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Estimation of Fasting Lipid Profile Parameters for Early Detection of Gestational Diabetes Mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common pregnancy complication characterized by high blood sugar levels in pregnant women who have never had diabetes before. It can have detrimental effects on both the mother and the fetus if left undiagnosed and untreated. Therefor the Study aims to evaluate the Variations in Lipid Profile Parameters Across Different Trimesters and their impact on Early Detection of Gestational Diabetes Mellitus.

Methods: This prospective cohort study, conducted at the Mardan Medical Complex Teaching Hospital in Pakistan from September 2022 to November 2023, included pregnant women in their first trimester. Fasting lipid profiles were measured across three trimesters. The Oral Glucose Tolerance Test (OGTT) was utilized for GDM diagnosis. Statistical analyses employed included chi-squared tests, t-tests, Mann-Whitney U tests, ANOVA, Pearson correlation, and ROC curves with SPSS software version 27.0.

Results: The study included 92 pregnant women divided into GDM and non-GDM groups. GDM Women had a higher average age 30.87±3.08 years and BMI 29.89±2.97 compared to non-GDM. Lipid profile Parameters showed more significant abnormalities in GDM patients, with total cholesterol levels increasing markedly by the third trimester to 218.09±16.03 mg/dL. Triglycerides rose from 158.70±7.68 mg/dL to 213.11±14.96 mg/dL, LDL from 93.52±13.53 mg/dL to 149.26±9.72 mg/dL, and with the decrease in HDL from 47.24±4.07 mg/dL to 41.83±3.05 mg/dL from the first to the third trimester.

Conclusion: Lipid profile parameter changes across trimesters were a reliable method for early GDM detection, offering a non-invasive tool for identifying at-risk pregnant women.

Key-words: Gestational Diabetes Mellitus (GDM), Lipid Metabolism, Early Diagnosis, Pregnancy Complications, Biomarkers

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a major health issue worldwide, impacting a significant proportion of 5-20% of pregnancies.[1]

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GDM is defined by glucose intolerance that begins or is first identified during pregnancy. It not only endangers the health of the mother but also affects the well-being of the fetus, potentially leading to long-term consequences for both the mother and child.[2] Early identification and treatment of GDM are essential to prevent negative pregnancy results, such as preeclampsia, cesarean birth, and various neonatal issues, including macrosomia, hypoglycemia, and respiratory distress syndrome.[3] Traditionally, GDM diagnosis is based on OGTT, while effective may not be

the most practical or comprehensive tool for early detection and risk assessment. [4]

A recent study indicates that changes in lipid metabolism during pregnancy could be crucial in the onset of GDM, [5] providing possible early indicators for its detection. Lipids are vital in hormone production, energy storage, and cell membrane development. They undergo substantial modifications throughout pregnancy to aid fetal growth and prepare the body for lactation. [6] Physiological changes might affect lipid profile measures such as triglycerides, cholesterol, and lipoproteins, which may indicate metabolic dysregulation linked to GDM.

These physiological changes can cause insulin resistance, which is expected to a certain extent during pregnancy but can worsen or expose underlying metabolic disorders, increasing the risk of developing gestational diabetes in certain people.[7] Monitoring lipid profiles throughout pregnancy can offer important information about the mother's metabolic health and the likelihood of developing gestational diabetes.

Identifying GDM early with lipid profile screening could significantly change how GDM is managed. Identifying high-risk individuals earlier in pregnancy allows healthcare practitioners to introduce lifestyle changes and glucose monitoring promptly, potentially slowing down the development of GDM and decreasing the occurrence of associated problems.[8] Furthermore, analyzing the changes in lipid profiles that are unique to the development of gestational diabetes mellitus could provide valuable information about the disease's underlying mechanisms, aiding in the creation of tailored treatments and individualized care plans.

Ideally, assessing fasting lipid profile parameters for early identification of GDM shows potential for enhancing health outcomes for mothers and newborns. Enhancing our knowledge of lipid metabolism in pregnancy and its impact on GDM development can improve early identification, refine risk assessment models, and provide better management strategies for this prevalent pregnancy issue. Comprehending how lipid profile changes evolve during pregnancy is crucial for identifying women at risk for GDM. The current study aims to analyze the changes in lipid profile parameters during various trimesters and their influence on the diagnosis of GDM. This involves thoroughly examining how lipid profiles evolve during pregnancy and identifying the crucial periods when these alterations most indicate GDM. It aims to improve the timing of lipid profile screening for assessing the risk of gestational diabetes mellitus, potentially providing a less intrusive and more thorough approach to early identification.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of Gynecology of the Mardan Medical Complex Teaching Hospital in Khyber Pakhtunkhwa, Pakistan. The study took place from September 2022 to November 2023. The study used a convenience sampling technique.

Inclusion Criteria- This study includes pregnant women aged 18-45 years who receive prenatal care at selected healthcare facilities and Pregnant women in their first trimester (≤12 weeks' gestation).

Exclusion Criteria- Patients with pre-existing Type 1 or Type 2 diabetes mellitus, chronic conditions impacting lipid metabolisms like hyperthyroidism, hypothyroidism, pre-existing lipid abnormalities, and those using medications known to influence lipid levels, such as statins and corticosteroids were excluded.

