



## An Observational Study to Evaluate Serum Lipid profile during 14-20 weeks of Pregnancy as Predictor of Hypertensive Pregnancy

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### Abstract

**Introduction:** Hypertensive disorders of pregnancy (HDP), including preeclampsia and gestational hypertension, remain major contributors to maternal and perinatal morbidity and mortality. Early identification of women at risk is critical to improving outcomes. Dyslipidemia during pregnancy has been proposed as potential predictive marker for HDP, with abnormal lipid metabolism contributing to endothelial dysfunction, vascular injury, and hypertension. This study aimed to evaluate whether serum lipid profile assessed between 14–20 weeks of gestation can predict development of HDP.

**Material and Methods:** A prospective observational cohort study was conducted in the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur, from October 2023 to May 2024. A total of 242 pregnant women between 14–20 weeks of gestation were enrolled after applying inclusion and exclusion criteria. Fasting venous blood samples were collected to assess lipid parameters (total cholesterol, triglycerides, HDL, LDL, and VLDL). Participants were followed until delivery for development of HDP. Data were analyzed using SPSS v23, with chi-square tests, t-tests, ANOVA, and ROC curve analysis applied.

**Results:** Of 242 women, 36 (14.87%) developed HDP. Among them, 12.40% had abnormal lipid profiles. Elevated total cholesterol was significantly associated with HDP ( $202.35 \pm 52.48$  vs.  $172.82 \pm 29.64$  mg/dL,  $p=0.0001$ ). Triglycerides, VLDL were higher in HDP cases but did not reach statistical significance. Total cholesterol showed highest diagnostic accuracy (80.12%), with specificity of 83.95%. Maternal age also significantly correlated with HDP risk, with higher prevalence in women  $>28$  years.

**Conclusion:** Serum lipid profile, particularly elevated total cholesterol in early second trimester, is a useful, non-invasive, cost-effective predictor of hypertensive disorders of pregnancy. Incorporating lipid screening into routine antenatal care may enable early risk stratification, closer monitoring, timely interventions to improve maternal and fetal outcomes.

**Keywords:** Hypertensive disorders of pregnancy, Preeclampsia, Lipid profile, Total cholesterol, Pregnancy prediction

### Introduction

Hypertensive disorders of pregnancy are a major global health concern, affecting about 10% of pregnancies worldwide. Among these, preeclampsia is the most severe form, complicating 3–5% of pregnancies and characterized by new-onset hypertension with signs of organ dysfunction, particularly involving the kidneys and liver. Pregnancy-induced hypertension, another subtype, manifests as elevated blood pressure after 20 weeks of gestation without proteinuria, and is seen in nearly 4% of pregnancies. Both conditions contribute significantly to maternal and perinatal morbidity and mortality, accounting for serious complications such as eclampsia, preterm delivery, and intrauterine growth restriction<sup>[1, 2]</sup>.

Hypertension in pregnancy is generally defined as a systolic blood pressure  $\geq 140$  mmHg and/or a diastolic blood pressure  $\geq 90$  mmHg, measured at least twice, four hours apart, after 20 weeks of gestation in a previously normotensive woman. The diagnosis may or may not be associated with proteinuria, which is considered significant when 24-hour urine protein exceeds 300 mg, a protein-to-creatinine ratio is  $\geq 0.3$ , or a dipstick test show  $\geq 2+$ . This classification encompasses chronic hypertension, gestational hypertension, and preeclampsia, reflecting the broad spectrum of hypertensive disorders encountered in clinical practice<sup>[3]</sup>.

The underlying pathogenesis of hypertensive disorders of pregnancy is complex and primarily attributed to abnormal

placentation and systemic endothelial dysfunction. Impaired trophoblastic invasion results in placental ischemia, oxidative stress, and increased secretion of anti-angiogenic factors, which disrupt vascular homeostasis. The resulting maternal endothelial cell injury manifests as hypertension, proteinuria, and systemic inflammation. Elevated levels of soluble fms-like tyrosine kinase-1 (sFlt-1) and other circulating factors further deplete vascular growth mediators, perpetuating the imbalance. Resolution of symptoms after delivery underscores the central role of the placenta in disease progression<sup>[4, 5]</sup>.

