SERUM LIPID PROFILE AMONG PREGNANT WOMEN WITH GESTATIONAL AGE OF 10-16 WEEKS: A HOSPITAL BASED STUDY

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ABSTRACT

BACKGROUND

Pregnancy greatly increases demand for metabolic fuels that are needed for growth and development of the foetus and its support structures. The major change in energy expenditure and in the accumulation of fat occurs at different times during pregnancy. Altered metabolic and hormonal status of the body in pregnancy leads to changes in lipid profile. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. Abnormal lipid metabolism seems important in the pathogenesis of Pregnancy Induced Hypertension (PIH). The association of serum lipid profile with gestational proteinuric hypertension is highly suggested to reflect some new diagnostic tools.

This study was done to investigate the effect of pregnancy on lipid profile changes during 10 to 16 weeks of pregnancy.

MATERIALS AND METHODS

A total of 497 pregnant women between the age group of 17 and 43 years were enrolled after getting written informed consents from the patients. Patients with diabetes and ultrasound diagnosed foetal congenital anomaly were excluded. Data were computerised and analysed.

RESULTS

Mean (SD) triglyceride and total cholesterol levels were 189.9 (36.85) and 209.9 (28.670) respectively. Mean (SD) of triglyceride values was visibly higher in PIH group than that of normotensive.

CONCLUSION

Conclusively, altered maternal serum lipid profile increases in susceptibility to the development of PIH and gestational proteinuric hypertension and other foetal diseases induced preterm birth and intrauterine growth restriction. Therefore, lipid profile estimation and monitoring should be made a part of routine investigation during antenatal period. Further studies are needed to determine if certain women are at increased risk of cardiovascular, hypertensive diseases in later life because of effects on their lipid profile during pregnancy.

KEYWORDS

Pregnant Women, Lipid Profile, PIH.


INTRODUCTION

Pregnancy is a new sequence of events after fertilisation of ovum. It is accompanied by changes in maternal lipoprotein, which may serve for satisfying a foetus nutritional demand.[1] In pregnant woman, lipid profile changes during pregnancy are a result of physiological adaptation to the state of pregnancy. There are increases in the blood concentration of Cholesterol, Triglycerides, LDL cholesterol, VLDL cholesterol and decreases in HDL cholesterol.[2]

The lipid profile tests include total Cholesterol, Triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol. Several studies have shown that endothelial dysfunction is related to hyperlipidaemia.[3] The most important feature in preeclampsia is hypertension, which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain.[4] The recognition of abnormality in lipid profile during early pregnancy is important for the welfare of the mother as well as the growing foetus.

Hypertension during pregnancy is an important problem globally. Hypertensive disorder affects up to 8% of all pregnancy. A variety of biochemical markers has been proposed for the purpose of predicting the development of pre-eclampsia later in pregnancy. At present four hypothesis are the subject of extensive investigation; these include placental ischaemia, altered endothelial cell function, immune maladaptation and genetic imprinting. Placenta is the known primary trigger of Pregnancy Induced Hypertension (PIH). Women with PIH have hyperplacentosis or abnormal placentation maternal plasma lipids are significantly elevated during pregnancy. There are also evidences suggesting that
abnormal lipid metabolism during early pregnancy could be the factors for subsequent development of PIH.\(^{(4,5)}\)

In the present study, we estimated maternal serum lipids during 10 to 16 weeks of pregnancy to investigate the clinical utility of second trimester maternal serum lipid level as a predictive test for PIH. In this study, pregnancy induced hypertension will refer to both transient hypertension (Unaccompanied by proteinuria) and pre-eclampsia (Proteinuric hypertension of pregnancy).

**MATERIALS AND METHODS**

This study was carried out in the Department of Biochemistry, Jawaharlal Nehru Institute of Medical Sciences, Imphal in collaboration with the Department of Obstetrics and Gynaecology during the period of May 2014 to April 2015. After getting approval from Institutional Ethics Committee, a total of 493 pregnant women between the age of group 17 and 43 years who attended the ante-natal outpatient department of Obstetrics and Gynaecology were selected for the study. All the subjects were similar low economic status and dietary habit. They were abstained from smoking and alcoholism.

