Effect of Minerals on Markers of Risk of Pre-Eclampsia in Pregnant Women: A Hospital Based Study

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Abstract

Introduction: Pregnancy specific complication characterised by hypertension, proteinuria, after 20 weeks of the gestation, and along with various signs of damage to organ systems, haemolysis, elevated levels of liver enzymes and low platelet count (HELLP syndrome) is collectively termed as eclampsia.

Method: Cross-sectional study with 3 groups of pregnant women, were taken followed by inclusion and exclusion criteria for characterisation. The study was approved by ethical board of DMIMSU. Minerals and their relationship were estimated using different method. Preeclamptic group with and without supplementation and pregnant women without preeclampsia were included in the study. Significant differences were seen in Na+, K+, Ca, Mg, Se, and Mn when compared with each group.

Result and Observation: The levels of K were increased significantly ($P < 0.001$) in pre-eclamptic group as compared to control group. There was significant change in levels of Mn when pre-eclamptic group was compared to control. Mn was also found to decrease significantly ($P < 0.001$) in cases as compared to control. However, the levels of Se, Mg, Ca and Na between cases and control were not highly significant. In supplementation and without supplementation group, Significant differences were seen in levels of Na, K, Ca and very significant difference was seen in levels of Mn. ($p<0.0001$).

Conclusion: Pre-eclamptic pregnant women have higher levels of serum potassium and our finding on Mn, an essential trace mineral, provides new insight into a potentially modifiable way to prevent preeclampsia. In multi-ethnic, predominantly urban and low-income pregnant women high level of Mn is associated with pre-eclampsia.

Keywords: *Mn, Na, K, Se, Ca and Preeclampsia.*

Introduction

Pregnancy specific complication characterised by hypertension, proteinuria, after 20 weeks of the gestation, and along with various signs of damage to organ systems, haemolysis, elevated levels of liver enzymes and low platelet count (HELLP syndrome) is collectively termed as eclampsia.[1]

Eclampsia is simply convulsions of pregnancy due to rise in blood pressure. Pre-eclampsia maybe seen before a eclampsia, condition where swelling can be seen on feet, face and urine usually consists proteins.[2]

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WHO, recognise eclampsia as major cause of fetal and maternal morbidity and mortality.[3]

Prevalence of pre-eclampsia stands around 3 to 10% in world population. Whereas factor such as obesity, diabetes, calcium deficiency advanced maternal age, oxidative stress, placental ischaemia, genetic factors and immune maladaptation have been implicated. [4] In addition, the American heart association recently added preeclampsia as a risk factor for future cardiovascular diseases in women. [5]Also, modified lipid profile has a possible role in the development of endothelial dysfunction and preeclampsia expression. Early detection of such lipid parameters will benefit pregnant patients in preeclampsia by avoiding maternal and fetal complications, which can also enhance preeclampsia management.[6] Only low dose of aspirin maybe effective in preventing the pre-eclampsia here in women at high risk.[7]

Some of the evidences from various line for examples the essential mineral manganese (Mn) and Selenium (Se) toxic heavy metals such as cadmium, lead and mercury. These minerals have opposing roles in the development of the preeclampsia.[8-10] and for early detection of PE and eclampsia serum uric acid, serum creatinine and serum urea are better diagnostic and predictive marker. With the help of these parameters most cases are detected early in the pregnancy before they can progress to eclampsia.[11] Due to limited number of studies result on epidemiologic studies on Mn have varying results. Se in pregnancy, reduce oxidative stress and also improve preeclampsia features in rats. Although need of large-scale studies in human is required.[12-17]

Aims and Objectives: The present study was undertaken in the Department of Biochemistry and Dept. of OBGY at Jawaharlal Nehru Medical College, and AVBRH (Datta Meghe Institute of Medical Sciences) Sawangi, Meghe, Wardha, in collaboration with Datta Meghe Medical College and Shalinitai Meghe Hospital and Research Centre Hingana, Nagpur, Maharashtra India with the following aims and objectives: -

Aim of Study: To estimate role of minerals, in patients with pre-eclampsia.

Objectives of study:

1. To estimate sodium, potassium, magnesium, calcium, manganese and selenium in pregnant women with pre-eclampsia and eclampsia.

2. Find out correlation of sodium, potassium, magnesium, calcium, manganese and selenium in pre-eclampsia and compare with normal pregnant women.

Material and Method

Study Area: The present study was undertaken in the Department of Biochemistry of Jawaharlal Nehru Medical College, and AVBRH (Datta Meghe Institute of Medical Sciences) Sawangi, Meghe, Wardha in collaboration with Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre, Hingana, Nagpur, Maharashtra India.