Early identification of women at risk for preeclampsia is critical for improving outcomes. Prophylactic measures such as low-dose aspirin initiated in high-risk pregnancies have been shown to reduce the incidence of early-onset preeclampsia, preterm birth, and intrauterine growth restriction by enhancing placental function. Predictive models have incorporated maternal demographic factors, uterine artery Doppler studies, and angiogenic biomarkers such as placental growth factor (PlGF) to improve detection rates. Metabolomic and biochemical markers, including uric acid, beta-hCG, alpha-fetoprotein, and inflammatory mediators, have also been studied as early predictors, although their utility remains variable<sup>[6, 7]</sup>.

Recently, dyslipidemia has emerged as a promising predictive marker of hypertensive disorders of pregnancy. Physiological hyperlipidemia is a normal feature of pregnancy, driven by elevated estrogen and insulin

resistance, but in preeclampsia this response is exaggerated. Elevated triglycerides, total cholesterol, very-low-density lipoprotein (VLDL), and low-density lipoprotein (LDL), accompanied by reduced high-density lipoprotein (HDL), are frequently observed in affected women. These abnormalities promote endothelial dysfunction, vasoconstriction, and thrombotic changes, all of which are central to the pathophysiology of hypertensive disorders [8, 9].

The mechanisms linking dyslipidemia to hypertensive disorders include estrogen-driven hepatic synthesis of triglyceride-rich VLDL particles and hyperinsulinemia that exacerbates lipid abnormalities. This imbalance alters prostaglandin metabolism, reducing the prostacyclin-to-thromboxane ratio, thereby favoring vasoconstriction and platelet aggregation. These vascular effects create a milieu conducive to the development of hypertension and proteinuria. Thus, abnormal lipid metabolism is thought to play a crucial role in the progression from normal pregnancy physiology to preeclampsia [10].

Serum lipid profiling during pregnancy offers a simple, cost-effective, and widely available tool for risk assessment. Unlike more advanced and expensive endocrine or angiogenic markers, lipid measurements can be routinely integrated into antenatal care. Several studies have suggested that lipid abnormalities detected as early as the second trimester, particularly between 14 and 20 weeks of gestation, may predict later development of hypertensive disorders. This window represents a critical period where early intervention strategies could be applied [11].

Uncontrolled hypertensive disorders during pregnancy can lead to life-threatening complications for the mother, including stroke, renal failure, and disseminated intravascular coagulation, as well as severe perinatal outcomes such as stillbirth, prematurity, and fetal growth restriction. Long-term effects extend beyond pregnancy, with evidence suggesting that offspring of affected mothers may have an increased risk of developing cardiovascular and metabolic diseases, including hypertension and diabetes, later in life [12].

Given these serious maternal and fetal consequences, the importance of identifying high-risk women early in pregnancy cannot be overstated. The present study was designed to evaluate the predictive potential of serum lipid profiles during 14–20 weeks of gestation, focusing on their association with hypertensive disorders of pregnancy. By exploring alterations in lipid metabolism during this key period, the study aimed to establish whether lipid profiling could serve as a reliable and cost-effective early marker. Detecting dyslipidemia in early pregnancy would not only allow closer monitoring but also facilitate timely interventions to improve maternal and perinatal outcomes [13].

Hypertensive disorders of pregnancy remain a leading cause of maternal and neonatal morbidity and mortality. The identification of predictive markers is central to prevention and early intervention. Dyslipidemia, as an emerging predictor, offers a practical and accessible option for risk assessment. Monitoring lipid profiles in early pregnancy has the potential to become an integral part of routine antenatal care, contributing to better management and reduction of complications associated with these disorders [14].

The aim of the study was to evaluate the serum lipid profile during 14–20 weeks of pregnancy as a predictor of hypertensive disorders of pregnancy. Specifically, the objectives were to analyze the serum lipid profile in pregnant women within this gestational period and to examine the association between abnormal lipid levels and the subsequent development of hypertensive disorders of pregnancy.

### Material and Methods

This prospective observational study was conducted at the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur from October 2023 to May 2024. Ethical approval has been obtained from the Ethical Approval Committee of SMS Medical College, Jaipur.

