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Lipid Profile as a Predictor of HbA1c in Women with Gestational Diabetes Mellitus

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A B S T R A C T

Gestational diabetes mellitus (GDM) is associated with adverse maternal and fetal outcomes. While glycemic control is paramount, the role of lipid profiles in predicting HbA1c levels, a marker of long-term glycemic control, remains under-investigated in Indonesian populations. This observational study enrolled 250 women diagnosed with GDM at the primary healthcare centers in Soppeng Regency. Fasting lipid profiles (total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol) and HbA1c levels were measured at diagnosis and at 24-28 weeks gestation. Statistical analyses included correlations, regression models, and receiver operating characteristic (ROC) curve analysis. HbA1c levels were significantly correlated with triglyceride and LDL-cholesterol levels at both time points. Regression analysis revealed that triglycerides were the strongest independent predictor of HbA1c. ROC curve analysis showed moderate discriminatory power for triglycerides in predicting elevated HbA1c (AUC 0.72). Lipid profiles, particularly triglycerides, may serve as early predictors of HbA1c levels in women with GDM. These findings underscore the importance of monitoring lipid profiles alongside glucose control in this population.

1. Introduction

Gestational diabetes mellitus (GDM) stands as a multifaceted metabolic disorder that arises during pregnancy, presenting significant challenges to maternal and fetal well-being. Affecting an estimated 14% of pregnancies globally, GDM is a growing public health concern with far-reaching consequences. In Indonesia, the prevalence of GDM is alarmingly high, ranging up to 10%, emphasizing the urgent need for targeted research and effective management strategies in this population. GDM is characterized by impaired glucose tolerance that emerges during pregnancy. The underlying pathophysiology involves a complex interplay of hormonal changes, insulin resistance, and pancreatic beta-cell dysfunction. The hormonal milieu of pregnancy, particularly the surge in placental hormones, acts as a diabetogenic force, increasing insulin resistance and demanding greater insulin secretion to maintain euglycemia. In predisposed individuals, this physiological stress can overwhelm the pancreatic beta cells, leading to inadequate insulin production and consequent hyperglycemia.[1,2]

The implications of GDM extend beyond pregnancy, with both immediate and long-term consequences. In the short term, GDM increases the risk of adverse maternal outcomes, such as preeclampsia, a potentially life-threatening hypertensive disorder, and increased susceptibility to infections. Fetal complications are equally concerning, including macrosomia (excessive birth weight), neonatal hypoglycemia, respiratory distress syndrome, and increased risk of stillbirth. The long-term sequelae of GDM are equally profound. Women with a history of GDM face a significantly elevated risk of developing type 2 diabetes mellitus (T2DM) later in life, with estimates suggesting a sevenfold increase in risk compared to women without GDM. Furthermore, GDM has been linked to an increased risk of cardiovascular

disease, metabolic syndrome, and other chronic conditions. These enduring effects underscore the importance of early detection, meticulous management, and comprehensive follow-up care for women with GDM. Beyond glycemic dysregulation, GDM is also associated with significant alterations in lipid metabolism. During pregnancy, physiological changes lead to a natural increase in circulating lipids, providing energy for fetal growth and development. However, in GDM, these changes are amplified, resulting in dyslipidemia, a state of abnormal lipid levels. Triglycerides, a type of fat found in the blood, are particularly elevated in GDM. High triglyceride levels have been implicated in insulin resistance, inflammation, and oxidative stress, all of which contribute to the pathogenesis of GDM and its associated complications.[3-5]

The role of HbA1c, a measure of average blood glucose over the preceding 2-3 months, in GDM management is well-established. HbA1c serves as a crucial marker of long-term glycemic control, guiding treatment decisions and predicting pregnancy outcomes. However, the utility of lipid profiles, particularly triglycerides, as predictors of HbA1c levels in women with GDM remains less explored. Understanding the interplay between lipid profiles and HbA1c levels in GDM is of paramount importance. If specific lipid parameters, such as triglycerides, can reliably predict HbA1c levels, this could open new avenues for personalized GDM management. Early identification of women at risk of suboptimal glycemic control based on their lipid profile could facilitate timely interventions, such as dietary modifications, exercise programs, or pharmacological therapies, to optimize maternal and fetal health.[6,7] This study, conducted in the Soppeng Regency of South Sulawesi, Indonesia, aims to shed light on this critical question. By investigating the relationship between lipid profiles and HbA1c levels in Indonesian women with GDM, we seek to advance our understanding of GDM pathophysiology, identify potential biomarkers for predicting glycemic control, and inform evidence-based clinical practices in this unique population.

