



Evaluation of serum calcium and zinc in preeclamptic patients – a case control study

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ABSTRACT

Preeclampsia being one of the major causes of maternal mortality and pregnancy related complication is a matter of intensive research in this field. Main aim of the study was to evaluate and compare serum calcium and zinc in preeclamptic and normal pregnant women. This was a case control study done in the department of Biochemistry at IGIMS Patna, Bihar, India. 50 patients of preeclampsia as case and 50 normal pregnant women of matched age were taken as control. Calcium and zinc levels were measured in the serum of the participants which showed significantly lower level in study group than control group. This study concludes that decreased serum calcium and zinc in pregnant women may be a risk factor for the development of preeclampsia. Therefore, early estimation of serum level of these minerals during antenatal visit and their supplementation if needed may decrease the incidence of preeclampsia.

KEYWORDS : Preeclampsia, Hypertension, calcium and zinc.

Introduction

Previously preeclampsia was defined as onset of high blood pressure ($\geq 140/90$ mmHg) and proteinuria (>300 mg/day) after 20 weeks of pregnancy in a previously normal woman with no past history of hypertension (Hawfield et al., 2009). According to the new ACOG guidelines, high level of protein in urine i.e. proteinuria is no longer essential for the diagnosis of preeclampsia. Preeclampsia is now diagnosed by persistent high blood pressure that develops for the first time during pregnancy or during the postpartum period that is associated with excessive amount of protein in the urine or the new development of decreased platelet count, defect in the kidney or liver, fluid filled lungs, or signs of brain involvement such as seizures and/or visual disturbances (American College of Obstetricians and Gynecologists, 2013).

Preeclampsia and eclampsia complicate 2–8% of pregnancies and, overall, 10–15% of maternal deaths are due to these conditions (Duley, 2009). Because of its dreadful complication of development of eclampsia which is fatal both for fetus and mother, it should be detected early and managed appropriately. Preeclampsia affects ten million women each year around the world. According to recent data, 76,000 pregnant women die each year from preeclampsia and other hypertensive disorders. About 500,000 babies of these preeclamptic mother die each year (Kuklina et al., 2009). In developing countries, a woman is seven times more prone to develop preeclampsia than a woman in a developed country (Maternal mortality, 2007).

In developing country like India, pregnant women have been reported to consume diet

that is deficient in minerals and vitamins (Adam et al., 2001, Begum et al., 2000).

Low level of calcium, either due to insufficient dietary intake or altered calcium metabolism have been linked by several researchers and laboratory studies to higher blood pressure, or hypertension (McCarron et al., 1994, Morris et al., 1995). "National Centre for Health Statistics" conducted a large study to examine this relationship. They found that there is a threshold of 400–600mg of dietary calcium daily; the chances of high blood pressure increases significantly at levels below this threshold (McCarron et al., 1994). The threshold is increased in pregnant women, who require a higher calcium intake in order to meet fetal need (such as bone mineralization).

82% pregnant women worldwide have inadequate zinc in their diet. Alteration of zinc in diet has been found to be related to preeclampsia (Pathak et al., 2003, Nourmohammadi et al., 2008).

Zinc is an important element in numerous proteins and plays a significant

role in different cell functions such as cell proliferation and apoptosis, defense against free radicals, and DNA repair. For e.g., superoxide dismutase (SOD) is an important first-line defense enzyme against oxygen radical species (Oteiza et al., 2001).

All preeclamptics have certain factors that reduce vasodilatation, enhance vasospasm and initiates oxidative stress supported by the finding of low level of magnesium (which is essential for maintenance of vascular tone), low calcium level (which is essential for the synthesis of endothelial-derived NO), and low zinc level (which is essential for antioxidant function) (Faisal et al., 2009).

Material and methods:

Fifty pregnant women of gestational age ≥ 28 weeks who were diagnosed with preeclampsia were taken as case and fifty normal primigravida of matched gestational age and singleton pregnancy were taken as control from department of Obstetrics and Gynecology, IGIMS Patna during the period from February 2014 to June 2015. Those who were on mineral supplements were not enrolled in study.

Inclusion Criteria for cases:

1. Pregnant women with first and singleton pregnancy.
2. Blood pressure of 140/90 mm Hg or more measured twice, 6 hours apart.
3. Proteinuria of at least 300mg / 24 hours.

Exclusion criteria for cases:

1. Any previous history of hypertension.
2. Pregnant women with multiple or molar pregnancy.
3. History of any chronic illness or on drugs.

