SERUM MINERALS CALCIUM, MAGNESIUM, COPPER AND ZINC IN PREGNANCY INDUCED HYPERTENSION

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SUMMARY
Antenatal and postnatal estimation of serum minerals - calcium, magnesium, copper and zinc, were carried out in 50 cases of Pregnancy Induced Hypertension (PIH). Healthy normal pregnant and non-pregnant women provided the data for comparison. Patients with mild PIH showed significantly lower serum zinc and calcium levels; severe PIH group in addition had significantly lower magnesium estimates; values for copper were higher in pregnant and also in women with severe PIH than the other groups. Postnatal estimates of calcium, magnesium and zinc were no different from antenatal values in all the groups studied. However, the levels of copper were found to be higher in postnatal samples.

INTRODUCTION
Pregnancy induced hypertension (PIH) is one of the commonest complications of pregnancy and it contributes significantly to the maternal as well as perinatal morbidity and mortality. Despite decades of research, the etiology of the disease has remained elusive, but has helped to understand the pathophysiology of it. Changes in the serum minerals have been noted and studies are carried out to determine the significance of deficiency or otherwise of various minerals, albeit individually.

Correlation between magnesium deficit diets and microcirculatory changes leading to hypertension is documented (Altura et al, 1984). However, no significant reduction was noted in the incidence of high blood pressure or edema in women receiving magnesium supplementation (Spatling and Spatling, 1988). Findings of rise in blood pressure in calcium deprived pregnant rats were extrapolated to human conditions and blood pressure reduction with calcium supplementation was achieved (Belzian et al, 1983). Strong association of low zinc levels with the incidence of PIH is
noted by some (Cherry et al, 1981), while the practice of zinc supplementation was admonished by others (Hytten, 1985). Relatively high serum copper levels are described for PIH (Schenker, 1969; Fattah et al, 1976), but, Friedman and associates (1969) did not find such correlation.

Because of such difference in the observations of various minerals by different authors, a prospective study to determine serum levels of some of the trace minerals - calcium, zinc, magnesium and copper, in PIH patients of the region was undertaken.

MATERIAL AND METHODS
Status of serum minerals was estimated in 80 hospital attending women. Of them, there were 25 with mild PIH, 25 with severe PIH, 15 healthy pregnant and 15 healthy non pregnant normotensives.

A pregnant woman with hypertension was labelled as one complicated by PIH and grouped as mild or severe, according to the classification of Cunningham et al (1989). In the healthy pregnant group were included gravides with no complications. And, in the healthy non pregnant group were included women who were normotensive, acceptors of interval laparoscopic tubal sterilization, who had not used hormonal contraceptives or copper containing intrauterine devices.

Fasting venous blood samples were collected twice from pregnant women, once during antenatal period after 36 weeks of gestation, and the second time after delivery; and from non pregnant women only once in the first week after the menses.

Collected blood samples were assayed for various minerals estimates; Calcium using oxalate-permanganate method (Varley, 1976); magnesium by modified method of Garner, Neil and Neely and copper and zinc by atomic absorption spectroscopy following a simple $1:5$ (Vol/vol) dilution of the serum with deionised water.

Significance of the differences in the mean estimates of any two groups was determined using student t-test.

RESULTS
Age and gravidity/parity were comparable in all the groups studied.

Estimates of serum minerals studied is shown in Table I.

Healthy pregnant women had significantly high serum copper concentrations than non-pregnant controls ($138 \text{ vs } 107 \text{ mg/dl, } p < 0.001$). But, other minerals showed no change in their levels in pregnancy.

Patients with PIH tended to have lowered calcium magnesium and zinc levels and high copper levels than in healthy pregnant women. This difference were strikingly significant with severe PIH group.

Postnatal blood levels showed not much of alternations than antenatal estimates for calcium, magnesium and zinc. Whereas, postnatal copper values were higher than in antenatal period in all the pregnant groups and significantly so in healthy pregnant women ($191 \text{ vs } 158 \text{ mg/dl, } p < 0.05$).

