Role of lipids, ionized calcium, and alkaline phosphatase in progress of pregnancy induced hypertension - A prospective study in Kolkata

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Abstract

Background: Pregnancy induced hypertension may complicate to preeclampsia and eclampsia. The pathophysiology of the former is still confusing, many authors suggested different opinions, and indicated different parameters for the prognosis of this.

Aim: To evaluate serum HDL and LDL cholesterol, alkaline phosphatase, ionized calcium in pregnancy induced hypertension patients.

Materials and methods: We had selected normal non-pregnant females (Group 0), pregnant normotensive females (Group I) and pregnancy induced hypertensive females (Group II). All the above mentioned parameters were estimated in them. Statistical analysis was done by SPSS 17 software; ANOVA and post hoc Bonferroni analysis were used to compare them.

Results: Significant increase of LDL and alkaline phosphatase as well as significant decrease of HDL and ionized calcium were found in Group II females.

Conclusion: HDL and LDL cholesterol, alkaline phosphatase, ionized calcium can indicate the severity of gestational hypertension. Normalization of those parameters can prevent the complications like preeclampsia and eclampsia.

Key words

Pregnancy induced hypertension, Lipids, Alkaline phosphatase, Ionized calcium.
Introduction
Hypertensive diseases contribute 5 to 10% of all pregnancies, when associated with hemorrhage and infection leading to maternal mortality and morbidity [1]. Hypertension appears after 20 weeks of pregnancy and resolve within 10 days of postpartum, in a previously normotensive women, without other features of pre eclampsia is called pregnancy induced hypertension (PIH) [2, 3, 4]. This PIH or gestational hypertension, affecting 2-5% of women and can progress to pre-eclampsia and eclampsia which can end in a grave consequence like maternal and perinatal mortality [5].

The pathophysiology of gestational hypertension is still unclear, but different studies postulated that metabolic abnormalities like dyslipidemias and insulin resistance may contribute to it [6]. Lipids may accumulate at the arterial intimal cells leads to endothelial dysfunction and altered lipid profile causes lowering in prostaglandin thromboxane ratio which is a significant pathway for development of PIH [7].

Epidemiological evidences suggested that the women with PIH are at risk of cardiovascular diseases (CVD), hypertension, stroke and death from ischemic heart diseases in later life [5].

Different authors highlighted on different parameters which can prevent the progression of PIH but still there is a scarcity of a reliable predictor.

Placental synthesis of alkaline phosphatase (ALP) during pregnancy has a role in division of normal and transformed cells. This enzyme is responsible for active transport of phosphate [8]. Lowering of serum ALP in pregnancy may be an indicator of intra uterine growth retardation (IUGR) ALP was also noticed to be increased in pre-eclampsia [9].

Epidemiological studies also documented that calcium intake is negatively correlated with PIH. A recent study found that calcium supplementation decreases the risk of hypertension in pregnancy [10]. Altered lipid metabolism, during pregnancy ensures the continuous supply of nutrients to the growing fetus [11].

The aim of the present study was to analyze the serum calcium, ALP, and lipid parameters between normal women without pregnancy, pregnant mothers with PIH, and pregnant mothers without PIH, and to find out whether any significant alteration exists between the groups.

Material and methods
The present study was undertaken in the Department of Biochemistry, Calcutta National Medical College, Calcutta. It was a case control, observational study and the study period extended from 01.06.2014 to 31.05.2015.

Selection of cases and controls
Total 101 pregnant women of 20-35 years old were selected and grouped as follows.

Group 0: Non pregnant women with normal blood pressure (<120/80 mmHg) (n=34)

Group I: Women having normal uncomplicated pregnancy without hypertension (<120/80 mmHg) (n=35)

Group II: Women with pregnancy-induced hypertension (PIH) (>140/90 mmHg) (n=32)

Inclusion criteria
Gestational age ranges from 24 weeks to term. All the subjects in the group were in the third trimester of pregnancy.

Criteria for making a diagnosis of gestational hypertension
The diagnosis of gestational hypertension was based on two consecutive measurements of systolic and diastolic blood pressure ≥140/90 mmHg 6 hours apart, one measurement of diastolic blood pressure of 110 mmHg or more or a rise of 30 mmHg or 15 mmHg above the normal pre-pregnancy systolic and diastolic blood pressures after the 20th week of pregnancy.

[5] while Urinalysis was done using COMBI-URISCREEN reagent strips. Persistent elevation of the blood pressure on two occasions without proteinuria was used to make a diagnosis of gestational hypertension.

**Exclusion criteria**

Exclusion criteria was preexisting hypertension, ischemic heart disease (IHD), chronic renal failure (CRF), diabetes mellitus (DM), patient under treatment with drugs which can interfere lipid profile. The pre-eclampsia patients were diagnosed by the presence of persistent hypertension (more than 140/90 mmHg) gross proteinuria (tested by heat test of urine) and pathological edema.