**Inclusion Criteria**

Pregnant women with gestational age between 10 to 16 weeks were selected irrespective of parity ultrasound screening was done, if menstrual history and clinical examination findings were not correlating, to find the exact period of gestation. Detail history of height, weight and blood pressure of all the study subjects were taken and noted down at the time of blood sample collection. Maternal education, religion, race, socio-economic status, family history of pre-eclampsia, past medical history and physical activity during pregnancy were noted. Systemic examination with special reference to blood pressure and gestational week were carried out and relevant antenatal investigations were done.

**Exclusion Criteria**

Pregnant women with hypertension diagnosed before 12 weeks of gestation, multiple pregnancy and ultrasound proof of congenital foetal anomaly were excluded. Out of the 497 pregnant women selected initially, 448 women who completed their pregnancy and delivered at our hospital were evaluated. Definition were used for pregnancy induced hypertension and proteinuria. PIH was defined as systolic blood pressure of 140 mmHg with a > 30 mmHg rise and/or diastolic blood pressure of 90 mmHg with a rise of 15 mmHg occurring on two or more occasions after 16 weeks of gestation. Pre-eclampsia was defined as gestational hypertension and proteinuria of at least 2+ or 1 gm per litre on dip stick or 24-hour urinary protein excretion more than 0.3 gm. Fasting venous blood (3 mL) was collected and tests were carried out on the same day. Serum lipid level estimation was done by enzymatic colorimetric test with Lipid Clearing Factor (LCF) using kits marketed by Human Gesellschaft fur Biochemica and Diagnostica mbH, Max-Planck-Ring 21, D65205 Wiesbaden, Germany. LDL – cholesterol and VLDL - cholesterol in values in mg/dL are indirectly calculated. The cases were followed up regularly in the antenatal OPD till delivery. All the detailed data were collected from delivery log book.

Statistical Analysis

Statistical analysis was performed by the SPSS version 18. Means±SD of all the parameters of interest were calculated for PIH and for normal separately and difference of means between groups was tested by t-test. Multiple logistic regression model was used to estimate the causal effect of each predisposing factor on response variables. Their effects were measured in terms of Odds Ratio for better and easy interpretation.

**RESULTS**

A total of 497 cases were analysed in the study; 80 cases developed PIH, while 417 cases remained normotensive. The prevalence rate of 17.66% were observed among the PIH group. Maximum PIH developed in the elderly primiparous group (52%) belonging to the age group of 30-34 years. Among the study group, the mean age ±SD was 27.71±6.170. Table 1 Blood pressure for PIH cases at the time of delivery was significantly higher than that of normotensive group (p 0.000). Total cholesterol and very low density lipoprotein values for PIH cases were significantly higher than the corresponding total cholesterol and very low density lipoprotein values for normotensive woman (p < 0.000 and p 0.27, respectively). The mean value of high density lipoprotein among PIH and normotensive group was similar. Mean±SD of triglyceride values was visibly higher in PIH group than that of normotensive group. Table 2 comparison of blood pressure at the time of booking (10-16 weeks) between the study and the normotensive group did not vary significantly. Median values for age, weight and haemoglobin were found to be the same for both the groups. However, median values of all the total cholesterol, very low density lipoprotein and low density lipoprotein for PIH group were found to be higher than the corresponding values of normotensive group. Out of 80 PIH cases, 77 had dyslipidaemia and the percentage detection of PIH dyslipidaemia as markers was 96.25%.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr.)</td>
<td>17-43</td>
<td>27.71 (6.170)</td>
</tr>
<tr>
<td>TC</td>
<td>146.2-309.0</td>
<td>209.9 (28.670)</td>
</tr>
<tr>
<td>TG</td>
<td>114.28-333.3</td>
<td>189.9 (36.85)</td>
</tr>
<tr>
<td>HDL</td>
<td>32.94-80</td>
<td>46.8 (9.95)</td>
</tr>
<tr>
<td>VLDL</td>
<td>22.86-66.6</td>
<td>38.1 (7.52)</td>
</tr>
<tr>
<td>LDL</td>
<td>71.16-193.0</td>
<td>122.4 (22.65)</td>
</tr>
</tbody>
</table>

