Evaluation of Predictor like Maternal Serum Lipid Profile in 2nd Trimester in Pregnancy Related Hypertensive Disorders

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Authors’ contributions

This work was carried out in collaboration between both authors. *All authors read and approved the final manuscript.

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ABSTRACT

Background: The most leading cause of perinatal and maternal deaths and morbidity in developed and developing countries like India is pregnancy related hypertensive disorders especially pre-eclampsia. PIH is defined as; in previously normotensive and normoproteinuric women, hypertension of >_140/90 mmHg with or without proteinuria measured on two occasions 6 hours apart after gestational age (20 weeks). Women with pregnancy related hypertensive disorders experience varied and altered lipid changes. Increased TG, low-density lipoprotein cholesterol (LDL-C), cholesterol and decreased high-density lipoprotein cholesterol (HDL-C) concentrations leading to dyslipidemia was found in majority of the studies.

Aim: The study aims to evaluate predictor like maternal sr. lipid profile in 2nd trimester in pregnancy related hypertensive disorders.

Objective: To evaluate the occurrence of normal maternal and altered maternal serum lipid profile in 2nd trimester of pregnancy in pregnancy related hypertensive disorders and compare them.

Materials and Methods: The design of the study will be prospective as well as observational.

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Conducted from September 2020 to August 2022 with an estimated sample size of 1000. Patients included were normotensive and non-proteinuric in second trimester (13-20 weeks of gestation). Subjects will be evaluated on the basis of preformed and pretested proforma consisting of history, clinical symptoms and presentation and investigations. Blood samples for serum lipid profile will be collected in plain bulb with aseptic conditions and analyzed at the biochemistry laboratory by enzymatic method.

**Expected Results:** We expect that from our results, altered maternal serum lipid profile in 2nd trimester will be positively associated with pregnancy related hypertensive disorders.

**Keywords:** Maternal serum lipid profile; hypertensive disorder; second trimester.

### 1. INTRODUCTION

One of the most leading cause of perinatal and maternal morbidity conditions as well as deaths in developed as well as developing countries is pregnancy related hypertensive disorders especially pre-eclampsia.

PIH is defined as; in previously normotensive and normoproteinuric women, hypertension of > 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).

It is also a continuous effort by obstetricians to recognize and if possible, foresee the risk involved in pregnancy. Prevention will follow automatically if predicting becomes feasible. Several approaches have been suggested to classify pregnant women who are at risk of hypertensive disorders. This include the roll over test, angiotensin II pain reaction, tests like isometric hand grip exercise, and test of mean arterial pressure (MAP). Yet none were generally accepted as screening procedures in the clinical trial. But none has been accepted widely as screening test in the clinical setting, because of their complex nature, the high chances of false positive results and observational subjective nature of interpreting the results. There is currently no single, easily available, reliable and cost effective screening test for hypertensive disorders of pregnancy.

Of all the pregnancies, pregnancy related hypertensive disorders complicate 5-10% and together they are the members of the dreadful triad- also including hemorrhage as well as infection- that contributes highly to maternal morbidity 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 [2].

Women who develop pregnancy related hypertensive disorders experience drastic lipid changes. Most studies indicate increased TGS, cholesterolloiprotein with low-density cholesterol (LDL-C) and decreased lipoprotein with high-density cholesterol (HDL-C) levels leading to dyslipidemia [3-4].

There are currently no clinically effective screening tests to detect the onset of preeclampsia. A fall in the PGI2:TXA2 ratio is observed due to alteration in lipid synthesis; which becomes an essential means of pathogenesis in pregnancy-related hypertensive disorders.

**Aim:** The study aims to evaluate maternal serum lipid profile in 2nd trimester of pregnancy as a predictor of pregnancy related hypertensive disorders.

#### 1.1 Objectives

- To evaluate the occurrence of normal maternal serum lipid profile in second trimester of pregnancy in pregnancy related hypertensive disorders.
- To evaluate the occurrence of altered maternal serum lipid profile in second trimester of pregnancy in pregnancy related hypertensive disorders.
To compare the above two objectives

1.2 Research Question

Does altered maternal serum lipid profile in 2nd trimester of pregnancy is a predictor of pregnancy related hypertensive disorders.

2. MATERIALS AND METHODS

2.1 Place of Study

The study will be carried out in the Department of OBGY, at AVBRH at Sawangi (Meghe), Wardha, Maharashtra, India.

