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Original Research Article

Study of Serum Calcium and Magnesium levels in Pre-eclampsia at DMC, Laheriasarai, Bihar

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Abstract

Background: Pre-eclampsia (PE) is a pregnancy disorder characterised by hypertension and proteinuria after 20 weeks of pregnancy in patients who were previously normotensive and non-proteinuric. If an emergency delivery is not performed, pre-eclampsia may progress to eclampsia, seizures, and maternal and foetal death. The aetiology of pre-eclampsia may be influenced by environmental and dietary variables. In impoverished nations, pregnant women consume fewer critical minerals and vitamins in their diets. Among other things, there is a change in the metabolism of calcium (Ca) and magnesium (Mg) during pregnancy, which may be a cause of pre-eclampsia. The goal of the current study was to evaluate, compare, and correlate the levels of serum total calcium, magnesium, and uric acid in pre-eclampsia and normotensive pregnancy.

Materials and Methods: This comparative cross-sectional study, which was situated on hospitals, was carried out between August 2021 and July 2022. Ca, Mg, and uric acid in the blood, as determined by an automatic analyzer. SPSS version 21.0 was used to analyse the data.

Results: Mean serum calcium and magnesium levels were considerably lower in PE than in normotensive pregnant women (8.69±1.59 mg/dL and 1.91±0.36 mg/dL versus 10.13±0.66 mg/dL and 2.08±0.12 mg/dL, respectively). In contrast, serum uric acid and creatinine levels were higher in PE than in control women.

Conclusion: The results of this study show that pre-eclampsia has lower serum total Ca and Mg levels than normal pregnancy does. Although the conclusion was statistically insignificant, the amount of serum total Ca was observed to decrease with the severity of pre-eclampsia.

Keywords: Electrolytes, Gestational Hypertension, Pregnancy, Uric acid

Introduction

Hypertensive disorders, which affect between 2 and 10% of all gestations, are a common cause of pregnancy complications [1,2]. Pre-eclampsia is a pregnancy disorder

characterised by high maternal systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg measured on two occasions separated by at least six hours, along with associated proteinuria of at least 300 mg or persistent >30 mg/dL (more than one dipstick) in random urine sample [3]. In the third trimester of pregnancy, the disease typically advances and gets worse [4,5]. Pre-eclampsia and gestational hypertension patients share risk factors include older maternal age, obesity, low serum Ca and Mg levels, and higher uric acid concentrations [5]. The aetiology of pre-eclampsia may be influenced by environmental and dietary variables. In developing nations, pregnant women typically consume diets with lower levels of important minerals and vitamins. An insufficient intake could be hazardous to both the mother and the developing foetus. Despite the fact that the exact cause of this illness is unknown, placental ischemia is thought to play a significant part in its pathophysiology [6].

Material and Methods

A comparative cross-sectional study centred at a hospital was carried out from August 2021 to July 2022. This study was conducted at the Darbhanga Medical College and Hospital in Laheriasarai, Bihar, in conjunction with the department of Obstetrics and Gynaecology. Informed agreement was obtained from each study participant, and convenient sampling was used to enlist participants.

Sample Size Calculation

Because the minimal mean difference was lower in Mg than in Ca, 0.12 mg/dL, sample size was determined based on Mg level. On the basis of this, assume that Mg is regularly distributed with S.D. in each group. 0.11, and the actual variation from the mean is 0.12 mg/dL. In order to reject the null hypothesis, 19 cases in each arm must be enrolled. The difference in mean between the two groups is equal with a 90% power probability and a 5% level of significance.

The study sample was increased by 10%, bringing the total sample size to 21 in each group.

The inclusion criteria for the case and control

For case (n=37): American College of Obstetricians and Gynecologists (ACOG), 2002 guidelines were applied for recruitment of cases that are maternal systolic blood pressure (SBP) 140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg measured on two occasions separated by at least 6 hours, with associated proteinuria >300 mg/day or persistent >30 mg/dL (>1+ dipstick).

For the control group (n=37), pregnant women with normal blood pressure and no proteinuria were used.

Existence of any self-reported acute illness, diagnosed cardiac, renal, or hepatic disease, any current treatment for cardiac or blood pressure-related morbidities, history of any surgeries, heavy alcohol or recreational drug use, and unwillingness to participate in the study were among the exclusion criteria.

Normal foetal morphology, the lack of concurrent illness, and gestation between 24 and 36 gestational weeks were the common inclusion criteria for both groups.

Cases and controls were recruited using a practical sample strategy, and each participant gave informed consent before being included in the study.

Biochemical Analysis

The 5-nitro-5'-methyl-BAPTA (NM-BAPTA) method was used to estimate serum Ca, while a photometric decrease in xylidyl blue absorbance was used to estimate serum Mg. By using the Uricase, peroxidase, and kinetic Jaffe's methods to

evaluate the amounts of serum uric acid and creatinine, respectively. In the Semi Autoanalyser, all the parameters were evaluated.

