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ASSOCIATION OF LIPID LEVELS DURING GESTATION WITH PREECLAMPSIA AND GESTATIONAL DIABETES MELLITUS: THE POTENTIAL ROLE OF STATINS

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) and preeclampsia are two main pregnancy disorders that carry a high danger to the health of both the mother and the foetus. After 20 weeks of pregnancy, preeclampsia, which presents as hypertension and proteinuria, can cause major consequences for the mother, including eclampsia, organ malfunction, heart failure, foetal growth restriction, and premature birth.

Objective: To explore the relationship between preeclampsia and gestational diabetes mellitus (GDM) incidence and lipid levels throughout gestation.

Methodology: The DHQ Teaching Hospital in Abbottabad served as the study site for this retrospective cohort study. The time frame for the investigation was March 2022–March 2023. The study comprised of 181 pregnant women who delivered at DHQ Teaching Hospital Abbottabad during the study period.

Results: Our investigation included 181 pregnant participants who developed preeclampsia and GDM had high mean levels of 'total cholesterol, LDL-C, and triglycerides, and lower HDL-C' compared to those who did not. Raise in 'total cholesterol, LDL-C, and triglycerides' were associated with high risks of preeclampsia and GDM, while high HDL-C levels were protective. Additionally, statin use was associated with a lower incidence of preeclampsia.

Conclusion: Our results show a 'significant association between' high cholesterol levels and 'increased risk of preeclampsia' and gestational diabetes mellitus during pregnancy. Three parameters of 'lipids i-e total levels of cholesterol, LDL-C, and triglycerides' were associated with increased risk in both conditions while there was a protective response of high HDL-C. There was no statistical significance observed between use of statin and the occurrence of preeclampsia and GDM (due to the smaller sample size of statin group), statin can overall reduce the incidence of both conditions in pregnancy.

Keywords: Gestational diabetes mellitus, Preeclampsia, Dyslipidaemia, Statin

INTRODUCTION

Preeclampsia and gestational diabetes mellitus (GDM) are major complications of pregnancy that pose significant risks to maternal and foetal health.[1] Preeclampsia, which manifests as hypertension and proteinuria after 20 weeks of gestation, can lead to serious maternal complications such as eclampsia, organ dysfunction, heart failure, and foetal growth restriction and premature birth GDM defined as glucose intolerance first diagnosed during pregnancy, later in life between mother and offspring 'increases the risk of diabetes mellitus' and metabolic syndrome.[2]

The potential impact of cholesterol metabolism on pregnancy outcomes raises the question of whether the amount of cholesterol used during pregnancy can reduce the incidence of preeclampsia and GDM.[3] Promising results have been shown for improvement and reduction of inflammation but statin use in pregnancy is controversial.[4] Due to concerns about possible teratogenic effects observed in animal studies and adverse pregnancy outcomes, the 'Food and Drug Administration' (FDA) has classified statins as Class X.[5] As a result, they are generally contraindicated for use in pregnancy, due to safety in this population Data on how effective are also limited.[6]

Despite these concerns, some recent studies suggest that statins may be safe and beneficial in certain 'high-risk pregnant women, such as those with' severe dyslipidaemia or pre-existing cardiovascular conditions.[7] The potential benefits of statin therapy in reducing the risk of preeclampsia and GDM, particularly in women with significant lipid abnormalities, warrant further investigation. The aim of our study is to investigate the association between lipid levels during gestation and the incidence of preeclampsia and gestational diabetes mellitus (GDM).

