

ORIGINAL ARTICLE

# Relationship between Serum Zinc Levels and Preeclampsia at the University Teaching Hospital, Lusaka, Zambia

L Chababa,<sup>1</sup> M Mukosha,<sup>2</sup> G Sijumbila,<sup>1</sup> B Vwalika<sup>3</sup>

<sup>1</sup> University of Zambia, School of Medicine, Department of Physiological Sciences, Zambia

<sup>2</sup> University of Zambia, School of Medicine, Department of Pharmacy, Zambia

<sup>3</sup> University of Zambia, School of Medicine, Department of Obstetrics and Gynaecology, Zambia

## ABSTRACT

**Background:** Preeclampsia is one of the common conditions in the pregnant mothers in Zambia. This condition has been shown in some studies to be associated with increased oxidative stress. This study aimed at evaluating the association of zinc, an important cofactor in the antioxidant metalloproteins in the aetiology of preeclampsia

**Methods:** A comparative cross-sectional study design was employed on conveniently sampled 41 preeclamptic and 57 non-preeclamptic pregnant women over a four month period at the University Teaching Hospital in Lusaka, Zambia. Serum samples from participants were analysed for Zinc concentration by Atomic Absorption Spectrometry.

**Results:** There was no significant difference in the mean serum Zinc levels between the preeclamptic and the non-preeclamptic pregnant women.

**Conclusion:** Based on our findings serum zinc level is not associated with the occurrence of preeclampsia.

## INTRODUCTION

Preeclampsia is a multisystem disorder characterized by the new onset of hypertension (>140/90mmHg) often accompanied by proteinuria in the second half of pregnancy.<sup>1,2</sup> It can be deleterious to both maternal and foetal health if not managed early. It is estimated globally

that 5-7% of all pregnancies are affected by preeclampsia and it is "one of the most common yet least understood disorders of pregnancy".<sup>3</sup>

While cases of preeclampsia are found worldwide, they are said to be more prevalent in developing countries.<sup>1</sup> In Zambia, according to Ministry of Health (MoH) records, hypertension related problems are among the leading causes of death for expectant mothers. Their prevalence has been on the rise in the previous decades.

Preeclampsia is believed to be caused by multiple factors and the search continues for its associated risk factors in order to gain further insights into the pathogenesis of this syndrome. Among numerous other hypotheses, one that seems to have sparked attention is the proposed possible role of serum zinc deficit in the pathophysiology of preeclampsia. In this regard, several studies have attempted to explore the possible link of not just zinc, but also magnesium, calcium, copper and other minerals, but the results of various studies remain controversial and inconclusive.<sup>4</sup> Zinc is found in all cells and has many functions which include synthesis of macromolecules, immune protection and anti-oxidative properties as well.<sup>5</sup> The antioxidant effects of zinc have been shown to be acute and chronic. In the acute phase zinc protects the sulfhydryls of protein and prevents the formation of hydroxyl radicals from hydrogen peroxide and the chronic effects is through the induction of metalloproteins which have the antioxidant properties.<sup>6</sup> Since high blood pressure has been associated with increased oxidative stress its logical to assume that adequate levels of serum zinc with its antioxidant properties can reduce blood pressure and vice versa.<sup>7,8</sup>

## Corresponding Author

Likando Chababa,  
University of Zambia, School of Medicine,  
Department of Physiological Sciences, Zambia  
E-mail: [gsijumbila@yahoo.co.uk](mailto:gsijumbila@yahoo.co.uk)

Though the aetiology of preeclampsia is not yet fully elucidated, it is now generally accepted that the placenta plays a major role in the development of the disease. It is believed that abnormal development of vasculature in the placenta leads to under perfusion, ischaemia, and hypoxia which in turn lead to the release of pathogenic soluble factors into the maternal circulation responsible for the widespread endothelial dysfunction present in preeclampsia.<sup>9</sup> In addition elevated levels of peroxynitrite and lowered levels of antioxidants, such as superoxide dismutase a metalloenzyme, have been observed in preeclamptic states.<sup>10</sup> In line with the above observations, it has also been reported that women who were deficient in dietary intake of antioxidant minerals such as zinc and selenium were at a higher risk of developing preeclampsia.<sup>11,12</sup>

