

**Serum Lipid Profile in 2nd Trimester as a Predictor of Hypertensive Disorder in Pregnancy**Arulmozhi<sup>1\*</sup>, Gayatri<sup>2</sup>, Pravallika M<sup>3</sup><sup>1</sup>Assistant Professor, Department of Obstetrics and Gynecology, Government Mohan Kumaramangalam Medical College, Salem<sup>2</sup>Assistant Professor, Department of Obstetrics and Gynecology, Government Mohan Kumaramangalam Medical College, Salem<sup>3</sup>Senior Resident, Thiruvallur Medical College and Hospital, Thiruvallur

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Conflict of interest: Nil

**Abstract:**

**Background:** Hypertension disorders represent the most common medical complication of pregnancy. Studies state that abnormal placentation and endothelial dysfunction are the key factors in the development of pre-eclampsia. Lipid levels in the early pregnancy can be a good predictor of development of preeclampsia. Dyslipidemia in early pregnancy leads to more oxidative stress by the formation of lipid peroxidases and reactive oxygen species, thus predisposing to development of pre-eclampsia. The pathological state of hypertension at the maternal period predisposing the condition of pre-eclampsia occurs due to reduced capacity of perfusion in placenta enhance the dysfunction of vascular endothelial system which arises from lesser invasion of cytotrophoblasts into the arteries of uterus. The research aims to estimate the lipid concentration in the second trimester of pregnancy for prediction of hypertension.

**Materials and Methods:** This study was done as a prospective cohort study at antenatal clinic, department of obstetrics and gynecology at Government Mohan Kumaramangalam medical college, Salem. Pregnant women with singleton pregnancy with LMP and USG confirmed pregnancy between 14 to 28 weeks of gestation were included in the study. A descriptive analysis was done among 100 pregnant women; they were subjected for routine investigations and clinical examination. Fasting blood samples collected from the selected pregnant women's for lipid profile analysis.

**Results:** The incidence of gestational hypertension in study was 34.3%. The total cholesterol ranging in the individuals tends to have the mean ranging  $214.76 \pm 72.25$  mg/dl and these individuals have greater range of mean score of TG level  $250.12 \pm 66.81$  followed by LDL mean score as  $116.28 \pm 45.55$  mg/dl with the lowest range of VLDL mean scoring predicted as  $36.34 \pm 19.54$  mg/dl. The total cholesterol, TG levels and VLDL have a significant effect on gestation hypertension in maternal period with the mean ranging as 25.32 and TG denoted as 277.69 whereas the values of HDL and LDL does not have any effect on GHTN.

**Conclusion:** The lipid profile acts as the most promising biomarker in identifying the condition of hypertension in the pregnancy. Lipid profile analysis in early 2<sup>nd</sup> trimester is a simple noninvasive and economical for the prediction of hypertensive disorders in pregnancy.

**Keywords:** Serum Lipid, HDL, LDL, Gestational Hypertension, Cholesterol, VLDL.

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**Introduction**

Hypertension disorders represent the most common medical complication of pregnancy. [1] According to world health organization (WHO) systemic review on maternal mortality globally hypertensive disease remains leading cause of maternal mortality. [2] Hemorrhage, hypertension, and infection forms the triad contributes to morbidity and mortality during pregnancy and childbirth. Studies state that abnormal placentation and endothelial dysfunction are the key factors in the development of pre-eclampsia. Lipid levels in the early pregnancy can

be a good predictor of development of preeclampsia. [3] Dyslipidemia in early pregnancy leads to more oxidative stress by the formation of lipid peroxidases and reactive oxygen species, thus predisposing to development of pre-eclampsia. The pathological state of hypertension at the maternal period predisposing the condition of pre-eclampsia occurs due to reduced capacity of perfusion in placenta enhance the dysfunction of vascular endothelial system which arises from lesser invasion of cytotrophoblasts into the arteries of

uterus. [4] This results in the hypoxic state of placenta inducing the inflammatory conditions and imbalances the angiogenic factors by stimulating the aggregation of platelets and causes the dysfunction of endothelium and results in pre-eclampsia.