Data collection- Data such as age, education level, family history of PCOS, Family history of diabetes, Maternal history of preeclampsia, Family history of cardiovascular disease, History of GDM in previous pregnancies, contraceptive drug use, mode of delivery, Obstetric history (gravidity, parity), sleep patterns, diet assessment, use prenatal vitamins during pregnancy, use of fertility treatments, History of miscarriages, gestation age, and Body Mass Index (BMI) were collected through interviews and standardized questionnaires. Initially, lipid profile parameters were conducted on all pregnant patients in their first trimester (≤12 weeks' gestation) and were followed up in each subsequent trimester (second and third trimesters) for repeated laboratory tests. Five millilitres of fasting blood samples were obtained from each patient during the three trimesters for blood tests. Roche Cobas c111 analyzers were used to estimate fasting lipid profile parameters (Cholesterol, triglycerides, high-density (HDL) and low-density lipoproteins (LDL)), Biomarkers such as Non-High Density Lipoprotein (HDL) as "Cholesterol - HDL", and Very Low-Density Lipoprotein (VLDL) as "Triglycerides ÷ 5" high-density (HDL)/ Cholesterol ratio as "Cholesterol ÷ high-

density (HDL)/, high-density (HDL)/ triglycerides ratio as "triglycerides ÷ high-density (HDL)/, were calculated using these formulas.

All patients were separated into two groups. We used specific criteria to diagnose GDM and Non-GDM.

We initiated the screening process by doing a glucose challenge test (GCT), usually between 24 and 28 weeks of pregnancy. A 50-gram oral glucose dose was given during the test, and blood glucose levels were tested one hour later. We conducted additional tests if the blood glucose level was above 140 mg/dL. Following that, we conducted confirmatory testing with the OGTT. This required fasting from eating overnight and consuming a 100-gram oral glucose solution. Blood glucose levels were assessed at fasting and one, two, and three hours after consuming glucose. The diagnostic criteria for GDM were determined based on oral glucose tolerance test (OGTT) findings and included specific thresholds.

- Fasting glucose levels equal to or greater than 92 mg/dL (5.1 mmol/L)
- Fasting blood sugar level of 180 mg/dL (10 mmol/L) or higher after one hour
- Fasting blood sugar level of 153 mg/dL (8.5 mmol/L) after a two-hour glucose tolerance test.
- Fasting blood sugar level more than or equal to 140 mg/dL (7.8 mmol/L) after three hours.

We diagnosed GDM, if one or more of these thresholds were reached or surpassed during the testing process. [9]

Statistical Analysis- The mean and standard deviation were used to summarize continuous variables, whereas frequencies and percentages were used to describe categorical variables. The differences in baseline characteristics between the two groups were assessed using the chi-squared test for categorical variables and the t-test or Mann-Whitney U-test for continuous variables, depending on the data's distribution. ANOVA krushkul wails one way was used to study intergroup differences between the lipid profile parameters and NON-GDM, GDM patient's groups. The correlation analysis was performed using Pearson correlation coefficients to examine the relationship between lipid profile parameters and the study's variables, which were significant in chi-squared test and t-test or Mann-Whitney U. Simple linear regression in scatter plots was employed for the relationship of lipid profile parameters and testing weeks across all trimester. The discriminating ability of all lipid profile parameters in predicting gestation diabetes mellitus was evaluated by receiver operating characteristic (ROC) curve analysis and quantifying the area under the curve (AUC). An area graph was used to study the mean increase difference of lipid profile parameters between non-GDM and GDM patient's groups. A p-value below 0.05 was deemed statistically significant. The statistical analyses were performed using the SPSS software (version 27.0).

Ethical Approval- This study was conducted after approved (Approval Number: 461/BKMC) by the Institutional Review Board (IRB). Informed consent was obtained from all participants before enrollment. Participants were informed of their right to withdraw from the study without affecting their standard of care. All personal information was kept confidential and used solely for research purposes.

RESULTS

Ninety-two patients were evenly split between non-GDM and GDM groups, and significant differences were found in various categories. GDM patients had a higher mean age (30.87±3.08 years) compared to non-GDM patients (28.80±3.48 years) and elevated BMI (29.89±2.97 vs. 26.30±1.73). GDM patients had higher systolic (125.09±7.11 mmHg) and diastolic (87.11±3.58 mmHg) blood pressures compared to non-GDM patients (116.91±4.77 and 81.13±4.60 mmHg, respectively). Literacy rates were 47.83% for non-GDM and 56.52% for GDM patients. Previous gestational diabetes was more common in the GDM group (67.39%) than in the non-GDM group (52.17%). Previous Maternal preeclampsia was reported by 28.26% of GDM patients and 19.56% of non-GDM patients. GDM patients showed greater means in gravidity (1.89±1.17) and parity (0.99±1.74) compared to non-GDM patients (1.04± 0.78±and 1.02± 0.77, respectively. Lifestyle factors like contraceptive pill use (60.86%) and prenatal vitamin use (93.48%) were more significant in GDM patients than non-GDM patients. Different sleep patterns were observed, with GDM patients sleeping 6.02±0.87 hours and non-GDM patients 6.71±1.51 hours. The gestational age at enrollment was earlier for GDM patients (2.24±1.13 weeks) compared to non-GDM patients (2.76±1.05 weeks) (Table 1).

