

In Brief**Comparison of Lipid Profile of A Normal Pregnant Women with A Pregnant Women of Gestational Diabetes Mellitus and A Pregnant Woman with Hypertensive Disorder - A Comparative Study***Kalyanikutty. K. P.¹, Poonguzhalai Subramanian^{2*}*¹*Department of Physiology, MES academy of Medical Sciences, Perinthalmanna, Kerala, India*²*Department of Physiology, Sri Manakula Vinayagar Medical College, Pondicherry, India*

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Corresponding Author: *Poonguzhalai Subramanian* Email: poongu85@gmail.com**ABSTRACT**

Background: Pregnancy induces significant physiological changes, including alterations in lipid metabolism to support fetal development. However, exaggerated lipid shifts may contribute to complications such as gestational diabetes mellitus (GDM) and pregnancy-induced hypertension (PIH).

Objective: The objective of this study is to assess the changes in lipid profiles during pregnancy at each trimester and investigate their correlation with GDM and PIH.

Methods: This prospective observational study included pregnant women attending antenatal clinics, categorized into normal, GDM, and PIH groups based on established clinical guidelines. Fasting blood samples were collected during each trimester to assess serum total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) using standard enzymatic methods. Atherogenic indices such as TC/HDL-c and TG/HDL-c ratios were also calculated. Comparative and trend analyses were performed across trimesters and between groups.

Results: All participants exhibited a physiological rise in TC, TGs, and LDL-c across trimesters. However, women with GDM and PIH showed significantly elevated levels in the third trimester compared to normotensive, euglycemic pregnancies. Interestingly, HDL-c levels were also increased in GDM and PIH, reflecting complex metabolic adaptations. Lipid ratios were markedly higher in high-risk groups, suggesting increased cardiovascular risk.

Conclusion: Abnormal lipid trajectories during pregnancy, particularly elevated TGs and lipid ratios, are associated with GDM and PIH. Monitoring lipid profiles throughout gestation may aid in early identification of at-risk pregnancies and guide preventive strategies.

Keywords: Pregnancy, Lipid profile, Gestational diabetes mellitus, Pregnancy-induced hypertension, Trimesters, HDL cholesterol

1. INTRODUCTION

Pregnancy is a unique physiological state characterized by complex metabolic adaptations that support fetal development and maternal health. Among these changes, maternal lipid metabolism undergoes significant alterations. One of the most notable metabolic shifts is the progressive increase in lipid fractions, including triglycerides (TGs), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c),

particularly during the second and third trimesters of gestation [1]. These alterations are considered an essential physiological response to meet the growing energy demands of the fetus and placenta, especially in late pregnancy when fetal lipid requirements peak [2].

However, when these physiological adaptations become exaggerated or dysregulated, they may contribute to maternal metabolic syndromes, such as gestational diabetes mellitus (GDM) and pregnancy-induced hypertension (PIH).

Hyperlipidemia, a central component of metabolic syndrome, is a known risk factor for adverse health outcomes, not only in the general population but also in pregnant women [3, 4]. In the obstetric context, maternal dyslipidemia has been increasingly implicated in poor pregnancy outcomes, including macrosomia, preterm birth, intrauterine growth restriction, preeclampsia, and stillbirth [5]. Furthermore, these women are at elevated risk of developing systemic hypertension, type 2 diabetes mellitus, and cardiovascular diseases later in life [6].

In recent years, a growing body of evidence has demonstrated that pregnant women with GDM or PIH often exhibit significantly elevated lipid levels compared to those with normotensive, euglycemic pregnancies [7]. This observation has prompted further investigation into the potential role of early pregnancy lipid profiling as a predictive marker for these metabolic complications. Despite these findings, the clinical utility of lipid profile assessment in early pregnancy remains controversial. Some studies suggest that lipid derangements precede the clinical onset of GDM or PIH, indicating a possible window for early identification and intervention. Nevertheless, inconsistencies in study design, population characteristics, and lipid thresholds have limited the development of consensus guidelines.

Compounding this issue is the rising global burden of metabolic disorders during pregnancy. Epidemiological data estimate that GDM affects approximately 7-10% of pregnancies [8, 9], while PIH affects about 5-8%. Lifestyle changes, increased maternal age, obesity, and genetic predisposition have all contributed to this trend. Given the potential for long-term maternal and fetal consequences, there is an urgent need to identify reliable biomarkers that can facilitate early risk stratification and management of metabolic complications during pregnancy.