2.2 Duration of Study

From September 2020 to August 2022 (Two years).

2.3 Study Design

Prospective observational study.

2.4 Sample Size

Estimated Sample size is 1000 based on study duration, Calculated by using the following formulae

\[ N = \frac{(Z_{a})^2 \times [p \times q]}{d^2} \]

Symbol ^ means ‘to the power of’  
* means; multiplied by’  
p=prevalence of population  
q=(100-p)  
d -the precision of the estimate.(20% of prevalence)

3. ENROLLMENT CRITERIA FOR SUBJECTS UNDER STUDY

3.1 Inclusion Criteria

- Live singleton pregnancy
- Normotensive and non-proteinuric at the time of enrollment
- Second trimester (gestational 13-20 weeks)
- Willing to participate in the study

3.2 Exclusion Criteria

- Clinical proof of medical and metabolic condition in pregnancy including critical hypertension, pregestational diabetes, renal failure
- Multiple gestation
- Congenital malformations
- Molar pregnancy

4. METHODOLOGY

The study will be done on all the eligible pregnant, normotensive, non-proteinuric women who attended the antenatal OPD between the second trimester (gestational age of 13–20 weeks). They will be screened for eligibility for inclusion in the study. Eligible women as per criteria will be enrolled. Written informed consent will be taken. Subjects will be analyzed on the basis of preformed and preevaluated proforma with respect to history, investigations and clinical examinations. Blood samples for serum lipid profile will be collected in plain bulb with aseptic conditions.

These will then be analyzed at the biochemistry laboratory by enzymatic method. We shall be applying for funding from intramural grant or ICMR grant or concession for synopsis.

Hypertensive disorders in pregnancy are included when systolic bp is >140mmhg and diastolic >90 mmhg 6 hours apart on any two events within 24 hours with or without proteinuria. All such patients have commonly other attached symptoms like blurring of vision, seeing dark spots, photophobia, headache etc. Routine hematological investigations along with serum lipid profile will be sent for such patients. Urinalysis will be done in the The cases will be followed before the conclusion of infancy for the occurrence of hypertensive diseases linked to pregnancy. Gestational age would be determined at the time of entry from the accurate dates of menstrual records by history questioning and early ultrasonographic foetal crown rump length calculation. Richter's mercury msphygmonanometer, the gold standard for blood pressure measurements, will measure blood pressure.

After making the patient relaxed, BP can be registered to ensure that there is no extreme exertion, feeding or smoking or exposure to cold in at least half an hour prior to the recording. It would strip all tight clothes from the arm. Blood pressure tests will be taken with the patient seated with the cuff positioned snugly over the brachial artery based on her right arm, ensuring that the lower mercury column was at the level of
the breast, with her forearm supporting on a side table and the manometer on a flat surface.

4.1 Statistical Analysis

In numbers and percentages, the continuous data will be tabulated as mean and standard deviation and discrete categorical percentage. The t-test of an individual student would be extended to continuous comparative variables such as (Lipid profile: TC, TG, HDL-C, VLDL-C, LDL-C; Blood pressure: SBP and DBP). The chi-square ($\chi^2$) test will be used to evaluate significance of the study.

Univariate binary logistic regression analysis will be used to determine risk factors associated with the lipid profile. Modified multivariate logistic regression study will be carried out in order to evaluate the relevant independent indicator for hypertensive pregnancy disorders.

Adjusted demographic variables will be used to do the univariate and multivariate study. The statistical significance of $p<0.05$ will be considered significant. All analysis will be carried out using the 24.0 version of SPSS.

5. EXPECTED RESULTS

We expect that from our results, altered maternal serum lipid profile in second trimester will be positively associated with pregnancy related hypertensive disorders.

6. DISCUSSION

For both mother and infant, hypertensive disorders can be life-threatening, raising both foetal and maternal morbid conditions and deaths. Cardiovascular disease in the mother occurs later in life, such as ischemic heart disease, chronic hypertensive disorders and stroke in PIH patients [5].

