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The role of Trace Elements (Zinc, Copper, Magnesium and Calcium) in Pregnant Women with Preeclampsia in third trimester and fetal cord blood after delivery

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Abstract

Trace element such as zinc and copper display antioxidant activity and act as peroxynitrate scavenger while others such as magnesium and calcium essential micronutrients. The aim of this study to determine the status of these elements in preeclamptic pregnant women and to find any relationship between changes in serum level of zinc, copper, magnesium and calcium in preeclamptic women and healthy women and to assess the relation to severity of the disease in Al-Najef city. The patients included in this study were divided into two groups control group who are normotensive (50) and study group who are preeclampsia (50 patients, 31 mild preeclampsia and 19 severe preeclampsia). Parameters include age, parity, urine albumin, liver function test, renal function test and platelets count. Maternal blood aspirated and cord blood sample taken to measure serum copper, zinc, magnesium and calcium using commercial kits. There is significant decrease in the level of trace elements between the control and preeclamptic groups. The mean serum level of calcium, magnesium, copper and zinc between the preeclamptic group and control group was significantly different. It seems that these trace elements are involved in the pathogenesis of preeclampsia.

Key words: Preeclampsia; Zinc; Copper; Magnesium; Calcium; Cord blood

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Introduction

Preeclampsia is leading cause of maternal death. The world Health Organization estimates that globally between 50000 and 75000 women die of this condition each year. Furthermore, preeclampsia is frequently accompanied by fetal growth restriction (FGR) which is responsible for

considerable perinatal morbidity and mortality, Although fetal growth is controlled by a number of factors including genetic predisposition and Maternal nutritional status [1, 2].

Trace elements such as zinc, copper, display antioxidant activity and act as peroxynitrite, while other such as Magnesium and Calcium are essential micronutrients. The disturbance in the metabolism of these elements may be a contributing factor in the development of certain diseases such as pre-eclampsia [3]. Dietary supplementation with these elements may help to prevent pre-eclampsia, at least in susceptible women, especially in developing countries [4].

Nutritional deficiencies are common during pregnancy and pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins. An inadequate dietary intake before and during pregnancy might be a high risk not only for the mother but also for the fetus [5]. Deficiencies of trace elements such as zinc, copper and magnesium have been implicated in various reproductive events like infertility, pregnancy wasted, congenital anomalies, preeclampsia, placental abruption, premature rapture of membrane, still birth and low birth weight [6].

Some studies have shown that changes in the levels of blood trace elements in pre-eclamptic patients may implicate its pathogenesis, while others have failed to show an association of blood levels of trace elements and prevalence of preeclampsia. The aim of this study is to determine the states of the trace elements (Calcium, Magnesium, Copper and Zinc) in pregnant women with preeclampsia and to find any relationship between changes in serum level of these trace elements and risk of developing preeclampsia and to assess the relation to severity of the disease in Al. Najaf city.

Methods

A total of 100 pregnant women, 50 patients with preeclampsia (31 patients mild, 19 patients severe preeclampsia and this is depend on her blood Pressure, albumin urine, signs and symptoms and other laboratory parameters) and 50 patients normotensive their age ranges 16 – 45 years, in third trimester (37-40 weeks) who were attending obstetrics and gynecology department in AL-Zahraa Teaching hospital in Al-Najaf city were investigated for analysis of serum levels of trace element, history sheet was completed where date pertaining to age, parity, blood Pressure, BMI, urine analysis for albumin, liver function test and renal function test. A written consent was obtained from all qualified pregnant women after explaining the purpose of the study and the confidentiality of collected data and results.

We exclude pregnant women who had a history of essential hypertension, multiple pregnancy, diabetes mellitus, heart disease, smoking or any medical diseases.

Blood samples were collected from participating women during the third trimester, and cord blood samples were collected from umbilical cord after delivery of fetus and before delivery of the placenta. Zinc, copper, calcium and magnesium were determined by flame atomic absorption spectrophotometry.

