

# Biochemical studies of various risk factors and important minerals in pre-eclamptic patients

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## Abstract

**Background:** The hypertensive disorders of pregnancy are major causes of morbidity and mortality. They may lead to eclamptic conditions causing seizures, comatose conditions and death in hypertensive mothers. It will also lead to disastrous conditions for fetus. The demographic, anthropometric factors like age, parity and obesity are vital in investigating the etiology of the disorder. The changes in biochemical parameters like total protein, albumin contents along with minerals like calcium, phosphorous and magnesium in pregnancy may implicate their possible role in pregnancy-induced hypertension. This study assessed serum mineral levels in women in PE (pre-eclampsia) cases and the control group which were statistically analyzed. **Methods :** This case-control study was conducted on 90 confirmed pre-eclamptic patients ( $\geq 20$  weeks gestation), admitted in B. Y. L. Nair Ch. Hospital, Mumbai Central, Mumbai 400008 India, and 90 healthy, age-matched pregnant women (controls), attending OPDs of same department. The demographic, anthropometric, clinical and obstetric data were gathered using an interview-based questionnaire. Venous blood samples were drawn for the estimation of total protein, albumin, calcium, phosphorus and magnesium. **Results:** The prevalence of PE was highest in the age group of 20 to 30 years. Primigravidae PE cases were more predominant (75.5 %), than multigravidae. Women with hypertensive disorders (PE) had significantly lower serum calcium and magnesium levels than those in the control group ( $p < 0.0001$ ). The decreased serum total protein content and calcium could be correlated positively with that of magnesium ( $p < 0.01$ ) in PE cases. These results might offer the guidelines for etiology of the disorder. **Conclusion:** In this study, age of pregnant woman, BMI along with serum total protein, albumin, calcium and magnesium levels were lower in PE cases than in normal control group. The supplementation of balanced diet and the minerals during the antenatal period may reduce the problem significantly and the occurrence of hypertensive disorders in pregnancy.

**Keywords:** Pregnancy-induced hypertension, Preeclampsia, Calcium, Magnesium

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## INTRODUCTION

Preeclampsia (PE), the condition of pregnancy induced hypertension (PIH) with proteinuria, causes about 50,000 maternal deaths annually in the world including the developed countries. Globally 3-10% of maternal deaths

are caused by this disorder<sup>1</sup>. In India, the maternal mortality rate is quite very high and hypertensive disorders are observed to be responsible for 6 % of all maternal deaths<sup>1,2</sup>. Pre-eclamptic conditions can lead to mortality and morbidity in mother (seizures and comatose conditions leading to death finally) and in child (the stillbirths or morbidity because of fetal growth restriction, low-birth weight, preterm delivery, respiratory distress syndrome and similar disorders)<sup>3</sup>. Therefore, there is a need to identify the causative factors, the alterations in various risk factors and important biochemical parameters in the preeclampsia (PE) during pregnancy. During PIH obesity, pre-existing diabetes and hypertension are some of the important factors implicated. Duckitt and Harrington carried out the controlled study and assessed the various risk factors for preeclampsia<sup>2</sup>. Other research groups also evaluated the risk factors like the advanced

age, diabetes, multiple pregnancies, multiparity and cardiovascular disorders along with obesity, as the causative factors of PIH. Pregnancy is a physiological state associated with increase in the need of calcium (Ca), phosphorous (P) and magnesium (Mg) for the growth of fetus. The dietary factors like Ca and Mg have been implicated in the pathophysiology of preeclampsia<sup>3,4</sup> Borella *et al* tried to correlate Ca and Mg content with PIH. Many research workers tried hypocalcaemia to correlate with preeclampsia.<sup>3,4,10</sup> Ca/Mg ratio was observed to be decreased in the extreme PIH condition. According to Seely *et al* the low ionized Ca can also be the source for the disorder Sudden Death Syndrome in infants<sup>5</sup>. Taking into account earlier studies conducted, the aetiology of the condition were still elusive.<sup>1,3,4</sup> There was a need to get the insight into the risk factors affecting the outcome of pregnancy and the alterations in metabolisms of important minerals like Ca, P and Mg in PE patients.