Preeclamptic patients also have an increased risk of placental abruption, acute renal failure, and neurological complications. Hypertensive conditions cause 15 per cent of all premature births, blindness, seizures, deafness, respiratory and learning difficulties in infants, in addition to causing complications and mortality in pregnant hypertensive women [6]. The perinatal mortality rate among preeclamptic pregnancies is five times as high as non-preeclamptic pregnancies in developed nations. In later life, babies born to pre-eclamptic mothers have an elevated chance of developing hypertension and diabetes mellitus [7]. Increament in diastolic blood pressure above 110 mmHg with signs of vascular retinal spasm suggest changes in the maternal portion of placental vascular system leading to IUGR [8].

This particular trophoblast converts into endothelial phenotype cells during the placental invasion, replacing the maternal endothelium’s spiral arteries in a phase called ‘pseudovasculogenesis.’

In preeclampsia, due to characteristic pathophysiological events, this process has not been significant. Invasion of cytotrophoblasts is shallow, limited to the upper layer of the decidua because they fail to mimic a vascular adhesion like phenomenon. They cannot convert the maternal spiral arteries to capacitance vessels which are high caliber, and they remain resistance vessels which are small caliber. Consequently, the placental morphology consists of small myometrial arteries and less number of arteriovenous shunts. As the fetus keeps growing, these placental vessels are not sufficient to provide sufficient perfusion. Consequently, the failed trophoblastic invasion and the impaired vascular remodeling lead to hypo perfusion of the placenta [9].

The clinical manifestation of pregnancy related hypertensive disorders is very much caused by dyslipidemia, particularly increased triglyceridemia and increased lipoprotein levels and thus may be of demographic and pathophysiologic importance in pregnancy related hypertensive disorders [10]. Endothelial dysfunction is induced by elevated plasma lipid and lipoprotein leading to oxidative stress. Dyslipidemia may come in the way of trophoblastic invasion thus contributing to a series of events that causes pregnancy related hypertensive disorders [11].

We ought to determine whether measurement of maternal serum lipid profile might have a predictive value in pregnancy related hypertensive disorders, because preeclampsia is a trophoblastic disorder and altered lipid metabolism seems to be of significant value in the pathogenesis [12-13]. A number of related studies were reported. Yadav et al. reported about serum lipid profile of women with preeclampsia and normotensive pregnancy [14]. Ambad et. al. studied association of lipid profile and uric acid levels in normotensive,
pre-eclamptic pregnancy [15]. Few of the relevant studies and cases were reviewed [16-18]. Issues related to antenatal care and services in this region were reported [19-25].

7. CONCLUSION

There exists positive correlation between serum lipid profile as a marker of pregnancy related hypertensive disorders. In present time, there is need of validation of non-invasive tests like biomarkers for disease detection. So the study is planned to determine altered levels of serum lipids in women with singleton pregnancy with hypertensive disorders of pregnancy.

Our finding that abnormally elevated lipid levels are predictive markers of hypertensive disorders can be beneficial as this screening can help classify antenatal women into high and low risk groups. Those at high risk could then be targeted for appropriate risk specific intervention before developing the overt disease to give better fetal outcome and to decrease fetal as well as maternal morbidity and deaths. This will be of great value in rural areas where there are limited resources, lack of awareness and difficult access to modern methods. This will also help in periphery so that early referral to higher centres can be planned.

IMPLICATIONS

As serum lipid profile collection is easy, non-invasive, cost-effective requiring simple instruction for collection. So such testing will be a useful predictor for monitoring hypertensive disorders at community and hospital setting.

Thus, from a practical side of view, we suggest that maternal serum lipid level can be used as a screening test for early diagnosis of hypertensive disorders and a efficient, cost-effective, non-invasive additional to clinical management to identify patients at risk of hypertension.

LIMITATIONS

Further studies with large sample size will be required to study the levels of sr. lipids in pregnancy for prediction of hypertensive disorders in pregnancy.

Limitations were

1. The sample size for this study was small.
2. Patients were lost to follow up because of lack of awareness.
3. A single spot serum lipid profile estimation in early second trimester and its correlation to development of hypertensive disorders has been attempted.

SUGGESTED STUDIES

Further such studies are needed with a larger sample size and sr. lipid profile should be repeated to evaluate the increasing trend of pregnancy related hypertensive disorders.

ETHICAL APPROVAL

Ethical Clearance will be taken from the ethical committee of JNMC, Sawangi, (Meghe), Wardha.

CONSENT

All the details about the way of study methodology and its significance in the study were explained to all patients selected for the study. Informed valid written consent was recorded from all eligible subjects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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