Study Population: 250 subjects were included in the study and were grouped as under.

Group 1: 100 pre-eclampsia diagnosed subjects without any mineral supplementation.

Group 2: 50 pre-eclampsia diagnosed subjects with mineral supplementation.

Group 3: 100 Normal pregnant women.

Study Type: Cross sectional interventional study

Data collected was entered into Microsoft Excel Worksheet and statistically analysed by using SPSS (Statistical Package for Social Sciences) version 20. For quantitative data mean, standard mean, standard deviation, t-test and Karl Pearson's Coefficient of Correlation were calculated. P value < 0.05 (0.01) will be considered as statically significant (highly significant) at 95% confidence interval. The proposed study was undertaken subject to approval by Institutional Ethical Committee.

Observations and Results

Table 1. Serum minerals levels in pregnant women with preeclampsia and norm tension.

Serum minerals	Group III	Group I	'P' Value
Potassium	4.38 ± 0.80	4.95±0.99	P<0.001
Sodium	140±1.12	139±1.95	p<0.01
Calcium	7.27±1.46	7.96±0.22	P<0.05
Magnesium	1.37±0.22	1.42±0.19	P<0.05
Manganese	0.13 ±0.077	0.072±0.068	P<0.001
Selenium	62.33±9.42	58.23±8.44	P<0.0014

Table no 1 showed the levels of serum trace elements in control and preeclamptic women are seen in table 1. Analysis of trace elements found that mean values of K, Na, Ca, Mg, Mn and Se were 4.38 ± 0.80, 140±1.12, 7.27±1.46, 1.37±0.22, 0.13 ±0.077 and 62.33±9.42. in control group and 4.95±0.99, 139±1.95, 7.96±0.22, 1.42±0.19, 0.072±0.068, and 58.23±8.44 women with pre-eclampsia respectively. The levels of K were increased significantly ($P < 0.001$) in pre-eclamptic group as compared to control group.

There was significant change in levels of Mn when pre-eclamptic group was compared to control. Mn was also found to decrease significantly ($P < 0.001$) in cases as compared to control. However, the levels of Se, Mg, Ca and Na between cases and control were not highly significant.

Table 2. Serum minerals level in pregnant women with preeclampsia and eclampsia without and with supplementation.

Serum minerals	Group I	Group II	'P' Value
Potassium	4.95±0.99	4.23±0.98	P<0.001
Sodium	139±1.95	141±1.40	P<0.001
Calcium	7.96±0.22	8.53±0.21	P<0.001
Magnesium	1.42±0.19	1.39±0.21	P<0.3803
Manganese	0.072±0.068	0.131±0.058	P<0.0001
Selenium	58.23±8.44	60.48±7.63	P<0.1144

Table no 2 showed the levels of serum minerals in cases with pre- eclampsia with and without any supplementation are depicted in table 2. On the analysis of serum minerals among patients with pre-eclampsia without supplementation the levels for K, Na, Ca, Mg, Mn and Se were 4.95±0.99, 139±1.95, 7.96±0.22, 1.42±0.19, 0.072±0.068 and 58.23±8.44 respectively. And the levels for K, Na, Ca, Mg, Mn and Se in patients with supplementation were 4.23±0.98, 141±1.40, 8.53±0.21, 1.39±0.21, 0.131±0.058 and 60.48±7.63 respectively. Significant differences were seen in levels of Na, K, Ca and very significant difference was seen in levels of Mn. (p<0.0001).

Table no 3 showed the levels of serum minerals in cases of pre- eclampsia with supplementation and normal pregnant women are depicted in table 2. On the analysis of serum minerals among patients of pre-eclampsia with supplementation the concentration of K, Na, Ca, Mg, Mn and Se were 4.23±0.98, 141±1.40, 8.53±0.21, 1.39±0.21, 0.131±0.058 and 60.48±7.63. In normal

pregnant the concentration of K, Na, Ca, Mg, Mn and Se were 4.38 ±0.80, 140±1.12, 7.27±1.46, 1.37±0.22, 0.13 ±0.077 and 62.33±9.42 respectively.

Table 3. Serum minerals level in pregnant women with preeclampsia and eclampsia without and with supplementation.

Serum minerals	Group II	Group III	'P' Value
Potassium	4.23±0.98	4.38 ± 0.80	P < 0.3177
Sodium	141±1.40	140±1.12	P < 0.0001
Calcium	8.53±0.21	7.27±1.46	P < 0.0001
Magnesium	1.39±0.21	1.37±0.22	P < 0.5950
Manganese	0.131±0.058	0.13 ±0.077	P < 0.9355
Selenium	60.48±7.63	62.33±9.42	P < 0.2303

No Significant differences were seen in levels of K, Mg, Mn and Se (P < 0.3177, P < 0.5950, P < 0.9355 and P < 0.2303) respectively, but in levels of Na and Ca significant difference was seen. (p<0.0001).