2. Methods

This study employed a prospective, observational design to investigate the relationship between lipid profiles and HbA1c levels in women with gestational diabetes mellitus (GDM). The research was conducted in the Soppeng Regency of South Sulawesi, Indonesia, a region characterized by a diverse population and varying socio-economic backgrounds. The study setting encompassed primary healthcare centers (PHCs) across the regency, ensuring a representative sample of women with GDM from both urban and rural areas. Participants were recruited through a systematic process involving collaboration with healthcare providers at the PHCs. Women attending antenatal care clinics were screened for GDM using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. These criteria recommend a 75g oral glucose tolerance test (OGTT) for all pregnant women between 24 and 28 weeks gestation, with GDM diagnosed if fasting plasma glucose is ≥5.1 mmol/L or 2-hour plasma glucose is ≥8.5 mmol/L. Women diagnosed with GDM were invited to participate in the study after receiving detailed information about the study's purpose, procedures, and potential risks and benefits. Written informed consent was obtained from all participants prior to enrollment. Inclusion criteria for the study were Age 18 years or older, Singleton pregnancy, Diagnosis of GDM according to the IADPSG criteria, Willingness to participate, and informed consent. Exclusion criteria were Pre-existing diabetes mellitus (type 1 or type 2), Multiple gestation, Chronic kidney disease, Liver disease, Use of medications known to affect lipid metabolism, and inability or unwillingness to comply with study procedures. The sample size was determined using a power analysis based on previous studies investigating the association between lipid profiles and HbA1c in GDM. With a significance level of 0.05 and a power of 80%, a sample size of 250 participants was calculated to be sufficient to detect a moderate correlation between triglycerides and HbA1c.

Data collection involved two-time points: Baseline: At the time of GDM diagnosis, following the OGTT.

Follow-up: Between 24 and 28 weeks gestation. At each time point, participants underwent a comprehensive assessment, including: Demographic data: Age, ethnicity, education level, occupation, parity, and socioeconomic status. Anthropometric measurements: Height, weight, body mass index (BMI). Medical history: Preexisting conditions, family history of diabetes, gestational age at GDM diagnosis. Obstetric history: Previous GDM, pregnancy complications, mode of delivery. Dietary assessment: Food frequency questionnaire to assess dietary intake of fats, carbohydrates, and protein. Physical activity assessment: International Physical Activity Questionnaire (IPAQ) to assess physical activity levels. Fasting blood samples were collected at both time points and analyzed at a certified laboratory. The following parameters were measured: Lipid profile: Total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C). HbA1c: Measured using high-performance liquid chromatography (HPLC). Laboratory personnel were blinded to the study hypotheses and participant characteristics to minimize bias. Quality control measures were implemented to ensure the accuracy and reliability of laboratory results.

Data analysis was performed using SPSS statistical software. Descriptive statistics were used to summarize participant characteristics and laboratory values. The normality of data distribution was assessed using the Shapiro-Wilk test. Spearman's rank correlation coefficient was used to assess the relationship between lipid profiles and HbA1c, given the non-normal distribution of some variables. Multiple linear regression models were employed to identify independent predictors of HbA1c, controlling for potential confounders such as age, BMI, gestational age, and dietary and physical activity levels. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the discriminatory power of lipid profiles, specifically triglycerides, in predicting elevated HbA1c. The optimal cutoff point for triglycerides was determined using the Youden index, which maximizes the sum of sensitivity and specificity. The study was approved by the Institutional Review Board of Universitas Megarezky, Indonesia. All participants provided written informed consent after receiving detailed information about the study procedures, potential risks and benefits, and their right to withdraw at any time without consequences. Data confidentiality was maintained throughout the study, and participant identities were anonymized.

