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Study of Serum Calcium, Magnesium and Uric acid Levels in Pre-eclampsia and Normal Pregnancy.

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Abstract:
Introduction*: Pre-eclampsia is the major cause of maternal morbidity and mortality and is also associated with increased perinatal problems. There are studies to show that the relationship between aggravation of hypertensive complication with changes in concentration of various chemistries in mothers serum. The purpose of this study was to estimate and compare the relationship between the levels of serum calcium, magnesium, uric acid in women with pre-eclampsia, and normal pregnant women as controls.*
Methodology*:The study included 30 pre-eclamptic patients as cases and 30 normal pregnant women was taken as controls. All the cases and controls were in the age group of 18-35 years. Blood pressure was checked and microalbuminuria was analysed to identify cases and controls. The serum calcium was estimated by Arsenazo-III method, magnesium by xylidyl blue colorimetric method, and uric acid enzymatic colorimetric method.*
Results*: The levels of serum calcium in pre-eclamptic women (9.14 ± 0.52 mg/dl) was significantly lower when compared to controls (9.92 ± 0.44) (P < 0.05). Serum magnesium levels in pre-eclamptic and normal pregnant was 2.37± 0.48 and 2.50 ± 0.28 respectively with p value of >0.05. Serum uric acid in pre-eclamptic women was significantly higher (6.14 ± 1.5 mg/dl) in comparison to control 2.79±0.49 (P < 0.05).*
Conclusion*: Based on the results of the present study, it is clear that in pre-eclampsia, the serum levels of calcium was significantly decreased while uric acid is increased, suggesting the possible role of these factors in the etiology and severity of pre-eclampsia. There was a insignificant decrease in serum magnesium in pre-eclampsia compared to normal pregnant .*

Key Words: *Serum calcium, Serum magnesium, Serum uric acid, microalbuminuria, Pre-eclampsia.*

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I. Introduction

Pre-eclampsia is a medical complication occurring during pregnancy and is associated with high incidence of maternal and fetal morbidity and mortality. Its incidence is 4-8% of pregnancies [1, 2]. Pre-eclampsia is high blood pressure (>140/90mm of Hg) with proteinuria, edema or both, induced by pregnancy usually after 20th week of gestation and sometimes earlier in cases of multifetal pregnancy or when there are extensive hydatiform changes in the chorionic villi [3].

It is very essential to treat pre-eclampsia at the earliest and if left undiagnosed and untreated pre-eclampsia in its severe form may be associated with cerebral or visual disturbances, oliguria, elevated serum creatinine and uric acid along with the presence of epigastric pain. These changes when accompanied with convulsions or coma without pre-existing neurological disease like epilepsy, may lead to eclampsia [4]. Pre-eclampsia resolves within 24 hrs of placental delivery. The underlying pathophysiological mechanism is that there is a failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta [5]. Recent studies have shown the relationship between the hypertensive complications and the changes in concentration of various biochemical parameters such as serum uric acid, calcium, magnesium in pre-eclamptic women. [6,7,8, 9].

The lowering of serum calcium and increase of intracellular calcium can cause an elevation of blood pressure in pre-eclamptic mothers..The serum magnesium also decreases in women with pre-eclampsia [9]. Magnesium has been known as an essential cofactor for many enzyme systems. Magnesium plays an important role in neurochemical transmission and peripheral vasodilatation, therefore magnesium sulphate has been used as a drug of choice in severe pre-eclampsia and eclampsia treatment [10].

Besides the alterations in the levels of serum calcium and magnesium, uric acid levels are also increased in pre-eclampsia. There are several proposed mechanisms for this increase in uric acid in pre-

eclampsia such as decreased renal excretion that occurs as a consequence of pre-eclampsia, increased tissue breakdown, acidosis and a rise in the activity of xanthine oxidase/dehydrogenase enzyme [11]. Therefore the modification of calcium, magnesium and uric acid metabolism during pregnancy could be one of the potential causes of pre-eclampsia.

However the role and status of serum calcium, magnesium, uric acid in pre-eclamptic women is still being discussed. The aim of the present study was to measure and compare the levels of serum calcium, magnesium, uric acid in women with pre-eclampsia and normal pregnant women also to find out their relationship if any.