**Sample analysis for test parameters**

Blood samples were drawn from all the subjects following a fast of 12 hours and analyzed for serum HDL and LDL cholesterol by enzymatic end point method with the help of kits on ERBA chem-5 semi-auto analyzer.

(S) LDL by Direct method [12] (Erba Lachema, diagnostics).

(S) HDL by PEG/CHOD-PAP method [13] (Crest Biosystems).

Serum Alkaline phosphatase determined by kinetic assay (Pnpp-AMP method) [14] and Serum ionized calcium was analysed by 9180 Electrolyte Analyser [15]. Principle based on Ion Selective Electrode (Roche Diagnostics GmbH Mannheim Germany).

**Statistical analysis**

It was done by using SPSS 17 Software. To see the differences in between the groups, one way analysis of variance (ANOVA) procedure using the Statistical Package for the Social Science (SPSS) program (SPSS Statistics 22.0) was applied. The differences between the individual pairs were done by post hoc Bonferroni Correction. The P values were given at appropriate places. A statistically significant difference was considered at p < 0.05.

**Results**

ANOVA showed significant of difference between different groups in various parameters as per Table – 1. Post hoc Bonferroni analysis showed significance between various groups was as per Table – 2. Significant increase of LDL and alkaline phosphatase as well as significant decrease of HDL and ionized calcium was found in Group II females.

**Table - 1:** ANOVA showing significance of difference between different groups in various parameters.

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant (GROUP-00) n=34</th>
<th>Pregnancy without complications (GROUP-I) n=35</th>
<th>Pregnancy induced hypertension (PIH) (GROUP-II) n=32</th>
<th>Levels of significance between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum HDL in mg/dl (mean±SD)</td>
<td>47.03±1.42</td>
<td>47.14±1.47</td>
<td>40.84±1.73</td>
<td>F= 178.309 p&lt;0.0001</td>
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<td>Serum LDL in mg/dl (mean±SD)</td>
<td>142.40±6.96</td>
<td>116.19±4.88</td>
<td>131.66±12.7</td>
<td>F= 225.498 p&lt;0.0001</td>
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<td>Serum alkaline phosphatase in IU (mean±SD)</td>
<td>136.25±3.07</td>
<td>288.06±11.25</td>
<td>402.39±21.07</td>
<td>F= 3160.924 p&lt;0.0001</td>
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<td>Serum Ionized Calcium in mmol/l (mean±SD)</td>
<td>1.2±0.09</td>
<td>1.1±0.08</td>
<td>0.92±0.11</td>
<td>F= 63.200 p&lt;0.0001</td>
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</table>

ANOVA performed with SPSS version 17.0 for windows to show the significance between different groups at 95% confidence interval.
Table - 2: Post hoc Bonferroni analysis showing significance between various groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Difference (I-J)</th>
<th>Std. Error</th>
<th>Sig.</th>
<th>95% Confidence Interval Lower Bound</th>
<th>Upper Bound</th>
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Discussion
In our study, we didn’t find any significant alteration of HDL in normotensive pregnant mothers when compared with non pregnant females. A significant decrease of HDL has been found in PIH mothers when compared with non pregnant females and normotensive pregnant mothers.

The above mentioned findings correlate with the findings of De J, et al. [16] the low levels of HDLC may be due to hyperoestrogenemia and also due to insulin resistance [16, 17, 18].

A significant lowering of LDL was found in normotensive pregnant participants in comparison to non pregnant females in our study. Jayantha C [19] also observed the similar results. They also documented significant rise of LDL in PIH which corroborates our finding.

The rise of LDL in PIH may be contributed by endothelial dysfunction, caused by hypoestrogenemia, predominance of smaller and denser LDL particles [20, 21, 22].

Many authors reported the rise of serum ALP in 2nd and 3rd trimester of pregnancy which coincides with the period of calcification of fetal skeletal growth. Placental ALP (PALP) facilitates the mobilization of calcium ions from mother to fetus. PALP gradually increases with the gestational weeks [21].

Mangal A, et al. [23] observed the rise of PALP activity is directly related to the rise of BP. We also found the same observations. Similar results were also found by Lopez P, et al. [24].

During pregnancy, there is a great demand for calcium for development of fetal skeleton. PALP causes this shift of calcium from mother to fetus. So without adequate intake, the maternal calcium concentration will fall below the normal level which will aggravate during PIH, since PALP increases with hypertension. Furthermore, there is dilution of cations due to expanded extracellular fluid volume and to the normal hypercalciuria of pregnancy [24]. Serum ionized calcium concentration depends on adequate calcium intake [25].

Conclusion
From the above mentioned results, we can assume that the serum HDL and LDL estimation is helpful in the prevention of complications of PIH. High level of ALP in PIH is attributed to increased blood pressure. High PALP activity can be explained by ischemia resulting from maternal hypertension.

Low levels of serum ionized calcium in PIH can be corrected by calcium supplementation, we can hypothesize that maintenance of all these parameters within normal range can control the PIH.

References