Statistical Analysis

Data was gathered, inputted using Microsoft Excel TM, and examined using SPSS version 11.5 of the statistical package for social science. The Kolmogorov and Smirnov test was used to determine the data's normality. All information was presented as a number, percentage, mean, and standard deviation. The demographic information was expressed using descriptive statistics. Independent t-tests and the Pearson correlation coefficient were employed to analyse the relationship between quantitative variables for parametric variables. In order to determine how the factors related to SBP and DBP, linear regression was performed. The correlation between serum Ca, Mg, and uric acid levels in mild versus moderate and mild versus severe pre-eclampsia, respectively, was examined using logistic regression analysis. Statistics are deemed significant at $p < 0.05$ or higher.

Results

[Table -1] shows the demographic data as well as the mean blood pressure.

Table 1: Demographic and clinical characteristics of the study

General Characteristics	Pre-eclampsia (n=37)	Control (n=17)	P-value
Age (years)	26.72±5.39	25.97±4.97	0.542
POG (weeks)	36.00±2.90	31.17±4.30	0.001
BMI (kg/m^2)	29.26±5.40	24.08±3.66	0.001
SBP (mmHg)	143.61±17.26	108.61±8.33	0.001
DBP (mmHg)	97.22±9.44	67.78±6.80	0.001
MAP (mmHg)	208.42±21.75	153.79±11.30	0.001

P value <0.05 statistically significant.

Preeclampsia was shown to have significantly higher POG, BMI, SBP, DBP, and MAP values than the control group ($p<0.001$). The comparison of biochemical characteristics between the groups is shown in [Table -2]. Between PE and the healthy control group, we found a significant difference in the serum levels of calcium, magnesium, creatinine, and uric acid.

Table 2: Biochemical parameters of the study

Biochemical Parameters	Pre-eclampsia (n=37)	Control (n=17)	P-value
Calcium (mg/dL)	8.69±1.59	10.13±0.66	0.001
Magnesium (mg/dL)	1.91±0.36	2.08±0.12	0.001
Creatinine (mg/dL)	0.49±0.24	0.30±0.07	0.001
Uric acid (mg/dL)	4.40±2.14	2.70±0.80	0.001

P value <0.05 statistically significant.

When compared to the healthy control group, pre-eclampsia patients' mean serum total Ca and Mg levels were significantly lower, according to biochemical characteristics of the study population. Multi-linear regression analysis of serum Ca, Mg, and uric acid revealed that each predicts the outcome of SBP as shown in [Table-3]: serum Ca (regression coefficient= -6.91, p-value=0.001), Mg (regression co-efficient= -16.76, p-value= 0.76), and uric acid (regression coefficient= 4.34, p-value= 0.001).

Table 3: Multiple linear regression analysis of SBP

Variables	Co-efficient	SE	t-value	p-value
Intercept	189.56	19.54	-	-
Calcium (mg/dL)	-6.91	1.50	-4.5	0.001
Magnesium (mg/dL)	-16.76	17.83	-0.94	0.35
Uric acid (mg/dL)	4.34	1.15	3.7	0.001

P value <0.05 statistically significant.

Similar to how serum Ca, Mg, and uric acid were found to predict the outcome of DBP in [Table -4], multi-linear regression analysis of these three variables revealed that serum Ca (regression coefficient= -4.88, p-value= 0.001), Mg (regression co-efficient= -5.66, p-value= 0.68), and uric acid (regression coefficient= 3.75, p-value= 0.001).

Table 4: Multiple linear regression analysis of DBP

Variables	Co-efficient	SE	t-value	p-value
Intercept	119.80	15.29	-	-
Calcium (mg/dL)	-4.88	1.15	-4.21	0.001
Magnesium (mg/dL)	-5.66	13.74	-0.41	0.68
Uric acid (mg/dL)	3.75	0.88	4.22	0.001

P value <0.05 statistically significant.

The level of serum Ca, Mg, and uric acid is not significantly correlated with the severity of pre-eclampsia, defined as from mild to moderate or mild to severe pre-eclampsia, according to a multinomial regression analysis of the study variables in pre-eclampsia. Our research indicates, despite the statistical insignificance of the correlation, that a drop in serum Ca levels is linked to an increase in pre-eclampsia severity.[Table-5].

Table 5: Multiple regression analysis for severity of pre-eclampsia

Variables	□ (regression coefficient)	Standard error	Level of Significant
Mild v/s Moderate Pre-eclampsia			
Calcium (mg/dL)	-0.314	0.643	0.69
Magnesium (mg/dL)	1.214	1.268	0.33
Uric acid (mg/dL)	0.188	0.792	0.81
Mild v/s Severe Pre-eclampsia			
Calcium (mg/dL)	-0.194	0.95	0.83
Magnesium (mg/dL)	1.378	1.371	0.31
Uric acid (mg/dL)	0.138	0.958	0.88

P value <0.05 statistically significant.

