A correlation of zinc and copper levels with blood pressure in normal pregnancy and preeclampsia

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Abstract
Objective: To estimate the levels of zinc and copper in the cases of preeclampsia. To know the importance of the same in pregnancy.
Materials and Methods: 30 preeclamptic cases and 30 pregnant women with normal blood pressure were estimated for serum zinc and copper levels.
Results: The levels of the trace elements, zinc and copper were found to be decreased in preeclamptic pregnancy when compared to the normal pregnancy without complications.
Conclusion: The decreased levels of zinc and copper in preeclampsia might be responsible for the complications in pregnancy as well as post-pregnancy complications.

Keywords: Zinc, Copper, Preeclampsia, Pregnancy.

Introduction
Preeclampsia, an important disorder in pregnancy, complicates almost 10% worldwide of all pregnancies and is responsible for both maternal and fetal mortality and morbidity.¹ The condition is more common in developing countries as their dietary intake of these micronutrients are low.²

Preeclampsia is a progressive, multisystem disease characterized by a triad of symptoms – increased blood pressure (≥ 140/90 mmHg), pedal edema and proteinuria in the second trimester.³ During pregnancy there are decreased levels of nutrients such as magnesium and zinc in maternal serum. This may be due to multiple reasons like hemodilution, transfer of these minerals from mother to the fetus, increased excretion through urine and accelerated metabolism.⁴ The risk increases with pregnancy because of increased requirements of these nutrients by the growing fetus as well.⁵,⁶,⁷

This study was taken into consideration to estimate the levels of zinc and copper among in preeclampsia and to highlight their importance in preventing the complications of pregnancy.

Materials and Methods
A total of 60 pregnant women attending the Out-patient department of Obstetrics and Gynecology at our Medical College Hospital participated in the study and were grouped as A and B with 30 in each.

Inclusion criteria for Group A:
Age 21-35 years and normal Blood pressure (≤ 120/80 mmHg) and no symptoms of pedal edema or proteinuria.

Inclusion criteria for Group B:
Age 21-35 years and high Blood pressure (≥ 140/90 mmHg), pedal edema and proteinuria developing after 20 weeks of gestation.

Exclusion criteria for Group A and B:
Patients with a history of diabetes mellitus, multiple gestations, and those who were suffering from chronic hypertension, cardiovascular disease, renal disease and liver diseases were excluded from the study.

5ml of venous blood sample was collected from all participants. The blood was allowed to clot and serum was separated by centrifugation at 3000 RPM for 10 minutes. The serum was stored at -20°C. Zinc and Copper were measured in Auto Analyzer by using standard enzyme kits.

Table 1: Parameters with the methods of estimation.

| Parameter | Method          |
|-----------|-----------------|
| Zinc      | Turbidimetry    |
| Copper    | Turbidimetry    |

Results
The study was enrolled with a total of 60 pregnant women, of which 30 were of normal pregnancy under group A and 30 were preeclamptic under group B.

The biochemical study parameters were analyzed with the help of Statistical Product and Service Solutions (SPSS) 22 software.

Table 2: Mean and standard deviation of measured parameters in group A (Normal pregnancy)

| Parameters       | Mean | Standard deviation |
|------------------|------|--------------------|
| SBP (mm Hg)      | 108.7| 9.8                |
| DBP (mm Hg)      | 74.2 | 6.2                |
| MAP (mm Hg)*     | 95.7 | 7.4                |
| Zinc (µg/dl)     | 70.6 | 11.8               |
| Copper (µg/dl)   | 106.9| 18.9               |

*Mean Arterial Pressure = (SBP+2(DBP))/3
Table 3: Mean and standard deviation of measured parameters in group B (Preeclampsia)

| Parameters     | Mean  | Standard deviation |
|----------------|-------|--------------------|
| SBP (mm Hg)    | 154.4 | 15.1               |
| DBP (mm Hg)    | 92.7  | 4.9                |
| MAP (mm Hg)*   | 113.2 | 9.3                |
| Zinc (µg/dl)   | 24.3  | 15.7               |
| Copper (µg/dl) | 44.9  | 20.8               |

Calculation of Group Means difference and the statistical significance by student’s t test.

