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ASSOCIATION OF SERUM CALCIUM AND MAGNESIUM LEVELS WITH PRE-ECLAMPSIA AND ECLAMPSIA IN PATIENTS ATTENDING TERTIARY CARE OF PESHAWAR

Samreen Rahim [1], Beena Rehman [2], Asma Abdul Rehman[3], Asia Habib [4], Zainab Abbas Mirza [5], Ubaid Ullah [6], Farhana Jabeen Shah [7*]

[1]MBBS , Post Graduate Resident Obstetrics And Gynaecology ,Mardan Medical Complex ,Mardan, Kpk, Pakistan.
[2] MBBS ,FCPS ,Assistant Professor Obstetrics And Gynaecology ,Maqsood Medical College And General Hospital ,Peshawar ,Kpk ,Pakistan.
[3]MBBS, Post Graduate Resident Obstetrics And Gynaecology, MTI Khyber Teaching Hospital ,Peshawar ,Kpk ,Pakistan
[4]MBBS, MCPS,FCPS , Associate Professor Obstetrics And Gynaecology , Qazi hussain Ahmad Medical Complex ,Nowshera,Kpk ,Pakistan.
[5]MBBS ,MCPS,FCPS(CPSP) ,Assistant Professor in Department Of Gynaecology And Obstetrics, Kpk, Pakistan.
[6] MBBS ,MPhil Biochemistry, Demonstrator in Department Of Biochemistry ,Khyber Medical College , Peshawar,Kpk ,Pakistan.
[7*]MBBS ,MPH , CHPE,CHR, Associate Professor ,Department of Community Medicine ,Kabir Medical College, Gandhara University , Peshawar Kpk,Pakistan .

***Corresponding Author** : Farhana Jabeen Shah
*Email Address : Farhana.J25@Yahoo.Com

Abstract:

Background: In developing countries, women of reproductive age are frequently confronted with deficiencies in both micro and macro nutrients. There is epidemiological evidence linking insufficient calcium in the diet to an increased risk of preeclampsia, which suggests that pregnant women's altered calcium metabolism plays a role in the development of this condition. The aim of the study was to find out the association of serum levels of calcium and magnesium in pre-eclamptic and eclamptic pregnancies compared to normal pregnancies.

Materials and Methods: Hospital-based cross-sectional and comparative study design was chosen across three groups i.e., normotensive pregnant women, women with pre-eclampsia, and women with eclampsia. Study duration was of 6month from August 2021 till Feb 2022. The population of the current study included pregnant women having 18 to 40 years of age having gestational age of 20 weeks or more, who are attending the HMC for antenatal or emergency obstetric care. The sample size of 150 was considered with 50 individuals in each of the three Groups. Non-probability purposive sampling technique was used. This questionnaire delivered involved the collection of demographic information (such as age, body mass index, and parity), clinical information (such as blood pressure and gestational age), and laboratory results (such as serum calcium and magnesium levels). Following the receipt of informed consent, five millilitres of venous blood were drawn from each participant and then transported to the laboratory of the hospital for examination. Standard techniques, such as

spectrophotometry, were utilised in order to determine the levels of calcium and magnesium in the serum.

Results: The results showed that proteinuria and convulsions show highly significant associations with diagnosis group — confirming their diagnostic relevance. While the mean serum calcium level was significantly lower in pre-eclampsia and eclampsia groups compared to normotensive women **(**$p < 0.001$**).** This suggests a strong inverse relationship between calcium levels and severity of hypertensive disorders in pregnancy. Similarly, the mean serum magnesium level also showed a significant decline from normotensive to eclampsia group **(**$p < 0.001$**).** These findings of the study support the study objective, thus indicating that low serum calcium and magnesium levels are significantly associated with hypertensive pregnancy disorders**.**

Conclusion: The study found that women with eclampsia and pre-eclampsia had significantly lower serum levels of calcium and magnesium compared to those with normal pregnancies. Future research is needed to explore the potential of mineral supplementation as a preventive or therapeutic intervention in pre-eclampsia

Keywords: Serum Calcium, Serum Magnesium, Pre-Eclampsia, Eclampsia

Introduction

Preeclampsia is an abnormality in pregnancy characterized by an increase in blood pressure levels and change in blood trace elements levels. Preeclampsia is commonly defined by a systolic blood pressure≥140 mmHg or diastolic pressure≥90 mmHg [1]. One of the leading causes of maternal and foetal death and disability is preeclampsia. Estimates put the prevalence of preeclampsia in poor countries between 4 to 18%. Both the mother and the baby are at increased risk for serious illness, disability, and mortality due to hypertensive disorders of pregnancy [2]. Among the many maternal mortality causes in the world, hypertensive disorders during pregnancy account for around 10% in Asia and 25% in Latin America. Both pre- and eclampsia, which are hypertension illnesses that may develop during pregnancy, are among the leading causes of death and disability for mothers and their babies. By promptly and effectively treating women who arrive with pre-eclampsia and eclampsia, the vast majority of maternal mortality may be prevented. One way to reach the Millennium Development Goals (MDGs) is to improve healthcare so that hypertension problems in women may be better prevented and treated [3]. The World Health Organization (WHO) has developed these evidence-based guidelines to encourage the most effective therapeutic practices in the treatment of pre-eclampsia and eclampsia [4].