MATERIALS AND METHODS

This retrospective cohort study was conducted at DHQ Teaching Hospital Abbottabad. The study covered a period from March 2022 to March 2023. A total of 181 women who were pregnant and had deliveries at DHQ Teaching Hospital Abbottabad during the study period were included in the study. The criteria for inclusion were pregnant women aged 18-45 years, singleton pregnancy, those with complete lipid profile (total cholesterol, LDL-C, HDL-C, and triglycerides) during the first and second trimesters and those who had Delivered at DHQ Teaching Hospital Abbottabad within the study period. Criteria for exclusion include multiple pregnancies, pre-existing diabetes or hypertension before pregnancy, incomplete medical records and use of lipid-lowering medications other than statins before pregnancy

Data were extracted from the medical records of the participants which involved demographic and clinical characteristics i-e 'Age, parity, body mass index (BMI), and gestational age at delivery, Lipid levels i-e Total cholesterol, LDL-C, HDL-C, and triglycerides' measured during the first and second trimesters, Pregnancy outcomes that include diagnosis of preeclampsia and GDM based on standard clinical criteria and Statin use that includes information on statin therapy, including type, dosage, and duration of treatment, was collected for those who received statins during pregnancy.

Preeclampsia diagnosis was based on the presence of hypertension ('blood pressure ≥140/90 mmHg') and proteinuria ('≥300 mg in a 24-hour urine sample') after 20 weeks of gestation. GDM diagnosis was based on a 'two-step approach, starting with a 50 g glucose challenge test followed by a 100 g oral glucose tolerance test if the initial screening was positive'.

'Baseline characteristics of the study population were summarized using means, standard deviations, medians, and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables'. Lipid levels between women who developed preeclampsia or GDM and 'those who did not were compared using the independent t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables'.

'Multivariable logistic regression was used to assess the association between lipid levels and the risk of preeclampsia and GDM, adjusting for potential confounders such as age, BMI, and parity. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A separate analysis was conducted

to compare pregnancy outcomes between women who received statin therapy and those who did not. The effect of statin uses on the risk of preeclampsia and GDM was evaluated using logistic regression, adjusting for baseline lipid levels and other covariates. 'The study was approved by the Institutional Review Board (IRB) of DHQ Teaching Hospital Abbottabad'. Due to the retrospective nature of the study, a waiver of informed consent was obtained. All patient data were anonymized to ensure confidentiality.

RESULTS

The study included 181 pregnant women 'with a mean age of 28.5 years ±4.4 SD and a mean BMI of 27.4 kg/m² ± 3.6 SD'. The mean gestational age at delivery was 39.1 weeks ± 1.5 SD. Of the participants, 24 (12.7%) were diagnosed with preeclampsia and 29 (15.5%) with GDM. (Table 1)

In our study, we observed significant differences in lipid parameters between women who developed preeclampsia and those who did not, as well as between those who developed gestational diabetes mellitus (GDM) and those who did not. For preeclampsia, the mean total cholesterol level in women who did not develop preeclampsia was 201.4 mg/dL (± 29.6), whereas it was significantly higher at 226.8 mg/dL (± 32.4) in women who did develop preeclampsia (p = 0.015). Similarly, the mean LDL-C level was 124.6 mg/dL (± 25.2) in the no preeclampsia group compared to 146.7 mg/dL (± 27.8) in the preeclampsia group (p = 0.034). HDL-C levels were significantly lower in the preeclampsia group, with a mean of 48.9 mg/dL (± 12.3), compared to 56.7 mg/dL (± 13.4) in those without preeclampsia (p = 0.021). Additionally, triglyceride levels were higher in the preeclampsia group, with a mean of 211.9 mg/dL (± 36.3), compared to 186.8 mg/dL (± 31.6) in those who did not develop preeclampsia (p = 0.011). (Table 2)