### Study Population

The study population comprised pregnant women with singleton pregnancies between 14 and 20 weeks of gestation, confirmed by first-trimester ultrasonography, who attended the antenatal clinic at SMS Medical College and provided informed consent. Women with pre-existing chronic hypertension, diabetes, renal disorders, thyroid dysfunction, lipid metabolism disorders, or those on lipid-lowering therapy were excluded. Multiple gestations, systemic illnesses affecting lipid metabolism, and refusal to participate or follow-up were also considered exclusion criteria.

### Data Analysis

Data were compiled and analyzed using SPSS version 23.0, with descriptive statistics expressed as mean  $\pm$  standard deviation for continuous variables and percentages for categorical data. Inter-group comparisons were performed using the Chi-square test for categorical variables and independent sample t-test or ANOVA for continuous variables. Receiver Operating Characteristic (ROC) curve analysis assessed the predictive value of lipid parameters, while diagnostic performance was evaluated using sensitivity, specificity, PPV, NPV, and accuracy. A p-value  $< 0.05$  was considered statistically significant.

### Results

**Table 1:** Incidence of HDP and Normotensive Across Subgroups

Group	Description	Number (N)	Percentage (%)
Group A	Normal Lipid + Normotensive	115	47.52%
Group B	Normal Lipid + HDP	6	2.48%
Group C	Abnormal Lipid + Normotensive	91	37.60%
Group D	Abnormal Lipid + HDP	30	12.40%
Total		242	100.00%

$\chi^2 = 17.26, df = 1, p < 0.001$

Out of 242 women, 14.88% developed HDP, with a significantly higher prevalence among those with abnormal lipid profiles (12.40%) compared to normal lipids (2.48%), showing a strong association between dyslipidemia and HDP ( $\chi^2 = 17.26, p < 0.001$ ).

The analysis of age group distribution between normotensive women and those with hypertensive disorders of pregnancy (HDP) revealed significant differences. Among normotensive women, the largest proportion was aged 23–27 years (31.8%), followed by 28–32 years (29.4%). In contrast, HDP was most common in women aged 28–32 years (30.6%) and 33–37 years (25.0%), with a notably higher proportion also seen in the 38–42 years group (11.1%) compared to only 2.3% among normotensive women of the same age. Statistical analysis ( $\chi^2 = 11.30, df = 4, p = 0.023$ ) confirmed a significant association between age and HDP, indicating that the likelihood of developing HDP increases with advancing maternal age.

**Table 2:** Descriptive Statistics of Age in Normotensive and HDP Groups

Parameter	Normotensive (N=206)	HDP (N=36)
Mean $\pm$ SD	27.05 $\pm$ 5.48	30.04 $\pm$ 6.10
Median	27	31
Range	18 - 42	18 - 42
$t = -3.57, p = 0.0005$		

Women who developed HDP had a significantly higher mean age (30.04 years) compared to normotensive women (27.05 years), with the difference being statistically significant ( $p = 0.0005$ ).

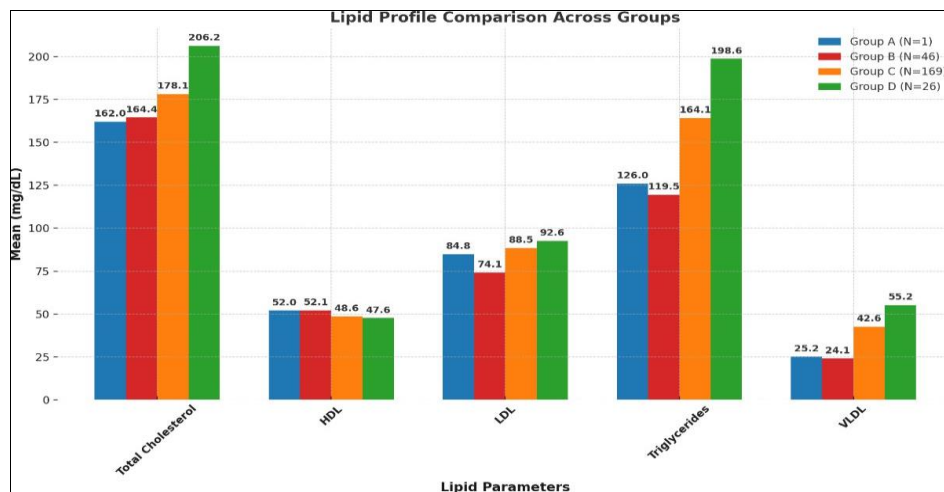
The study cohort had a mean maternal age of 27.85 years, mean gestational age at sampling of 17.12 weeks, baseline BP within normal range, mean gestational age at birth of 38.24 weeks, and a predominance of primigravida women (64.5%), reflecting a representative antenatal population.