Statistical analysis

The statistical package for the social sciences (SPSS) software package was used for statistical analysis and graphical expression by Microsoft excel software. Values obtained from this study were expressed as mean and standard deviation when compared using the independent t-test Pearson and Annora correlation coefficient was used to measure the level of association between variables. Variables results were regarded as significant at $P < 0.05$.

Results

Characteristic	Normal (50)	Mild pe (31)	Sever pe (19)	P value
	Mean±SD	Mean±SD	Mean±SD	
Age	25.02±5.516	26.45±6.521	28.58±6.727	<0.006
Para	1.10±1.515	1.71±1.736	1.63±1.383	<0.008
Systolic blood pressure	115.50±6.095	144.03±5.231	165.53±6.432	<0.001
Diastolic blood pressure	70.30±5.556	94.35±4.608	107.63±8.558	<0.001
Body mass index	27.100±2.1783	28.681±2.1384	30.332±3.9719	<0.001

Table 1.

Demonstrate the mean and standard deviation of normal, mild, and severe preeclampsia in regard to demographic characteristics**.**

Characteristic	Normal (50)	Mild pe (31)	Sever pe (19)	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
SGOT	26.62±6.250	32.77±8.582	33.84±9.564	<0.001
SGPT	17.04±4.389	19.32±3.970	21.16±6.768	0.003
ALP	201.14±49.955	202.52±34.662	211.22±34.640	0.593
blood urea	24.42±4.440	28.58±8.445	32.32±8.327	<0.001
serum creatinine	0.7620±0.21466	0.9613±0.20925	1.0700±0.18616	<0.001
serum uric acid	4.1170±0.93617	4.8455±1.27006	5.5879±1.08043	<0.001
TSB	0.6560±0.20389	0.5468±0.22499	0.6189±0.23709	0.063

Table 2.

Comparison between different groups regarding biochemistry results.

Characteristic	Normal (50)	Mild pe (31)	Severe pe (19)	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
Calcium	9.1660±0.50451	7.4065±0.59941	7.3579±0.64232	<0.001
Magnesium	2.0820±0.29602	0.8677±0.32801	0.9579±0.28542	<0.001
Zinc	94.7800±16.00316	69.5290±6.27855	69.1632±7.45059	<0.001
Copper	116.9340±17.79279	82.9194±8.19103	84.7947±8.79195	<0.001

Table 3.

Comparison between different groups regarding minerals.

Characteristic	Mild pe (31)	Sever pe (19)	P value
	Mean ±SD	Mean ±SD	
Calcium	7.4065±0.59941	7.3579±0.64232	0.451
Magnesium	0.8677±0.32801	0.9579±0.28542	0.746
Zinc	69.5290±6.27855	69.1632±7.45059	0.313
Copper	82.9194±8.19103	84.7947±8.79195	0.794

Table 4.

Comparison between mild and severe preeclampsia regarding minerals.

Variables	Cord blood (controls)	Cord blood (mild PE)	Cord blood (sever PE)	P value
	mean±SD	Mean±SD	Mean±SD	
Magnesium	1.0730±0.16326	1.0935±0.49121	1.0579±0.43374	0.936
Zinc	97.2400±7.24374	81.6806±11.22026	86.8053±9.12168	<0.001
Copper	44.9000±10.85197	62.4581±12.09840	58.9526±9.97070	<0.001
Calcium	9.0860±0.77354	7.4613±0.74774	7.7263±0.77592	<0.001

Table 5.

Demonstrates the difference in cord blood between normal, mild, and severe pre-eclampsia regarding different minerals.

The SGPT, SGOT, blood urea, serum creatinine, serum uric acid significantly increase in preeclampsia group in comparison with control group (P<0.001), but there is no significant difference in the level of ALP and TSB between these groups as in table 2.

