

# Comparison of Serum Magnesium and Zinc Levels between Pre-Eclamptic and Normotensive Pregnant Women

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## ABSTRACT

**Objective:** To find the levels of serum magnesium and zinc in pregnant women and to compare their levels in PE and normotensive pregnant women.

**Methodology:** This study was conducted in the outpatient & in-patient departments of the Obstetrics and Gynaecological unit of the Hayatabad medical complex, MTI, Peshawar. Pregnant female were included via non-probability convenient sampling. Informed verbal & written consent was obtained, 5ml venous blood was withdrawn for estimation of serum zinc and serum magnesium levels.

**Results:** A total of 110 patient's pregnant women [pre -eclamptic =46; normotensive pregnant women=64] were included in the final analysis. Mean age of study participants was 26.41±4.71 years. Obstetric characteristics of the pregnant women revealed that most 84.55% (n=93) of the women were multi-gravida and similarly more than half of the women were multipara. Low serum zinc was noted in pre-eclamptic pregnant women compared to normotensive pregnant women but the difference was statistically insignificant (68.16±20.60 Vs. 74.96±32.23, p=0.385). Similarly, comparable results were noted for serum magnesium level, with mean level of 1.68±0.39 in women in pre-eclamptic group as compared to 1.86±0.34 in normotensive females.

**Conclusions:** Our findings suggested that there was no correlation between PE in pregnant female and the serum levels of zinc and magnesium. Clinical implication of serum zinc and magnesium in PE is questionable. However, more research into the involvement of serum levels of zinc and magnesium in PE is required since they might serve as early indicators of PE.

**Keywords:** Hypertension, Magnesium Level, Pre-Eclampsia, Pregnancy, Zinc Level.

### Authors' Contribution:

<sup>1,2</sup>Conception; Literature research; manuscript design and drafting; <sup>2,3</sup>Critical analysis and manuscript review; <sup>3,4</sup>Data analysis; Manuscript Editing.

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## Introduction

Pre-eclampsia (PE) is one of the notable causes of morbidity and mortality in the world. PE is the new onset of serious hypertension in pregnancy with substantial proteinuria, with the clinical sign typically occurring in 20<sup>th</sup> week of pregnancy or later.<sup>1</sup> It is "one of the most prevalent yet least understood illnesses of pregnancy" and it is thought

to affect 5-8% of all pregnancies globally.<sup>2</sup> It has been estimated that nearly 40% fetal 18% maternal deaths are attributed to PE globally.<sup>3-5</sup> Globally, more than 50000 annual deaths of pregnant females are due to PE and even in developed countries it is responsible for almost 1/4<sup>th</sup> of all cases of intrauterine growth retardation and 15% of premature births.<sup>6</sup> According to the "International

Society for the Study of Hypertension in Pregnancy (ISSH)", PE in clinical practice is described as the presence of hypertension with proteinuria and/or edema after twenty weeks of pregnancy in an earlier normotensive woman that totally settles by the 6<sup>th</sup> postpartum week.<sup>6,7</sup>

The exact etiology of PE is still unknown. There are many theories and hypothesis which explains the causes of PE. These include oxidative stress during pregnancy as a cause of endothelial dysfunction and ultimately a cause of preeclampsia. Another theory hypothesized incomplete invasion of 2<sup>nd</sup> wave of spiral arteries.<sup>8,9</sup> one of the study reported that long term complications of this pregnancy specific hypertensive disorder, pregnant women having PE were at a two-fold higher risk of cardiovascular disease(CVD) and a 5 to 12-fold greater possibility of the end stage renal stage in future.<sup>10</sup> The micronutrients and their contributory role in preeclampsia has been much hypothesized, with their fundamental role in oxidative stress on the body during pregnancy and preeclampsia.<sup>11</sup> Zinc is an important micronutrient that is part of the anti-oxidant system and is a cofactor for superoxide dismutase. All cells contain zinc, which is involved in the creation of macromolecules, immunological defense, and anti-oxidative qualities.<sup>12</sup> Additionally, pre-eclamptic conditions have been associated with increased amounts of proxy nitrite and decreased levels of antioxidants like superoxide dismutase, a metalloenzyme.<sup>13,14</sup> In accordance with the aforementioned findings, it has also been revealed that women who did not consume enough Zn and selenium, two antioxidant minerals, in their diets were more likely to develop PE.<sup>15</sup>