**Table 3:** Comparison of lipid profile (mg/dl) between Normotensive and HDP Groups

Lipid Profiles	HDP (N = 36)	Normotensive (N= 206)	p- value
Total Cholesterol (mg/dL)	202.35 $\pm$ 52.48	172.82 $\pm$ 29.64	0.0001
HDL (mg/dL)	47.95 $\pm$ 9.85	49.45 $\pm$ 10.98	>0.05
LDL (mg/dL)	90.12 $\pm$ 26.75	84.72 $\pm$ 27.95	>0.05
Triglycerides (mg/dL)	198.87 $\pm$ 95.45	152.36 $\pm$ 40.58	>0.05
VLDL (mg/dL)	53.12 $\pm$ 34.75	37.85 $\pm$ 30.92	>0.05

Total cholesterol was significantly higher in the HDP group (202.35 mg/dL) than in normotensive women (172.82 mg/dL,  $p = 0.0001$ ), while triglycerides, VLDL, LDL, and

HDL showed no significant differences, indicating cholesterol as the key predictor of HDP.



**Fig 2:** Comparison of lipid profile between different sub-groups

Lipid profile comparison showed significantly higher total cholesterol, triglycerides, VLDL, and LDL in women with abnormal lipids and HDP (Group D), while HDL

differences were not significant, indicating dyslipidemia—except HDL—is strongly associated with hypertensive disorders of pregnancy.

**Table 4:** Sensitivity, specificity, PPV and NPV of lipid profile for predicting HDP

Variables	Sensitivity (%)	Specificity (%)	AUC	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Total Cholesterol	46.15	83.95	0.66	28.12	92.75	80.12
HDL	18.25	85.45	0.53	14.05	89.85	78.92
Triglycerides	57.85	52.35	0.54	13.78	90.65	53.1
VLDL	70.25	48.85	0.59	14.88	92.75	50.23
LDL	35.95	71.12	0.53	12.92	90.1	66.45

Among lipid parameters, total cholesterol showed the best predictive performance for HDP with high specificity (83.95%) and diagnostic accuracy (80.12%), while VLDL had the highest sensitivity (70.25%) but low specificity, and other markers like triglycerides, HDL, and LDL demonstrated limited standalone predictive value.

## Discussion

Hypertensive disorders of pregnancy (HDP), including preeclampsia and pregnancy-induced hypertension (PIH), affect 5–10% of pregnancies worldwide and remain a leading cause of maternal and perinatal morbidity and mortality. Preeclampsia alone complicates 3–5% of pregnancies and is defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP) and the American College of Obstetricians and Gynecologists (ACOG) as blood pressure  $\geq 140/90$  mmHg after 20 weeks of gestation, with or without proteinuria. The pathophysiology of HDP involves defective placentation, ischemia, oxidative stress, and endothelial dysfunction, mediated partly by anti-angiogenic factors such as soluble fms-like tyrosine kinase-1 (sFlt-1). Risk factors include chronic hypertension, diabetes, obesity, renal disease, advanced maternal age, and *in vitro* fertilization, while environmental and lifestyle factors also play important roles [15, 16].

Early diagnosis is crucial to prevent complications such as eclampsia, placental abruption, and maternal stroke. Predictive models such as the FMF triple test, which incorporates maternal factors, uterine artery Doppler indices, and angiogenic markers like PlGF, have shown utility in early screening. In addition, metabolomic studies suggest biochemical changes occur before the onset of HDP. Dyslipidemia is an emerging predictor, as pregnancy-induced hyperlipidemia is often exaggerated in preeclampsia, with increased triglycerides (TG), very-low-density lipoproteins (VLDL), total cholesterol (TC), and LDL, alongside decreased HDL. These abnormalities contribute to vascular injury, vasoconstriction, and thrombosis. Mid-pregnancy lipid profiling, particularly between 14–20 weeks, may therefore serve as a simple and cost-effective predictor [17].