II. Methodology

The study population consisted of 30 pregnant women with pre-eclampsia and 30 normal pregnant women, consenting outpatient and inpatient in the department of Obstetrics and Gynecology. The age of cases and control varied from 18-35 years with singleton pregnancy and gestational period was ≥ 28 weeks. The cases were selected on the basis of simple random sampling method. The results were compared with 30 normal, age matched, healthy pregnant women. The study protocol was approved by the institutional ethical committee and informed consent was obtained from the subjects under study.

Inclusion criteria for cases were pre-eclampsia patients with blood pressure of ≥ 140/90 mmHg along with microalbuminuria ≥ 30mg/dl . The exclusion criteria included patients with disorders such as chronic renal disease, chronic hypertension, molar pregnancy, intrauterine fetal death, urinary tract infection and twin pregnancy. Patients were excluded if they were on calcium supplementation. Controls groups are normal pregnant women with blood pressure < 140/90 and microalbumunuiria < 30mg/dl. Blood pressure was checked in supine position with sphygmomanometer. Spot urine sample was collected.

Under all aseptic precautions, about 3 ml of venous blood was collected in gel tubes from the study group comprising of the cases and controls. The blood was allowed to clot and it was centrifuged at 5000rpm for 3 min. The serum separated was then used for the estimation of calcium, magnesium and uric acid.

Serum calcium was estimated by Arsenazo-III colorimetric method, magnesium was estimated by xylidyl blue method and uric acid was estimated by enzymatic method. Urinary albumin was estimated by immunoturbidimetric method. All the analyses were performed using the DAYTONA Autoanalyzer (Randox, UK) using commercially available kits (Randox, UK). The data was analyzed with SPSS soft ware package version 16. Students independent t test and Pearson's correlation coefficient was applied. A p-value <0.05 was considered to be statistically significant.

III. Results

The clinical characteristics of the patient are shown in Table-1. Age and gravida was matched between cases and controls group. Systolic blood pressure in cases and controls was 155.86 ± 17.26 and 98.4± 9.5, respectively. Mean diastolic blood pressure in cases and controls was 116.86±9.27 and 74.93 ± 4.86, respectively. Microalbuminuria in cases and controls was 310.21±71.94 and 26.44±16.54 respectively. This fulfills the inclusion criteria for cases and controls.

The levels of biochemical parameters are shown in table -2. The mean serum calcium in pre-eclampsia was 9.14 ± 0.52 mg/dl and in controls it was 9.92 ± 0.44 mg/dl. There is a significant decrease in mean serum calcium values in pre-eclamptic patients, when compared with normal healthy pregnant women ($p<0.001$). The mean serum uric acid levels in pre-eclamptic cases were 6.14± 1.58 mg/dl whereas in the control group it was 2.79± 0.49 mg/dl. There was statistically significant increase in the mean uric acid levels in pre-eclamptic cases when compared to the normal healthy pregnant women ($p<0.001$). The mean serum magnesium levels were not significant. In pre eclamptic patients the magnesium levels were 2.37± 0.428 mg/dl, and in the control group it was 2.50± 0.280 mg/dl ($p>0.05$).

Table-3 shows the pearson's correlation between serum calcium, magnesium, uric acid and microalbuminuria between cases and controls. The serum calcium is negatively correlated with serum uric acid and microalbuminuria, and this correlation is statistically significant ($p < 0.01$). The serum calcium is positively correlated with magnesium with significant p value of < 0.05. There is also a positive correlation between serum uric acid and microalbuminuria ($p < 0.01$). Serum magnesium is negatively correlated with uric acid and microalbuminuria and p value is insignificant (>0.05).

Table 1: Clinical characteristics of study subjects

	Cases (30)	Controls (30)
Mean age(years)	23.37 ± 3.06	22.53 ± 2.29
Gravida • Primigravida • Multigravida	 19 (63.3%) 11 (36.7%)	 16 (53.3%) 14 (46.7%)
Blood pressure • Mean systolic blood pressure (mm Hg) • Mean diastolic blood pressure (mm Hg)	 155.86 ± 17.26 116.86 ± 9.27	 98.4 ± 9.5 74.93± 4.86
Microalbuminuria	310.21 ± 71.94	26.44 ± 16.54

Table 2. Serum calcium, magnesium and uric acid levels in pre-eclampsia and normal pregnancy.