The lipid level variations decrease the synthesis of prostaglandins and the thromboxane A2 concentration which paves the pathway for hypertension in pregnancy. Placenta serves a main pathway for synthesis of HCG but in case of hypertension due to hypoxic condition of placenta there was a trophoblastic invasion into the placenta and tends to rise the oxidative stress and peroxidation of lipid prone to dyslipidemia. [5]

PIH is defined as; in previously normotensive and normoproteinuric women, hypertension of  $\geq 140/90$  mmHg after gestational age of 20 weeks with/without proteinuria measured on two different times 6 hours apart [1]. The American College of Obstetricians and Gynaecologists (ACOG) has categorized pregnancy hypertensive disorders into four categories: gestational hypertension, where resting blood pressure (BP) is  $140/90$  mmHg or greater during the 20th gestation week; chronic hypertension, which develops before pregnancy or starts during gestational age till 20 weeks; preeclampsia (raised BP and edema or proteinuria)

Of all the pregnancies, pregnancy related hypertensive disorders complicate 5-10% and together they are the members of the dreaded triad-also including hemorrhage as well as infection-that contributes highly to maternal morbid conditions and deaths. Out of these, the most dangerous is pre-eclampsia syndrome, alone or superimposed on chronic hypertension. In all pathological consequences, oxidative stress is of utmost importance occurring in pregnancy related hypertensive disorders and correlated with poor placental perfusion

Hypertensive disorders are responsible for not only maternal death but also substantial morbidity for the pregnant women. Long term impact of hypertension in pregnancy in the form of chronic hypertension and increased lifetime cardiovascular risk. Hypertension disorders also carry risk for baby. Hypertension and or proteinuria is the leading single identifiable risk factor in pregnancy associated with stillbirth. [6] Pre-eclampsia is strongly associated with fetal growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome and cerebral palsy. Maternal mortality is much lower in high income countries than developing countries. About 16% of maternal deaths were attributed to hypertensive disorders in developed countries. Hypertensive disorders in pregnancy found to be the

second leading cause of maternal death. Based on this aim of our study is to estimate the lipid concentration in the second trimester of pregnancy for prediction of hypertension.

### Materials and Methods

This study was done as a prospective cohort study at antenatal clinic, department of obstetrics and gynecology at Government Mohan Kumaramangalam medical college, Salem. Pregnant women with singleton pregnancy with LMP and USG confirmed pregnancy between 14 to 28 weeks of gestation were included in the study.

A descriptive analysis was done among 100 pregnant women within 14-28 weeks admitted in the antenatal ward in Department of Obstetrics and Gynecology were selected based on inclusion and exclusion criteria after obtaining their informed consent. All selected women were subjected to a detailed history of age, parity, body weight, medication history, family history, detailed obstetrics history including previous history of gestational hypertension. They were subjected for routine investigations and clinical examination. Fasting blood samples collected from the selected pregnant women's for lipid profile analysis.

These patients were regularly followed up in the antenatal OPD once in 2 weeks and regular blood pressure monitoring, urine routine. According to International society for the study of hypertension (ISSHP) defined as systolic blood pressure  $>140$  mmHg or diastolic blood pressure  $>90$  mmHg.

The qualitative variables were expressed using frequency and percentages and the quantitative variables were expressed using mean and standard deviation. To compare distribution of qualitative variable, chi square test was employed. To compare the mean between two groups, independent sample -student 't' test was employed. P value of less than 0.05 was considered to be statistically significant. SPSS version 24 was used for analysis

### Results

In our study population of 100 pregnant women, 37% were in the age group 21 to 23 years and 32% in the age group 24 to 26 years. The mean age among the participants was  $23.34 \pm 2.77$  years. Among 100 women 32% were primi and 19% were G2P1L1. Also 34% were in 17<sup>th</sup> to 20<sup>th</sup> week of gestation and 33% were in 13 to 16<sup>th</sup> week of gestation. In our study group 42% belonged to upper lower class and 31% lower class.

Among 100 pregnant women in our study group. 72% participants had previous history of gestational hypertension. In our study group mean height among the participants was  $150.11 \pm 6.25$  cms. The mean weight among the participants was  $55.70 \pm$

9.53 Kgs. The mean BMI among the participants was  $27.21 \pm 3.34 \text{ Kg/m}^2$ .

The mean total cholesterol was  $214.76 \pm 72.25 \text{ mg/dl}$ . The mean HDL was  $57.45 \pm 19.75 \text{ mg/dl}$ . The mean LDL was  $116.28 \pm 45.55 \text{ mg/dl}$ . The mean TGL was  $250.12 \pm 66.81 \text{ mg/dl}$ , The mean VLDL was  $36.34 \pm 19.54 \text{ mg/dl}$ .

Among 100 women in our study group 35% participants developed GHTN during the study period. Among the participants who had developed GHTN, 34.3% belonged to age group 24 to 26 years and 28.6% belonged to age group 21 to 23 years while among those normal, 41.5% belonged to age group 21 to 23 years and 30.8% belonged to age group 24 to 26 years. Both the groups were similar with regard to distribution of age with P value of more than 0.05 (0.378).