This study of 242 women supports this association, showing that 12.40% of women with abnormal lipid profiles developed hypertensive disorders of pregnancy compared to only 2.48% with normal lipid levels ( $\chi^2 = 17.26$ ,  $p < 0.001$ ). Spracklen CN, *et al*; 2014, highlighted that elevated total cholesterol, triglycerides, LDL, and VLDL, along with reduced HDL, are linked to a higher risk of preeclampsia, reinforcing the predictive potential of dyslipidemia in early pregnancy [18].

Maternal age was another significant factor in the current study, which showed that women aged 28–32 years had the highest prevalence of hypertensive disorders of pregnancy (30.6%), while those above 33 years also faced increased risk. The mean age was notably higher in the HDP group (30.04 years) compared to normotensive women (27.05 years,  $p = 0.0005$ ). Zerihun E, *et al*; 2025, suggested that advancing maternal age contributes to a greater likelihood of developing hypertensive disorders during pregnancy [19]. Baseline characteristics of the study cohort included a mean maternal age of 27.85 years, mean gestational age at blood sampling of 17.12 weeks, and predominance of

primigravida women (64.5%). Most were normotensive at baseline, reflecting a representative antenatal population. Gootjes DV, *et al*. 2021 compared from the Generation R cohort emphasized long-term cardiometabolic consequences in offspring rather than maternal predictors, highlighting complementary research perspectives [20].

In terms of lipid parameters, total cholesterol was significantly higher in HDP women (202.35 mg/dL) than in normotensive women (172.82 mg/dL,  $p = 0.0001$ ), whereas TG, VLDL, LDL, and HDL showed no significant differences. Shaikh MK & Mittal S. 2018, who observed broader dyslipidemia—including elevated TG, LDL-C, and VLDL-C, and reduced HDL-C—in hypertensive women later in pregnancy. The discrepancy may be explained by the timing of lipid assessment, as the present study focused on early second trimester [21].

Further subgroup analysis showed the highest lipid levels in women with both abnormal lipid profiles and HDP, particularly for TC, TG, VLDL, and LDL. Similar patterns were reported by Arora N, *et al*; 2017, who demonstrated significantly elevated TG, LDL, and VLDL, along with reduced HDL and elevated  $\beta$ -hCG, as strong predictors of PIH. Both studies underscore the amplified risk when dyslipidemia coexists with other pregnancy complications [22].

Diagnostic performance analysis revealed that total cholesterol had the best specificity (83.95%) and overall accuracy (80.12%), making it the most reliable individual predictor. VLDL showed the highest sensitivity (70.25%) but lower specificity, while TG, HDL, and LDL had limited diagnostic value. Abdelaziz A, *et al*; 2012, in contrast, demonstrated superior prediction using integrated first-trimester biomarkers such as mean arterial pressure, uterine artery Doppler indices, and soluble endoglin, with AUC values above 0.80. Similarly, Abdelaziz A, *et al*; 2012, achieved higher accuracy (AUC 0.848) by combining BMI, cholesterol, uric acid, and proteinuria into a nomogram [23].

Xu X, *et al*; 2024, highlighted that mid-pregnancy dyslipidemia—particularly elevated total cholesterol—is significantly associated with hypertensive disorders of pregnancy. Maternal age further increases risk, and lipid profiling may serve as a simple, non-invasive screening tool. However, given the moderate predictive value of lipid parameters alone, integration into multifactorial risk models remains essential. Early lipid monitoring, alongside established predictive approaches, could improve risk stratification and enable timely intervention to reduce HDP-related complications [24].

## Conclusion

This study highlighted that dyslipidemia in the early second trimester is strongly linked to an increased risk of hypertensive disorders of pregnancy, with total cholesterol proving the most reliable predictor due to its moderate sensitivity and high specificity. While VLDL, triglycerides, and LDL were elevated, their predictive accuracy was lower, and HDL showed no significant difference. These results emphasize the role of endothelial dysfunction and metabolic imbalance in preeclampsia, suggesting that routine lipid profiling could help identify high-risk pregnancies early and reduce HDP-related maternal and fetal complications.

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