3. Results and Discussion

The baseline characteristics outlined in Table 1 provide a comprehensive snapshot of the 250 women diagnosed with gestational diabetes mellitus (GDM) who participated in this study. These characteristics offer valuable insights into the demographic and clinical profile of the study population, enabling a deeper understanding of the factors that may influence lipid profiles and HbA1c levels in this specific context. The mean age of the participants was 28.5 years, suggesting that GDM is a significant concern for women of reproductive age in Soppeng Regency. The range of ages (20 to 40 years) indicates that GDM can affect women across a broad spectrum of reproductive years. The majority of participants were of Bugis ethnicity, reflecting the predominant ethnic group in the region. However, the inclusion of women from other ethnic groups (Makassar and others) ensures a degree of diversity in the sample, enhancing the generalizability of the findings to the wider population. The mean body mass index (BMI) of 26.5 kg/m^2 indicates that overweight and obesity are prevalent among women with GDM in this study. This finding aligns with previous research demonstrating a strong association between elevated BMI and increased risk of GDM. The range of BMI values (18.5 to 39.5 kg/m^2) further underscores the heterogeneity of the study population, encompassing women with varying degrees of adiposity. The educational attainment of the participants varied, with most having completed secondary education. This suggests that GDM is not confined to a particular educational stratum. However, the presence of women with lower educational levels

underscores the importance of culturally sensitive and accessible healthcare interventions for GDM management. The majority of participants were housewives, which is consistent with the socioeconomic landscape of the region. This finding highlights the need to tailor GDM management strategies to the specific needs and lifestyle patterns of women who may have limited time and resources for healthcare. The mean gestational age at GDM diagnosis was 22.5 weeks, falling within the recommended timeframe for GDM screening (24-28 weeks). However, the range of gestational ages (16 to 30 weeks) suggests that GDM can be diagnosed earlier or later in pregnancy, emphasizing the importance of vigilance throughout prenatal care. The mean parity of 1.8 indicates that most participants had given birth previously, suggesting that GDM risk may increase with subsequent pregnancies. However, the range of parity values (0 to 5) highlights the need to consider GDM risk in both nulliparous and multiparous women. Overall, the baseline characteristics presented in Table 1 provide a comprehensive overview of the study population, enabling a nuanced interpretation of the subsequent findings. The heterogeneity of the sample, encompassing women with diverse ages, ethnicities, BMI values, education levels, occupations, and obstetric histories, strengthens the generalizability of the research and underscores the importance of tailoring GDM management to the individual needs of each woman.

Table 1. Baseline characteristics of study participants.

Characteristic	Mean (SD) or n (%)	Range
Age (years)	28.5 (4.2)	20 - 40
Ethnicity		
Bugis	170 (68%)	
Makassar	55 (22%)	
Other	25 (10%)	
Body mass index (kg/m^2)	26.5 (4.8)	18.5 - 39.5
Education level		
Primary school	30 (12%)	
Secondary school	138 (55%)	
Tertiary education	82 (33%)	
Occupation		
Housewife	155 (62%)	
Employed	70 (28%)	
Unemployed	25 (10%)	
Gestational age at diagnosis (weeks)	22.5 (3.1)	16 - 30
Parity	1.8 (1.2)	2 - 5

Table 2 provides a comparative analysis of lipid profile parameters (total cholesterol, triglycerides, LDL-C, HDL-C) and HbA1c levels at two crucial time points in the study: baseline (at GDM diagnosis) and follow-up (between 24-28 weeks gestation). The data presented in this table offers valuable insights into the dynamic changes in lipid metabolism and glycemic control that occur during the course of GDM pregnancy. The most striking observation is the significant increase in triglyceride and LDL-C levels from baseline to follow-up ($p < 0.001$). This finding aligns with previous research demonstrating that GDM is associated with elevated levels of these atherogenic lipids. The observed increase may be

attributed to the hormonal changes of pregnancy, insulin resistance, and altered lipid metabolism characteristic of GDM. Total cholesterol levels showed a slight increase from baseline to follow-up, but this change was not statistically significant. This suggests that while GDM impacts specific lipid fractions, it may not significantly alter overall cholesterol levels during pregnancy. HDL-C levels exhibited a slight decrease at follow-up, although this change was not statistically significant. This observation warrants further investigation, as HDL-C is considered the "good" cholesterol due to its protective role against cardiovascular disease. A decline in HDL-C, even if not statistically significant, may have implications for long-term metabolic health in women with GDM. HbA1c levels showed a marginal increase at follow-up, but this change was not statistically significant. This suggests that glycemic control remained relatively stable during the study period, despite the observed changes in lipid profile. However, the slight increase in HbA1c warrants close monitoring, as even small elevations can impact pregnancy outcomes and future diabetes risk.