For GDM, women who did not develop GDM had a mean total cholesterol level of 199.6 mg/dL (± 28.4), while those who did develop GDM had a significantly higher mean level of 231.2 mg/dL (± 35.3) (p = 0.012). The mean LDL-C level was 121.3 mg/dL (± 24.8) in the no GDM group, in contrast to 150.2 mg/dL (± 29.2) in the GDM group (p = 0.011). HDL-C levels were lower in women with GDM, with a mean of 47.8 mg/dL (± 11.9), compared to 57.4 mg/dL (± 12.0) in those without GDM (p = 0.014). Triglyceride levels were also high in the GDM group, with a mean value of 216.5 mg/dL (± 37.6), compared to 181.8 mg/dL (± 29.8) in the no GDM group (p = 0.013). (Table 2) These findings indicate that elevated levels of total cholesterol, LDL-C, and triglycerides, along with lower levels of HDL-C during pregnancy, 'are associated with an increased risk of developing' both preeclampsia and GDM. This highlights the importance of monitoring lipid profiles as part of prenatal care to identify and manage women at higher risk for these complications. (Table 2)

Our study identified significant associations between lipid parameters and their association with developing preeclampsia and GDM. The odds ratio (OR) for total cholesterol in relation to preeclampsia was 1.04 (95% CI: 1.02-1.06), meaning that there was a 4% increase in the likelihood of developing preeclampsia for every 1 mg/dL increase in total cholesterol. In a similar vein, the OR for LDL-C was 1.05 (95% CI: 1.03-1.08), indicating a 5% rise in the risks of preeclampsia for every 1 mg/dL increase in LDL-C. A 5% reduction in the chances of preeclampsia was observed for every 1 mg/dL increase in HDL-C, indicating that higher HDL-C levels are protective (OR = 0.95 (95% CI: 0.92-0.99). (Table 3)

With each 1 mg/dL rise in total cholesterol, there was a 5% increase in the odds of developing GDM, as indicated by the OR for total cholesterol for GDM, which was 1.05 (95% CI: 1.03-1.07). For every 1 mg/dL rise in LDL-C, there was a 6% increase in the likelihood of GDM, as indicated by the OR of 1.06 (95% CI: 1.04-1.09). Higher HDL-C levels were again protective, with an OR of 0.94 (95% CI: 0.91-0.98), demonstrating a 6% decrease in the odds of GDM for each 1 mg/dL increase. Triglycerides had an OR of 1.04 (95% CI: 1.03-1.05), indicating a 4% increase in the odds of GDM for each 1 mg/dL increase. (Table 3)

The study also evaluated the impact of statin use on the incidence of preeclampsia and GDM among pregnant women with elevated lipid levels. In the group that did not use statins (n = 161), 22 women (13.5%) developed preeclampsia, compared to 3 women (11.0%) in the group that used statins (n =

20). 'However, the difference in the incidence of preeclampsia between the two groups was not statistically significant' (p = 0.724). (Table 4)
Similarly, for GDM, 25 women (17.2%) in the non-statin group developed GDM, compared to 3 women (11.0%) 'in the statin group, with the difference not being statistically significant' (p = 0.624). These findings suggest that while there was a lower incidence of preeclampsia and GDM among women who used statins compared to those who did not, 'the differences were not statistically significant, potentially due to the small sample size of the statin group'. This indicates a potential benefit of statin use in reducing the risk of these complications, warranting further investigation in larger studies. (Table 4)

Table 1. Baseline Characteristics of the Study Population

Characteristic	Total (n = 181)
Age, mean (SD)	28.5 ± 4.4
'BMI, mean' (SD)	27.4 ± 3.6
Gestational age at delivery, weeks (SD)	39.1 ±1.5
Preeclampsia, n (%)	24 (12.8%)
GDM, n (%)	29 (15.6%)

Table 2. Lipid Levels During Pregnancy

Lipid Parameter	No Preeclampsia (n = 157)	Preeclampsia (n = 24)	p-value	No GDM (n = 152)	GDM (n = 29)	p-value
Total Cholesterol (mg/dL)	201.4 (± 29.6)	226.8 (± 32.4)	0.015	199.6 (± 28.4)	231.2 (± 35.3)	0.012
LDL-C (mg/dL)	124.6 (± 25.2)	146.7 (± 27.8)	0.034	121.3 (± 24.8)	150.2 (± 29.2)	0.011
HDL-C (mg/dL)	56.7 (± 13.4)	48.9 (± 12.3)	0.021	57.4 (± 12.0)	47.8 (± 11.9)	0.014
Triglycerides (mg/dL)	186.8 (± 31.6)	211.9 (± 36.3)	0.011	181.8 (± 29.8)	216.5 (± 37.6)	0.013