In our study population who had developed GHTN, 51.4% were primi and 14.3% were G2P1L1 while among those normal, 21.5% were primi and G2P1L1, respectively. Both the groups were found to be statistically similar with P value of more than 0.05(0.078). Among the participants with GHTN, 34.3% were in gestational age 17 to 20 weeks and 31.4% were in gestational age of 13 to 16 weeks. Among those normal, 33.8% belonged to gestational age 13 to 16 weeks and 17 to 20 weeks,

respectively. Both the groups were similar with regard to distribution of gestational age with P value of more than 0.05(0.991).

In our study among mothers with GHTN, 42.9% were middle class and 37.1% were upper middle while among those normal, 44.6% were upper lower and 36.9% were lower. The proportion of participants in middle class was more in GHTN group than in the normal group with P value of more than 0.05(0.304). Coming to previous history among the participants with GHTN, 65.7% had previous history and among those normal, 75.4% had previous history. Both the groups were similar with regard to previous history with P value of more than 0.05. The mean height among the GHTN was  $149.29 \pm 4.91 \text{ cms}$  and that of the normal was  $150.55 \pm 6.86 \text{ cms}$ .

The mean height was similar in both the groups with P value of more than 0.05. The mean weight among the GHTN was  $54.47 \pm 9.16 \text{ Kgs}$  and that of normal was  $56.31 \pm 9.74 \text{ Kgs}$ . The mean weight was similar in both the groups with P value of more than 0.05. The mean BMI among the GHTN was  $27.17 \pm 3.07 \text{ Kg/m}^2$  and that of normal was  $27.23 \pm 3.49 \text{ Kg/m}^2$ . The mean BMI was similar between those developed GHTN and normal with P value of more than 0.05.

**Table 1: Comparison of mean total cholesterol and triglycerides between GHTN and normal**

Variable	GHTN		Normal		t value	P value
	Mean	SD	Mean	SD		
Total cholesterol (mg/dl)	253.22	64.19	194.05	68.12	4.22	0.001
Triglycerides (mg/dl)	277.69	71.73	235.28	59.42	3.16	0.002

The mean total cholesterol among the GHTN was  $253.22 \pm 64.19 \text{ mg/dl}$  and that of normal was  $194.05 \pm 68.12 \text{ mg/dl}$ . The mean total cholesterol was significantly more in the GHTN group than in the normal with P value of less than 0.05. The mean triglycerides among the GHTN was  $277.69 \pm 71.73 \text{ mg/dl}$  and that of normal was  $235.28 \pm 59.42 \text{ mg/dl}$ . The mean triglycerides were significantly more in the GHTN group than in the normal with P value of less than 0.05.

**Table 2: Comparison of mean HDL, LDL and VLDL between GHTN and normal**

Variable	GHTN		Normal		t value	P value
	Mean	SD	Mean	SD		
HDL (mg/dl)	57.39	17.46	57.49	21.01	0.023	0.981
LDL (mg/dl)	119.82	39.01	114.37	48.89	0.569	0.571
VLDL (mg/dl)	45.83	23.68	31.22	4.73	3.80	0.001

The mean HDL among participants with GHTN was  $57.39 \pm 17.46 \text{ mg/dl}$  and that of normal was  $57.49 \pm 21.01 \text{ mg/dl}$ . The mean HDL level was found to be similar between GHTN developed and normal participants with P value of more than 0.05.

The mean LDL among the GHTN was  $119.82 \pm 39.01 \text{ mg/dl}$  and that of normal was  $114.37 \pm 48.89 \text{ mg/dl}$ . The mean LDL level was found to be similar between GHTN developed and normal participants with P value of more than 0.05. The mean VLDL among the GHTN was  $45.83 \pm 23.68 \text{ mg/dl}$  and that of normal was  $31.22 \pm 4.73 \text{ mg/dl}$ . The mean

VLDL was significantly more in the GHTN group than in the normal with P value of less than 0.05.

### Discussion

Hypertension during maternity is becoming the greatest concern as it tends to affect the overall healthy life of individuals. The hypertension particularly occurring at the maternal period poses the greater risk to the life of the offspring and this problem continues to persist in the entire world.

Various multiple factors trigger the person to be susceptible to the systemic disorders which includes excessive storage of fat in the body parts

includes lack of exercise, irregular intake of dietary patterns and lifestyle behavioral habits, stress etc.

