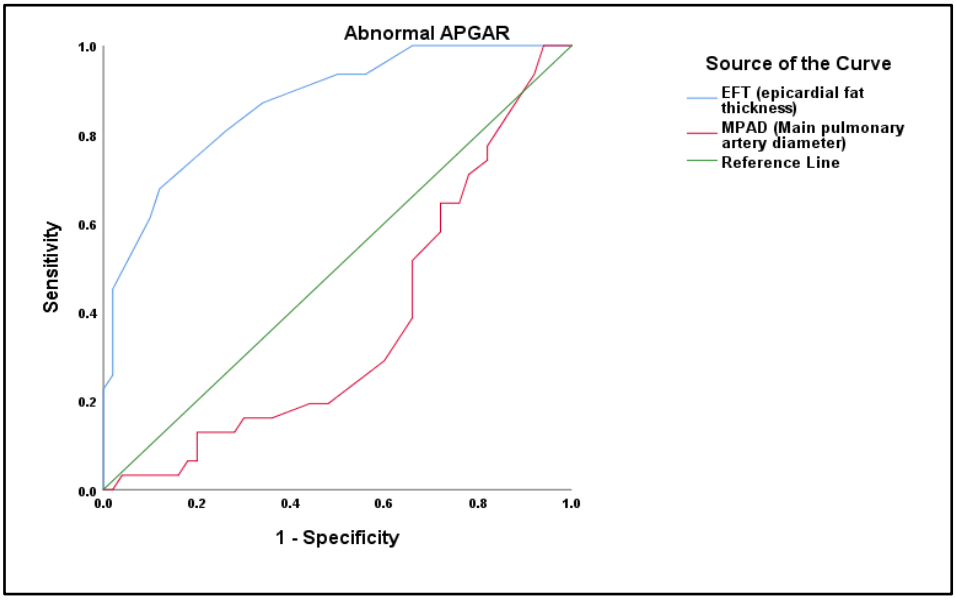

Figure (5): ROC curve fEFT and MPAD for prediction of abnormal APGAR.

Univariate logistic regression analysis showed that AC, EFW, fEFT, birth weight, delivery time, maternal HbA1c, and AFI were significant predictors in univariate analysis and accordingly they entered in multivariate analysis where delivery time was significant predictor (Table 7).

Table (7): Logistic regression for predictors for respiratory distress among studied participants

Variable	Univariate				Multivariate			
	cOR	95% CI		P value	aOR	95% CI		P value
		Lower	Upper			Lower	Upper	
Gravidity	1.238	0.946	1.622	0.120	---	---	---	---
MPAD	0.530	0.271	1.038	0.064	---	---	---	---
Age (Years)	1.125	1.038	1.219	**0.004***	0.896	0.674	1.190	0.448
BMI (Kg/m^2)	1.347	1.163	1.560	**<0.001***	1.240	0.755	2.037	0.396
Parity	1.391	1.005	1.927	**0.047***	1.536	0.504	4.679	0.450
Abdominal circumference (mm)	1.036	1.014	1.059	**0.001***	0.961	0.888	1.041	0.330
Estimated weight (gm)	1.003	1.001	1.004	**0.001***	0.992	0.982	1.001	0.087
AFI Normal (Reference) Abnormal	57.333	13.668	240.492	**<0.001***	0.012	0.000	1.172	0.058
fEFT	44372.582	397.120	4958014.163	**<0.001***	27404.146	0.032	23250275804	0.142
HbA1c	4.724	2.413	9.249	**<0.001***	1.313	0.317	5.441	0.708
Delivery Time (Weeks)	0.158	0.068	0.368	**<0.001***	0.010	0.000	0.348	**0.011***
Birth weight (gm)	1.004	1.002	1.006	**<0.001***	1.007	0.998	1.016	0.147

*: Significant.

DISCUSSION

After applying the inclusion and exclusion criteria, 54 instances of diabetes (27 with pre-gestational diabetes mellitus (PGDM) and 27 with gestational diabetes mellitus (GDM)) were found during the study period. These cases were matched with controls based on the gestational age at which FEFT and MPAD were measured.