Table 1: Baseline Characteristics of Non-Gestational Diabetes Mellitus vs Gestational Diabetes Mellitus patients

Characteristic	All patients	Non-Gestational Diabetes Mellitus	Gestational Diabetes Mellitus	p-value
Total patients	92(100)	46(50.00)	46(50.00)	
Age	29.87±3.84	28.80±3.48	30.87±3.08	0.005
Body mass index	28.10±2.97	26.30±1.73	29.89±2.97	0.00
Blood pressure				
Systolic Pressure	121.00±7.29	116.91±4.77	125.09±7.11	0.00
Diastolic Pressure	84.12±5.08	81.13±4.60	87.11±3.58	0.00
Education level				
Literate	48(52.17)	22(47.84)	26(56.52)	0.91
Illiterate	44(47.82)	24(52.17)	20(43.47)	
Family history of diabetes				
NONE	32(34.78)	19(41.30)	13(28.26)	0.59
Type 1	13(14.13)	6(13.04)	7(15.21)	
Type 2	23(25)	11(23.91)	12(26.08)	
GDM	24(26.08)	10(21.73)	14(30.43)	
History of GDM in previous pregnancies	55(59.78)	24(52.17)	31(67.39)	0.04
Maternal history of preeclampsia	22(23.91)	9(19.56)	13(28.26)	0.03
Gravidity	1.08±1.47	0.78±1.04	1.89±1.17	0.004
Parity	1.38±0.95	1.02±0.77	1.74±0.99	0
History of polycystic ovary syndrome	19(20.65)	11(23.91)	8(17.39)	0.11
History of miscarriages	27(29.34)	15(32.60)	2(26.08)	0.49
Use of fertility treatments	63(68.47)	32(69.56)	31(67.39)	0.82
Mode of delivery				
vaginal delivery	55(59.78)	27(58.69)	28(60.86)	0.24
C-section	37(4.21)	19(41.30)	18(39.13)	
contraceptive drug use	45(48.91)	17(36.95)	28(60.86)	0.042
Family history of cardiovascular disease	19(20.65)	10(21.73)	9(19.56)	0.79
Diet assessment				
Dietary fiber intake	28(30.43)	19(41.30)	9(19.56)	0.06
Total caloric intake	37(40.21)	20(43.47)	17(36.95)	
saturated fat intake	27(29.34)	7(15.21)	20(43.47)	
Sleep patterns	6.36	6.71±1.51	6.02±0.87	0.01
Use of prenatal vitamins during pregnancy	46(50.00)	39(84.78)	43(93.74)	0.00
Gestational age at enrollment	2.50±1.12	2.76±1.05	2.24±1.13	0.002

Data is presented as mean and standard deviation or frequency and percentages
p-value <0.05 is statically significant

Comparison of lipid profile parameter values over the three trimesters between Non-GDM and GDM patients shows substantial differences. Non-GDM patients' total cholesterol levels increased from the first to second trimester (172.30±11.01 to 197.35±10.84 mg/dL) and reduced somewhat in the third trimester (195.26±9.34 mg/dL), but not significantly (p=0.21). Over trimesters, triglycerides levels increased considerably (143.67±4.91 to 179.46±6.48 mg/dL, p<0.00), while VLDL levels increased significantly (28.73±0.98 to 37.89±1.30 mg/dL, p<0.00). HDL levels fluctuated slightly (47.02±0.45 to 46.37±3.18 mg/dL, p=0.28), whereas LDL and Non-HDL levels were consistent with modest changes without statistical significance. GDM patients had more substantial lipid profile abnormalities. Total cholesterol levels were lower than non-GDM in the first trimester (169.78±9.89 mg/dL). Still, they considerably rose by the third trimester (218.09±16.03 mg/dL, p<0.00 triglycerides, non-HDL, LDL, and VLDL all showed significant increases across trimesters (158.70±7.68 to 213.11±14.96 mg/dL), non-HDL (122.54±9.29 to 176.26±14.87 mg/dL), LDL (93.52±13.53 to 149.26±9.72 mg/dL), and VLDL (31.73±1.53 to 42.62±2.99 mg/dL) (p<0.00). HDL levels dramatically reduced from the first to third trimester (47.24±4.07 to 41.83±3.05 mg/dL, p<0.00), showing a worsening lipid profile in GDMA worrying rising trend in GDM patients' Cholesterol/HDL and Triglycerides/HDL ratios indicated a worsening cardiovascular risk profile as pregnancy continued. In GDM patients, the CHO/HDL ratio increased significantly from 3.61±0.32 in the first trimester to 5.24±0.52 in the third trimester (p<0.00), while the TRIGLYCERIDES /HDL ratio increased from 3.38±0.34 to 5.12±0.54 (p<0.00) (Table 2).

