

The Study of Serum Copeptin, Calcium and Magnesium in Normal and Preeclamptic Pregnant Women

M. Sarala¹, P. Srilaxmi², N.R.V. Krishna Swamy³, T. Sunitha⁴

ABSTRACT

Introduction: Pre-eclampsia is a disorder of pregnancy characterized by the onset of high blood pressure and increased amount of proteins in urine, preeclampsia begins after 20 weeks of pregnancy. The present study was done to compare the levels of copeptin, blood pressure, Proteinuria, calcium and magnesium in preeclampsia with normal pregnant women.

Materials and methods: A total of 80 subjects were included, out of which 40 were cases and 40 were controls. We have included 24-30 weeks of gestation with singleton pregnancy of age 20-40 years. The levels of serum copeptin, calcium, magnesium, total proteins and urinary proteins were estimated. Data was statistically analyzed using SPSS 17th version.

Results: The results shows that there is convincingly elevation of serum copeptin and Proteinuria in preeclampsia women.

Conclusion: The present study suggests that serum copeptin is a significant marker in preeclampsia in assessing the severity.

Keywords : Preeclampsia, Copeptin, Calcium, Magnesium.

INTRODUCTION

Preeclampsia is a common obstetrical progressive pregnancy associated disorder. It is characterized by the hypertension (systolic/diastolic blood pressure $\geq 140/90$ mm Hg), and pathological edema after 20 weeks of gestation.¹ Around 5% to 8% of world wide population are suffering from preeclampsia which is the main cause of maternal, fetal, and neonatal morbidity and mortality.² It is diagnosed on two occasions and two positions with 4 hrs difference which shows the systolic BP more than 140mmHg and diastolic BP more than 90mmHg at 20 weeks of gestation in a woman with previously normal blood pressure and Proteinuria (≥ 300 mg per 24 hour urine collection or ≥ 1 by dipstick method) Copeptin is a 39-amino acid glycopeptide, is co synthesized in the hypothalamus with vasopressin, which is also an anti diuretic hormone. Copeptin used as indicator because copeptin are more stable in plasma and serum when compared with vasopressin.³ In addition to the reflecting individual stress levels, vasopressin also has hemodynamic and osmoregulatory effects. Copeptin act identically with vasopressin during the disorders associated with osmoregulatory system and copeptin levels are directly correlated with plasma vasopressin in both healthy people and ill patients.⁴

Deficiency of calcium and magnesium has been shown to have a harmful effect on the pregnant mother and growing fetus and possibly complicate preeclampsia.⁵

Deficiency of magnesium has been established to play a role in blood pressure regulation and hence development of preeclampsia.⁶

During pregnancy there is high demand for calcium intake for the process of fetal bone formation. Physiologically, calcium is an important macro mineral. Intracellular calcium levels are useful for muscle contraction, hormone secretions, neuronal activity and cell death. Extracellular calcium is useful for bone mineralization and blood coagulation.⁷ Changes in plasma calcium levels have shown to alter the blood pressure.⁸ Around 200 mg/day of calcium is deposited in fetal skeleton via placenta in last trimester of pregnancy, whereas maternal urinary calcium excretion is two times more in last trimester.⁹ Low serum calcium level stimulate the release of rennin and parathyroid hormones. By the action of rennin and parathyroid hormone increases the intracellular calcium in vascular smooth muscle cells. This increased calcium leads to vasoconstriction and increased peripheral vascular resistance. This will cause increased blood pressure.¹⁰ Thus, abnormalities in calcium homeostasis may contribute to the vasculopathy that has been already manifested in preeclampsia.¹¹

MATERIAL AND METHODS

The subjects were divided into two groups. Group I is normal healthy pregnant women as controls (40), group II included women with preeclampsia (40). Venous blood was collected and analyzed for the study. We have included 24-30 weeks of gestation with singleton pregnancy of age 20-40 years. We have excluded cases with multiple pregnancies, gestational diabetes mellitus, chronic hypertension, poly hydromnios, sexually transmitted diseases, prior renal diseases and evidence of acute or chronic inflammation.

¹Assistant Professor, Department of Biochemistry, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, ²Assistant Professor, Department of Biochemistry, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, ³Associate Professor, Department of Biochemistry, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, ⁴Professor and HOD, Department of Biochemistry, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India.