There are significant difference between normal and pre-eclamptic group in the level of trace element (there is decrease in level of trace element in pre-eclamptic group) table 3. While, no significant different between mild and severe pre-eclamptic group in level of trace element, table 4. There are significant different in the level of zinc, copper and calcium but not significant in magnesium in the cord blood sample. Also the level of copper increase in cord blood while Zinc and calcium decrease. There is no significant different in level of trace elements in cord blood sample between mild and severe preeclampsia as in table 5.

Discussion

Our knowledge of preeclampsia has increased dramatically in the past 10 years. The role of diet and the potential for micronutrient supplements or therapy has not been adequately studied in light of this knowledge. Minerals have important influence on the health of pregnant women and growing fetus. They are necessary during pregnancy and these elements should be supplemented as a daily requirement in pregnant women [7]. In developing countries, nutritional deficiency of essential trace elements is a common health problem, particularly among pregnant women because of increased requirements of various nutrients [8]. Accordingly, this study was initiated to compare trace elements status in women with or without pre-eclampsia.

Result obtained from this study show a significant decrease in all the trace elements in preeclamptic women when compared to the control group, this suggests a possible effect of zinc, copper, magnesium and calcium in development and pathogenesis of preeclampsia, similar results found by Leila Farzin, et al [8] who observe significant decline in Zn, Se, Ca and Mg levels between patients with pre-eclampsia and control group. However; this results must be interpreted with caution. This is because, we did not analyses the dietary intake of pre-eclamptic women to confirm whether the reduced levels of trace elements reported here is due to nutritional deficiencies. However our data in agreement with that of Mohammed et al [9] who reported reduced zinc concentration in women with eclampsia and Serefden Acikgoz [10],who reported that zinc and copper levels were low in the placentas of pre-eclamptic patients which might cause insufficiency of superoxide dismutase, an antioxidant enzyme. Furthermore, deficiency in placental zinc also plays a role in the biosynthesis of connective tissue, maintaining its integrity, which might have an impact on the structure of the spiral arteries.

It has reported an increased incidence of preeclampsia in zinc deficient regions and it was later found that zinc supplementation reduced the high incidence of the disease [11]. Furthermore, decreased levels of zinc, selenium and copper have been observed in patients with preeclampsia [11, 12] as zinc is an important trace element has been shown to function as Co-factor for Synthesis of a number of enzymes, deoxyribonucleic (DNA) and ribonucleic acid (RNA).

Akinloge et al [3] reported that zinc deficiency has been associated with complication of pregnancy part of which is preeclampsia, during pregnancy there is a decline in circulating zinc level and this increases as the pregnancy progresses possibly due to decrease in zinc binding and increased transfer of Zinc from the mother to the fetus.

This study show decease in the serum zinc and magnesium concentration of preeclampsia patient compared to the controls and this supports the study of Tamura et al [13] and Mahomed et al

[9] who found that low concentration of zinc and magnesium in the serum exposes the subject to a risk of pregnancy complications which includes preeclampsia, Idogun et al [14] assess magnesium and calcium in the plasma and cerebrospinal fluid of Nigerian women with preeclampsia and eclampsia plasma calcium was significantly lower in patients than controls test. The CSF calcium and magnesium levels were lower in patients than controls, there is extracellular calcium and magnesium reduction in patients with preeclampsia and eclampsia.

This reduction may have a cause and effect relationship with these disorders. This agree with the idea of Lu and Nightingale [15], who reported a reduced in development of preeclampsia with introduction of a low dose of magnesium sulphate. Thus the success of magnesium therapy as treatment for eclamptic seizures in severe preeclampsia suggest that magnesium might be deficient in women with preeclampsia. In addition, Touyz, Power, Skjaerven et al [16, 17, 18] confirms that Ca and Mg are very important for cellular metabolism such as muscle contractility, secretions, neuronal activity, as well as cellular death.