Table 2: Comparison of Lipid Profiles parameters between Non-Gestational Diabetes Mellitus and Gestational Diabetes Mellitus Patients across Trimesters

Lipid profile parameters	Non-Gestational Diabetes Mellitus Trimesters			p-value	Gestational Diabetes Mellitus Trimesters			p-value
	1ST	2ND	3RD		1ST	2ND	3RD	
Total CHO	172.30±11.01	197.35±10.84	195.26±9.34	0.21	169.78±9.89	203.65±12.40	218.09±16.03	0.00
TG	143.67±4.91	160.78±7.40	179.46±6.48	0.00	158.70±7.68	198.61±13.08	213.11±14.96	0.00
HDL	47.02±.45	49.41±4.79	46.37±3.18	0.28	47.24±4.07	42.72±1.68	41.83±3.05	0.00
NHDL	125.28±11.20	149.93±11.10	149.89±15.32	0.07	122.54±9.29	155.93±12.25	176.26±14.87	0.00
LDL	96.57±14.56	101.30±6.93	96.91±11.08	0.19	93.52±13.53	113.96±15.78	149.26±9.72	0.00
VLDL	28.73±0.98	32.16±1.48	35.89±1.30	0.00	31.73±1.53	39.72±2.62	42.62±2.99	0.00
HDL/CHO ratio	3.69±0.39	4.13±0.44	4.23±0.43	0.03	3.61±0.32	4.66±0.32	5.24±0.52	0.00
HDL/TG ratio	3.08±0.31	3.35±0.36	3.85±0.28	0.00	3.38±0.34	4.66±0.36	5.12±0.54	0.00

Data is presented as mean and standard deviation; p-value<0.05 is statically significant
HDL=High density lipoproteins; NHDL=Non-high density lipoproteins; LDL=Low density lipoproteins; VLDL=Very low density lipoproteins; CHO=Cholesterol; TG=Triglycerides

Demographic and clinical variables and lipid profiles in GDM patients significantly correlate across trimesters. Triglycerides and Very Low-Density Lipoprotein (VLDL) are positively correlated with age at 0.34 and negatively correlated with HDL at -0.31. BMI affects lipid metabolism by positively affecting triglycerides and VLDL at 0.59 and negatively affecting HDL at -0.39. Systolic and diastolic blood pressures positively correlate with triglycerides (0.37 and 0.30) and LDL (0.38 and 0.25), showing that blood pressure affects lipid parameters.

GDM history in prior pregnancies slightly correlates with triglycerides at 0.21, suggesting it affects present lipid profiles. Contraceptive drug use increases triglycerides and VLDL levels at 0.31 and lowers HDL at -0.19, while diet evaluation correlates with triglycerides at 0.438 and HDL at -0.39, indicating food's influence on lipid levels. Triglycerides and LDL marginally correlate with supplement use at 0.22 and 0.23. Sleep patterns are negatively correlated with triglycerides at -0.28 and LDL at -0.27, suggesting better sleep improves lipid profiles (Table 3).

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Table 3: Correlation Analysis between Demographic and Clinical Factors with Lipid Profiles parameters in Gestational Diabetes Mellitus across all trimesters

Variables	Total CHO	TG	HDL	NHDL	LDL	VLDL	HDL/TG ratio	HDL/CHO ratio
Age	0.006	0.34**	-0.31**	0.04	0.26**	0.34**	0.38**	0.24*
Body mass index	0.24*	0.59**	-0.39**	0.03	0.48**	0.59**	0.45**	0.27**
Systolic pressure	0.05	0.37**	-0.28**	0.11	0.38**	0.37**	0.33**	0.33**
diastolic pressure	0.03	0.30**	-0.22**	0.07	0.25**	0.30**	0.34**	0.28**
History of GDM in previous pregnancies	-0.01	0.21*	-0.09	-0.02	-0.04	-0.11	-0.23*	-0.07
Maternal history of preeclampsia	0.01	0.07	-0.01	0.02	0.06	0.07	0.06	0.033
Contraceptive drug use	0.06	0.31**	-0.19*	0.02	0.24*	0.31**	0.21*	0.09
Gravidity	0.02	0.28**	-0.26**	0.05	0.09	0.28**	0.32**	.328*
Parity	0.03	0.28**	-0.23*	0.05	0.10	0.28**	0.30**	0.11
Diet assessment	0.05	0.43**	-0.39**	0.10	0.21*	0.39**	0.41**	.32**
Use of supplements	0.09	0.22*	-0.05	0.10	0.23*	0.02	0.03	0.09
Sleep patterns	-0.01	-0.28*	0.08	-0.03	-0.27*	-0.08	-0.10	-0.06

***Significant at 0.01; *Significant at 0.05*

HDL=High density lipoproteins; NHDL=Non-high density lipoproteins; LDL=Low density lipoproteins; VLDL=Very low density lipoproteins; CHO=Cholesterol; TG=Triglycerides

According to receiver operator characteristic curve analysis, GDM patients' lipid profile characteristics have distinct predictive values throughout trimesters. Triglycerides and VLDL have good diagnostic power in the first trimester, with an AUC of 0.94 (p<0.00, 95% CI: 0.89-0.99) showing great predictive accuracy. The High-Density Lipoproteins/Triglycerides (HDL/triglycerides) ratio demonstrates good prediction, with an AUC of 0.73 (p<0.00, 95% CI: 0.63-0.83). Total cholesterol, HDL, non-HDL, LDL, and HDL/cholesterol ratios had lower and non-significant predictive values. In the second trimester, triglycerides and VLDL achieve a perfect AUC of 1 (p<0.00), indicating accurate prediction. HDL/triglycerides ratio has a near-perfect AUC of 0.99 (p<0.00, 95% CI: 0.98-1), while HDL and HDL/Cholesterol ratios had good predictive values of 0.84 (p<0.00, 95% CI: 0.75-0.92) and 0.82 (p<0.00, 95% CI: 0.74-0.91)—modest predictive accuracy for total cholesterol, non-HDL, and LDL. The third trimester shows strong predictive values, with LDL obtaining a perfect AUC of 1 (p<0.00). Triglycerides, VLDL, and HDL have good predictive accuracy with AUCs of 0.93 (p<0.00, 95% CI: 0.88-0.98), 0.93 (p<0.00), and 0.95 (p<0.00, 95% CI: 0.90-0.99). The HDL/triglycerides and HDL/Cholesterol ratios show strong diagnostic potential, with AUCs of 0.989 (p<0.00, 95% CI: 0.97-1) and 0.902 (p<0.00, 95% CI: 0.84-0.96) (Table 4 & Fig. 1).