Corresponding author: Dr. T. Sunitha, Professor and HOD, Department of Biochemistry, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India

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This study was approved by an institutional review board and informed consent was obtained from all subjects involved in the study. From each pregnant women included in the study, a written informed consent was obtained. Detailed history was taken, vital measurements and examination were done. Participants were in the supine position for 5 to 10 minutes before venipuncture and 5ml of venous blood was collected. Serum was separated within one hour after sample collection. Care was taken to avoid hemolysis. Serum and urine from all 80 subjects was analyzed for the following parameters:

1. Estimation of Serum Copeptin by Enzyme Linked Immunosorbent Assay – Non Competitive, Sandwich Assay.
2. Serum calcium was estimated by the Arsenazo III, End Point method using A25 & ERBA – CHEM 5x automated analyser.
3. Estimation of Serum magnesium by Calmagite method using ERBA – CHEM 5x automated analyser.
4. Estimation of total protein in serum Biuret, End Point method using A25 & ERBA – CHEM 5x automated analyser.
5. Total protein in urine is estimated by DIP‘N’READ Strips method

Statistical analysis was done by SPSS (statistical package for social science) software. Results were expressed as mean, \pm SD. Statistical correlation was done using partial correlation test and significance was expressed in the form of ‘p’ value. ‘p’ value of <0.05 was considered statistically significant and ‘p’ value <0.001 was considered highly significant.

RESULTS

The study was conducted in 80 pregnant women who were divided into two groups to assess the severity of preeclampsia by estimating the serum copeptin and related biochemical parameters. The results of the study was shown in the table 1.

DISCUSSION

The study was conducted to estimate the levels of serum copeptin in preeclamptic patients and normal pregnant women. And also it was aimed to compare the findings with other established parameters such as serum proteins, urinary proteins and serum calcium and magnesium. Preeclampsia is a progressive pregnancy specific disorder which is associated with increased maternal and fetal morbidity and mortality especially in developing countries.¹² Copeptin is a biomarker of arginine vasopressin which acts on vascular system to

increase blood pressure and water retention. As a potential biomarker of PE, we prospectively evaluated opeptin levels among women who consequently developed PE and other pregnancy complications.¹³ The serum copeptin levels were significantly elevated in women with PE compared with the normal pregnancy supports the study of Santilan et al. who stated that serum copeptin were significantly higher throughout preeclamptic pregnant women when compared with normal pregnant women.¹⁴ Yeung et al evaluated that the copeptin is predictive marker for preeclampsia and association between circulating copeptin and the development of preeclampsia or other pregnancy-associated disorders.¹⁵

In preeclampsia, there is oxidative stress and inflammation will cause vasospasm, ischemia and hypoxia. This leads to endothelial dysfunction. This cellular injury leads to increased intracellular calcium influx into the cell and loss of calcium homeostasis.¹⁶ So thus, serum calcium plays an important role in development of preeclampsia. So we consider the serum copeptin is a sensitive test for early detection of preeclampsia.¹⁷

Similar studies conducted in sub-Saharan Africa using the same method of assay (atomic absorption spectrophotometry), in determining serum calcium and magnesium levels showing varying results.^{18,19,20} Ugwuja et al, in a study conducted among Nigerian women using atomic absorption spectrophotometry for assaying serum calcium and magnesium, found no significant difference in serum calcium but significantly reduced serum magnesium in preeclamptic women when compared with normal pregnant women.¹⁹

The results in this study have shown that serum copeptin levels are positively correlated with early-onset of preeclampsia, potentially reflecting the presence of relatively increased physiological stress. In addition to the serum copeptin levels were associated with elevated systolic and diastolic blood pressure. So that the study reveals that serum copeptin is a novel biomarker which is useful for assessing the severity of preeclampsia.

CONCLUSION

From the above results we concluded that serum copeptin is a novel bio marker for preeclampsia. Therefore, early diagnosis of biomarkers is a great importance. Not only for the early diagnosis of disease but identification of new therapeutic targets. That could result in the development of more effective treatment options for preeclampsia .

Parameters	Normal pregnancy	Preeclampsia	P Value
Systolic Blood Pressure (mmHg)	108.13 \pm 4.35	160.21 \pm 7.6	< 0.001
Diastolic Blood Pressure (mmHg)	70.3 \pm 2.4	108.31 \pm 4.27	< 0.001
Serum Copeptin (pg/ml)	230.61 \pm 45.04	480.21 \pm 70.20	< 0.001
Serum Calcium (mg %)	9.82 \pm 0.58	7.02 \pm 0.31	< 0.001
Serum Magnesium (mg %)	1.82 \pm 0.22	0.85 \pm 0.24	< 0.001
Serum Proteins (g%)	7.02 \pm 0.41	3.01 \pm 0.02	< 0.001
Urinary Proteins (mmol/l)	5 (Trace)	60 \pm 3	< 0.001

Table-1: Mean and SD of various parameters in different groups

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