Table 2. Lipid profile and HbA1c levels at baseline and follow-up.

Parameter	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	p-value
Total cholesterol (mg/dL)	205.3 ± 38.5	210.2 ± 42.3	0.23
Triglycerides (mg/dL)	180.5 ± 52.6	220.8 ± 65.4	<0.001
LDL-C (mg/dL)	115.8 ± 30.2	132.5 ± 35.7	<0.001
HDL-C (mg/dL)	48.7 ± 12.3	46.5 ± 11.8	0.11
HbA1c (%)	5.8 ± 0.8	5.9 ± 0.9	0.08

Spearman's correlation data (Table 3) reveals intriguing relationships between HbA1c (a marker of long-term glycemic control) and various lipid parameters in women with gestational diabetes mellitus (GDM). The strong positive correlation between HbA1c and triglycerides at both baseline (r = 0.62) and follow-up (r = 0.65) indicates a robust association. This means that higher triglyceride levels tend to coincide with higher HbA1c levels in women with GDM. This relationship persists throughout pregnancy, suggesting that elevated triglycerides may be an early and ongoing indicator of suboptimal glycemic control in this population. Similarly, the strong positive correlation between HbA1c and LDL-C at both baseline (r = 0.58) and follow-up (r = 0.60) reinforces the link between dyslipidemia and glycemic control in GDM. Higher LDL-C levels are associated with higher HbA1c levels, further emphasizing the importance of monitoring and managing lipid profiles in this context. The weak and non-significant negative correlations between HbA1c and HDL-C at both time points suggest that HDL-C levels may not be a reliable predictor of glycemic control in women with GDM. While HDL-C is generally considered cardioprotective, its role in GDM pathophysiology and its relationship with HbA1c require further investigation.

Table 3. Correlation of HbA1c and lipid profile.

Correlation pair	Baseline (r, p-value)	Follow-up (r, p-value)
HbA1c vs. Triglycerides	0.62, <0.001	0.65, <0.001
HbA1c vs. LDL-C	0.58, <0.001	0.60, <0.001
HbA1c vs. HDL-C	-0.12, 0.15	-0.08, 0.32

Table 4 presents the results of a multiple linear regression analysis aimed at identifying the independent predictors of HbA1c levels in women with gestational diabetes mellitus (GDM) at 24-28 weeks gestation (follow-up). The analysis adjusted for several potential confounders, including age, BMI, gestational age at diagnosis, dietary fat intake, and physical activity level. Triglycerides emerged as the most potent independent predictor of HbA1c levels. The standardized beta coefficient of 0.35 indicates a substantial positive association, meaning that higher triglyceride levels are strongly linked to higher HbA1c levels, even after accounting for other factors in the model. LDL-C also demonstrated a significant positive association with HbA1c, with a standardized beta coefficient of 0.28. This suggests that elevated LDL-C levels are an independent risk factor for poorer glycemic control in women with GDM. Age and BMI showed a positive association with HbA1c, but their effects were less pronounced compared to triglycerides and LDL-C. The standardized beta coefficients of 0.05 and 0.10, respectively, indicate a relatively weaker influence on HbA1c levels. Gestational age at diagnosis, dietary fat intake, and physical activity level were not found to be significant predictors of HbA1c in this model. This suggests that these factors, while potentially important for overall GDM management, may not directly influence HbA1c levels independently of other variables. The model explained 45% of the variance in HbA1c levels (R-squared = 0.45), indicating a moderate fit. This implies that other factors not included in the model, such as genetic predisposition, insulin sensitivity, and other metabolic parameters, also contribute to the variability in HbA1c levels. The findings underscore the critical role of lipid management in optimizing glycemic control in women with GDM. Targeting triglycerides and LDL-C through lifestyle modifications and, if necessary, pharmacological interventions may lead to improved HbA1c levels and better pregnancy outcomes. The relatively weaker influence of age and BMI suggests that while these factors are relevant, they may not be as readily modifiable as lipid levels. However, addressing overweight and obesity before or during pregnancy may still be beneficial for overall metabolic health. The non-significant predictors emphasize the complex nature of GDM and highlight the need for multifactorial interventions that address various aspects of the disease, including diet, exercise, and medication adherence.

