

# Serum and Urinary Levels of Micronutrients in Preeclamptic and Healthy Pregnant Women: A Case-Control Study

Afsaneh Tabandeh<sup>1</sup>, Samira Eshghinia<sup>2</sup>, Hamid Reza Joshaghani<sup>3</sup>, Mashallah Azarian<sup>1</sup>, \*Saba Besharat<sup>2</sup>

<sup>1</sup>School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran <sup>2</sup>Clinical Research Development Unit (CRDU), Sayad Shirazi Hospital, Golestan University of Medical Sciences, Gorgan, Iran <sup>3</sup>Biochemistry and Metabolic Disorders Research Center, Golestan University of Medical Sciences, Gorgan, Iran

### ABSTRACT

**Introduction:** Preeclampsia is the most common cause of prenatal and maternal mortality worldwide and the second most common cause of maternal death in Iran. Deficiency of some trace elements such as zinc, calcium and magnesium in pregnant women may play a role in preeclampsia. Therefore, the aim of this study was to measure serum and urinary levels of zinc, calcium and magnesium in preeclamptic and healthy pregnant women. **Materials and Methods:** This cross-sectional study was performed on 100 pregnant women (at second trimester of pregnancy) referred to the gynecology clinic of Sayyad Shirazi hospital in Gorgan, Iran, during 2014-15. The subjects were divided into a preeclampsia group (N=50) and an age-matched healthy control group (N=50). Serum and urinary levels of zinc, calcium and magnesium were measured by enzymatic method. Data were analyzed in SPSS (version 19) using t-test. P-values less than 0.05 were considered statistically significant. **Results:** Mean serum calcium level in the preeclampsia group ( $8.17 \pm 0.64$  mg/dl) was significantly lower than that in the control group ( $8.70 \pm 0.40$  mg/dl) ( $P < 0.001$ ). Moreover, mean urinary calcium level in the preeclampsia group ( $222.33 \pm 19.35$  mg/dl) was significantly higher than that in the control group ( $158.61 \pm 40.16$  mg/dl) ( $P < 0.001$ ). **Conclusions:** Women with preeclampsia have significantly lower serum calcium level compared to healthy pregnant women, but the level is still within the normal range. Moreover, preeclampsia has no significant effect on the serum zinc and magnesium concentrations. Women with preeclampsia have significantly higher urinary calcium and significantly lower urinary magnesium levels compared to healthy pregnant women.

**KEYWORDS:** Preeclampsia, serum and urine, zinc, magnesium, calcium

\***Correspondence:** Saba Besharat, Address: Clinical Research Development Unit (CRDU), Sayyad Shirazi hospital, Sayyad Shirazi Boulevard, Gorgan, Iran, Telephone: +98173225190, Email: saba\_besharat@yahoo.com

### INTRODUCTION

Preeclampsia is a disorder characterized by hypertension, edema and proteinuria, affecting about 2 to 8% of pregnant women worldwide [1-7]. Deficiencies of trace elements such as calcium, magnesium, zinc and copper are thought to be associated with risk of preeclampsia [8-13]. These micronutrients are all essential for the antioxidant defense system [10]. Disruption in the balance between oxidant-generating system and antioxidant defense system results in oxidative stress. Oxidative stress-induced endothelial dysfunction is one of the main events proposed in the pathogenesis of preeclampsia [10].

Despite numerous studies, there is not sufficient evidence about the exact role of trace elements [14]. Calcium has a major role in development of clinical hypertension. A balance between calcium and magnesium

(vasodilation and vasoconstriction) level is required for the normal regulation of blood pressure. Therefore, magnesium may be considered as a calcium channel blocker that increases intracellular calcium concentrations, resulting in vasodilatation [1].

The aim of this study was to evaluate serum and urinary level of zinc, calcium and magnesium in preeclamptic and healthy women in Gorgan, Northeast of Iran.

### MATERIALS AND METHODS

This cross-sectional study was performed on 100 pregnant women (at second trimester of pregnancy) referred to the gynecology clinic of Sayyad Shirazi hospital in Gorgan, Iran, during 2014-15. The subjects were divided into a preeclampsia group (N=50) and an age-matched healthy control group (N=50).

Informed consent was taken from all participants and a questionnaire was completed to collect data on age and gravidity. The subjects were free to withdraw from the study at any time.

