

## A Study of Serum Copper Levels in Preeclampsia and its Correlation with the Severity of Pre-Eclampsia

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### Abstract

**Background:** Pre-eclampsia is a disease of unknown etiology characterized by development of hypertension to the extent of 140/90 mm of Hg or more with proteinuria after the 20th week in a previously normotensive and non-proteinuric patient. Incidence of Pre-eclampsia varies from 8-10% in India, being 10% in the primigravidae and 5% in multigravidae. **Objective:** The present study, conducted in the department of Biochemistry of a tertiary care teaching hospital, proposes the value of serum copper levels as marker in etiopathogenesis and in assessment of the severity of pre-eclampsia. **Methods:** The serum copper levels were measured in sixty newly diagnosed pre-eclampsia patients admitted in the wards of Department of Obstetrics and Gynecology of the tertiary care teaching hospital and sixty age and sex matched normal healthy relatives of patients attending the Out Patient Departments. **Result:** The outcome of the study indicated that the levels of serum copper were increased statistically significantly in the pre-eclampsia cases group when equated to the normal pregnant control group. Moreover when levels of serum copper were correlated with the systolic and the diastolic blood pressure in pre-eclampsia patients, significant positive correlation was detected. **Conclusion:** Hence the result obtained concludes that serum copper level may be considered as an influence having a role in the etiopathogenesis of the disease and may also be used as severity indicator in patients with pre-eclampsia.

**Keywords:** Copper, Pregnancy Induced Hypertension, Preeclampsia, Correlation

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### Introduction

Many complex biochemical changes occur during pregnancy due to physiological stress which is exaggerated in various complications of pregnancy like Pregnancy Induced Hypertension (PIH). PIH is reported with incidence of about 10% of first pregnancies and 20% to 25% of women with previous chronic hypertension.<sup>1</sup> The incidence of PIH varies among different hospitals, regions and countries. Pre-eclampsia is the most common medical complication that develops during pregnancy<sup>(1)</sup> and is responsible for large number of maternal mortality<sup>(2)</sup>.

Preeclampsia is the most frequently encountered hypertensive disorder with medical complications occurring during pregnancy<sup>(3)</sup>. According to "WHO recommendations for treatment and prevention of Preeclampsia and Eclampsia", Preeclampsia is the onset of a new

episode of hypertension during pregnancy characterized by persistent hypertension (Diastolic BP  $\geq$  90 mm Hg) and substantial proteinuria ( $>0.3$  g/24 hr)" (4). Hypertensive disorders of pregnancy occur in about 10 % of pregnant women in the world and 7.8% in Indian scenario while Preeclampsia occur in about 5.4% of pregnant population in India (5).

Despite of many clinical researches, the etiology behind the development of Preeclampsia has not been clearly identified (6). In developing countries like India essential nutrient deficiencies has been indicated as one of the predisposing factors likely to be indicated in the etiology of Preeclampsia (7,8). Many researches have documented an evidence that changes in the levels of serum Copper may have a role as etiopathogenesis of preeclampsia (9-11).

A mean comparison of serum level of copper in Preeclampsia and normal pregnancy may help in indicating whether the changes in the levels might be involved in the etiology of Preeclampsia and correlation between serum Copper and mean systolic & diastolic BP may help in establishing serum Copper as a severity marker in Preeclampsia. Additionally only a handful of studies have been conducted in the Indian setup regarding this scenario where a majority of pregnant women have a poor consumption of micronutrients.

### Objectives

1. To estimate the level of serum Copper in Preeclamptic cases and normal pregnant control group.
2. To correlate between serum Copper and the mean levels of systolic & diastolic blood pressure in Preeclamptic group.

### Materials And Methods

The study was conducted in a tertiary care hospital over a period of one & half years.

**Study design-** Hospital based cross-sectional study with comparison groups.

**Study population-** Sixty cases of preeclampsia and sixty healthy pregnant women controls.

#### Inclusion criteria

1. Preeclamptic primigravidae in the third trimester of pregnancy,
2. Age between 18-35 years,
3. BP $>$ 140/90 mm Hg in third trimester,
4. Urinary albumin  $\geq$  1+ dipstick or 300 mg per 24 hour urine,
5. Normal pregnant women in the third trimester were taken as controls.

#### Exclusion criteria

1. Multigravidae,
2. Previous history of diabetes,
3. Hypertension,
4. Thyroid disorder,
5. Renal disorder,
6. Dyslipidemia,
7. Family history of preeclampsia,
8. Previous history of convulsions.

**Collection of blood sample-** 2 ml blood was collected from veins in antecubital fossa in a plain bulb. After clotting, the bulb was centrifuged and serum collected.