Table 4: Comparison of variables with groups A and B

| Variable | Group | Group | Mean Difference (A-B) | Std. Error | Significance P | 95% Confidence Interval |
|----------|-------|-------|-----------------------|------------|----------------|-------------------------|
| MAP      | A     | B     | 17.5                  | 2.17       | < 0.0001       | 13.16; 21.85            |
| Zinc     | A     | B     | -46.3                 | 3.59       | < 0.0001       | -53.48; -39.12          |
| Copper   | A     | B     | -62.0                 | 5.13       | < 0.0001       | -72.27; -51.73          |

Table 5: Comparison of Zinc and MAP within group A and group B

| Zinc | MAP | Mean Difference (A-B) | Std. Error | Significance P | 95% Confidence Interval |
|------|-----|-----------------------|------------|----------------|-------------------------|
| Group A | Group A | 25.1                | 2.54      | < 0.0001       | 20.01; 30.19            |
| Group B | Group B | 88.9                | 3.33      | < 0.0001       | 82.23; 95.57            |

Table 6: Comparison of copper and MAP within group A and group B

| Copper | MAP | Mean Difference (A-B) | Std. Error | Significance P | 95% Confidence Interval |
|--------|-----|-----------------------|------------|----------------|-------------------------|
| Group A | Group A | -11.2                | 3.71       | 0.0037         | -18.62; -3.78           |
| Group B | Group B | 68.3                 | 4.16       | < 0.0001       | 59.97; 76.63            |

Discussion

The trace elements are required because of their vital functions in the human body. Their daily requirement is increasing during the pregnancy period due to different reasons. According to the World Health Organization, a pregnant woman in the third trimester needs almost double the daily zinc requirement.\(^9\) When this increased need is not met, it results in various complications during and post pregnancy like preeclampsia, thereby increasing morbidity and mortality both for the mother and fetus.

There are various studies which assessed the reasons behind preeclampsia and its association with zinc and copper.

According to a study conducted by Ikgos et al, it was found that concentrations of zinc and copper were low in the placental tissues in preeclamptic pregnancy when compared to healthy pregnancy.\(^10\)

The functions of zinc and copper were analyzed by various studies as enzyme cofactors like Metallothionein, Ceruloplasmin and Super oxide dismutase, says a study by Cetin et al.\(^11\)

Our study showed a decrease in zinc concentration in preeclampsia than in normal pregnancy. This was in accordance with the study conducted by Joshi et al, Ette et al and Ilhan et al.\(^12\)-\(^14\)

Lower level of copper was found in group B pregnancy with preeclampsia when compared to group B pregnancy with normal blood pressure. This was supported by others like Akinloye et al and Ugwuja et al.\(^15,16\)

In contrast to our study, higher levels of zinc were also estimated among preeclampsia like the studies conducted by Borella et al and Ajayi et al.\(^17,18\)

There was also studies conducted by Golmohammad et al and a study conducted by Prema K, which showed both the trace elements, zinc and copper to be in normal concentrations among pregnant women with preeclampsia.\(^19,20\) This was also in contrast to our study.

Conclusion

The present study showed a decrease in zinc and copper levels in preeclampsia both mild and severe preeclampsia when compared to the normotensive pregnancy controls, explaining their importance and role in normal pregnancy.

Since there is a significant decrease, the estimation of micronutrients in pregnancy might becomes an important in early diagnosis and treatment of pre-eclampsia. The study thereby recommends the clinicians to include minerals zinc and copper in the prenatal period to prevent preeclampsia and other complications.
Limitations of the Study: A smaller study group limits the study to come to a major conclusion.

Ethical Standards: The study was conducted in Department of Biochemistry collaborated with Department of Obstetrics and Gynecology at a Medical College Hospital and Research Centre. The study was approved by the Institutional Ethical Committee.

An informed consent was taken from all the participants in the study group and control group.

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Conflicts of Interest: None.

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