Inclusion criteria were blood pressure of  $>140/90$  mmHg and proteinuria after 20 weeks of gestation.

Exclusion criteria were presence of eclampsia and other epileptic disease, pregnancy-induced hypertension and other hypertensive disorders, and cardiovascular disease requiring medication.

A questionnaire was completed to collect data on age and gravidity. Calcium, magnesium and zinc levels were measured by enzymatic method using Pars Azmun kits (Iran) for calcium and magnesium, and Dialab kits (Austria) for zinc.

Urinary level of the trace elements was assessed by 24-hour urine collection. Data were analyzed in SPSS (version 19) using t-test. P-value of less than 0.05 was considered statistically significant.

## RESULTS

The mean age ( $\pm$ standard deviation) of subjects was 28.42 ( $\pm 6.03$ ) years. Table 1 represents the serum level of calcium, zinc and magnesium in both study groups. Serum calcium level was significantly lower in the preeclampsia group compared to the control group ( $P < 0.001$ ), but no calcium deficiency was found. There was no significant difference in the serum zinc and magnesium levels between the two study groups.

**Table 1. Mean ( $\pm$ standard deviation) serum levels of micronutrient in the preeclampsia and control group**

Micronutrients	Women with preeclampsia	Healthy pregnant women	P-value
Calcium (mg/dl)	8.17 ( $\pm 0.64$ )	8.70 ( $\pm 0.40$ )	$<0.001$
Zinc (mg/dl)	70.50 ( $\pm 19.94$ )	75.89 ( $\pm 18.96$ )	0.17
Magnesium (mg/dl)	1.82 ( $\pm 0.53$ )	1.83 ( $\pm 0.18$ )	0.895

Mean urinary level of calcium was significantly higher in the preeclampsia group, but mean urinary level of zinc was

significantly lower in the preeclampsia group. There was no significant difference in the urinary level of magnesium between the patients and controls (Table 2).

**Table 2. Mean ( $\pm$ standard deviation) urinary level of micronutrients in the preeclampsia and control group**

Micronutrients	Cases with preeclampsia	Healthy control group	P-value
Calcium (mg/dl)	222.33 ( $\pm 19.35$ )	158.61 ( $\pm 40.16$ )	0.012
Zinc (mg/dl)	647.11 ( $\pm 58.33$ )	950.99 ( $\pm 80.13$ )	0.003
Magnesium (mg/dl)	187.11 ( $\pm 36.60$ )	148.75 ( $\pm 23.79$ )	0.682

## DISCUSSION

The present study was designed to evaluate the alterations in the serum levels of calcium, zinc and magnesium in women with preeclampsia. Our findings showed that preeclamptic women had significantly lower serum calcium levels compared to healthy pregnant women. This is in line with results of some previous studies [4, 6, 9, 10, 15]. Increased intracellular calcium in smooth

muscle cells has been reported during pregnancy, which could be due to elevated secretion of parathyroid hormone and renin in response to hypocalcemia. This rise in calcium leads to vasoconstriction and increased vascular resistance, which results in the subsequent development of high blood pressure in pregnancy [4].

In this study, serum zinc level was lower in preeclamptic women compared to healthy controls. However, this difference was not statistically significant. In addition, the urinary level of zinc was significantly lower in women with preeclampsia. Similar to our study, most previous studies reported decreased serum zinc levels in patients with preeclampsia [4, 9]. Low serum concentration of zinc leads to oxidative stress and reduces the activity of the antioxidant enzyme-superoxide dismutase, which itself may increase blood pressure [4]. Due to the increased transfer of zinc from mother to the growing fetus, decreased serum zinc level and increased urinary zinc excretion are observed in preeclamptic women [4]. On the other hand, elevated lipid peroxidation in preeclampsia lowers concentrations of transporter protein and estrogen, resulting in a decrease in serum zinc level [4].

Unlike previous reports, we found no significant difference in the serum and urinary magnesium levels between the two groups [4,9,10]. It has been reported that preeclamptic women have lower serum magnesium, calcium and zinc levels. Concentrations of magnesium significantly affects the tone and contractility of vascular smooth muscles [4].

Pregnancy-induced hypertension could be due to increased vascular resistance, and low serum concentrations of calcium and magnesium may play a role in constriction of vascular smooth muscles. Moreover, decreased magnesium concentrations may have a vasodilatory effect that results in increased blood pressure [4].