Discussion

Pre-eclampsia has been regarded as a condition with an unidentified pathogenesis. In view of this dangerous pregnant complication, many etiologies have been proposed [7-9]. Various trace element concentrations have been observed to change during pregnancy [10,11]. Two intracellular ions, serum Ca and Mg, are crucial for cellular metabolism, including muscular contraction, secretion, neuronal

activity, and cellular death [7]. There have been reports of changes in the levels of calcium, magnesium, and copper in all three trimesters of pregnancy as well as zinc in the middle and late stages of pregnancy and the postpartum period. Additionally, a decrease in serum calcium, magnesium, and zinc during pregnancy has been linked to a number of PE etiologies, suggesting that dietary supplementation with these nutrients may be highly beneficial in preventing this life-threatening disease [10].

According to the current study, preeclampsia patients have lower serum Ca and Mg levels than normal pregnant women do (8.69±1.59 mg/dL versus 10.13±0.66 mg/dL and 1.91±0.36 mg/dL versus 2.08±0.12 mg/dL, respectively). This is consistent with research that has been reported from other parts of the globe. For more than 40 years, maternal hypocalcemia during pregnancy has been recognised.

In healthy pregnant women, total serum Ca tends to drop with time, and it drops dramatically during pre-eclampsia. The degree of Ca intracellular concentration may be able to explain how serum Ca affects changes in blood pressure. Lower levels of total serum Ca eventually result in higher levels of intracellular Ca, which constricts the smooth muscles in blood vessels and raises vascular resistance [11–14].

The most common time to find decreased Mg is also during pregnancy. The majority of pregnant women have hypomagnesaemia, which is correlated with hemodilution, pregnancy-related renal clearance, and elevated foetal demand.

Magnesium concentrations may significantly affect cardiac reactivity, vascular tone, contractility, and excitability. Thus, low Mg levels can result in increased neuronal burst, cerebral vasospasm, and decreased cerebral blood flow [15].

Additionally, earlier studies contend that elevated blood pressure levels are connected to altered Ca homoeostasis, as seen by increased Ca excretion [16]. Low serum Ca levels can also raise blood pressure by triggering the production of renin and parathyroid hormone, both of which raise the intracellular Ca in smooth muscle and cause vasoconstriction. The 2011 WHO guideline, which discovered a greater incidence of pre-eclampsia in pregnant women with low dietary intake of Ca and advised supplementation for such women [17], lends more credence to the observation. This suggests that Ca levels might be involved in pregnancy-related hypertension problems.

Pre-eclampsia has been linked to serum uric acid as a pathogenic factor [18]. According to research done by Niraula A *et al*., Powers RW *et al*., Pramanik T *et al*., and Patel T *et al*., the results from the current study show considerably higher serum uric acid in pre-eclampsia patients compared to normal pregnant women. Numerous biochemical indicators are reported in the literature for predicting the severity of pre-eclampsia, however none of them exhibit the desired sensitivity and specificity. Serum uric acid has a substantial correlation with the severity of pre-eclampsia, according to retrospective investigations.

This conclusion is also confirmed by the current study, which shows that pre-eclampsia patients have higher mean serum uric acid levels (4.40±2.14 mg/dL) than healthy pregnant women (2.70±0.80 mg/dL), with the difference between the two groups being statistically significant.

In PE, hyperuricemia is primarily brought on by decreased GFR and increased tubular reabsorption, but it can also be brought on by increased placental uric acid production brought on by increased placental purine metabolism, acidosis, or an increase in the

activity of xanthine oxidase/dehydrogenase. As such, hyperuricemia is not only a sign of pathological state and renal dysfunction, but it also contributes to the pathogenesis of the disease.

As reported by numerous research, multi-logistic regression has demonstrated that pregnancy in advanced maternal age (40 years) was linked to a two- to five-fold increase in the risk of getting PE. Low serum Ca levels have been identified as one of the causes of the development of pregnancy-related hypertension, which ultimately results in pre-eclampsia. According to the current study, the serum Ca and Mg levels of preeclamptic patients are much lower. The correlation between serum Ca, Mg, and uric acid levels in patients with mild, moderate, and severe pre-eclampsia shows that Ca was negatively associated, but the difference between mild and moderate and mild and severe pre-eclampsia was statistically insignificant.

Conclusion

According to the current study, pre-eclampsia is linked to low serum levels of Ca and Mg, which may contribute to the onset and development of the condition. Additionally, the current study shows a correlation between serum Ca levels and pre-eclampsia severity. Thus, these trace elements would undoubtedly be useful in the appropriate management of pre-eclampsia combined with other blood indicators.

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