Table 4: Receiver operator characteristic curve analysis of lipid profile parameters across trimesters in gestational diabetes mellitus patients

Test Result Variable(s)	AUC	Std. Error	p-value	95% cl	
				Lower Bound	Upper Bound
Trimester 1st					
Total cholesterol	0.43	0.06	0.31	0.32	.55
Triglycerides	0.94	0.02	0.00	0.89	.99
High density lipoproteins	0.48	0.06	0.78	0.36	.60

Non-High-density lipoproteins	0.42	0.06	0.21	0.30	.54
Low density lipoproteins	0.43	0.06	0.31	0.32	.55
Very Low-density lipoproteins	0.94	0.02	0.00	0.89	.99
High density lipoproteins/Triglycerides ratio	0.73	0.05	0.00	0.63	.83
High density lipoproteins/cholesterol ratio	0.43	0.06	0.25	0.31	.55
Trimester 2nd					
Total cholesterol	0.50	0.06	0.94	0.38	0.62
Triglycerides	1.00	0.00	0.00	1.00	1.00
High density lipoproteins	0.84	0.04	0.00	0.75	.92
Non- High-density lipoproteins	0.61	0.05	0.06	0.49	.72
Low density lipoproteins	0.71	0.05	0.00	0.61	.82
Very Low-density lipoproteins	1.00	0.00	0.00	1.00	1.00
High density lipoproteins/Triglycerides ratio	0.99	0.00	0.00	0.98	1.00
High density lipoproteins/cholesterol ratio	0.82	0.04	0.00	0.74	.91
Trimester 3rd					
Total cholesterol	0.72	0.05	0.00	0.51	.74
Triglycerides	0.93	0.02	0.00	0.88	0.98
High density lipoproteins	0.95	0.02	0.00	0.90	0.99
NON- High-density lipoproteins	0.75	0.05	0.00	0.65	0.85
Low density lipoproteins	1.00	0.00	0.00	1.00	1.00
Very Low-density lipoproteins	0.93	0.02	0.00	0.88	0.98
High density lipoproteins/Triglycerides ratio	0.98	0.00	0.00	0.97	1.00
High density lipoproteins/cholesterol ratio	0.90	0.03	0.00	0.84	0.96

AUC: Area under the curve, 95% CL: 95% confidence interval, Std. Error: Standard Error
p-value<0.05 is statically significant

