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Study of Serum Vitamin D and Lipid Profile in Pre-Eclampsia

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HIGHLIGHTS

1. Investigating Vitamin D levels in pre-eclampsia.
2. Correlating lipid profile with disease severity.
3. Assessing vitamin-lipid interaction in pregnancy.
4. Evaluating pre-eclampsia's impact on lipids.
5. Analyzing serum markers in affected women

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ABSTRACT

Introduction: Pre-eclampsia, a serious pregnancy complication characterized by hypertension and organ dysfunction after 20 weeks of gestation, poses significant maternal and fetal health risks. Recent studies suggest a link between dyslipidemia, Vitamin D deficiency, and pre-eclampsia, emphasizing the need for further investigation. **Objective:** This study aims to explore the role of serum Vitamin D and lipid profiles in pre-eclampsia by comparing these biomarkers between pre-eclamptic and normotensive pregnant women and examining the correlation between Vitamin D levels and triglycerides in pre-eclampsia. **Methods:** A one-year case-control study was conducted at Tezpur Medical College & Hospital, Assam, India, involving 100 pregnant women. The participants were divided into two groups: 50 pre-eclamptic (cases) and 50 normotensives (controls). Serum Vitamin D levels and lipid profiles, including HDL, LDL, total cholesterol, and triglycerides, were measured and compared between the groups. Statistical analysis was performed to assess the significance of differences and correlations. **Results:** The pre-eclampsia group exhibited significantly lower HDL (36.3 ± 5.2 mg/dL) and Vitamin D levels (15.65 ± 2.67 ng/mL) and higher LDL (159.36 ± 20.28 mg/dL), total cholesterol (251.84 ± 32.37 mg/dL), and triglycerides (199.89 ± 55.21 mg/dL) compared to the normotensive group. A moderate negative correlation between Vitamin D levels and triglycerides was observed ($r = -0.565$, $p < 0.0001$), indicating that lower Vitamin D levels are associated with higher triglycerides in pre-eclamptic women. **Conclusion:** The study reveals significant alterations in lipid metabolism and Vitamin D deficiency in pre-eclampsia, with a notable inverse relationship between Vitamin D levels and triglycerides. These findings suggest that monitoring these biomarkers could help identify women at risk of pre-eclampsia, enabling early intervention. Further research should investigate the potential therapeutic benefits of lipid-lowering agents and Vitamin D supplementation in managing pre-eclampsia.

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INTRODUCTION

Pre-eclampsia is a serious pregnancy complication that typically arises after 20 weeks of gestation, characterized by sudden high blood pressure and often accompanied by protein in the urine. This condition affects millions of women worldwide each year, leading to significant maternal and perinatal morbidity and mortality. Women who survive pre-eclampsia face long-term health risks, including an increased likelihood of stroke and cardiovascular disease[1]. Additionally, babies born to mothers with pre-eclampsia are at a higher risk of premature birth and various health issues later in life.

Pre-eclampsia is classified based on the gestational age at onset—preterm, term, or postpartum—which helps guide clinical management. However, recent research suggests that classifying pre-eclampsia solely based on timing may underestimate the severity of early-onset cases. Severe complications associated with pre-eclampsia include eclampsia (seizures), HELLP syndrome (a variant involving liver and blood complications), stroke, and renal failure[2]. Despite these variations, all cases of pre-eclampsia pose a risk of rapid deterioration. As a result, guidelines now advise against distinguishing between severe and mild forms of the condition during ongoing pregnancies. There is ongoing research into whether symptom-based classification could enhance understanding and treatment, potentially aiding in the development of predictive tests and preventive strategies tailored to different onset times of pre-eclampsia[3].

The International Society for the Study of Hypertension in Pregnancy (ISSHP) defines pre-eclampsia as the development of systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg on two separate occasions at least four hours apart in previously normotensive women, occurring after 20 weeks of gestation. Diagnosis also requires accompanying new-onset conditions such as proteinuria (≥30 mg/mmol protein: creatinine ratio, ≥300 mg/24 hours, or ≥2+ on a dipstick test) or evidence of maternal organ dysfunction[4]. This dysfunction can manifest as acute kidney injury, liver involvement indicated by elevated liver enzymes, neurological complications like eclampsia or stroke, and hematological abnormalities such as thrombocytopenia or hemolysis. Uteroplacental dysfunction, including fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth, further characterizes pre-eclampsia[5].