This context underscores the importance of examining the relationship between lipid metabolism and pregnancy complications. If lipid profile parameters can be validated as early indicators of GDM or PIH, they could serve as accessible, cost-effective tools for routine antenatal screening. Such an approach could

enable targeted lifestyle or pharmacological interventions, ultimately improving maternal and neonatal outcomes.

In this study, we aimed to evaluate the changes in lipid fractions-including TGs, TC, LDL-c, HDL-c, and lipid ratios-across all three trimesters of normal pregnancy and to compare them with those in non-pregnant women of reproductive age. Furthermore, we sought to compare the lipid profiles of normal pregnant women with those diagnosed with GDM and PIH, to explore the extent of dyslipidemia associated with these conditions. Through this comparative analysis, we aim to contribute to the growing understanding of maternal lipid metabolism as a potential early marker for metabolic syndromes in pregnancy.

2. Materials and Methods

The study was conducted by following the ethical principles outlined in the Declaration of Helsinki. Informed verbal consent was obtained from all participants after explaining the purpose and procedures of the study. A detailed clinical history was recorded, and thorough physical examinations were performed to rule out any major illnesses or comorbid conditions.

Study Design and Participants

This was a cross-sectional comparative study conducted at Calicut Medical College. The participants were grouped into four main categories based on pregnancy status and the presence of pregnancy-related metabolic complications.

- Group I: 20 non-pregnant women of reproductive age (students and staff of the medical college), serving as healthy controls.
- Group II: 60 normal pregnant women, further subdivided into:
 - Subgroup II-1: 20 women in the first trimester (≤ 12 weeks gestation)
 - Subgroup II-2: 20 women in the second trimester (13–27 weeks gestation)
 - Subgroup II-3: 20 women in the third trimester (≥ 28 weeks gestation)
- Group III: 40 pregnant women diagnosed with pregnancy-induced hypertension (PIH), further subdivided into:

- Subgroup III-1: 20 women in the second trimester
- Subgroup III-2: 20 women in the third trimester
- Group IV: 20 pregnant women with gestational diabetes mellitus (GDM), all in the third trimester

Inclusion and Exclusion Criteria

Only healthy pregnant women with no prior medical illnesses were included. Pre-pregnancy weight and height were used to calculate body mass index (BMI). Pregnant women with a high BMI or any underlying chronic illnesses (such as thyroid disorders, renal or hepatic disease, or pre-existing diabetes or hypertension) were excluded from the study.

Diagnosis of GDM and PIH

- Gestational Diabetes Mellitus (GDM): Diagnosed between 24–28 weeks of gestation using the Oral Glucose Tolerance Test (OGTT), in accordance with the criteria set by the International Association of Diabetes and Pregnancy Study Groups (IADPSG).
- Pregnancy-Induced Hypertension (PIH): Defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, occurring after 20 weeks of gestation in previously normotensive women.

Biochemical Analysis

All participants were instructed to undergo a 12-hour overnight fast before sample collection. Venous blood samples were collected and analysed for lipid profile, which included:

- Total Cholesterol (TC): Estimated using the cholesterol oxidase–peroxidase method.
- Triglycerides (TGs): Measured by the glycerol phosphate oxidase–peroxidase method.
- High-Density Lipoprotein Cholesterol (HDL-c) and Low-Density Lipoprotein Cholesterol (LDL-c): Estimated by direct methods.

Lipid fractions and lipid ratios were compared across all study groups to assess the impact of pregnancy, trimester-wise changes, and the influence of GDM and PIH.

Sample size calculation

A study done among the Indian Pregnant Mothers (Ghodke et. al.) [10] showed the mean and SD of triglycerides in pregnant mothers with hypertension and gestational diabetes were 243 ± 15 and 230 ± 17 respectively. Expecting similar results with one sided hypothesis, 5% alpha error and 80% power the sample size was calculated to 20 in each group using nMaster software version 2.0

3. Results

Baseline Characteristics

The mean age of participants across all groups ranged from 25.45 ± 3.13 to 26.7 ± 3.1 years, with no statistically significant age difference between groups. The mean BMI of study participants ranged from 23.5 ± 3.01 to 24.5 ± 1.99 kg/m², indicating a relatively homogeneous cohort with regard to age and body composition.