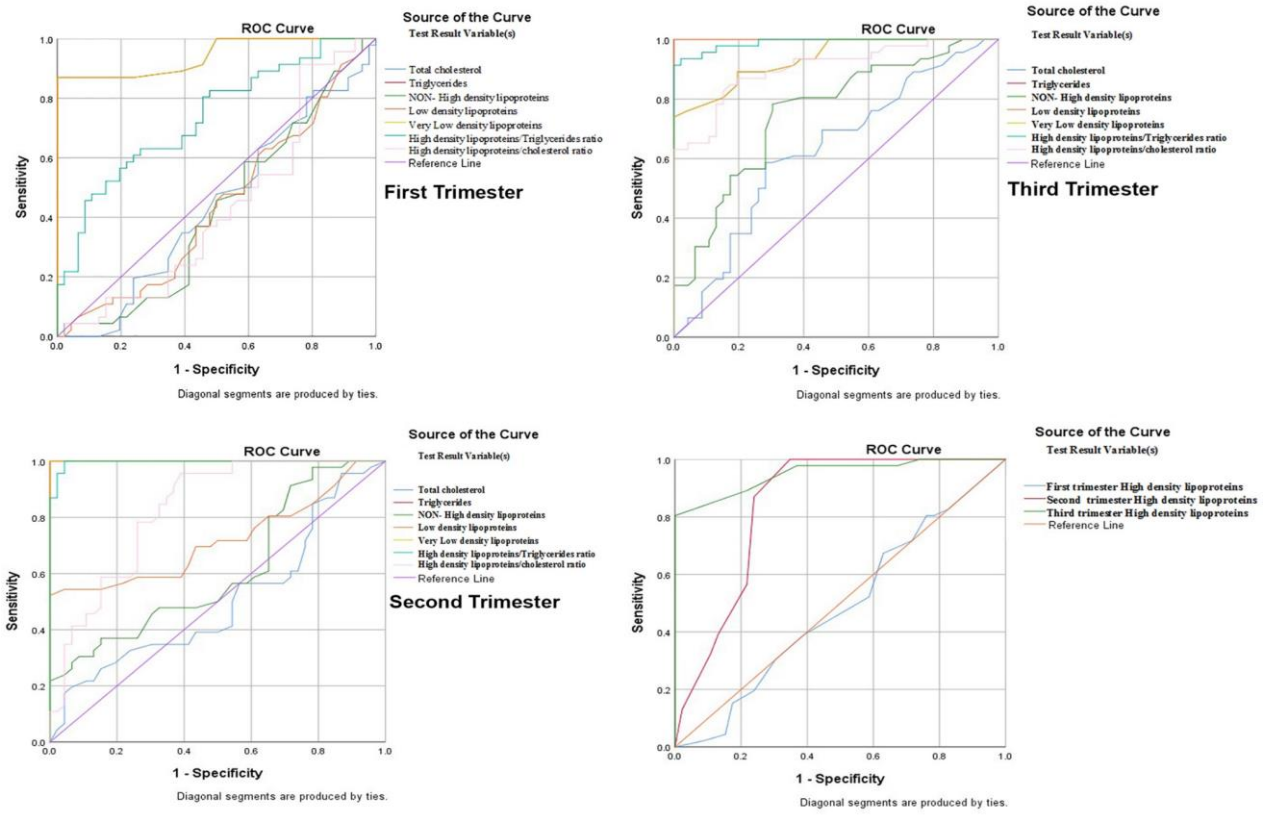

Fig. 1: ROC Curves for Lipid Profile Parameters Across Trimesters in Predicting Gestational Diabetes Mellitus

Four scatter plots show the association between lipid profile parameters and pregnancy weeks, indicating trimesters. The first plot displays rising total cholesterol and triglycerides levels during pregnancy, with R^2 values of 0.71 and 0.69, indicating a significant linear association. The second plot shows LDL-C levels, with the blue group showing a considerable increase R^2=0.72 and VLDL-C R^2=0.69, indicating similar patron to cholesterol and triglycerides. R^2 values of 0.27 for HDL and 0.74 for NON-HDL indication poor to stronger linear fit in the third plot during pregnancy. In the fourth plot, HDL/triglycerides ratio significantly increase R^2=0.69 and less for HDL/total cholesterol ratio R^2=0.66 (Fig. 2).

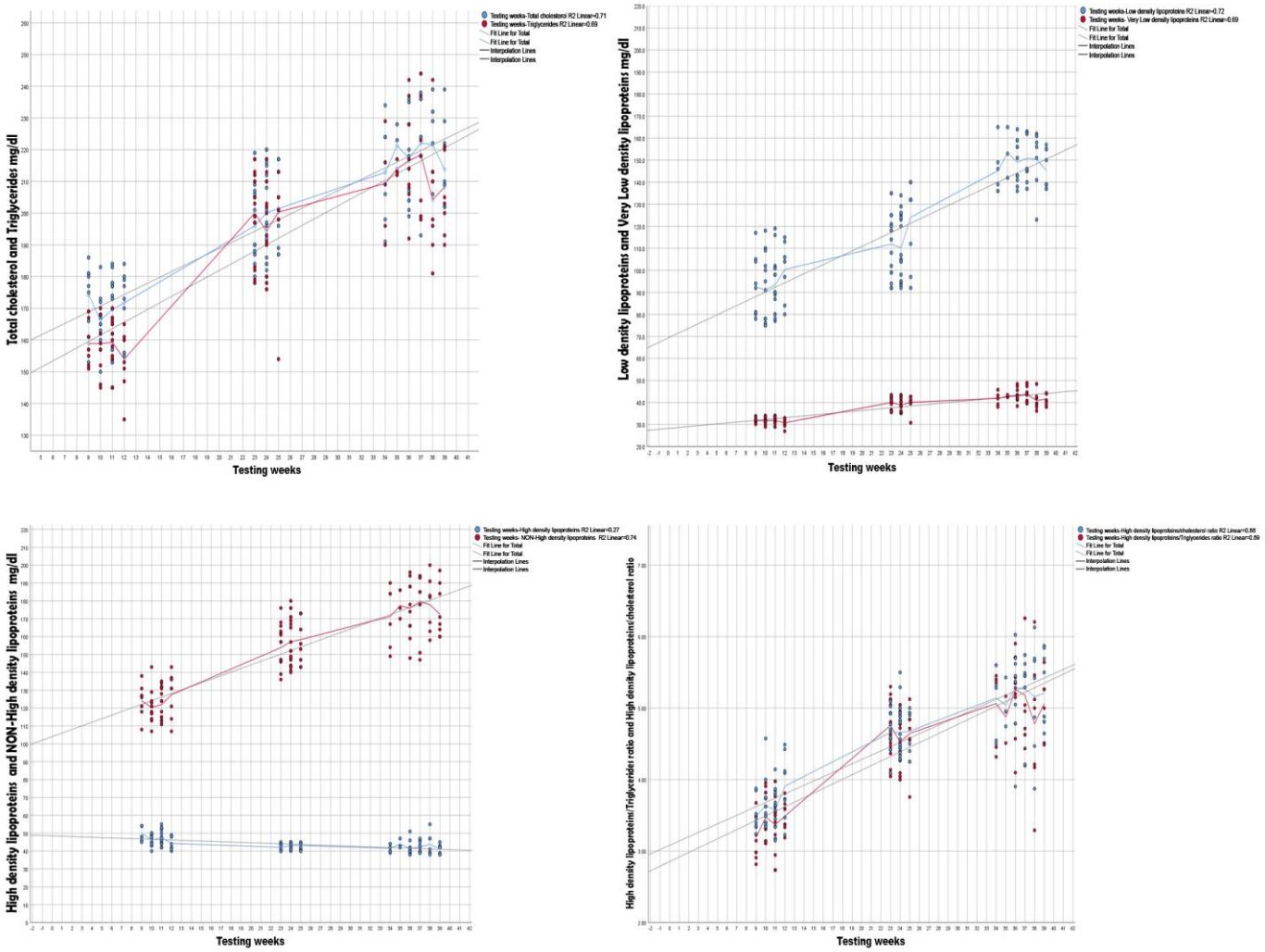

Fig. 2: Temporal Trends in Fasting Lipid Profiles During Pregnancy for the Early Detection of Gestational Diabetes Mellitus