#### Method of estimation

No.	PARAMETER	METHOD
1.	Serum Copper	Di-Br-PAESA colorimetric method (12)

**Normal Range of Serum Copper-**

80-140 µg/dL

**Statistical analysis**

- The values of serum Copper and systolic & diastolic BP are expressed as mean ± SD.
- p value <0.05 was considered as statistically significant, that<0.001 was considered as statistically highly significant.
- To find out the correlation between serum Copper and the mean systolic & diastolic blood pressure, Pearson's correlation coefficient (r) was calculated.

**Results****Demographic & anthropometric data**

There was statistically no difference between the mean levels of age, gestational age of pregnant women and the body mass index of the participants belonging to the preeclampsia group and healthy pregnant women group. (Table: 1)

**Table 1: Comparison of age, Gestational age and BMI among cases and controls**

Parameter	Cases (n=60)	Controls (n=60)	p-value
Age (Yrs)	23.13 ± 2.75	22.81 ± 2.48	0.5098*
Gestational Age (Wks)	34.2 ± 2.40	34.45 ± 2.38	0.5685*
BMI (kg/m <sup>2</sup> )	22.75 ± 1.99	23.01 ± 2.02	0.4854*

\*p>0.05= statistically insignificant

**Blood Pressure**

The mean levels of systolic and the diastolic blood pressures were raised statistically significantly in the cases compared to healthy pregnant controls. (Table: 2)

**Table 2**

Vital parameter	Cases	Controls	p-value
Systolic blood pressure (mm Hg)	167.23 ± 11.58	119.23 ± 8.79	<0.0001**
Diastolic blood pressure (mm Hg)	103.4 ± 8.22	77.56 ± 5.32	<0.0001**

\*p<0.05= statistically significant;

\*\*p<0.001= statistically highly significant

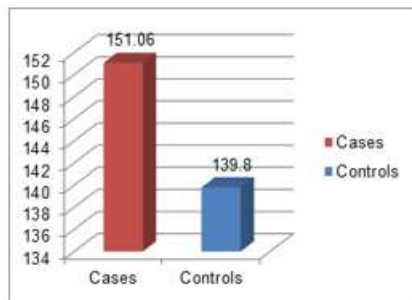
**Serum Copper**

Serum Copper level was increased statistically highly significantly in preeclampsia cases compared to healthy pregnant controls. (Table: 3, Graph: 1)

**Table 3**

Parameter	Cases	Controls	p-value
Serum Copper (µg/dL)	151.06 ± 19.73	139.8 ± 17.98	0.0014*

\*p<0.001= statistically highly significant



**Graph 1: Serum Copper (µg/dL)**

**Correlation of severity**

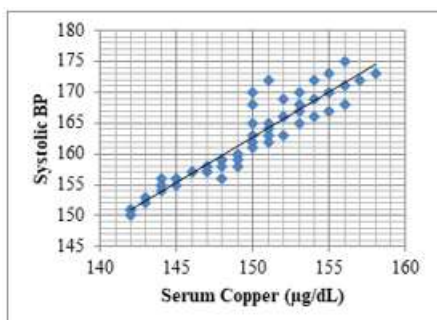
A statistically significant positive correlation was obtained when serum Copper level was correlated with mean systolic and diastolic blood pressure. (Table:4, Graph:1 & Graph: 2)

**Table 4**

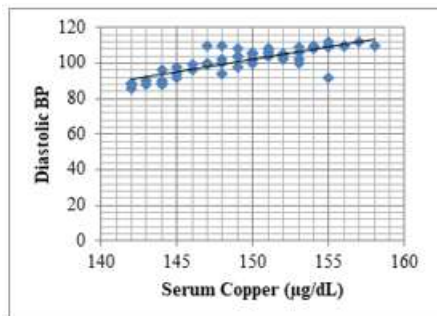
Parameter	Serum Copper
Systolic blood pressure	r= 0.9405; p= 0.0001
Diastolic blood pressure	r= 0.8248; p= 0.0001

where,

r - Karl Pearson correlation Co-efficient (-1: Negative correlation to +1: Positive correlation).  
p<0.05= statistically significant; p<0.001= highly significant.



**Graph 2: Correlation between Serum Copper and Systolic BP**



**Graph 3: Correlation between Serum Copper and Diastolic BP**

## Discussion

The study was carried out with the aim to assess the difference in the levels of serum Copper between Preeclamptic cases and healthy controls to find out if serum level of Copper has any association in the etiology of Preeclampsia and to assess the correlation between serum Copper and the blood pressure. The cases and controls were comparable with each other in relation to the age, gestational age and the Body mass index.

Higher BMI is associated with development of hypertension (13). However in this study; both the groups were comparable on the basis of BMI. Hence BMI was excluded as an etiological factor in preeclampsia.