Investigations of the zinc status of pregnant women in Africa are limited, but there is increasing evidence that they may be especially vulnerable to zinc deficiency due to impoverished nutrition. Previous studies of pregnant women in various African countries, including Nigeria, Egypt, DR Congo, and Malawi, have all reported lower plasma zinc concentrations compared to pregnant women from developed countries.<sup>13</sup> Evidence seems to point to the fact that decreased serum levels of zinc and other trace minerals are associated with the risk of preeclampsia in pregnant women, though there is still need for further research in various populations to establish the external validity of various findings.<sup>3,12,14</sup>

This study therefore aimed at finding out whether there was a relationship between serum zinc levels and preeclampsia at the University Teaching Hospital in Lusaka, Zambia.

## METHODS

This was a comparative cross-sectional study design which compared mean serum zinc levels of preeclamptic and non-preeclamptic pregnant women.<sup>15</sup> The study was conducted at the Maternity Clinic of the University Teaching Hospital (UTH). The target population comprised Zambian women who were more than 20 weeks pregnant attending antenatal clinics. For

inclusion in the study women had to be Zambian, more than 20 weeks pregnant, over 18 years old who were willing to participate. The ones who were non-Zambian, on mineral supplementation or with history hypertension before pregnancy were excluded. The study recruited 41 preeclamptic and 57 non-preeclamptic participants. Systolic and diastolic blood pressure readings and levels of proteinuria were accurately determined and used to distinguish preeclamptic participants from non-preeclamptic ones. Those with systolic blood pressure readings above 140mmHg and/or diastolic blood pressure above 90mmHg with significant proteinuria were considered preeclamptic.

Blood amounting to 8mls was drawn from the ante cubital vein using a sterile needle and syringe into an appropriate specimen bottle. Serum was prepared by centrifugation (Allegra 6R, Beckmann Coulter, USA) of the blood samples in the plain tubes for 10 min at 4000 rpm and stored at -20°C until the stage of zinc analysis.

Serum samples were assayed for concentration of zinc in microgram per decilitre using Atomic Absorption Spectroscopy (AAS) technique at the Food and Drugs control laboratory as done elsewhere.<sup>16</sup> In brief a light beam is used to excite atoms that are in the ground state in a flame. The light absorption (by these ground state atoms) is measured and related to concentration.

Data was analysed using Stata version 14 (Stata Corporation, College Station, Texas). In all comparisons, significance was determined at  $p=0.05$ . The protocol was reviewed and approved by Eres Converge ethics committee.

## RESULTS

### Demographic characteristics

Comparison of demographic characteristics shows that the proportion of participants did not significantly differ with regards to age group, gestational age, family history of preeclampsia, and residential area density with exception of age group 18-30 and 30-40 and gestational age of 25-30 weeks (Table 1).

**Table 1: Demographic statistics for the pre-eclamptic pregnant women and the non-pre-eclamptic participants**

Variables	Pre-eclamptic n=41	Non-Pre-eclamptic n=57	T test P-value
	(mean±SD)	(mean±SD)	
<b>Age group</b>			
18-30	0.32±0.47	0.60±0.50	0.006
30-40	0.61±0.49	0.37±0.49	0.018
40+	0.073±0.26	0.04±0.19	0.403
<b>Gestational Age (weeks)</b>			
20-25	0.12±0.33	0.26±0.44	0.088
25-30	0.24±0.43	0.04±0.19	0.002
30+	0.63±0.49	0.70±0.46	0.487
<b>Family History of pre-eclampsia</b>			
No	0.85±0.36	0.82±0.38	0.704
Yes	0.15±0.36	0.18±0.38	0.704
<b>Residential Area Density</b>			
High	0.51±0.51	0.56±0.50	0.634
Low	0.12±0.33	0.16±0.37	0.620
Medium	0.37±0.49	0.280±0.45	0.377

**Comparison of mean serum Zinc levels**

Table 2 below summarizes the comparisons between mean serum zinc levels in both groups in general (preeclamptic group 89.17± 47.19 mg/dL, non-preeclamptic group 76.20± 35.23mg/dL, p=0.122) and within specific variables that could be deemed to be confounding. It seems apparent that serum zinc levels do not significantly differ in all the listed categories and in the whole group comparisons, with exception of participants from the medium residential area density (p<0.05).