**Table 1: Mean (SD) and Range of Serum Lipid Profile in the Study Population (n=497)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>PIH (n=80) Mean±SD</th>
<th>Normotensive (n=417) Mean±SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>237.19±33.95</td>
<td>204.15±23.74</td>
<td>0.000</td>
</tr>
<tr>
<td>TG</td>
<td>213.94±51.07</td>
<td>197.78±59.20</td>
<td>0.590</td>
</tr>
<tr>
<td>HDL</td>
<td>48.88±11.76</td>
<td>48.08±12.59</td>
<td>0.753</td>
</tr>
<tr>
<td>VLDL</td>
<td>52.70±11.86</td>
<td>46.48±13.08</td>
<td>0.27</td>
</tr>
<tr>
<td>LDL</td>
<td>135.47±27.12</td>
<td>109.30±17.28</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Table 2: Comparison of Mean±SD of Serum Lipid Profile between PIH Patients and Normotensive Pregnant Women Group**
DISCUSSION
In this study, 497 pregnant women including primigravids (66%) were recruited from the antenatal OPD. The cases were divided into the study group comprising of 80 pregnant women who subsequently developed PIH and the remaining 417 women who remained normotensive as the control group giving the prevalence rate of 17.66%. The present study shows that there is an association between maternal early pregnancy dyslipidemia, particularly hypertriglyceridaemia and the subsequent risk of pre-eclampsia. Those pregnant women who developed pre-eclampsia had increased cholesterol and low density lipoprotein cholesterol concentrations as compared to pregnant women who remained normotensive. The inverse relationship between pre-eclampsia risk and high density lipoprotein concentration was not evident. The association between dyslipidemia and the risk of pre-eclampsia is biologically plausible. The principle modulator of this hypertriglyceridaemia is oestrogen as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL. This process may be modulated by hyperinsulinism found in pregnancy. Serum triglycerides concentration also rose much more significantly in PIH of pregnancy in our study, which corroborated with the findings of many workers. The above mentioned interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction in gestosis. Increased TG found in pregnancy-induced hypertension is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small dense LDL.

In the study of Tanja G et al it was found that plasma TG levels, but not TC levels, in first term of pregnancy were independently and positively associated with adverse pregnancy outcomes, which is consistent with our study. Increasing evidence suggests that elevated plasma lipids may induce endothelial dysfunction. Dyslipidemia mediated activation of the endothelial cells to the placental-derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of placental-derived factors with the lipoproteins could be regarded as possible contributors for pathogenesis of PIH. Thus, the assessment of blood lipids may be helpful in prevention of complications in PIH.

Our results when considered with those of earlier prospective studies indicate that dyslipidemia, particularly hypertriglyceridaemia and elevated lipoprotein precede the clinical symptoms of pre-eclampsia. Thus dyslipidemia may be of aetiological and pathophysiological importance in this relatively common complication of pregnancy. There are at least three hypothesised mechanisms for the dyslipidaemia and pre-eclampsia association have been described in the literature. First, Lorentzen B et al in their study of plasma lipid and vascular dysfunction in pre-eclampsia have noted that elevated plasma lipid and lipoprotein may induce endothelial dysfunction secondary to oxidative stress. The second mechanism is the changes in pathological process via dysregulation of lipoprotein lipase resulting in a dyslipidaemic lipid profile. In a study by Lorentzen B, Drevon C et al shows that sera from pre-eclamptic women had both a higher ratio of free fatty acids to albumin and increased uptake of free fatty acids, which are further esterified to triglycerides. A third possible mechanism may be via the metabolic syndrome. Metabolic disorder like “insulin resistance syndrome” namely hyperinsulinaemia and hyperuricaemia are also present in pre-eclampsia. The most frequent lipid abnormality is hypercholesterolaemia. Hypercholesterolaemia and hypertriglyceridaemia have been attributed to the hormonal effect of progesterone and oestrogen. Maternal hypertriglyceridaemia is a characteristic feature during pregnancy and corresponds to an accumulation of triglycerides. Plasma lipid profiles in the second trimester of pregnancy may predict the incidence and severity of pre-eclampsia. Hence, the early recognition of moderate rise of cholesterol during early pregnancy case predict the pregnancy related complications. Lipid profile, at least total cholesterol and triglyceride must be measured in the first trimester of their pregnancy.

An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular disease. Pre-eclampsia and related disorder are known to affect function of various organ involved in lipid metabolism.

CONCLUSION
In conclusion, our result suggested that there is increase in susceptibility to the development of PIH and gestational proteinuric hypertension and other foetal diseases, induced preterm birth and intrauterine growth restriction. Therefore, lipid profile estimation and monitoring should be made a part of routine investigation during 10-16 weeks of pregnancy. Further studies are needed to determine if certain women are at increased risk of cardiovascular, hypertensive diseases in later life because of effects on their lipid profile during pregnancy.

REFERENCES