Mg is a significant intracellular cation that is necessary component for the production of both proteins and nucleic acids, and it also plays a crucial supporting role in a number of carriers and enzymatic activities, including guanosine triphosphate, phospholipase C, adenylate cyclase, and guanylate cyclase, among 300 additional metabolic enzymes. In a recent study, pregnant

Nigerian women's maternal hypomagnesaemia was linked to the development of unfavorable fetal outcomes, such as preterm birth with all of its manifestations.<sup>16,17</sup> This finding implies that preeclampsia is a condition with higher prenatal risks when hypomagnesaemia is present. The effectiveness of MgSo<sub>4</sub> administration in the management and prophylaxis of eclampsia and PE has been explored in connection to Mg blood levels and PE.<sup>18</sup>

This study was designed to compare of serum Mg and Zn levels between pre-eclamptic and control normotensive pregnant female in order to describe a general strategy for incorporating the results of this assessment into the formulation of a preventative intervention.

## Methodology

A cross-sectional study was conducted over a six-month period from July 2021 to December 2021. The study sample was selected from both outpatient and in-patient departments of the Obstetrics and Gynaecological unit of the Hayatabad Medical Complex-MTI, Peshawar. A total of 110 pregnant females were selected after 20 weeks of gestation. Calculation of gestational age was done from the date of last menstrual period or 1st trimester ultrasound,<sup>14</sup> (mean gestational age for both groups was about 33.34±5.26 weeks). Women having twin pregnancies, molar pregnancy, diabetes mellitus, chronic hypertension, renal disease, or any other infectious or inflammatory disease or on medication for the said diseases were excluded. The diagnosis of preeclampsia was done by women developing hypertension and proteinuria for the 1<sup>st</sup> time after 20weeks of gestation. Blood pressure was taken by mercury sphygmomanometer twice after interval of rest of about 15 min.<sup>15</sup>

After an informed verbal & written consent, 5ml venous blood was withdrawn with 5ml disposable syringes from the vein of subject under aseptic conditions. 5ml of the blood was transferred to

labeled plain vacuum tubes for calculation of serum zinc and serum magnesium levels blood samples were stored at pathology laboratory, Khyber Girl Medical College, Peshawar under the supervision of a Pathologist, and results were obtained following the manufacturers protocol. Collected data was analyzed by statistical package for social sciences (SPSS) V, 21 and presented as tables and graphs. Quantitative variables were presented as mean (standard deviation), and qualitative variables were expressed on frequency + percentage. Relationships between qualitative variables were determined using  $X^2$  test or Fisher's exact test where suitable. Association of quantitative (numerical variables) for means difference in pre-eclamptic pregnant women and normotensive pregnant women was done by student's independent t-test. A p-value of  $\leq 0.05$  was considered statistically significant for all statistically tests.

The study received **ethical approval** from the Khyber Medical University Advance Studies & Research Board (KMU-AS&RB) letter no DIR/KMU-AS&RB/CS/001209 dated 07-04-2021.

## Results

### Overview of Study Population

The study included a total of 110 pregnant women, with the sample size divided into two primary groups: pre-eclamptic (46 women) and normotensive (64 women). The mean age of participants was  $26.41 \pm 4.71$  years, and the age distribution was as follows: 39.09% of the women were aged between 18-24 years, 40.91% were aged between 25-31 years, and 20.00% were aged 32 years or older. The majority of participants were of Pashtun ethnicity (95.45%), and the rest (4.55%) were from other ethnic groups.

In terms of obstetric characteristics, 84.55% of the women were multi-gravida, with a mean gravida of  $3.94 \pm 2.29$ . The mean parity for the entire study group was  $2.36 \pm 1.92$ , and 58.18% of the women were multiparous. Pre-eclampsia was significantly

more common in older women, as evidenced by the mean age of  $29.26 \pm 3.86$  years in the pre-eclamptic group, compared to  $24.36 \pm 4.19$  years in the normotensive group ( $p < 0.001$ ).