In the present study, serum Ca and Mg levels in pre-eclamptic women were significantly lower than corresponding values in the control group, which is suggestive of some role of these elements in the rise of blood pressure. Although, Ca alone might play a role in the rise of blood pressure, a proper balance of Ca and Mg is of vital importance to control blood pressure because blood vessels need Ca to contract, but they also require sufficient Mg to relax and open up. Thus, Mg acts as a Ca channel blocker by opposing Ca dependent arterial constriction and by antagonizing the increase in intracellular Ca concentration leading to vasodilatation.

Copper has been shown to play in the function of several cuproenzymes that are essential for life [19] our finding indicated a decrease in serum concentration of copper in preeclampsia when compared to control subject this agree with find of Gifford et al [20].

This study show decrease serum level of calcium which play a role in endothelial function and antioxidant this is agree with the study of Mahmod et al [9], who reported allow intake of calcium during pregnancy decrease risk of preeclampsia development deficiency or decreased levels of various trace element such as zinc, copper, magnesium and calcium, have been shown to be associated with many complication related to pregnancy outcome [21].

In this paper there is no significant different between mild and sever preeclamptic group in level of trace element, while a study done by Katz [22] shows that severe PE is associated with abnormal

concentrations of Zn, Cu and Se. Therefore, trace elements may have a crucial role in the pathogenesis of severe PE.

In our study the level of copper increase in cord blood while Zinc and calcium decrease. Finding of decrease serum levels of zinc in cord blood observed in this study agrees with study done by Awadallah [23], but Katz [22] report that found that Zn levels (µg/L) were significantly higher in fetal arterial and venous blood of the PE group. While elevated level of copper in cord blood in our study disagree with same study Cu levels (µg/L) and Katz [22] were significantly lower in fetal arterial and venous cord blood but agree with Roberts [24].

This is a attributed to increased copper and zinc up take by the fetus and placenta, increased transfer of plasma zinc to maternal erythrocytes, expanded plasma volume and deceased serum albumin availability for zinc binding during pregnancy and specially in sever preeclampsia patient . furthermore zinc transports such as Zn that are localized in placenta may play an important role in acceleration zinc uptake from the mother`s blood to the developing fetus. Thus, the level of zinc would be expected to be higher in cord blood than that in material blood [25].

Our study show decrease calcium level in cord blood sample in preeclampsia this is agreeing with study of mahmod [9] and study of Awadallah [23], while disagree with a study of Ziael [26] who found no relation between preeclampsia and level calcium in the fetus.

In conclusion; the mean serum level of calcium, magnesium, copper and zinc between the preeclamptic group and control group was significantly different. It seems that these trace elements are involved in the pathogenesis of pre-eclampsia, in the light of the concentration of these elements ,dietary supplementation or replacement therapy of these trace elements is suggested for women with preeclampsia.

Competing interests

The authors declare that there is no conflict of interest.

Author Contributions

All authors wrote, read and approved the final manuscript.

References

1. Philip. N. Baker, Louise Ckenny, Obstetrics by ten teachers 19th edition, Chapter 10, page 120-122 ; 2011.

2. D. Keith Edmonds, Dewhurst's Text book of obstetrics and Gynecology. 7th edition, Chapter 25, page 228-230; 2006.

3. Akinloye O, Oyewale OJ, Oguntibeju OO. Evaluation of trace elements in pregnant women with pre-eclampsia. Afr J Biotech 2010; 9:5196-202.

4. Adam B, Malatyaliogu E, Alvur M,Talu C. Magnesium, zinc and iron levels in per-eclampsia. J. Matern. Foetal Med 2001;10:246-250.

5. James M. Roberts, Judith L. et al. Nutrient Involvement in Preeclampsia. J. Nutr 2003;133: 1684S-1692S.

6. Black RE. Micronutrients in pregnancy. Br J Nutr 2001; 85 (suppl):193S-197S.

7. Rathore S, Gupta A, Batra HS, Rathore R. Comparative study of trace elements and serum ceruloplasmin level in normal and pre-eclamptic pregnancies with their cord blood. Biomed Res 2011; 22:207-10.