**Table 2: Comparison of mean serum zinc levels in preeclamptic verses non-preeclamptic pregnant women in various categories and in whole group**

Variables		Mean Serum Zinc Concentration levels (µg/dL)		P-value
		n=41	n=57	
		Pre-eclamptic	Non-Pre-eclamptic	
<b>Age group (years)</b>	18-30	87.11	76.84	0.3941
	30-40	94.32	76.69	0.1948
	40+	55.19	60.06	0.8876
<b>Gestational Age (Weeks)</b>	20-25	76.56	74.48	0.8590
	25-30	86.61	67.16	0.3296
	30+	92.59	77.29	0.2025
<b>Family History of pre-eclampsia</b>	Yes	81.95	71.65	0.4784
	No	90.41	77.16	0.1710
<b>Residential Area Density</b>	High	92.791	83.27	0.500
	Medium	87.83	67.26	0.0391
	Low	78.02	66.90	0.4161

Whole group 89.17± 47.19 76.20± 35.23 0.122

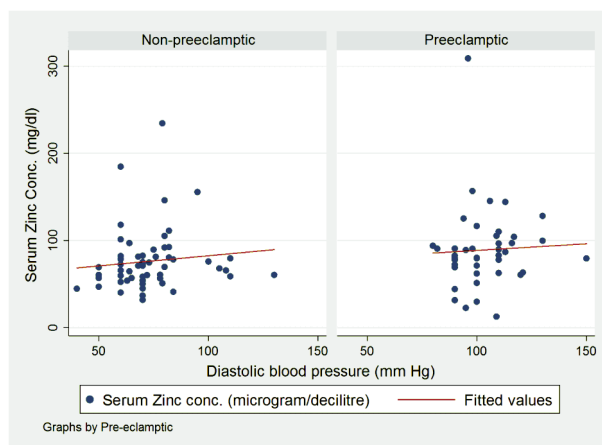
**Correlation between serum Zinc level and Systolic/Diastolic Blood Pressure**

Pearson's correlation between systolic blood pressure and serum zinc level was positive (r=0.1149) but insignificant (p=0.2599). Diastolic blood pressure also had a positive correlation with serum zinc level (r=0.1656) but it was also not significant (p=0.1031). See Table 3 and Figures 2 and 3 below.

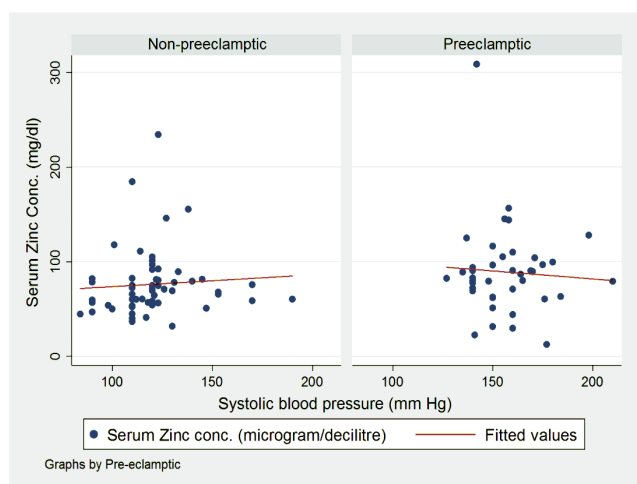
**Table 3: Correlation coefficients of systolic blood pressure and diastolic blood pressure verses serum Zinc levels**