DISCUSSION
Studies relating serum calcium levels with pregnancy and PIH have been few and the results contradictory. Sangal and Beavers (1982) and Kesteloot et al (1982) observed increased calcium levels in hypertensives, while studies by Belzian and associates (1983) noted decreased calcium levels in pre-eclampsia and achieved decrease in blood pressure with calcium supplementation. In the present study also significantly lower calcium levels were seen in PIH patients than in normotensives, decreasing further with severity of the disease. It is seen than when concentration of calcium is low in extracellular fluid, the amount of ionicaic calcium entering the cell will increase making vascular smooth muscle more sensitive to excitation (Ganong, 1979). However, ionised calcium
Table I

Antenatal and Postnatal Estimates of Serum Minerals

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Status</th>
<th>PIH Mild (25)</th>
<th>PIH Severe (25)</th>
<th>Healthy Pregnant (15)</th>
<th>Healthy Non Pregnant (15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>Antenatal</td>
<td>8.7 ± 0.6*</td>
<td>8.6 ± 1.4**</td>
<td>9.2 ± 0.7</td>
<td>9.5 ± 0.5</td>
</tr>
<tr>
<td>mg/dl</td>
<td>Postnatal</td>
<td>8.9 ± 0.9</td>
<td>8.4 ± 0.6</td>
<td>0.9 ± 0.7</td>
<td>—</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Antenatal</td>
<td>1.9 ± 0.3*</td>
<td>1.9 ± 0.2**</td>
<td>2.2 ± 0.3</td>
<td>2.1 ± 0.3</td>
</tr>
<tr>
<td>mg/dl</td>
<td>Postnatal</td>
<td>2.0 ± 0.3</td>
<td>1.8 ± 0.4</td>
<td>2.1 ± 0.4</td>
<td>—</td>
</tr>
<tr>
<td>Copper</td>
<td>Antenatal</td>
<td>185 ± 46</td>
<td>194 ± 43**</td>
<td>158 ± 33</td>
<td>107 ± 30***</td>
</tr>
<tr>
<td>ug/dl</td>
<td>Postnatal</td>
<td>200 ± 53</td>
<td>211 ± 76</td>
<td>191 ± 25+</td>
<td>—</td>
</tr>
<tr>
<td>Zinc</td>
<td>Antenatal</td>
<td>120 ± 37</td>
<td>110 ± 46*</td>
<td>143 ± 41</td>
<td>143 ± 34</td>
</tr>
<tr>
<td>ug/dl</td>
<td>Postnatal</td>
<td>101 ± 37</td>
<td>107 ± 53</td>
<td>148 ± 38</td>
<td>—</td>
</tr>
</tbody>
</table>

— Values are mean ± standard deviation
— Figures in parenthesis indicate number cases
— Statistically significant difference: with healthy pregnant estimates
  * p < 0.05
  ** p < 0.01
  *** p < 0.001
  + p < 0.05

was not measured in our study.

Pregnant women were found to have significantly higher copper levels than their non pregnant counterparts. Increase in copper levels in PIH patients was statistically significant and was found to increase with severity of PIH. These findings, are comparable to the results of longitudinal study by Schenker et al (1969). However, the physiological importance of these changes remains obscure. But, it is presumed that mobilisation of copper from maternal tissues especially liver associated with increase in oestrogen may be responsible for raised copper in pregnancy (Evans, 1973), and in addition, damage to the organs due to vasoconstriction in toxaeamias (Piskacek, 1960). Absence of foetal accrederion may be responsible for rise in immediate postnatal period.

Studies have shown an association of lower magnesium levels with pre-eclampsia (Pradhan et al 1964; Rizvi et al, 1979). The patients with PIH in this study also had significantly lower magnesium levels than the healthy pregnant women. Like calcium, lowered magnesium levels are thought to potentiate contractile response of vascular smooth muscle
to vasopressors (Prasad et al., 1980).

Similarly, lower zinc concentrations accompanying poor nutrition may result in abnormal susceptibility of blood vessels to pressor amines and Cherry et al. (1981), noted significantly lower zinc levels in patients with PIH. Likewise, were the findings in this study.

Some of the trace elements studies above through their associations in disease states, do point toward the causal/efficacy relationship with PIH. Hence, serum minerals profile in antenatal period may assume prophylactic importance, provided multicentric studies with large number of pregnant women confirm above findings and establish the norms.

REFERENCES