### Demographic and Obstetric Characteristics

Table 1 presents the demographic and obstetric characteristics of the study participants. The pre-eclamptic group had significantly higher maternal age compared to the normotensive group, with the mean age of pre-eclamptic women being  $29.26 \pm 3.86$  years versus  $24.36 \pm 4.19$  years in normotensive women ( $p < 0.001$ ). Additionally, the proportion of women in the age group 25-31 years and  $\geq 32$  years was higher in the pre-eclamptic group, while the normotensive group had a higher percentage of women in the 18-24 years category ( $p < 0.001$ ). Gravida and parity were also significantly different, with pre-eclamptic women having a higher mean gravida ( $4.67 \pm 2.21$ ) and mean parity ( $3.09 \pm 1.71$ ) compared to normotensive women ( $3.41 \pm 2.22$  and  $1.84 \pm 1.90$ , respectively).

**Table 1: Demographic and Obstetric Characteristics of the Pregnant Women (n=110)**

Characteristic	Pre-eclamptic Women (n=46)	Normotensive Women (n=64)	p-value
Maternal age (mean $\pm$ SD)	$29.26 \pm 3.86$	$24.36 \pm 4.19$	<0.001
18-24 years	7 (15.22%)	36 (56.25%)	<0.001
25-31 years	22 (47.83%)	23 (35.94%)	
$\geq 32$ years	17 (36.96%)	5 (7.81%)	
Gravida (mean $\pm$ SD)	$4.67 \pm 2.21$	$3.41 \pm 2.22$	0.004
Nulliparous (%)	0 (0%)	20 (31.25%)	<0.001
Multiparous (%)	36 (78.26%)	28 (43.75%)	0.001

Parameter	Pre-eclamptic Women (n=46)	Normotensive Women (n=64)	p-value
Serum Zinc (mean ± SD)	68.16 ± 20.60	74.96 ± 32.23	0.385
Serum Magnesium (mean ± SD)	1.68 ± 0.39	1.86 ± 0.34	0.085

### Serum Zinc and Magnesium Levels

Table 2 summarizes the serum zinc and magnesium levels in both pre-eclamptic and normotensive women. The mean serum zinc levels were slightly lower in the pre-eclamptic group (68.16 ± 20.60 µg/dL) compared to the normotensive group (74.96 ± 32.23 µg/dL), but this difference was statistically insignificant (p = 0.385). Similarly, serum magnesium levels were lower in pre-eclamptic women (1.68 ± 0.39 mg/dL) compared to normotensive women (1.86 ± 0.34 mg/dL), though the difference was not statistically significant (p = 0.085).

### Pre-eclampsia Features and Elemental Concentrations

Further analysis revealed that pre-eclamptic women with mild and severe features exhibited lower levels of zinc and magnesium compared to normotensive women. However, as shown in Table 3, the differences were statistically non-significant. The mean serum zinc level for pre-eclamptic women with mild features was 71.41 ± 22.50 µg/dL and 61.25 ± 14.72 µg/dL for those with severe features. Similarly, for serum magnesium, the mean levels were 1.73 ± 0.27 mg/dL for mild pre-eclampsia and 1.57 ± 0.60 mg/dL for severe pre-eclampsia.

### Clinical Characteristics and Statistical Analysis

The clinical characteristics, such as history of pre-eclampsia, diuretic use, and proteinuria, were significantly associated with the study groups. As shown in Table 4, a higher percentage of pre-eclamptic women had a positive history of pre-

eclampsia (71.74%) compared to normotensive women (0%), and the difference was statistically significant (p < 0.001). Proteinuria was also significantly more prevalent in pre-eclamptic women (95.65%) compared to normotensive women (26.56%) (p < 0.001). The mean proteinuria level for pre-eclamptic women was significantly higher (202.09 ± 229.69 mg/day) compared to normotensive women (7.73 ± 37.57 mg/day) (p < 0.001).