## CONCLUSION

Women with preeclampsia have significantly lower serum calcium level compared to healthy pregnant women, but the level is still within the normal range. Moreover, preeclampsia has no significant effect on the serum zinc and magnesium concentrations. Women with preeclampsia have significantly higher urinary calcium and significantly lower urinary magnesium levels compared to healthy pregnant women. Since this was a

cross-sectional study, conducting longitudinal and cohort studies would further clarify the possible association of micronutrient deficiency and preeclampsia.

## ACKNOWLEDGMENTS

This article has been derived from a thesis (code: 693) for completion of a degree in medicine (MD) at Golestan University of Medical Sciences, Iran.

## CONFLICT OF INTEREST

There is no conflict of interest to declare

## REFERENCES

1. Elmugabil A, Hamdan HZ, Elsheikh AE, Rayis DA, Adam I, Gasim GI. Serum calcium, magnesium, zinc and copper levels in sudanese women with preeclampsia. *PLoS one*. 2016;11(12):e0167495.
2. Adam I, Haggaz AD, Mirghani OA, Elhassan EM. Placenta previa and pre-eclampsia: analyses of 1645 cases at medani maternity hospital, Sudan. *Front Physiol*. 2013;4: 32.
3. Mistry HD, Gill CA, Kurlak LO, Seed PT, Hesketh JE, Méplan C, et al. Association between maternal micronutrient status, oxidative stress, and common genetic variants in antioxidant enzymes at 15 weeks' gestation in nulliparous women who subsequently develop preeclampsia. *Free Radic Biol Med*. 2015;78:147-55.
4. Al-Jameil N, Tabassum H, Ali MN, Qadeer MA, Khan FA, Al-Rashed M. Correlation between serum trace elements and risk of preeclampsia: A case controlled study in Riyadh, Saudi Arabia. *Saudi J Biol Sci*. 2017;24(6):1142-8.
5. Song X, Li B, Li Z, Wang J, Zhang D. High serum copper level is associated with an increased risk of preeclampsia in Asians: A meta-analysis. *Nutr Res*. 2017;39:14-24.
6. Kim J, Kim YJ, Lee R, Moon JH, Jo I. Serum levels of zinc, calcium, and iron are associated with the risk of preeclampsia in pregnant women. *Nutrition research*. 2012;32(10):764-9.
7. Pallavi P, Pranay A, Jasmin H. Changes in serum calcium and Magnesium level in preeclampsia vs normal pregnancy. *Intern J Biomed Adv Res*. 2012;3(6):511-3.

8. Hovdenak N, Haram K. Influence of mineral and vitamin supplements on pregnancy outcome. *Eur J Obstet Gynecol Reprod Biol.* 2012;164(2):127-32.
9. Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. *Biol Trace Elem Res.* 2010;133(2):162-70.
10. Negi R, Pande D, Karki K, Kumar A, Khanna RS, Khanna HD. Trace elements and antioxidant enzymes associated with oxidative stress in the pre-eclamptic/eclamptic mothers during fetal circulation. *Clinical nutrition.* 2012;31(6):946-50.
11. Pathak P, Kapil U. Role of trace elements zinc, copper and magnesium during pregnancy and its outcome. *Indian J Pediatr.* 2004;71(11):1003-5.
12. Bringman J, Gibbs C, Ahokas R, Syamal B, Ramsey R, Egerman R. Differences in serum calcium and magnesium between gravidas with severe preeclampsia and normotensive controls. *Am J Obstet Gynecol.* 2006;195(6):S148.
13. Kumru S, Aydin S, Simsek M, Sahin K, Yaman M, Ay G. Comparison of serum copper, zinc, calcium, and magnesium levels in preeclamptic and healthy pregnant women. *Biol Trace Elem Res.* 2003;94(2):105-12.
14. Trumbo PR, Ellwood KC. Supplemental calcium and risk reduction of hypertension, pregnancy-induced hypertension, and preeclampsia: an evidence-based review by the US Food and Drug Administration. *Nutr Rev.* 2007;65(2):78-87.
15. Amirabi A, Yazdian M, Pashapour N. Evaluation of serum calcium, magnesium, copper, and zinc levels in women with pre-eclampsia. *Iranian Journal of Medical Sciences.* 2015;33(4):231-4.