The results of our study showed that the level of serum Copper among Preeclampsia cases was increased statistically significantly compared to the health controls. (Table: 3, Graph: 1) The findings of our study corroborated well with the studies conducted by Ahsan T et al (14), Atamer Y et al (15), Borella P et al (16), Deepa Kanagal et al (17), Ruksana Anjum et al (18). The reasons cited behind increased levels associated with Preeclampsia include increased levels of Ceruloplasmin due to lipid peroxidation, production of highly reactive free radicals which is also associated with increased lipid peroxidation and further endothelial damage etc. Further when serum Copper was correlated with systolic and diastolic blood pressure, a statistically significant positive correlation was obtained in our study (Table: 4, Graph: 2 & Graph: 3). This may indicate a strong association between elevated Copper and risk of developing preeclampsia. These findings were also obtained in study conducted by Arash Rafeinia et al (19).

Studies conducted by Serefden Acikgoz et al (20) have reported a decrease in the level of serum Copper in Preeclampsia patients. Additionally some studies have indicated no association between serum Copper and blood pressure levels.

## Conclusion

Preeclampsia is a condition associated with changes in the nutrient levels in females like serum Copper. The results obtained in our study may help in understanding the pathophysiological process behind the occurrence of preeclampsia and may help in establishing strategies for prevention and reduction of severity of this disease. As some studies have shown different results compared to our study and the sample size was less, many studies are required to be carried out in Indian setup to establish the association between serum Copper levels and occurrence of Preeclampsia so that if association is proven, the estimation of copper levels at an early gestational age can be used as a predictive marker for early diagnosis preeclampsia taking into consideration the dietary pattern of the study groups.

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## Author Declaration

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**References**

1. James P, Nelson-Piercy C. Management of hypertension before, during and after pregnancy. *Heart* 2004; 90(12):1499-504.
2. Malas NO, Shurideh ZM. Does serum calcium in pre-eclampsia and normal pregnancy differ? *Saudi Med J*. 2001; 22(10):868-71.
3. Wang A, Rana S, Karumanchi SA. Preeclampsia: The Role of Angiogenic Factors in Its Pathogenesis: *Physiology (Bethesda)* 2009 June; 24:147-58.
4. World Health Organization. WHO Handbook for guideline development. Geneva, World Health Organization, 2010. Available from: URL [www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/9789241548335/en/index.html](http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548335/en/index.html).
5. Rastogi A. Preeclampsia. In *Gynecology & Obstetrics*: [nph.gov.in](http://nph.gov.in). [Internet]. Zahid. 2016 Jun. Available from: URL <https://www.nhp.gov.in/disease/gynaecology-and-obstetrics/preeclampsia>.
6. Bell MJ. A historical overview of preeclampsia-eclampsia. *J Obstet Gynecol Neonatal Nurs*. 2010;39(5):510-518. doi:10.1111/j.1552-6909.2010.01172.x.
7. Roberts J M, Balk J L, Bodnar L M, Belizán J M, Bergel E, Martinez A. Nutrient Involvement in Preeclampsia. *J Nutr*. 2003
8. Atamer Y, Koçyigit Y, Yokus B, Atamer A, Erden AC. Lipid peroxidation, antioxidant defense, status of trace metals and leptin levels in preeclampsia. *Eur J Obstet Gynecol Reprod Biol*. 2005 Mar 1;119(1):60-6. doi: 10.1016/j.ejogrb.2004.06.033. PMID:15734086.
9. Borella P, Szilagyi A, Than G, Csaba I, Giardino A, Facchinetti F. Maternal plasma concentrations of magnesium, calcium, zinc and copper in normal and pathological pregnancies. *Sci Total Environ*. 1990 Dec 1;99(1-2):67-76. doi: 10.1016/0048-9697(90)90212-d. PMID: 2270473.
10. Kanagal D V, Rajesh A, Rao K, Shetty H, Shetty P K, Ullal H. Zinc and copper levels in preeclampsia: a study from coastal South India. *Int J Rep Con Obs Gyn*. 2014; 3(2):370- 3.
11. Anjum R. Study of Serum Levels of Copper, Ceruloplasmin in Pregnant Women with preeclampsia. *Int J Cuae Med App Sci*. 2016 Jan; 9(2):60-4.
12. Rafeenia A, Tabandeh A, Khajeniazi S, Marjani AJ. Serum copper, zinc and lipid peroxidation in pregnant women with preeclampsia in gorgan. *Open Biochem J*. 2014 Nov;8:83-8. doi:10.2174/1874091X01408010083.
13. Açıkgoz S, Harma M, Harma M, Mungan G, Can M, Demirtas S. Comparison of angiotensin-converting enzyme, malonaldehyde, zinc, and copper levels in preeclampsia. *Biol Trace Elem Res*. 2006 Oct;113(1):1-8. doi: 10.1385/BTER:113:1:1. PMID: 17114810.