Table 1. Comparison of circulating levels of serum TGs (mg/dl)

Group 1	Group 2	P value
NOP 99.6 $\pm$ 31.88	NP 1 90.15 $\pm$ 32.62	0.36
	NP 2 168.55 $\pm$ 39.64	< 0.0001*
	NP 3 165.55 $\pm$ 34.89	< 0.0001*
	PIH 2 219.35 $\pm$ 78.05	< 0.0001*
	PIH 3 212.8 $\pm$ 62.05	< 0.0001*
	PDM 3 214.25 $\pm$ 63.97	< 0.0001*
NP 3 165.55 $\pm$ 34.89	PIH 3 212.8 $\pm$ 62.05	0.01*
	GDM 3 214.25 $\pm$ 63.97	0.01*

NOP: Non-pregnant women, NP 1: Normal pregnant women in 1st trimester, NP 2: Normal pregnant women in 2nd trimester, NP 3: Normal pregnant women in 3rd trimester, PIH 2: women with pregnancy induced hypertension in 2nd trimester, PIH 3: women with pregnancy induced hypertension in the 3rd trimester, GDM 3: Gestational diabetes mellitus in 3rd trimester.

As shown in Table 1, the mean serum TG level in non-pregnant women was 99.6 ± 31.88 mg/dL. There was a significant rise in TG levels during the 2nd (168.55 ± 39.64 mg/dL, $p < 0.0001$) and 3rd trimesters (165.55 ± 34.89 mg/dL, $p < 0.0001$) of normal pregnancy compared to non-pregnant controls.

Even more pronounced elevations were observed in women with PIH during the 2nd (219.35 ± 78.05 mg/dL) and 3rd trimesters (212.8 ± 62.05 mg/dL), and in women with GDM in the 3rd trimester (214.25 ± 63.97 mg/dL), all with $p < 0.0001$ when compared to controls.

When comparing TG levels in 3rd trimester normal pregnancies with those of PIH ($p = 0.01$) and GDM ($p = 0.01$), the differences were statistically significant, indicating higher dyslipidemia in complicated pregnancies.

Table 2. Comparison of circulating levels of serum LDL - c (mg/dl)

Group 1	Group 2	P value
NOP 94.5 ± 28.51	NP 1 71.90 ± 29.68	0.0187
	NP 2 89.7 ± 39.29	0.66
	NP 3 115.3 ± 48.04	0.1041
	PIH 2 153.75 ± 29.29	< 0.0001*
	PIH 3 157.1 ± 49.04	< 0.0001*
	PDM 3 115.8 ± 42.97	0.0725
NP 3 115.3 ± 48.04	PIH 3 157.1 ± 49.04	0.0097*
	GDM 3 115.8 ± 42.97	0.97

NOP: Non-pregnant women, NP 1: Normal pregnant women in 1st trimester, NP 2: Normal pregnant women in 2nd trimester, NP 3: Normal pregnant women in 3rd trimester, PIH 2: women with PIH in 2nd trimester, PIH 3: women with PIH in the 3rd trimester, GDM 3: GDM in 3rd trimester

As presented in Table 2, the mean LDL-c in non-pregnant women was 94.5 ± 28.51 mg/dL. There was no significant increase in LDL-c during the 1st (71.9 ± 29.68 mg/dL, $p = 0.0187$), 2nd (89.7 ± 39.29 mg/dL, $p = 0.66$), and 3rd (115.3 ± 48.04 mg/dL, $p = 0.10$) trimesters of normal pregnancy.

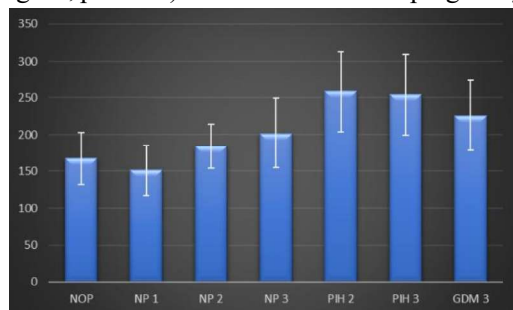


Figure 1: Comparison of circulating levels of serum TC (mg/dl)

However, women with PIH showed significantly elevated LDL-c in the 2nd (153.75 ± 29.29 mg/dL) and 3rd (157.1 ± 49.04 mg/dL) trimesters, both with $p < 0.0001$ compared to controls. Furthermore, comparing 3rd trimester normal pregnancy to PIH showed a significant increase ($p = 0.0097$), while the difference between normal pregnancy and GDM (115.8 ± 42.97 mg/dL) was not significant ($p = 0.97$).