The patients with gestational diabetes have a more atherogenic lipid profile than those without. Gestational Diabetes Mellitus patients had higher mean total cholesterol, triglycerides, non-HDL and LDL cholesterol, lower HDL cholesterol, and a higher triglycerides/HDL cholesterol ratio across all trimesters (Fig. 3).

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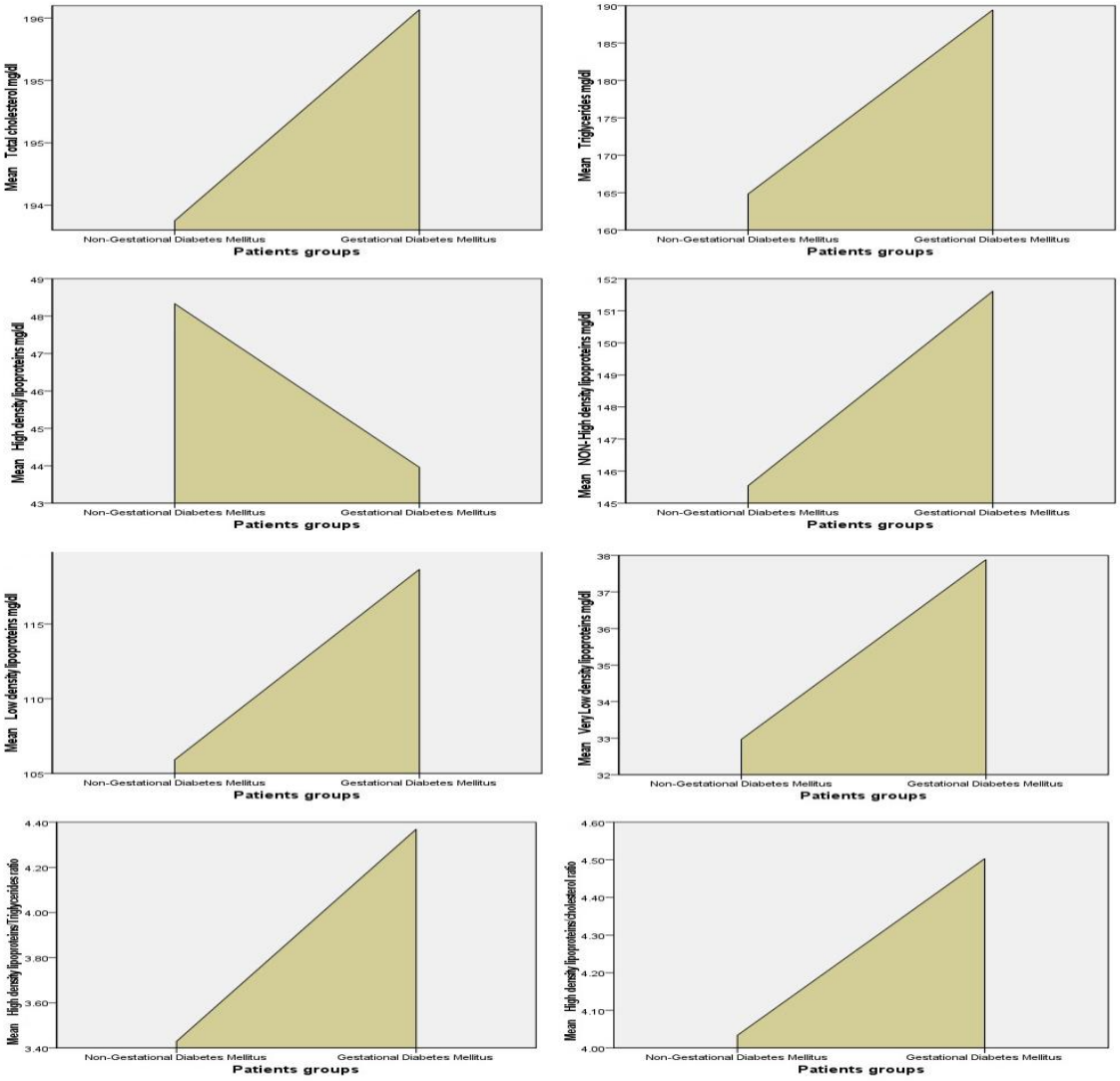

Fig. 3: Mean increase in lipid parameters among patients with gestational diabetes mellitus compared to non-gestational diabetes mellitus

DISCUSSION

Our study found significant connections between fasting lipid profile characteristics and the onset of GDM. We noticed notable changes in lipid levels in pregnant women who were later diagnosed with GDM compared to those who were non-GDM.