Table 4. Multiple linear regression analysis for predictors of HbA1c at follow-up.

Predictor	**Standardized β Coefficient**	**95% Confidence Interval**	**p-value**
Triglycerides (mg/dL)	0.35	0.28 - 0.42	<0.001
LDL-C (mg/dL)	0.28	0.21 - 0.35	<0.001
Age (years)	0.05	-0.02 - 0.12	0.16
Body mass index (kg/m^2)	0.10	0.03 - 0.17	0.005
Gestational age at diagnosis (weeks)	-0.03	-0.10 - 0.04	0.41
Dietary fat intake	0.08	-0.01 - 0.17	0.09
Physical activity level	-0.06	-0.13 - 0.01	0.08

Model Fit Statistics: R-squared: 0.45; Adjusted R-squared: 0.42; F-statistic: 25.6, $p < 0.001$.

Table 5 summarizes the results of a receiver operating characteristic (ROC) curve analysis, evaluating the performance of using triglyceride levels as a test to predict elevated HbA1c (≥ 6.5%) in women with gestational diabetes mellitus (GDM) at 24-28 weeks gestation. Area Under the Curve (AUC) of 0.72 indicates that the triglyceride test has moderate discriminatory power in predicting elevated HbA1c. This means that the test performs better than chance (AUC of 0.5), but it is not perfect (AUC of 1.0). In other words, it can distinguish between women with and without elevated HbA1c reasonably well, but there is

still room for improvement. The optimal cutoff point for triglycerides is 200 mg/dL. This means that if a woman's triglyceride level is 200 mg/dL or higher, the test considers her positive for elevated HbA1c. If her triglyceride level is below 200 mg/dL, the test considers her negative. This cutoff point was chosen because it offers the best balance between sensitivity and specificity. The sensitivity of 70% means that the test correctly identifies 70% of women who actually have elevated HbA1c (true positives). This is also known as the true positive rate. However, it also means that 30% of women with elevated HbA1c will be missed by the test (false negatives). The specificity of 65% means that the test correctly identifies 65% of women who do not have elevated HbA1c (true negatives). This is also known as the true negative rate. However, it also means that 35% of women without elevated HbA1c will be incorrectly flagged as having elevated HbA1c (false positives). A positive predictive value (PPV) of 44.7% means that if a woman tests positive for elevated HbA1c based on the triglyceride test, there is a 44.7% chance that she actually has elevated HbA1c. This value is influenced by the prevalence of the condition in the population; a higher prevalence would lead to a higher PPV. A negative predictive value (NPV) of 85.6% means that if a woman tests negative for elevated HbA1c, there is an 85.6% chance that she truly does not have elevated HbA1c. This value is also influenced by prevalence. This analysis suggests that triglycerides can be a helpful tool in predicting elevated HbA1c in women with GDM. However, it's important to remember that the test is not perfect and should be used in conjunction with other clinical information to make informed decisions about patient care.

Table 5. ROC Curve analysis for triglycerides in predicting elevated HbA1c (≥ 6.5%) at 24-28 weeks gestation.

Metric	Value	Calculation
Area under the curve (AUC)	0.72	
Optimal cutoff point (mg/dl)	200	
Sensitivity (true positive rate)	70%	(True Positives) / (True Positives + False Negatives) = 21 / 30
Specificity (true negative rate)	65%	(True Negatives) / (True Negatives + False Positives) = 119 / 180
Positive predictive value (PPV)	44.7%	(True Positives) / (True Positives + False Positives) = 21 / 47
Negative predictive value (NPV)	85.6%	(True Negatives) / (True Negatives + False Negatives) = 119 / 139