NOP: Non-pregnant women, NP 1: Normal pregnant women in 1st trimester, NP 2: Normal pregnant women in 2nd trimester, NP 3: Normal pregnant women in 3rd trimester, PIH 2: women with PIH in 2nd trimester, PIH 3: women with PIH in the 3rd trimester, GDM 3: GDM in 3rd trimester

Table 3: Comparison of serum total cholesterol levels in 3rd trimester of normal pregnancy with 3rd trimester of pregnancy induced hypertension and 3rd trimester of diabetic complicating pregnancy

Group 1	Group 2	P value
NP 3 202.04 ± 46.73	PIH 3 254.4 ± 55.24	0.0025*
	GDM 3 225.85 ± 47.79	0.1

As illustrated in Figure 1 and Table 3, the mean TC in non-pregnant women was 167.4 ± 36.02 mg/dL. A gradual rise was observed across trimesters, with a significant increase noted in the 3rd trimester (202.04 ± 46.73 mg/dL, $p = 0.01$).

Women with PIH had significantly higher TC levels in both 2nd (258.7 ± 54.6 mg/dL, $p < 0.0001$) and 3rd trimesters (254.4 ± 55.24 mg/dL, $p < 0.0001$) compared to controls. Women with GDM also showed elevated TC in the 3rd trimester (225.85 ± 47.79 mg/dL, $p = 0.0001$).

When comparing the 3rd trimester of normal pregnancy with PIH and GDM, the difference was significant with PIH ($p = 0.0025$) but not with GDM ($p = 0.1$).

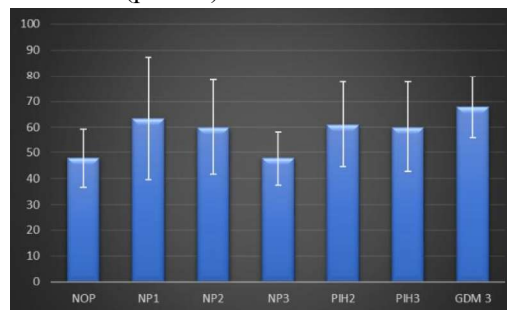


Figure 2: Comparison of circulating levels of serum HDL cholesterol (mg/dl)

NOP: Non-pregnant women, NP 1: Normal pregnant women in 1st trimester, NP 2: Normal pregnant women in 2nd trimester, NP 3: Normal pregnant women in 3rd trimester, PIH 2: women with PIH in 2nd trimester: PIH 3: women with PIH in the 3rd trimester, GDM 3: GDM in 3rd trimester.

Table 4: Comparison of serum HDL cholesterol levels in 3rd trimester of normal pregnancy with 3rd trimester of pregnancy induced hypertension and 3rd trimester of diabetic complicating pregnancy

Group 1	Group 2	P value
NP 3 47.85 ± 10.37	PIH 3 60.1 ± 17.52	0.01*
	GDM 3 67.9 ± 11.67	0.0001*

According to Figure 2 and Table 4, non-pregnant women had a mean HDL-c level of 47.95 ± 11.42 mg/dL. Significant increases were observed during the 1st (63.5 ± 23.9 mg/dL, $p = 0.01$) and 2nd (59.85 ± 18.35 mg/dL, $p = 0.01$) trimesters of normal pregnancy, but not in the 3rd trimester (47.85 ± 10.37 mg/dL, $p = 0.9$).

HDL-c levels were significantly elevated in women with PIH in the 2nd (61.1 ± 16.47 mg/dL, $p = 0.005$) and 3rd trimesters (60.1 ± 17.52 mg/dL, $p = 0.01$), as well as in GDM (67.9 ± 11.67 mg/dL, $p < 0.0001$) compared to controls. When compared to normal pregnancy in the 3rd trimester, HDL-c was significantly higher in both PIH ($p = 0.01$) and GDM groups ($p = 0.0001$).