When it comes to hypertension diseases, pre-eclampsia is particularly harmful to both the mother and the baby. In terms of maternal and perinatal death and morbidity, it is among the top causes globally. Nevertheless, our understanding of the pathophysiology of pre-eclampsia is still limited [5,6]. It is believed to be associated with early pregnancy placentation abnormalities, subsequent to systemic inflammation and increasing endothelial damage. Additional questions remain: how severe pre-eclampsia is, how to diagnose it, and how to screen for it are all contentious topics. It is commonly acknowledged, however, that pre-eclampsia may be diagnosed when a woman has a new episode of hypertension throughout her pregnancy (with a sustained diastolic blood pressure >90 mm Hg) and significant proteinuria (>0.3 g/24 h). Both hypertension and proteinuria often manifest in the second part of pregnancy; however, pathophysiological alterations such as insufficient placentation are present from the very beginning of the pregnancy [7]. These complications affect around 2-8% of all pregnancies. Maintaining normal blood pressure requires adequate calcium levels, since hypocalcemia may lead to dangerously high readings. The root cause of vasoconstriction is an increase in the amount of renin in vascular smooth muscle, which is caused by the activation of parathyroid hormone. Serum calcium levels may have an impact on hypertensive problems in pregnancy and pre-eclampsia, according to a small number of studies. For women with high-risk characteristics, the chance of pre-eclampsia is significantly reduced—by half—when they consume enough calcium [8]. Nevertheless, hypocalcemia has been identified in several investigations as a

potential cause of pre-eclampsia. Blood pressure regulation relies on maintaining an appropriate calcium and magnesium balance. When magnesium levels are high enough, blood vessels relax, and when calcium levels are high enough, blood vessels constrict. When intracellular calcium concentration increases, it may lead to vasodilation; magnesium counteracts this effect. As a calcium channel blocker, magnesium works by opposing the calcium-dependent constriction of the arteries [9,10]. Despite the importance of calcium and magnesium in maintaining cardiovascular health, there is limited research on their levels in eclamptic and pre-eclamptic women in the Pakistani population. To fill the gap in the literature, the current study investigated the association of serum calcium and magnesium levels with pre-eclampsia and eclampsia in patients attending tertiary care hospital of Peshawar. This study will help identify whether abnormal serum calcium and magnesium levels are significant risk factors for pre-eclampsia and eclampsia, enabling early detection and improved maternal care.

Materials and Methods

In this study, hospital-based cross-sectional and comparative study design was chosen to compare the serum calcium and magnesium levels across three groups i.e., normotensive pregnant women, women with pre-eclampsia, and women with eclampsia, considering the pregnant women attending the Department of Gynecology and Obstetrics at Hayatabad Medical Complex (HMC), Peshawar.

The population of the current study included pregnants women having 18 to 40 years of age having gestational age of 20 weeks or more, who were attending the HMC for antenatal or emergency obstetric care. The study population was categorized into 3 groups normotensive controls, pre-eclamptic patients, and eclamptic patients, based on clinical diagnosis.

The sample size was determined through below formula;

$n_0=Z^2p(1-p)/e^2$

n_0 stands for Sample size

Z stands for Z-value i.e., 1.96

p value is 0.5 for maximum variability

e is margin error i.e., 0.05

$n_0 = (1.96)^2 x\ 0.5\ x\ (1-0.5)/\ (0.05)^2$

$n_0 = 384.16$

Given the limited population, the formula for finite population adjustment was used as below;

$n = n_0/1+ n_{0/N}$

where the anticipated population is 250 and N is the size of the population;

$n = 384.16/1+ 384.16/250 = 151$

$n = 151$

To get an equal distribution between the all three groups, the sample size of 150 was considered with 50 individuals in each of the three Groups. Non-probability purposive sampling technique was employed to recruit participants based on diagnostic criteria at HMC.

The pregnant women having age 18 to 40 years, having gestational age ≥20 weeks, and willing to give informed consent were included in this study. Women having a history of the chronic hypertension, renal disease, the diabetes, and multiple gestations, or having taken the calcium or magnesium supplements within the last month were excluded from the study to avoid confounding factors. In this study, the Pre-eclampsia was defined as the blood pressure ≥140/90 mmHg with proteinuria, while eclampsia was defined as pre-eclampsia with convulsions.