### MATERIALS AND METHODS

Pregnancy is a metabolic stage involving the development of fetus Preeclampsia is the hypertension associated with pregnancy occurring after 20 weeks of gestation. Pregnant ladies with Blood pressure (BP)  $\geq$  140/90 mm of Hg (Systolic BP/Diastolic BP) and protienuria (+2) admitted in the Obs and Gynaec ward of T.N.M.C, Nair Hospital, Mumbai formed the test group. The set of confirmed PE cases (in-patients) formed the test group (Number 90) and normotensive pregnant women (attending OPDs of Ob. and Gynaec. Deptt.) were the controls (Number 90 matched age-wise). Patients with bone deformities, cancerous conditions and the endocrinological disorders were excluded in the studies. The study covered pregnant women ranging from 18 yrs to 40 yrs of their age. The risk factors like maternal age, gravidae, BMI, economic status and oedema were evaluated. Serum Calcium, Phosphorus and Magnesium are the important minerals assessed along with total protein and albumin contents using the Autoanalyzer of Olympus AU400. The Research study was approved by The Institutional Ethics Board of Topiwala National Medical College, Nair Hospital, Mumbai Central, Mumbai, India, one of the premium tertiary care hospitals in India. The participants were voluntary and the Informed Consent was obtained (in English, Marathi and Hindi) from all participants. The statistical analysis was carried out with help of standard formulae and SPSS software.

### RESULTS AND DISCUSSION

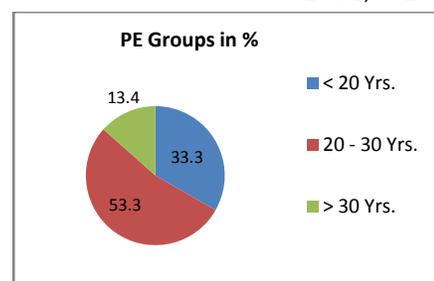
**Table 1:** Distribution of PE patients and Control groups and prevalence of various risk factors

No.	Risk Factors	PE group	Control group
a]	<b>Age</b>	<b>N = 90</b>	<b>N = 90</b>
	>20 yrs	30(33.3%)	30 (33.3%)
	20-30yrs	48(53.3%)	48 (53.3%)
b]	<b>Parity</b>		
	Primigravidae	68 (75.5%)	69(78.3%)
	Multigravidae	22(24.5%)	21 (21.7%)
c]	<b>Obesity</b>		
	BMI>25 Kg/met <sup>2</sup>	16 (18.4%)	24 (28.75%)
	BMI<25Kg/met <sup>2</sup>	74(21.6%)	66 (11.25%)
d]	<b>Economic Status</b>		
	High>Rs 200,000 / per Annum	NIL	NIL
	Low≤Rs 200,000 /per Annum	80 (100%)	30(100%)
e]	<b>Oedema</b>	6(6.7%)	1(1.1%)

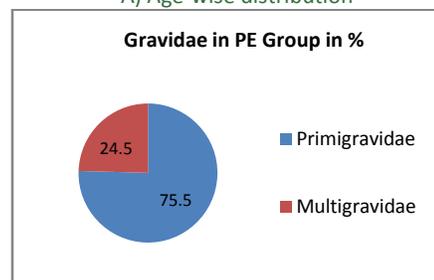
**Table 2** Mean serum Total protein, Albumin and mineral contents in PE patients and Control groups.

	Control	PE
	n = 90	n = 90
Total Protein (g /dl)	6.8 ± 0.476	5.5 ± 0.875*
Albumin (g/dl)	4.0 ± 0.427	3.5 ± 0.666 *
Calcium (mg / dl)	10.47 ± 0.48	9.49 ± 1.13 **
Phosphorus (mg/dl)	2.63 ± 0.41	2.90 ± 0.79 NS
Magnesium (mg / dl)	2.64 ± 0.25	1.05 ± 0.22 **
Ca / Mg ratio	3.9 ± 0.78	8.7 ± 0.31 **

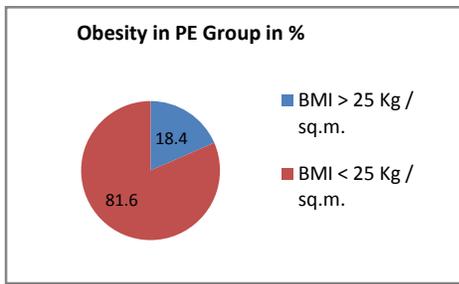
\* ≤ 0.01, \*\* ≤ 0.001



A) Age-wise distribution



b) Gravidae



### c) Obesity

Figure 1: Prevalence of the risk factor in the PE and control groups.

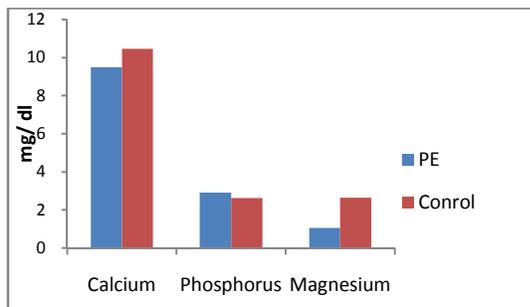


Figure 2: Mean Serum Calcium, Phosphorous and Magnesium contents in PE and Control groups