GDM is defined by the reduced ability to process glucose initially detected or occurs for the first-time during pregnancy. [10] The condition is associated with notable changes in lipid metabolism, resulting in dyslipidemia, which is marked by increased levels of triglycerides, total cholesterol, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL), as well as reduced high-density lipoprotein (HDL) levels [11]. Rahnemaei *et al.* [12] found that women with GDM have elevated levels of total cholesterol, triglycerides, and VLDL, as well as a higher triglycerides/HDL ratio than normal pregnancies. The findings align with our study. Our study supports these results by showing significant elevations in triglycerides, cholesterol, LDL, and VLDL levels and a reduction in HDL levels in GDM patients during all trimesters. The dysregulation of lipid metabolism impacts insulin sensitivity in GDM due to hormonal fluctuations during pregnancy, including elevated estrogen, progesterone, and human placental lactogen, which are recognized for their influence on lipid metabolism. [13] Emphasize the importance of lipid profile characteristics as markers for GDM risk, highlighting the necessity of early screening and monitoring to reduce related health risks.

Anjum *et al.* [14] studied the differences in serum lipid profiles between normotensive and hypertensive pregnant women. Her study showed that hypertension during pregnancy is linked to notable changes in lipid

levels, such as elevated triglycerides, total cholesterol, LDL, VLDL, and reduced HDL. Our study supports the idea that changes in lipid profiles have a role in GDM, as we detected similar abnormalities in lipid profiles.

Chen *et al.* [15] support our findings about the elevated average age and BMI among women with GDM. The study emphasizes that higher pre-pregnancy BMI raises the risk of GDM, particularly in mothers who are elderly. Another study discovered a substantial association between neck circumference and weight, waist circumference, and BMI, all of which are risk factors for GDM. Zhang *et al.* [16] indicating age and BMI as significant risk predictors for GDM.

Our study revealed a notable increase in the CHO/HDL and triglycrides/HDL ratios in GDM patients as pregnancy advanced, suggesting a deterioration in their cardiovascular risk profile. Takhshid and Zare [17] identified these ratios as indicators of postpartum cardiovascular risk in GDM patients. Hu *et al.* [18] discovered that high levels of triglycerides in the blood during the first and second trimesters are strongly linked to the onset of GDM. This highlights the need to evaluate maternal lipid profiles to predict cardiovascular risk in GDM patients. Our study highlights the importance of lipid ratios and triglyceride levels in assessing cardiovascular risk in GDM patients. This rise indicates a lipid profile that promotes atherosclerosis and is linked to insulin resistance and endothelial dysfunction, as reported by White *et al.* [19] highlighting the importance of these lipid ratios in evaluating cardiovascular risk in GDM patients.

Sweeting *et al.* [20] discovered that maternal lipid indicators, such as triglycerides and very low-density lipoprotein (VLDL), are useful for predicting the risk of GDM in early pregnancy. [20] Our study suggests that lipid profile parameters such as triglycerides, VLDL, and LDL have high predictive accuracy for diagnosing GDM, as shown by receiver operator characteristic (ROC) curve analysis. This implies their effectiveness in early GDM screening. The high AUC values for triglycerides, VLDL, and LDL indicate the diagnostic potential of these markers in the first and second trimesters.

The early identification of lipid profile deviations offers a window for intervention to mitigate GDM-related complications. Given the link between dyslipidemia and adverse pregnancy outcomes, including preeclampsia, preterm birth, and future cardiovascular disease (CVD) risk our findings advocate for the inclusion of lipid screening in prenatal care protocols. Such measures could facilitate the timely initiation of dietary, lifestyle, and pharmacological interventions aimed at optimizing maternal and fetal outcomes.

The conclusions of the current study have several limitations. First, the limited sample size and the single-center nature of our study may reduce the generalizability of our findings. To address this issue, future studies should aim to include larger sample sizes and involve multiple centers to validate our results. Second, we did not evaluate patients with comorbidities in our study. Future studies should investigate the impact of different comorbidities on lipid profile parameters, particularly in cardiovascular diseases, as we hypothesize that these patients may have higher lipid profile parameters. Third, most of our patients in the GDM group had higher body mass indexes. This introduces a potential bias as higher body mass index is known to be an independent risk factor for developing GDM. The findings from our study may not accurately represent the patient with normal BMI or lower BMI. Therefore, the generalizability of our results to normal BMI or lower BMI groups may be limited. Future studies should aim to include a more diverse range of BMI to obtain a comprehensive understanding of the symptoms and complications associated with GDM across different populations.

CONCLUSIONS

Our study suggests a significant change in the approach of detecting GDM early, supporting the inclusion of fasting lipid profile screens in routine prenatal care procedures. This method improves the early detection of GDM and provides a more thorough insight into maternal metabolic well-being. The study categorically shows that notable differences in lipid profile characteristics over several trimesters can accurately forecast the development of GDM. This finding highlights the effectiveness of early lipid profile testing as a non-invasive and practical method for identifying pregnant women who are at high risk for GDM. Healthcare practitioners might enhance the timing of therapies by identifying the key periods when alterations in lipid profiles best reflect GDM, which could lead to better pregnancy outcomes and a lower incidence of GDM-related problems. Early identification of high-risk

pregnant women and implementing specific interventions can help reduce the negative impacts of GDM on mothers and their children.

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