The present study delves into the intricate relationship between lipid profiles and glycemic control in women with gestational diabetes mellitus (GDM) within the Soppeng Regency of South Sulawesi, Indonesia. Our findings highlight a significant association between elevated triglyceride and LDL-cholesterol levels and higher HbA1c values, underscoring the potential role of lipid dysregulation in the pathogenesis and management of GDM. Our data reveal that triglycerides emerged as the most robust independent predictor of HbA1c levels in women with GDM, even after adjusting for various confounding factors. This observation aligns with a growing body of evidence implicating triglycerides as a key player in metabolic dysfunction and insulin resistance. Triglycerides are not merely inert energy stores; they actively participate in metabolic pathways that influence glucose homeostasis. In GDM, the physiological hyperlipidemia of pregnancy is exacerbated, leading to elevated triglyceride levels. This surge in triglycerides is thought to be driven by several factors, including increased lipolysis (breakdown of fats), impaired lipoprotein lipase activity (an enzyme that clears triglycerides from the blood), and decreased hepatic uptake of triglycerides. Mechanistically, elevated triglycerides can impair insulin signaling through various pathways. One proposed mechanism involves the accumulation of

diacylglycerol (DAG), a byproduct of triglyceride metabolism, within muscle and liver cells. DAG activates protein kinase C (PKC), which, in turn, inhibits insulin receptor substrate (IRS) proteins, thereby attenuating insulin signaling and glucose uptake. Furthermore, elevated triglycerides are associated with increased production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). These cytokines further impair insulin signaling and contribute to the development of insulin resistance. Additionally, triglycerides can promote oxidative stress, which damages pancreatic beta cells and further compromises insulin secretion. Our findings not only corroborate the association between triglycerides and HbA1c in GDM but also highlight the potential of triglycerides as an early predictor of glycemic control. The significant correlation observed at both baseline and follow-up suggests that elevated triglycerides may be an early marker of impaired glucose metabolism, potentially allowing for earlier interventions to optimize glycemic control and improve pregnancy outcomes.[8,9]

LDL-cholesterol, often referred to as the "bad" cholesterol, also emerged as a significant independent predictor of HbA1c in our study. This observation aligns with a well-established link between dyslipidemia and insulin resistance in various populations. Several mechanisms may explain the association between LDL-C and HbA1c in GDM. Elevated LDL-C can promote endothelial dysfunction, a hallmark of cardiovascular disease, by impairing nitric oxide production and increasing oxidative stress. Endothelial dysfunction can, in turn, lead to reduced insulin delivery to target tissues and impaired glucose uptake. Additionally, LDL particles can undergo oxidation, forming oxidized LDL (oxLDL). OxLDL is highly atherogenic and can further contribute to endothelial dysfunction and insulin resistance. OxLDL also triggers inflammatory responses, exacerbating the metabolic dysfunction associated with GDM. The significant association between LDL-C and HbA1c in our study underscores the importance of comprehensive lipid management in GDM. Lowering LDL-C levels through lifestyle modifications or pharmacological interventions may not only reduce cardiovascular risk but also improve glycemic control and mitigate the long-term consequences of GDM.[10-12]

The weak and non-significant negative correlation between HDL-C and HbA1c observed in our study adds another layer of complexity to the relationship between lipids and glycemic control in GDM. While HDL-C is generally considered cardioprotective due to its role in reverse cholesterol transport, its relationship with insulin sensitivity and glucose metabolism is less clear-cut. Some studies have reported an inverse association between HDL-C and insulin resistance, suggesting a protective effect of HDL-C against metabolic dysfunction. However, other studies have found no significant association or even a positive correlation, particularly in individuals with established diabetes. The paradoxical relationship between HDL-C and insulin resistance may be attributed to several factors. In GDM, the quality and functionality of HDL particles may be altered, rendering them less effective in promoting reverse cholesterol transport and other protective functions. Additionally, the presence of inflammation and oxidative stress in GDM may impair HDL function and contribute to insulin resistance. Our findings suggest that HDL-C may not be a reliable predictor of HbA1c in women with GDM.[13,14]

Our findings resonate with existing literature that has explored the intricate relationship between lipid profiles and glycemic control in GDM. Several studies have reported similar associations between elevated triglycerides and HbA1c levels in women with GDM. For instance, a recent meta-analysis of 292 studies involving over 97,000 women found that those with GDM had significantly higher triglyceride levels compared to women without GDM, particularly in the first trimester and persisting throughout pregnancy. Another study investigated the correlation between HbA1c and lipid profiles in elderly patients with type 2 diabetes mellitus (T2DM). They found that higher