The three cohorts' maternal demographics and obstetric histories revealed a statistically significant difference in age, BMI, and gravidity across the study cohorts (P value < 0.05). The PGDM cohort's cases had higher BMIs and gravidities and were substantially older than those in the control and GDM cohorts. These results are comparable to those that **Sever *et al.*** [8], reported**.**

Both the GDM and PGDM cohorts had significantly greater AFI, fEFT, and HbA1c levels than the control cohorts; the PGDM cohort had even higher values than the GDM cohort. The mean fetal EFT in moms with PGDM was 1.62 +/- 0.11 mm, which was substantially higher than the GDM cohort's 1.45 +/- 0.07 mm and higher than the control cohort's 1.24 +/- 0.12 mm. Similarly, **Akkurt *et al.*** [9] reported similar results**.**

In contrast, there was no statistically significant variation in the resistance and umbilical artery pulsatility indices across the cohorts.

These findings are consistent with those published by **Iskender *et al.*** [10] In terms of fetal outcomes, including delivery time, neonatal birth weight, APGAR (degree of RD), NICU admission, and newborn hypoglycemia, there was a statistically significant difference between research cohorts (P value < 0.05).

Diabetic pregnancies (both GDM and PGDM) were substantially more likely to result in adverse perinatal outcomes, such as RDS, neonatal hypoglycemia, and NICU admission. These results were comparable to those published by **Iskender *et al.*** [10] and **Omeroglu *et al.*** [11].

The findings of the ROC analysis showed that fEFT had 96% sensitivity and 81% specificity in diagnosing gestational DM at cutoff value ≥ 1.325, whereas MPAD had 59% sensitivity and 48% specificity at cutoff value ≥ 6.95.

In contrast to **Iskender *et al.*** [10] who suggested a cutoff value of fEFT 1.55 mm that can predict GDM in the third trimester with a specificity of 74.4% and a sensitivity of 75%. Furthermore, fEFT demonstrated remarkable diagnostic efficacy in identifying GDM and PGDM, with corresponding AUCs of 0.912 and 0.974.

Our study's ROC analysis revealed that, at a cutoff value of 1.425, fEFT showed 56% sensitivity and 53% specificity in predicting the C.S. mode of delivery and 75% sensitivity and 47% specificity in predicting the aberrant FHR.

Maternal hypoglycemia was predicted with fEFT with sensitivity of 67% and specificity of 94% at cutoff value ≥ 1.695, abnormal APGAR score with sensitivity of 81% and specificity of 74%, NICU admission with sensitivity of 74% and specificity of 77%, and neonatal hypoglycemia with sensitivity of 77% and specificity of 74% at cutoff value ≥ 1.475.

Maternal age, BMI, gravidity, parity, HbA1c, fetal AC, EFW, fEFT, MPAD, birth weight, AFI, and delivery time were all examined using logistic regression to determine their effects on the likelihood of respiratory distress in neonates as a primary outcome. Univariate analysis revealed that maternal HbA1c, AFI, AC, EFW, fEFT, birth weight, and delivery time were significant predictors in univariate analysis, which led to multivariate analysis, where delivery time was a significant predictor.

In addition to its prospective design, this study's strengths include being the first to examine fEFT and MPAD jointly in diabetic pregnancies and identifying a cutoff value that can identify both GDM and PGDM. Lastly, to the best of our knowledge, this is the first study to assess the relationship between MPAD and perinatal outcome and one of the few that assesses the relationship between fEFT and bad perinatal outcome.

CONCLUSION

The clinical utility of fEFT as a sensitive and non-invasive sonographic measure for forecasting unfavourable perinatal outcomes in pregnancies with diabetes is highlighted in this work. Both pregestational and gestational diabetic cohorts had considerably higher fEFT, which was also strongly correlated with neonatal problems such hypoglycemia, poor APGAR ratings, and NICU admission. On the other hand, the MPAD had less predictive power and lower correlations for worse outcomes.

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