The American College of Obstetricians and Gynecologists (ACOG) has expanded upon this definition to include cases where renal, hepatic, or hematological dysfunction is present without concurrent proteinuria. This broader criterion acknowledges that pre-eclampsia can present with varying patterns of maternal organ involvement beyond traditional markers like proteinuria, encompassing a wider spectrum of clinical presentations. This updated approach aims to enhance diagnostic accuracy and ensure appropriate management strategies are applied to all affected individuals, reflecting ongoing advancements in understanding and managing this co-

-mplex pregnancy complication[6].

Globally, the incidence of pre-eclampsia varies significantly, affecting between 2% and 10% of pregnancies. This condition, which can progress to eclampsia, shows notable disparities between developed and developing countries. According to the World Health Organization (WHO), pre-eclampsia occurs approximately seven times more frequently in developing nations, affecting around 2.8% of live births compared to about 0.4% in developed countries. In regions like North America and Europe, the incidence of eclampsia is relatively consistent, estimated at 5 to 7 cases per 10,000 deliveries[7]. However, in developing countries, the incidence varies widely, ranging from 1 case per 100 pregnancies to 1 case per 1700 pregnancies. In India, for example, pre-eclampsia affects approximately 8-10% of pregnant women, with hypertensive disorders of pregnancy, including pre-eclampsia, having a prevalence of 7.8% among the study population[8].

These statistics highlight significant regional differences in the occurrence of pre-eclampsia and eclampsia, influenced by factors such as socioeconomic conditions, healthcare access, and demographic characteristics. Understanding these variations is crucial for tailoring healthcare strategies and interventions to effectively manage and reduce the impact of these serious pregnancy complications worldwide[9].

Early pregnancy dyslipidemia has been identified as a potential risk factor for pre-eclampsia. During early pregnancy, the mother transitions into an anabolic state where lipids serve as a vital energy source for both fetal growth and maternal needs, particularly in the third trimester[10]. Several studies have shown that abnormalities in lipid profiles, such as elevated levels of triglycerides (TG), low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC), and very low-density lipoprotein (VLDL), are more prevalent in women who develop pre-eclampsia compared to those with uncomplicated pregnancies. Conversely, high-density lipoprotein (HDL) levels tend to be lower in pre-eclamptic women[11].

Lipid profile abnormalities and vitamin D deficiency are critical factors in pregnancy, particularly in the development of pre-eclampsia. As pregnancy progresses, lipid irregularities, such as elevated triglyceride levels, become more pronounced and are strongly associated with an increased risk of pre-eclampsia[12]. Similarly, vitamin D deficiency, which affects 8% to 70% of pregnant women based on skin pigmentation and sunlight exposure, is linked to adverse pregnancy outcomes, including pre-eclampsia, preterm birth, and gestational diabetes, with long-term impacts on offspring health. Adequate vitamin D levels may help protect against pre-eclampsia by supporting normal placentation. Monitoring both lipid profiles and vitamin D levels during pregnancy is crucial for early identification and management of pre-eclampsia risk, potentially improving maternal and fetal outcomes. These findings underscore the need for further research to optimize preventive strategies and refine guidelines for vitamin D supplementation in pregnant women

[13].

This study aims to investigate the role of Vitamin D and lipid profiles in pre-eclampsia by measuring and comparing serum Vitamin D and lipid levels in pre-eclamptic and normotensive patients, and exploring any potential correlation between serum Vitamin D levels and triglycerides (TG) in pre-eclamptic individuals.