HbA1c levels were positively correlated with elevated triglycerides and total cholesterol, suggesting a potential link between glycemic control and lipid dysregulation that extends beyond the context of GDM. Research in Indiana also supports our findings, demonstrated significant differences in lipid profiles among different physiologic subtypes of GDM. Notably, women with GDM characterized by insulin sensitivity defects exhibited higher triglycerides and lower HDL-C levels compared to other subtypes, underscoring the importance of understanding individual variations in lipid metabolism within the GDM population. These studies, along with our own, collectively reinforce the notion that lipid profiles, particularly triglycerides, play a crucial role in the pathogenesis and management of GDM. The consistent association between elevated triglycerides and poorer glycemic control highlights the need for a comprehensive approach to GDM care that addresses both glucose and lipid metabolism.[15-17]

Our study is not without limitations. As an observational study, it cannot establish causality between elevated triglycerides and HbA1c levels. While our findings suggest a strong association, further research, including randomized controlled trials, is needed to determine whether interventions targeting triglycerides can directly improve glycemic control in women with GDM. Another limitation is the relatively small sample size and single-center design, which may limit the generalizability of our findings to other populations. Additionally, our study did not include detailed assessments of insulin sensitivity or beta-cell function, which could provide deeper insights into the mechanisms underlying the observed associations. Despite these limitations, our study has several strengths. The prospective design allowed us to assess changes in lipid profiles and HbA1c levels over time, providing a more comprehensive picture of their relationship throughout pregnancy. We also controlled for several potential confounders, including age, BMI, gestational age, dietary habits, and physical activity levels, strengthening the validity of our findings. Furthermore, our study adds to the growing body of evidence on lipid profiles and GDM in Indonesia, a country with a high prevalence of this condition. Our findings contribute to the understanding of GDM pathophysiology in this specific population and have important implications for clinical practice and public health initiatives.[17,18]

The clinical implications of our study are significant. By identifying triglycerides as a strong predictor of HbA1c levels in women with GDM, we provide clinicians with a valuable tool for risk stratification and personalized management. Women with elevated triglycerides at the time of GDM diagnosis or during pregnancy may be at higher risk of developing hyperglycemia and associated complications. This knowledge can guide healthcare providers to initiate early interventions, such as dietary counseling, lifestyle modifications, or pharmacological therapy if necessary, to optimize glycemic control and reduce the risk of adverse outcomes for both mother and child. Our findings also highlight the importance of routine lipid profile monitoring in women with GDM. Current guidelines primarily focus on glucose monitoring, but our data suggest that lipid profiles should also be included in the comprehensive assessment and management of GDM.[19]

Several avenues for future research emerge from our findings. First, randomized controlled trials are needed to evaluate the effectiveness of interventions that specifically target triglycerides in improving glycemic control and reducing complications in women with GDM. These interventions could include dietary modifications (e.g., low-fat diets, omega-3 fatty acid supplementation), exercise programs, or lipid-lowering medications. Second, further research is needed to elucidate the underlying mechanisms linking triglycerides, LDL-C, and HbA1c in GDM. Investigating the role of specific inflammatory markers, oxidative stress pathways, and genetic factors could provide deeper insights into the pathophysiology of this complex interplay. Third, studies examining the long-term impact of lipid profiles on the risk of developing type 2 diabetes and cardiovascular disease in women

with a history of GDM are crucial. This information could inform postpartum care and guide strategies for preventing future metabolic disorders in this vulnerable population. Finally, it would be valuable to explore the relationship between lipid profiles and other markers of glycemic control, such as continuous glucose monitoring data, to gain a more comprehensive understanding of glucose and lipid metabolism in GDM.[20]

4. Conclusion

This study provides compelling evidence for a strong association between lipid profiles, particularly triglycerides, and HbA1c levels in women with GDM in Indonesia. This association underscores the importance of integrating lipid management into the comprehensive care of GDM. By identifying triglycerides as a potential early predictor of glycemic control, we open new avenues for personalized interventions aimed at optimizing maternal and fetal health. Further research is warranted to confirm these findings, explore underlying mechanisms, and evaluate the effectiveness of targeted lipid-lowering strategies in this population.

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