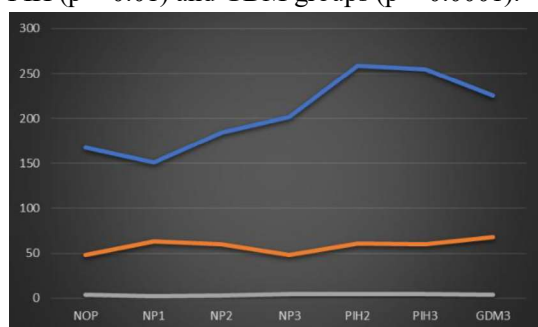


Figure 3: TC/HDL-c ratio

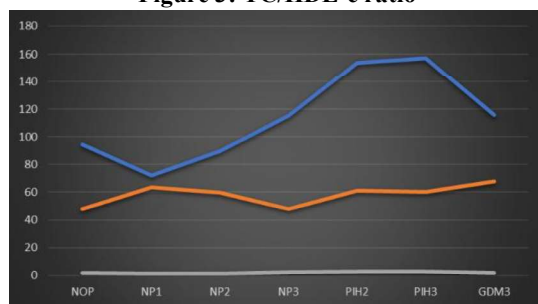


Figure 4: LDL-c/HDL-c ratio

The ratio was greater than 3 in all groups, suggesting an atherogenic lipid profile throughout pregnancy and in metabolic complications.

The ratio remained below 3 in all groups, which is generally considered acceptable, although higher values were noted in PIH groups.

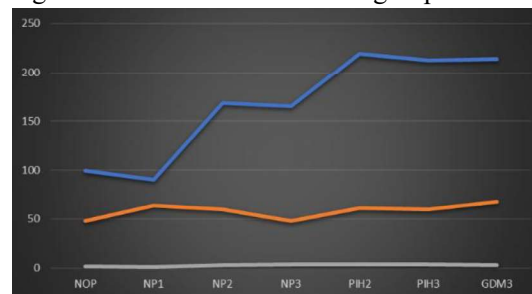


Figure 5: TG/HDL-c ratio

The ratio exceeded 3 in all groups except in non-pregnant women and those in the 1st trimester, indicating a shift towards insulin resistance and increased cardiovascular risk in later pregnancy stages and in PIH/GDM.

4. Discussion

This study aimed to evaluate the alterations in lipid profiles among non-pregnant women, normal pregnant women across all three trimesters, and those with pregnancy complications such as pregnancy-induced hypertension (PIH) and gestational diabetes mellitus (GDM) [7]. The findings confirm that pregnancy, both normal and complicated, is associated with significant modifications in lipid metabolism, reflecting physiological and pathological adaptations to support fetal development and maternal needs.

Lipid Profile Changes in Normal Pregnancy

Pregnancy is characterized by profound metabolic adaptations, including a progressive increase in lipid fractions such as triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c), particularly as gestation advances. The present study observed a gradual elevation of these lipid parameters from the first to the third trimester, with a marked increase in the third trimester [8]. These findings support earlier studies suggesting that lipid metabolism shifts towards a hyperlipidemic state in late pregnancy to ensure

a continuous energy supply for the rapidly growing fetus.

The increase in maternal TG levels, especially in the third trimester, is physiologically significant. The placenta facilitates the transfer of TG-derived free fatty acids (FFAs) to the fetus, as fetal growth is most rapid during this period [9, 10]. The elevation of TG, TC, and LDL-c in late pregnancy is largely attributed to hormonal influences, particularly rising estrogen levels, which enhance hepatic lipogenesis while suppressing lipoprotein lipase activity. This results in the accumulation of TG-rich lipoproteins. Additionally, increased levels of human placental lactogen (HPL) stimulate lipolysis, contributing to higher plasma FFA concentrations. These FFAs are utilized by the maternal liver for further lipid synthesis and by maternal tissues for energy [11, 12].

Dyslipidemia in PIH and GDM

In contrast to normal pregnancy, women with PIH and GDM exhibited significantly deranged lipid profiles, with disproportionately higher TG and LDL-c levels. These findings are consistent with previous literature, indicating a pathological intensification of the normal gestational hyperlipidemia [13, 14]. In PIH, hypertriglyceridemia contributes to endothelial dysfunction, a key pathogenic factor in the development of preeclampsia. The increased levels of circulating TGs may lead to excessive FFA release, promoting oxidative stress and inflammatory responses in the vascular endothelium [15].