8. Leila Farzin, Fattaneh Sajadi. Comparison of serum trace element levels in patients with or without pre-eclampsia. J Res Med Sci 2012; 17(10): 938-941.

9. Mahomed K, Williams MA, Woelk GB, et al. Leukocyte selenium, zinc, and copper concentrations in preeclamptic and normotensive pregnant women. Biol. Trace Elem. Res 2000; 75: 107-118.

10. Serefden A, Muge H, Mehmet H, et al. Comparison of angiotensin-converting enzyme, malonaldehyde, zinc, and copper levels in preeclampsia, Biological Trace Element Research, 2006; 113: 1-8.

11. Rayman MP, Bode P, Redman CW. Low selenium status is associated with the occurrence of the pregnancy disease preeclampsia in women from the United kingdom. Am J Obstet Gynaecol 2003;189:134-9.

12. Kumru S, Aydin S, Simsek M, Sahin K, Yaman M. Comparison of Serum Copper, Zinc, Calcium, and Magnesium Levels in Pre-Eclamptic and Healthy Pregnant Women. Biol Trace Elem Res 2003;94:105-12.

13. Tamura T, Goldenberg RL, Johnston KE, DuBard M. Maternal plasma zinc concentrations and pregnancy outcome. Am J Clin Nutr 2000;71:109-13.

14. Idogun ES, Imarengiaye CO, Momoh SM. Extracellular Calcium and Magnesium in Preeclampsia and Eclampsia. Afr J Reprod Health 2007;11:89-94.

15. Lu JF, Nightingale CH. Magnesium sulfate in eclampsia and pre-eclampsia: pharmacokinetic principles. Clin Pharmacokinet 2000;38(4):305-14.

16. Touyz RM. Role of magnesium in pathogenesis of hypertension. Mol Aspects Med 2003;24:107–36.

17. Power ML, Heaney RP, Kalkwarf HJ, et al. The role of calcium in health and disease. Am J Obstet Gynecol 1999;181:1560-9.

18. Skjaerven R, Wilcox A, Lie RT. The interval between pregnancies and the risk of pre-eclampsia. N Engl J Med 2002;346:33-8.

19. Al Ghazali B, Al-Taie AA, Hameed RJ. Study of the clinical significance of serum albumin level in Preeclampsia and in the detection of its severity. American Journal of BioMedicine 2014; 2(8) 899-902.

20. Gifford RW, August PA, Cunningham G, et al. Report of the National High Blood Pressure Education Program Working Group on high blood pressure in pregnancy. Am J Obstet Gynecol 2000;183(suppl):1-22.

21. Magri J, Sammnt M, Sayon C. Lead and other meals in gestational hypertension. Int. J. Gynecol. Obstet 2003; 83: 29-36.

22. Katz O, Paz-Tal O, Lazer T, et al. Severe pre-eclampsia is associated with abnormal trace elements concentrations in maternal and fetal blood. 2011;25(7):1127-30.

23. Awadallah SM, Abu-Elteen KH, Elkarmi AZ, et al. Maternal and Cord Blood Serum Levels of Zinc, Copper, and Iron in Healthy Pregnant Jordanian Women. The Journal of Trace Elements in Experimental Medicine 2004;17:1-8.

24. Roberts JM, Balk JL, Bodnar LM, Belizan JM, Bergel E, Martinez A. Nutrient Involvement in Preeclampsia. Journal of Nutrition. 2003;133:1684S-1692S.

25. Mc Gowan CA, MCAulifce FM. Materal nutrient intake and levels of energy underreporting during early pregnancy. Eur J Clin Nuts 2012;162(2):125-30.

26. Ziael S, Ranjkesh F, Faghihzadeh S. Evaluation of 24- hour copper in preeclamptic vs normotensive pregnant and non-pregnant women. Int. J. Fertil. Steril 2008; 2:9-12.