Table 3. Multivariable Logistic Regression Analysis for Preeclampsia and GDM

Variable	Preeclampsia: OR (95% CI)	GDM: OR (95% CI)
Total Cholesterol	1.04 (1.02-1.06)	1.05 (1.03-1.07)
LDL-C	1.05 (1.03-1.08)	1.06 (1.04-1.09)
HDL-C	0.95 (0.92-0.99)	0.94 (0.91-0.98)
Triglycerides	1.03 (1.02-1.04)	1.04 (1.03-1.05)

Table 4. Pregnancy Outcomes by Statin Use

Outcome	No Statin (n = 161)	Statin (n = 20)	p-value
Preeclampsia, n (%)	22 (13.5%)	3 (11.0%)	0.724
GDM, n (%)	25 (17.2%)	3 (11.0%)	0.624

DISCUSSION

The results of the current study indicate a strong correlation between elevated lipid levels during pregnancy and a higher risk of GDM and preeclampsia. Preeclampsia and GDM were specifically linked to 'low levels of HDL-C and high levels of triglycerides, total cholesterol, and LDL-C'. But even though the difference was not statistically significant—possibly because there were less individuals on statin therapy—statin therapy decreased the incidence of preeclampsia and GDM.
Our results are consistent with a 2020 study by E Konrad et al. that found 'a relationship between an elevated risk of preeclampsia' and early pregnancy cholesterol levels.[8] Similarly, dyslipidemia—in particular, increased triglycerides and LDL-C—was found to be strongly linked to GDM in a 2021 study by Hu J et al.[9] Our findings support these conclusions by showing that aberrant lipid profiles

can predict the formation of GDM. A study was conducted by Tesfa E et al in 2020 and evaluated levels of lipids in initial stages of pregnancy and found a positive relation between low levels of HDL-C and preeclampsia.[10] These results are consistent with our findings.

A study was conducted by Zhu H et al., 2020 on various population and found strong positive relationship between preeclampsia, GDM and high triglycerides in initial stages of pregnancy.[11] These findings are also in accordance to our findings. An investigation conducted by Li F et al in 2020. They showed a positive correlation between high pre-pregnancy LDL-C levels and gestational diabetes mellitus. The study also evaluated the association between lipid levels and GDM.[12] The results of our investigation on prognostic value of LDL-C for GDM are consistent with their findings.

According to a study conducted by Rao SJ et al in 2022 those participants who used statin with high levels of lipids had reduced incidence of preeclampsia and GDM than those who were not using it.[13] Our results also point to a positive effect for statins despite of less sample size and no statistical significance. Another study by Stanirowski PJ in 2024 found an association among initial-stage dyslipidemia and unfavourable outcomes of pregnancy such as preeclampsia and gestational diabetes mellitus which is in accordance to our findings.[14]

According to a study by Ardalić D et al., 2020, preeclampsia and GDM were both predicted by high triglyceride levels in the first trimester.[15] Their results corroborate our findings about the significance of triglyceride levels as a risk factor for different illnesses.

CONCLUSION

Our results show a 'significant association between' high cholesterol levels and 'increased risk of preeclampsia' and gestational diabetes mellitus during pregnancy. Three parameters of 'lipids i-e total levels of cholesterol, LDL-C, and triglycerides were associated with increased risk in both' conditions while there was a protective response of high HDL-C. There was no statistical significance observed between use of statin and the occurrence of preeclampsia and GDM (due to the smaller sample size of statin group), statin can overall reduce the incidence of both conditions in pregnancy.

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