Groups	Serum Calcium (mg/dl)	Serum Magnesium (mg/dl)	Serum uric acid (mg/dl)
Pre-eclampsia	9.14 ± 0.52	2.37 ± 0.48	6.14 ± 1.58
Normal Pregnancy	9.92 ± 0.44	2.50 ± 0.28	2.79 ± 0.49
P value	<**0.001**	>0.05	<**0.001**

Table 3. Correlation between serum calcium, magnesium, uric acid and microalbuminuria in pre-eclampsia.

	Magnesium	Uric acid	Microalbuminuria
Calcium: • Pearson's correlation • P value	 0.286 < 0.05	 -0.557 < 0.01	 -0.528 <0.01
Magnesium: • Pearson's correlation • p value		 - 0.193 >0.05	 -0.111 >0.05
Uric acid: • Pearson's correlation • P value			 0.809 < 0.01

IV. Discussion

In the present study, the mean serum calcium levels in pre-eclamptic women were decreased significantly compared to the controls, suggests calcium might be a cause of pre-eclampsia. The effect of serum calcium on changes in blood pressure could be explained by the intracellular calcium. There is influx of calcium into the cell and hence serum calcium falls down. This lead to constriction of smooth muscles in blood vessels and increase in vascular resistance [12].

Our findings are comparable with the study done by Sukonpan K et al., and Naser O. Malas et.al., who have show that serum calcium is decreased in pre-eclamptic cases as compared to controls [13, 14].The above findings show that hypocalcaemia could be a risk factor for the development of pre-eclampsia. There were no significant changes in the serum levels of magnesium in pre-eclamptic cases when compared with the control group. The findings of the present study are similar to the findings of the study done by Lou Golmohammed. S et.al., [15].The result of this study is contradictory to some studies which reported that the mean serum magnesium level in pre-eclampsia was lower than normal pregnancy [13].

Generally, the hypomagnesemia in most pregnant women is associated with hemodilution, renal clearance during pregnancy and consumption of minerals by the growing fetus [13].Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity [16].

The association between serum uric acid and pre-eclampsia has been investigated in many studies. In the present study, there was a statistically significant increase in uric acid levels in pre-eclamptic group compared to the control group. Our findings agree with the study done by Punthumapol Chanvitya et.al., who have shown that hyperuricaemia may induce hypertension and vascular disease [2].Roberts JM et.al., have shown the increase in serum uric acid level with the severity of pre-eclampsia [17].Study done by Taner C et.al., have also shown increase in serum uric acid in pre-eclamptic patients when compared to the controls [18]. Hyperuricaemia is believed to result from decreased renal urate excretion and is frequently found in women with pre-eclampsia. Soluble uric acid impairs nitric oxide generation in endothelial cells and also hyperuricaemia induces endothelial dysfunction and may induce hypertension and vascular disease [2].

The findings of the present study show that alteration in calcium, magnesium, uric acid metabolism during pregnancy could be one of the potential causes of pre-eclampsia. In the present study, we found that there was statistically significant correlation of calcium with magnesium, uric acid and microalbuminuria. There was no correlation of magnesium with uric acid and microalbuminuria. Early diagnosis and prompt treatment in pre-eclamptic patients can reduce the morbidity and mortality, associated with hypertensive disorders of pregnancy. Studies have shown possible beneficial role of calcium supplementation in pre-eclampsia.

V. Conclusion

Based on the results of the present study and data available from literature, it is clear that in pre-eclampsia, the serum levels of calcium, magnesium, uric acid are altered, suggesting the possible role of these factors in the etiology and severity of pre-eclampsia. But it remains to be known whether these changes are a cause or consequence of the disease. It is not clear which is the primary event that triggers the onset of hypertension in pre-eclampsia. This research shows abundant evidence that the pathophysiological changes of pre-eclampsia are present long before the clinical presentation of the disorder, which probably explains why all the management of PIH other than delivery are only palliative. This indicates that for a therapy to be successful, the therapy has to be instituted before clinically evident disease. Thus predictors of pre-eclampsia with high sensitivity and moderate specificity will be useful initially in the conduct of clinical trials and perhaps eventually for therapy. Many studies have shown that hypocalcemia and hyperuricemia play a role in severity and outcome of pre-eclampsia. The lowering of serum calcium can cause an elevation of blood pressure in pre-eclamptic mothers. Hyperuricemia induces endothelial dysfunction and may induce hypertension and vascular disease.

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