Parameter	Mild Pre-eclampsia (n=34)	Severe Pre-eclampsia (n=12)	Normotensive Women (n=64)	p-value
Serum Zinc (mean ± SD)	71.41 ± 22.50	61.25 ± 14.72	74.96 ± 32.23	0.468
Serum Magnesium (mean ± SD)	1.73 ± 0.27	1.57 ± 0.60	1.86 ± 0.34	0.128

Characteristic	Pre-eclamptic Women (n=46)	Normotensive Women (n=64)	p-value
History of Pre-eclampsia (%)	33 (71.74%)	0 (0%)	<0.001
Diuretics Used (%)	7 (15.22%)	0 (0%)	0.002
Presence of Proteinuria (%)	44 (95.65%)	17 (26.56%)	<0.001
Proteinuria (mean ± SD)	202.09 ± 229.69	7.73 ± 37.57	<0.001

## Discussion

Preeclampsia (PE) is a multi-organ condition that occur at 20 weeks of gestation or later. It can have a

range of unfavourable effects on women who are pregnant, including high blood pressure, proteinuria, liver impairment, placental abruption, and fetal growth retardation and complicates about 5% of pregnancies globally. It continues to be a significant contributor to maternal, fetal, and neonatal death, notably in lower income nations. Some experts suggested that trace elements may be crucial in the pathogenesis of PE. Even though they only make up 0.1% of the human body, but play a significant role in regulating health.

Magnesium (Mg) and zinc (Zn) are two critical essential nutrients. It serves as a cofactor and is an essential component of many biological processes in the human body. Abnormal serum Zn levels have been linked to conditions like breast cancer, TB, and cardiovascular events. Zn has a significant influence in both various hormonal adaptations and embryonic development throughout gestation.<sup>11-22</sup> It has been established that magnesium is a crucial co-factor for many metabolic enzymes. It is crucial for the propagation of neurochemicals and peripheral vasodilation.

Based on our results, it can be concluded that neither pre-eclamptic nor control group have a significant relationship between serum zinc levels, magnesium level and blood pressure.

A study postulated that these substances might not show a clinical meaning in the pathogenesis of pregnancy hypertension because they did not identify a correlation between serum levels of Ca, Mg, and Zn and gestational hypertension.<sup>23</sup> However, in our results, preeclamptic women rather than healthy controls had low mean zinc and Magnesium concentrations. Since Zn is necessary for the correct operation of antioxidant enzymes that guard against free radical damage, so PE is known to be characterized by an imbalance of oxidants and antioxidants in maternal vascular systems that favors the hypothesis that Zn plays a significant intermediate role in preeclampsia.<sup>24</sup>

Preeclampsia is a multisystem syndrome, widely characterized vasospasm and vascular endothelial

damage advancing to ischemia, hypoxia and cellular injury. Calcium and magnesium are imperative intracellular cations associated with muscular contractility; vascular spasm and neuromuscular secretion are calcium and magnesium.

Our results showed that, preeclamptic women's serum Mg levels were reduced than those of the normal group however the difference was statistically insignificant. Similar findings have been reported from various geographic locations.<sup>25,26</sup> By Kanchapan et al,<sup>25</sup> in Thailand and another study by Behairy,<sup>26</sup> Pre-Eclampsics were found to have low maternal serum magnesium concentrations. When compared to a normal pregnant control, Chanvitya reported no significant change in the mean mother serum Mg of both moderate and severe features of preeclampsics.<sup>27</sup>

## Conclusion

This study aimed to investigate the relationship between serum zinc and magnesium levels and pre-eclampsia in pregnant women. The results showed no significant difference in the serum levels of zinc and magnesium between pre-eclamptic and normotensive women, suggesting that these trace elements may not be reliable biomarkers for pre-eclampsia. While the observed trend of lower serum levels in pre-eclamptic women raises questions about the role of zinc and magnesium in the condition, statistical analysis did not find a strong correlation between these nutrients and blood pressure levels. Despite the lack of statistically significant findings, this study contributes to the growing body of research examining the complex mechanisms underlying pre-eclampsia. The results highlight the need for further research with larger sample sizes and more focused biochemical evaluations to better understand the potential roles of magnesium and zinc in pre-eclampsia. Future studies could explore other factors that might influence the levels of these trace elements and investigate their potential as early indicators of the

condition. While the study did not establish a direct link between serum zinc and magnesium levels and pre-eclampsia, it suggests that further exploration is needed to determine their exact role in the pathophysiology of the disease.

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