Similarly, GDM is characterized by insulin resistance, particularly in the second and third trimesters, driven in part by increased placental hormones such as HPL and progesterone. The insulin-resistant state reduces maternal glucose utilization, thereby channeling glucose to the fetus while the mother shifts to lipid metabolism for energy. The elevated TG and FFA levels observed in GDM contribute to this metabolic shift [16]. Additionally, the FFAs have been implicated in further impairing insulin signaling, creating a vicious cycle of insulin resistance [14, 17].

Interestingly, while most studies report a decrease in HDL-c levels in PIH and GDM

pregnancies considered a marker of adverse cardiovascular and metabolic risk [18, 19] this study found a proportional increase in HDL-c levels in these groups. This discrepancy may be attributed to variations in population genetics, diet, or regional differences. Notably, Zeynab Farsangi et al., [20] also reported elevated HDL-c levels in women with GDM, supporting our findings.

Lipid Ratios and Predictive Value

Beyond individual lipid components, the study analyzed lipid ratios such as TC/HDL-c, LDL-c/HDL-c, and TG/HDL-c, which are increasingly recognized as valuable predictors of cardiovascular and metabolic risks. Among these, the TG/HDL-c and TC/HDL-c ratios were significantly elevated in normal pregnant women, and even more so in PIH and GDM groups. These ratios provide a better reflection of atherogenic risk than absolute lipid levels and have been proposed as potential markers for identifying high-risk pregnancies [21, 22].

The LDL-c/HDL-c ratio, however, did not show significant variation across groups, suggesting it may be less sensitive in reflecting the lipid changes associated with gestational complications in this population. Nonetheless, TG/HDL-c ratio, in particular, has emerged as a robust indicator of insulin resistance and is strongly associated with GDM and PIH, as corroborated by our results.

Physiological and Pathological Implications

Hyperlipidaemia, in particular, is frequently detected in the second half of gestation and is considered a physiological adaptation to meet the growing energy and nutritional demands of the developing foetus. Lipid levels rise modestly during early pregnancy but show a significant increase in the later stages. These observed lipid alterations in normal pregnancy underline the maternal physiological adaptation necessary for fetal growth. In contrast, the exaggerated lipid abnormalities seen in PIH and GDM may reflect the pathological failure of metabolic regulation during pregnancy. The combination of increased estrogen, insulin resistance, & elevated placental hormones orchestrates a complex interplay that alters lipid metabolism [23]. However, in conditions like PIH and GDM, these mechanisms

are either exaggerated or impaired, leading to clinical complications that may jeopardize both maternal and fetal outcomes. Dyslipidemia, or altered lipid metabolism, contributes to insulin resistance and is associated with increased cardiovascular risk. Several mechanisms have been proposed to explain the atherogenic potential of small, dense LDL particles, including their reduced affinity for LDL receptors, increased susceptibility to oxidative stress, prolonged plasma half-life, strong binding to vascular wall components, and enhanced ability to penetrate the arterial intima [24]. Interestingly, recent hypotheses suggest that not only elevated but also dysregulated or altered estrogen levels may contribute to the pathogenesis of PIH and GDM [25]. These hormonal imbalances could disrupt normal lipid metabolism, leading to the atypical patterns observed in our study.

Comparison with Global Studies

The consistency of our findings with studies conducted globally including those by Wang *et al.*, [25] and Reda *et al.*, [26] confirms the universality of lipid changes in pregnancy, regardless of ethnicity or geography. Cross-population analyses [17] reveal similar trends, highlighting the importance of monitoring lipid profiles as a routine part of antenatal care, especially in high-risk pregnancies. Studies suggest that effective management of hyperlipidemia should involve a multidisciplinary team to implement dietary fat restriction, recommend appropriate supplementation, and initiate pharmacological treatment when necessary [27].

5. Conclusion

This study reinforces the notion that pregnancy is associated with significant changes in lipid metabolism, which become more pronounced in complications like PIH and GDM. Elevated TG levels and deranged lipid ratios in these conditions may serve as early biomarkers for identifying women at risk. Early identification and management of dyslipidemia during pregnancy may offer a pathway to reduce adverse maternal and fetal outcomes.

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