The research findings of this study stated majority of individuals belonged to the respective ages of 21 to 23(37%) and 34% individuals were belonged to the maternal period of 17 to 20 weeks. Almost majority of the persons belonged to the upper lower class (42%) followed by 31% people belonged to lower class. The 72% people had the history with the previous occurrence of GHTN with the BMI ranging with the mean of  $27.21 \pm 3.34$  kg/m<sup>2</sup>. Almost 65.7% individuals with condition of GHTN have the previous history related to HT. However, the previous occurrence of HT had no effect on the occurrence of HT in the maternal phase of people. Research stated BMI tend to cause major complication in individuals at their maternal life including Preeclampsia, GDM and HT and makes the person more susceptible to the complications of fatality. [7] The total level of cholesterol ranging in the individuals tends to have the mean ranging  $214.76 \pm 72.25$  mg/dl and these individuals have greater range of mean score of TG level  $250.12 \pm 66.81$  followed by LDL mean score as  $116.28 \pm 45.55$  mg/dl with the lowest range of VLDL mean scoring predicted as  $36.34 \pm 19.54$  mg/dl.

Wang et al [8] suggested that variations occurring in the levels of lipid range had an ultimate impact in determining the pressure variations in the blood of humans and simultaneously the CRP parameter also the key predominant variable in detecting the condition HT status along the triggering possible factor in the determination of PE and HT condition in individuals.

The current research reported 35% of the persons have the condition of HT at the gestational phase. The GHTN is predominant among the individuals with the respective age of 24-26 years during the maternal age of 17 to 20 weeks with the rate reported to be 34.3% and they don't have any influential effect on GHTN condition. The varied from the research estimated that 26% individuals had developed the condition pertaining to the state of hypertensive condition which was lower compared to the present research. [8]

The social economic variables had a greater significant effect on triggering the condition of HT in maternal phase with the prevalence to be maximum among people pertaining to the middle class with the range denoted as 42.9%. BMI does not have any influential effect on hypertension. This highly correlated with the research stated that SES had no effect in triggering the condition of hypertension at the maternity period.

Another study done by Maria et al [9] was differed from the present data stated that socio economic variable had a great significance in the occurrence of PIH. Present research stated that total

cholesterol, TG levels and VLDL have a significant effect on HT in maternal period with the mean ranging as 25.32 and TG denoted as 277.69 whereas the values of HDL and LDL does not have any effect on GHTN.

This highly correlated with study stated that lipid levels pertaining to the individuals suffering from PIH had greater range in respect of HDL, LDL and all form of cholesterols and are highly influential in triggering the development of HT.

Another research reported by De et al [4] that enhanced range of triglycerides specifically in the maternal time was seems to be more along with the highest range of VLDL was noted and also comparatively lowest LDL range reported in the persons with no any abnormality in maternity and there were no variations in the range particularly in HDL level seems particularly in the normal maternal period.

Hemanth deshpande et al [10] were reported cholesterol, LDL, VLDL and triglyceride levels were gradually increasing from Mild PIH to Severe PIH to Eclampsia, while HDL levels were gradually decreasing from Mild PIH to Severe PIH to Eclampsia. Many studies observed that preeclampsia preceded by dyslipidemia, particularly hypertriglyceridemia and elevated lipoprotein, which indicates they may be etiologic and pathophysiologic mechanism responsible for preeclampsia. Many mechanisms were investigated regarding association between dyslipidemia and preeclampsia. Altered lipid levels in serum results in oxidative stress stimulated by linoleic acid, which in turn cause endothelial dysfunction. This is one of the pathophysiologic events responsible for development of preeclampsia. Preeclamptic women had both a higher ratio

of free fatty acids to albumin and increased lipolytic activity, resulting in enhanced endothelial uptake of free fatty acids, which are further esterified to triglycerides. Thus, pre pregnant weight reduction and life style modification may help in reducing the occurrence of preeclampsia. [11]

## Conclusion

Detecting dyslipidemia before 20 weeks of gestation would help us to recognize pregnancies at high risk for preeclampsia even before the clinical syndrome. Early recognition would help us in offering better surveillance to detect and treat the disease earlier for a better maternal and perinatal outcome.

The determination of insulin levels, inflammatory markers in early pregnancy and then followed by a thorough assessment of the outcome through a large cohort study, may help in addressing the role of metabolic syndrome in causation of preeclampsia. Due to early detection of altered lipid profile in pre-eclampsia incidence of complication

can be decreased which in turn reduce the fetomaternal morbidity and mortality.

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