Discussion

Calcium as well as magnesium are very important for metabolism at the cellular level and are mandatory for muscle contraction, also for neuronal activity making it very essential in pregnancy[18,19]. **Mitchell et. al (1990)**discovered that eclampsia was in arrears to maternal deficiency in calcium through foetal absorption and held that good results were achieved by calcium administration. He stated that the hypocalcaemia of eclamptic patients led to an accumulation of fat in the liver and therefore impairment of its function resulting into sudden attacks[20]. **Knight and Keith (1992)** studied calcium supplementation on normotensive and hypertensive pregnant women. A significant inverse relationship was observed between dietary calcium intake and blood pressure[21]. **Jama (1997)** observed that pre-eclampsia still remains a dangerous entity with an elusive pathogenesis and causes significant morbidity in both, the mother and foetus[22]. It has been found that women on a high calcium diet have a low incidence of pre-eclampsia. It is also known that pre-eclamptic women have reduced urinary excretion of calcium, so there is an inverse relationship between the dietary consumption of calcium and events of eclampsia. **Walker (2000)** stated that calcium supplements lower the risk of pre-eclampsia and eclampsia because calcium is required for maintaining tone of muscles[23].

Present study finding showed no change in serum sodium levels in preeclamptic as compared to normotensive pregnancies. It also showed that serum magnesium level was significantly depleted in mothers with pre-eclampsia as compared to healthy control group. This finding suggests that hypomagnesemia may be one of the aetiologies of preeclampsia.

Serum Potassium levels were highly significantly increased in preeclamptic pregnant women as compared to normal. These findings are in close conformity with the findings of **Agyei Frampong et al**[24] who demonstrated that there was only slight correlation between the plasma sodium levels and diastolic blood pressure with no significant difference between normotensive and pre-eclamptic subjects. Serum potassium levels however, showed a highly significant increase in pre-eclamptic women. These results were consistent with earlier study by **Handwerker et al**[25] where the study group had significantly higher levels of serum potassium than control group. Normal pregnancy has been associated with a decrease in mean serum potassium possibly related to a physiologic increase in Na+/K+ adenosine triphosphatase activity in the cell membranes, causing a shift of K+ into cells with extrusion of Na+.

Seydoux J et al. study concludes that serummagnesium leveldecreases with progress in pregnancy.[26] These results are were consistent with earlier study by **Seydouse et al, Handworker et al and Zhao F**[27-28] where the study group has lower serum magnesium than control group.Our study on preeclamptic women with and without supplementation shows remarkable differences in calcium levels p<0.001.

Thus, our findings of higher extracellular K+ levels in toxaemia may be of interest and our study also concludes that minerals supplementation also decreases K+ levels in preeclamptic women after supplementation.

Furthermore, in a prospective cohort study of 620 pregnant women in Iran, **Goodarzi Khoigani et al**[29] reported that Mn intake in the third trimester, estimated using 48-hour dietary recalls, was significantly lower among women who developed preeclampsia compared with those who did not. In contrast, in a case–control study of 396 participants (31 preeclampsia cases) in Iran, **Vigeh et al**[30] reported that Mn concentration in umbilical cord blood, but not maternal blood, was associated with higher odds of preeclampsia after adjustment.

Conclusion

In the light of the above interpretations it can be determined that pre-eclamptic pregnant women have **higher levels of serum potassium**, **decreased level of serum calcium** and **magnesium** and **no significant difference in sodium** levels as compared to normotensive pregnant women in their pregnancy during third trimester.

Our finding on Mn, an essential trace mineral, provides new insight into a potentially modifiable way to prevent preeclampsia. In multi-ethnic, predominantly urban and low-income pregnant women high level of **Mn is associated with pre-eclampsia**. Our study also concluded thatserum **Se have no contribution in pre-eclampsia** and eclampsia.

Moreover, study of serum lipid profile in pre-eclampsia showed by **Shreya Yadav et. al**.[6]with our study helpful to early detection and used in better management of preeclampsia which is important to improve the maternal and fetal outcome. Further research with information on characteristic features of preeclampsia (such as severity of blood pressure and proteinuria) and clinical subtypes of preeclampsia (e.g. early-onset versus late-onset) is needed to elucidate the potential heterogeneity of mechanisms that are responsible for the effect of trace minerals.

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