MATERIALS AND METHODS

This one-year case-control study, conducted from May 1, 2023, to May 1, 2024, at Tezpur Medical College & Hospital, Assam, India, examines the relationship between serum Vitamin D levels, lipid profiles, and pre-eclampsia in pregnant women. The study involved 100 participants, split evenly between 50 pre-eclamptic women (cases) and 50 normotensive pregnant women (controls), recruited from the hospital's OPD and IPD. Inclusion criteria focused on pre-eclamptic women of all ages, while exclusion criteria eliminated those with pre-existing conditions such as diabetes, hypertension, renal failure, or other severe diseases.

RESULTS

Table 1: Age Distribution Analysis of Patients

	Count	Min Age	Max Age	Mean Age	Median Age	Std Dev Age
Normal	50	20	39	29.86	30	5.79
Pre-eclampsia	50	20	38	28.16	28	5.19
Total	100	20	39	29.01	28.5	5.54

The age distribution analysis of patients in normal (n=50) and pre-eclampsia (n=50) groups shows a mean age of 29.86 years (SD 5.79) for the normal group and 28.16 years (SD 5.19) for the pre-eclampsia group. The combined mean age across both groups is 29.01 years (SD 5.54), with ages ranging from 20 to 39 years. A t-test yielded a p-value of 0.091, indicating no statistically significant difference in mean age between the groups.

Table 2: Distribution of Pregnancy Stages Between Normal and Pre-Eclampsia Groups

Stage of Pregnancy	Normal	Pre-eclampsia	Total
First Trimester	18	15	33
Second Trimester	18	13	31
Third Trimester	14	22	36
Total	50	50	100

The distribution of pregnancy stages between normal and pre-eclampsia groups was analyzed, showing 18 cases in the first trimester, 18 in the second, and 14 in the third for the normal group. The pre-eclampsia group had 15 in the first trimester, 13 in the second, and 22 in the third. A chi-square test revealed no statistically significant difference in pregnancy stage distribution between the groups ($p > 0.05$), indicating that pregnancy stage does not significantly differ between normal and pre-eclampsia cases.

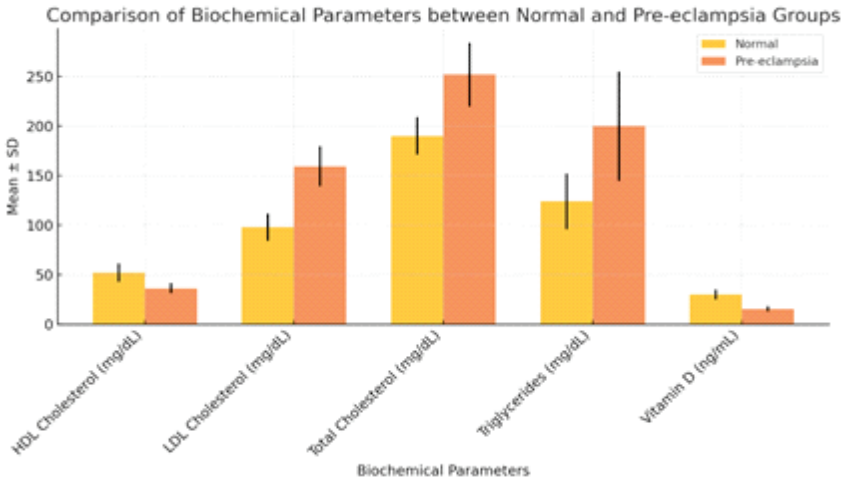

Figure 1: Comparison of Lipid profile and Vitamin D between Normal and Pre-eclampsia Groups

The comparison between Normal and Pre-eclampsia groups revealed significant biochemical differences. The Pre-eclampsia group had significantly lower HDL Cholesterol (36.3 ± 5.2 mg/dL) and Vitamin D levels (15.65 ± 2.67 ng/mL) and significantly higher LDL Cholesterol (159.36 ± 20.28 mg/dL), Total Cholesterol (251.84 ± 32.37 mg/dL), and Triglycerides (199.89 ± 55.21 mg/dL) compared to the Normal group. All differences were highly significant, with p-values indicating that these biochemical discrepancies are strongly associated with Pre-eclampsia, rather than due to chance.