Preeclampsia is a gestational hypertensive disorder with proteinuria observed in pregnant females, 20 weeks of gestation onwards. This disorder may lead to eclampsia with seizure, comatose conditions of prospective mother and/or stillbirth or similar lethal condition of fetus. There is a need to increase the chances of better survival of mother and fetus.<sup>1,2,19</sup> It is essential to study the probable causative factors of the disorder. The age-wise distribution of PE cases exhibited highest involvement of the test group of 20-30 years (53.3%) (Table 1a). Amongst the test group 75.5% population were primigravidae (Table 1b). Earlier studies indicated early pregnancy (<20 years) and late pregnancy (>30 years) could be more prone for PE.<sup>1,2,3,4</sup> Current study revealed the changing trends in pregnancy. The alterations of many socio-economic patterns, literacy, health awareness and change in marriageable age in Metro city like Mumbai may be responsible for the same. Higher BMI was observed in PE cases. This observation could be shared with other research outcomes.<sup>2,3,14</sup> Mean BMI in PE group was observed significantly higher than that of in Control group (Table 1c). BMI was thought to be promising parameter to predict elevated BP and PE condition.<sup>11,12</sup> The present study adds to implications on the aetiology of hypertension in pregnancy in urban population of India. Previous reports have considered the association between hypertensive disorders of pregnancy (PE and PIH) and serum electrolytes, particularly calcium and magnesium.<sup>10-13</sup> There are reports of reduced levels

of calcium and magnesium in pre-eclampsia<sup>12,13</sup>. PE group was observed to be associated with statistically significant hypocalcemia and hypomagnesemia, (Table - 2 and Figure 2). Other studies conducted from different parts of world also reported lowered calcium and magnesium levels<sup>4,6,8,12</sup>. The ratio of Ca: Mg was elevated in PE group despite of lowering individual levels. The trials were done to assess role of calcium in reducing possibility of development of PE. A recent report from Nigeria has indicated that apart from raised levels of sodium in pre-eclampsia, calcium and magnesium were within normal reference intervals.<sup>14</sup> To date, the similar studies on calcium and magnesium levels amongst Pregnant women presenting with PE and PIH are inethically the pregnant women, normal or pre-eclamptic, cannot be differed from calcium supplementation.

Magnesium sulphate alone found to be reasonably better antihypertensive to control hypertension in eclamptic women. It was found to be superior to number of other drugs for controlling seizures.<sup>9</sup> Hypertensive disorders are the commonest medical complications that develop during pregnancy, characterized by an increase in blood pressure. In accordance with presentation of the condition, Hypocalcemia may influence the hypertension. Its prevention and treatment through mineral supplementation during the antenatal period can be followed with WHO guidelines. The present study showed that systolic and diastolic blood pressure was significantly raised in women with PIH and PE<sup>9,18</sup>. Serum calcium and magnesium are very important for metabolism at the cellular level and are vital for muscle contraction, cell death and neuronal activity<sup>13</sup>, making it very essential in pregnancy. The observation of low calcium and magnesium levels is in agreement with other studies on hypertensive disorders in pregnancy.<sup>10,12,13</sup> A probable theory to this observation maybe that when serum calcium levels decreased, the levels of intracellular calcium increased, leading to constriction of smooth muscles in blood vessels and therefore increased blood pressure. A Cochrane review as well as the recommendations by WHO on prevention and management of pre-eclampsia and eclampsia have consistently supported that supplementation of these minerals in pregnancy is associated with a significant reduction in the risk of pre-eclampsia<sup>19,20</sup>. The observed low levels of magnesium in women with PE could be due to decreased dietary intake, increased clearance by the kidneys, haemodilution due to expansion of the extracellular space and increased consumption of minerals by the growing foetus.<sup>12,14,15</sup> This together with lowered calcium levels play a role in the development of hypertensive disorders in pregnancy. Other researchers have proposed that a reduction in the level of extracellular

magnesium causes partial membrane depolarization and decreased repolarisation along with opening of calcium membrane channels, leading to an intracellular calcium shift. Furthermore, the existing decrease in the foetal calcium and may also block bone resorption of calcium with a concurrent intracellular pool<sup>14,15</sup>. This phenomenon produces vasoconstriction together with an increase in the blood pressure, as seen in PIH and PE. The measures like salt restriction to reduce the hypertension may not be most effective as a line of maintenance and treatment. The effect of magnesium and calcium in the pathogenesis of hypertensive disorders in pregnancy is supported by the observed positive correlation between magnesium and calcium in PE group. Further correlation analysis showed a positive association between BMI and systolic blood pressure in all groups and was significant amongst both controls and those with PE.<sup>20,21</sup> The present study revealed that the age (20 – 30 years) and BMI more than 25 were the predominant demographic risk factors along with serum total proteins, albumin, calcium and magnesium. The supplementation of these minerals and proteins during the antenatal period along with balance diet may reduce the problem significantly.

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