After obtaining informed consent, 5 ml of venous blood was drawn from each participant from ante-cubital vein under aseptic precaution. Serum was separated and was used for the estimation of calcium and zinc. Serum calcium was estimated by photometric test using arsenazo III. Serum zinc was estimated by colorimetric method with 5-Brom-PAPS. All tests were done on fully automated clinical chemistry analyzer (Olympus AU 400) in department of Biochemistry, IGIMS Patna.

Statistical Analysis:

The data of the study were expressed as mean \pm SD. Students t-test was applied for statistical comparisons. P value < 0.05 was considered statistically significant.

Result:

In our study we found that serum calcium and zinc were significantly decreased in preeclamptic women compared to controls. Mean serum calcium was 8.46 ± 1.59 in preeclamptic women and 9.44 ± 1.27

in control group with p value <0.001 . Serum zinc was 8.63±0.87 in preeclamptic women and 9.07±0.87 in control group with p value <0.01 .

Table 1: comparison of serum calcium and zinc in different study groups

Minerals	Normal control (n=50)		Preeclamptic women(case) (n=50)		P value
	Mean	SD	Mean	SD	
Calcium(mg/dl)	9.44	1.27	8.46	1.59	<0.001
Zinc(µmol/l)	9.07	0.87	8.63	0.87	<0.01

Discussion

This study shows significantly lower serum calcium and zinc in preeclamptic women compared to normal pregnant women. Our study matched with different investigators. Sridevi M et al. (2015) reported decreased serum calcium in patients of preeclampsia. Similarly Guhan VN et al. (2014) reported decreased serum calcium and magnesium in patients of preeclampsia. Selina Akhtar et.al. (2011) reported decreased calcium and zinc in patients of preeclampsia.

Various studies have suggested that serum calcium has important role in smooth muscle cell contractility. Decreased level of serum calcium in pregnancy increases release of parathyroid hormone and renin which thus increases intracellular calcium in smooth muscle cells of vascular endothelium. This increased smooth muscle calcium causes vasoconstriction which increases vascular resistance leading to rise in blood pressure in patients of preeclampsia (Jain et al.,2010, Sukonpan et al.,2005, Punthumapol et al.,2008, Ritchie et al.,2000).

ROS (reactive oxygen species) are known to be increased during normal pregnancy and it is necessary for proper outcome (Yang et al., 2012). Difficulty in pregnancy occurs when balance between antioxidant host defenses and the pro-oxidant species is disturbed leading to preeclamptic pregnancy.

This leads to oxidative stress which promotes vascular smooth muscle cell proliferation its hypertrophy and collagen deposition, leading to thickening of the vascular media and narrowing of its lumen.

Further, increased oxidative stress damages endothelium, impairs vascular relaxation and also increases contractile activity of vascular endothelium. All these effects on the vasculature may explain how increased oxidative stress can cause hypertension (Grossman, 2008).

Zinc plays a significant role in antioxidant defense. It acts by various mechanisms like it is a cofactor of the superoxide dismutase enzyme; also it modulates the glutathione metabolism and metallothionein expression. It competes with iron and copper in the cell membrane and inhibit nicotinamide adenine dinucleotide phosphate-oxidase enzyme (Kyria et al., 2015).

Zinc is an important component of cytoplasmic as well as extracellular superoxide dismutase enzyme, which serves as the frontline of defense against reactive oxygen species (ROS). Zinc deficiency has been shown to aggravate hypertension. This explains how amelioration of oxidative stress with supplemented antioxidant therapy improves hypertension (Mujahid et al., 2011).

Not only this, zinc is an essential cofactor for more than 300 enzymes. It helps in reduction of free radicals and also in its neutralization (Prasad, 2008; Carocho et al.2013).

A study by Bernardo Rodriguez-Iturbe et al.(2003) demonstrated that diet rich in antioxidants like vitamin C, vitamin E, selenium and zinc decreases inflammation in renal interstitial tissue, and lowers the level of renal tissue content of malondialdehyde and thus improves hypertension .

Conclusion

This study shows that serum calcium and zinc were significantly lower in women with preeclampsia as compared to normal pregnancy. As preeclampsia is more prevalent in low socio economic group, low serum level of these minerals may be due to inadequate dietary intake and deficiency of these minerals may be one of the reasons for

development of raised blood pressure and preeclampsia. In light of reduction of these elements in patients of preeclampsia the obstetricians must monitor these minerals from beginning of the antenatal period and supplement it to pregnant women who show lower level of any of these minerals in their serum to reduce the incidence of preeclampsia.

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