Table 3: Comparison of Biochemical Parameters between Normal and Pre-eclampsia Groups

	Normal	Pre-eclampsia	p-value
ALP (U/L)	100.73 ± 22.16	151.66 ± 42.84	<0.0001
ALT (U/L)	30.96 ± 7.7	70.68 ± 24.09	<0.0001
AST (U/L)	25.26 ± 5.85	95.22 ± 30.32	<0.0001
Albumin (g/dL)	3.94 ± 0.27	2.77 ± 0.55	<0.0001
Direct Bilirubin (mg/dL)	0.25 ± 0.08	0.53 ± 0.18	<0.0001
Indirect Bilirubin (mg/dL)	0.61 ± 0.15	1.22 ± 0.4	<0.0001
Total Bilirubin (mg/dL)	0.85 ± 0.2	1.75 ± 0.52	<0.0001
Total Protein (g/dL)	6.99 ± 0.33	5.92 ± 0.56	<0.0001

The analysis revealed significant biochemical alterations in the Pre-eclampsia group compared to the Normal group. ALP, ALT, AST, and Direct Bilirubin levels were markedly higher in the Pre-eclampsia group, while Albumin levels were significantly lower. Specifically, the mean ALP was 151.66 U/L versus 100.73 U/L, ALT was 70.68 U/L versus 30.96 U/L, AST was 95.22 U/L versus 25.26 U/L, and Albumin was 2.77 g/dL versus 3.94 g/dL, all with highly significant p-values. These findings highlight the profound impact of Pre-eclampsia on liver function.

Table 4: Comparison of cholesterol-related ratios between the Normal and Pre-eclampsia groups

	Normal	Pre-eclampsia	p-value
HDL/VLDL	2.2 ± 0.61	0.99 ± 0.35	<0.0001
LDL/HDL	1.93 ± 0.39	4.49 ± 0.94	<0.0001
TC/HDL	3.77 ± 0.75	7.08 ± 1.4	<0.0001
TGL/HDL	2.44 ± 0.63	5.62 ± 1.8	<0.0001

The analysis revealed significant differences in cholesterol-related ratios between the Normal and Pre-eclampsia groups, indicating altered lipid metabolism in Pre-eclampsia. The Pre-eclampsia group had a significantly lower HDL/VLDL ratio (0.99 vs. 2.2), and higher LDL/HDL (4.49 vs. 1.93), TC/HDL (7.08 vs. 3.77), and TGL/HDL (5.62 vs. 2.44) ratios compared to the Normal group, all with highly significant p-values. These findings underscore the profound impact of Pre-eclampsia on cholesterol ratios and lipid metabolism.

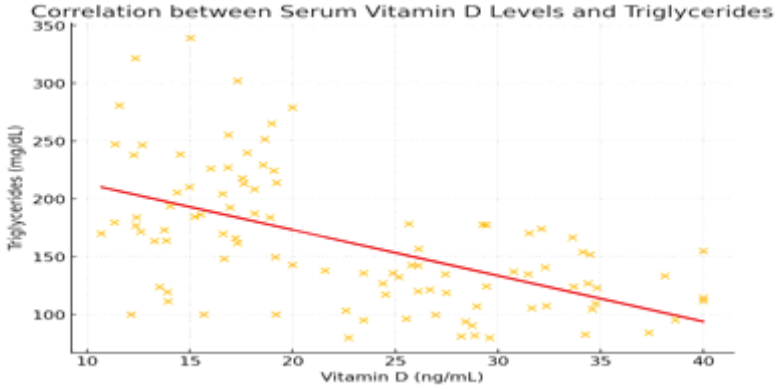

Figure 2: Correlation Between Serum Vitamin D Levels and Triglycerides (Tg)

The analysis revealed a moderate negative correlation between serum Vitamin D levels and Triglycerides (TG), with a correlation coefficient of approximately -0.565. This suggests that higher Vitamin D levels are associated with lower Triglyceride levels. The correlation was confirmed to be highlystatistically significant, with a p-value of $9.40\times10-10$, indicating that this inverse relationship is unlikely due to chance. The scatter plot further supports this, showing a downward trend between Vitamin D and Triglyceride levels.