Total sample Correlation matrix			
Variable	Serum Zinc Conc. (µg/dL)		
	n	correlation coefficient	p-value
Systolic BP	98	0.1149	0.2599
Diastolic BP	98	0.1656	0.1031

**Fig. 2 Correlation of systolic blood pressure and serum Zinc levels**



**Fig. 3 Correlation of diastolic blood pressure and serum zinc levels**



## DISCUSSION

It can be deduced from the above illustrated data that the findings show no significant association between serum zinc level and blood pressure in preeclamptics or non-preeclamptics. It might therefore follow that changes in serum zinc levels do not play a direct role in the pathogenesis of preeclampsia. In our study serum zinc levels were found to have no significant effect on systolic or diastolic blood pressure. There was a positive correlation between the serum zinc levels and blood pressure though insignificant.

Our results are supported by the findings of some other studies. In one study where 20 preeclamptic and 20 healthy pregnant women were recruited it was reported that serum zinc level was slightly lower in the preeclamptic than the healthy pregnancies, but the difference was not statistically significant.<sup>17</sup> It was argued that the lower serum zinc levels reported in other studies could be due to other factors, other than zinc deficiency, such as reduced albumin concentrations. Magri et al., did not find a relationship between the serum levels of calcium, magnesium, and zinc and gestational hypertension; therefore, they proposed that these elements might not clinically participate in the pathogenesis of the gestational hypertension.<sup>18</sup> Their findings and conclusions are compatible with the results of the present study as far as serum zinc is concerned. However, in our study a higher mean zinc concentration

was unexpectedly found in the preeclamptic rather than the normal pregnant women.

Others have reported significantly lower mean serum zinc in preeclamptic patients than in normal pregnancies and an inverse correlation of blood pressure and the mineral levels in pregnant women.<sup>19,20</sup> The studies done in Nigeria and Iran also concluded that levels of zinc were significantly low in preeclampsia and found a significant difference in the levels in cases versus controls ( $p < 0.001$ ).<sup>3,21</sup> This lack of consensus on the role of zinc on pregnancy outcome is largely due to contradictory results from researchers. Although many results seem to suggest that deficiency of serum zinc may predispose to preeclampsia other results have demonstrated no association at all. This can be due methods for measuring serum zinc not being sensitive or specific enough, variations in sample sizes and many other factors. Generally one would expect low serum zinc levels to be associated with preeclampsia as zinc has got significant antioxidant properties, which minimizes oxidative stress, one of the main factors associated with preeclampsia.<sup>22</sup> The role of zinc binding proteins may also play a major role in total serum zinc in pregnancy. For instance some researchers have demonstrated that hypoalbuminemia can predispose to reduced serum zinc levels and it has also been observed that in pregnancy the affinity of albumin for zinc tends to be reduced which can also predispose to low serum zinc level.<sup>23</sup> What this means is that serum zinc levels may be low in the presence of normal tissue levels because of reduced transport proteins.

It has also been argued that serum zinc may not really be an accurate biomarker of the actual zinc status that occurs at the cellular level of tissues. Serum zinc is under tight homeostatic regulatory mechanisms that keep the level fairly constant in spite of nutritional or pathological changes.<sup>24</sup>

Zinc has been thought to be an important intermediary factor in preeclampsia as it is required for the proper functioning of antioxidant enzymes which protect the epithelial lining of blood vessels from free radicals injury. Imbalance of oxidants and antioxidants in favour of the former in maternal vascular systems has been established as a hallmark of preeclampsia.<sup>25</sup> According to one study, nutritional supplementation of zinc was associated with lower incidence of preeclampsia though plasma zinc

levels remained fairly constant. In this vein it could be possible that zinc plays a role in preeclampsia but serum zinc level may not be the appropriate way of detecting that role.<sup>26</sup>

## CONCLUSION

Our conclusion therefore is that serum zinc level is not associated with the aetiology of preeclampsia.

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## DECLARATION OF INTEREST

The authors have no conflict of interest.

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