DISCUSSION

Pre-eclampsia, defined by ISSHP, is characterized by systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg in previously normotensive women after 20 weeks of gestation, accompanied by proteinuria, maternal organ dysfunction, or uteroplacental dysfunction. The American College of Obstetricians and Gynecologists includes cases without proteinuria but with other organ dysfunctions[14]. Affecting 2-10% of pregnancies globally, its incidence is higher in developing countries. Dyslipidemia, especially elevated TG and low HDL, and Vitamin D deficiency are linked to increased pre-eclampsia risk. This study aims to explore the role of Vitamin D and lipid profiles in pre-eclampsia[15].

Our study's analysis of age distribution in normal and pre-eclampsia groups, with mean ages of 29.86 and 28.16 years respectively, showed no statistically significant difference (p=0.091), consistent with findings by Al Subai et al. (2023) and Giourga et al. (2023). Additionally, our study found no significant difference in pregnancy stage distribution between the groups, aligning with results from Kumari et al. (2023) and Giourga et al. (2023). These studies suggest that neither age nor pregnancy stage significantly predicts pre-eclampsia, underscoring the need to consider other risk factors[16, 17, 18].

Our study found significantly lower HDL and Vitamin D levels, along with higher Total Cholesterol, Triglycerides, and LDL in the Pre-eclampsia group, consistent with findings by Bakacak et al. (2015) and Mummadi et al. (2019). Similar results were also reported by Salma et al., who observed elevated TC, TG, LDL, and lower Vitamin D levels in Pre-eclampsia. Additionally, our study's findings of elevated ALP, ALT, AST, and Direct Bilirubin, alongside reduced Albumin levels, align with Giourga et al. (2023) and Mummadi et al. (2019), reinforcing the pattern of dyslipidemia and liver dysfunction in Pre-eclampsia[17,19,20].

Our study revealed significant alterations in cholesterol-related ratios in the Pre-eclampsia group, including lower HDL/VLDL and higher LDL/HDL, TC/HDL, and TGL/HDL ratios, consistent with findings by Mummadi et al. (2019) and Gawade et al. (2019), who reported similar lipid disturbances in Pre-eclampsia. Additionally, we found a significant negative correlation between serum Vitamin D levels and Triglycerides, aligning with Al Refaie et al. (2024) and Han et al. (2021), who observed that low Vitamin D is associated with elevated Triglycerides. These studies collectively highlight the role of Vitamin D and lipid metabolism in Pre-eclampsia[20, 21, 22, 23].

Our study revealed a significantly elevated TGL/HDL ratio in the Pre-eclampsia group, often exceeding 10, compared to the more stable and lower ratios of 2-3 in the Control group. This elevated TGL/HDL ratio in Pre-eclampsia suggests a higher atherogenic risk and aligns with findings by Al Refaie et al. (2024), who reported similar increases in TGL/HDL ratios in Pre-eclampsia patients, indicating metabolic disturbances. Han et al. (2021) also observed elevated TGL/HDL ratios in conditions associated with metabolic stress, reinforcing the link between higher TGL/HDL ratios and increased cardiovascular risk in Pre-eclampsia. These correlations emphasize the metabolic alterations inherent in Pre-eclampsia[22, 23].

CONCLUSION

This study provides compelling evidence that pre-eclampsia is linked to significant alterations in lipid metabolism and Vitamin D levels. Women with pre-eclampsia exhibited an atherogenic lipid profile with elevated LDL, total cholesterol, triglycerides, and reduced HDL, alongside marked Vitamin D deficiency. A significant inverse relationship between Vitamin D levels and triglycerides was also observed. These findings suggest that dyslipidemia and Vitamin D deficiency may contribute to the endothelial dysfunction and inflammation characteristic of pre-eclampsia. Monitoring these parameters could help identify at-risk women, guiding early intervention. Future research should explore the therapeutic potential of lipid-lowering agents and Vitamin D supplementation.

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