A systematic questionnaire was used to collect data. This questionnaire involved the collection of demographic information (such as age, body mass index, and parity), clinical information (such as blood pressure and gestational age), and laboratory results (such as serum calcium and magnesium levels). Following the receipt of informed consent, five millilitres of venous blood were drawn from each participant and then transported to the laboratory of the hospital for examination. Standard techniques, such as spectrophotometry, were utilised in order to determine the levels of calcium and magnesium in the serum. In order to adhere to ethical norms, permission was sought from the

Hayatabad Medical Complex's Institutional Review Board (IRB). The data analysis was conducted through SPSS.

Results

Table 1: Comparison of Maternal Characteristics Among Study Groups

Variable	Normotensive (n=50)	Pre-eclampsia (n=50)	Eclampsia (n=50)	p-value
Age (years)	26.8 ± 4.2	27.9 ± 4.6	28.1 ± 4.8	0.168
Gravida (No. of pregnancies)	2.1 ± 1.1	2.5 ± 1.2	3.0 ± 1.3	0.008
Parity (No. of live births)	1.6 ± 0.9	2.0 ± 1.1	2.3 ± 1.2	0.021
Gestational Age (in weeks)	36.7 ± 1.8	34.9 ± 2.3	33.5 ± 2.6	<0.001
History of Pre-Eclampsia/Eclampsia (Yes %)	6%	16%	24%	0.015*

* $p < 0.05$.

Table 1 shows that the mean age of the participants was slightly higher in pre-eclamptic and eclamptic groups compared to the normotensive group, but the difference was not statistically significant (p = 0.168). Similarly, the mean gravida and parity were significantly higher in the eclamptic group compared to the normotensive group, indicating that women with more pregnancies and deliveries may have an increased risk of hypertensive disorders (p = 0.008 and 0.021, respectively).
The table also shows that the gestational age was significantly lower in the pre-eclampsia and eclampsia groups compared to normotensive women, suggesting that these conditions may lead to earlier deliveries (p < 0.001). While, a significantly higher proportion of women in the eclampsia group had a previous history of hypertensive disorders in pregnancy, indicating a possible recurrence risk (p = 0.015).

Table 2: Frequency Distribution of Clinical Features **(Chi-square test)**

Clinical Variable	Normotensive (n=50)	Pre-eclampsia (n=50)	Eclampsia (n=50)	p-value
Proteinuria				
- Absent	50 (100%)	5 (10%)	1 (2%)	
- Present	0 (0%)	45 (90%)	49 (98%)	<0.001
Convulsions (Seizures)				
- Absent	50 (100%)	48 (96%)	0 (0%)	
- Present	0 (0%)	2 (4%)	50 (100%)	<0.001
Supplement Use (Ca/Mg)				
- Yes	22 (44%)	15 (30%)	10 (20%)	
- No	28 (56%)	35 (70%)	40 (80%)	0.009

Table 2 shows that Proteinuria and convulsions show highly significant associations with diagnosis group — confirming their diagnostic relevance.
While Supplement use is significantly higher in normotensive women, possibly indicating a protective role of calcium/magnesium intake.

Table 3: Mean Blood Pressure at Admission **(One-Way ANOVA)**

Blood Pressure (mmHg)	Normotensive (n=50)	Pre-eclampsia (n=50)	Eclampsia (n=50)	p-value
Systolic BP (mean ± SD)	114.6 ± 6.5	147.3 ± 10.2	162.8 ± 12.1	<0.001
Diastolic BP (mean ± SD)	75.2 ± 4.3	96.1 ± 6.7	105.5 ± 8.0	<0.001

Table 3 shows that Systolic and diastolic blood pressure values increase significantly across the three groups, aligning with clinical progression from normotension to eclampsia. While, these values confirm the clinical criteria used for group classification and demonstrate the severity of hypertensive changes in eclampsia.

Table 4: Comparison of Serum Calcium and Magnesium Levels

Variable	Normotensive (n=50)	Pre-eclampsia (n=50)	Eclampsia (n=50)	p-value
Serum Calcium (mg/dL)	9.2 ± 0.6	8.4 ± 0.7	7.9 ± 0.8	<0.001
Serum Magnesium (mg/dL)	2.2 ± 0.3	1.8 ± 0.4	1.5 ± 0.3	<0.001

Significance level: $p < 0.05$

Table 4 of the study shows that the mean serum calcium level was significantly lower in pre-eclampsia and eclampsia groups compared to normotensive women **(**$p < 0.001$**).** This suggests a strong inverse relationship between calcium levels and severity of hypertensive disorders in pregnancy.

The mean serum magnesium level also showed a significant decline from normotensive to eclampsia group **(**$p < 0.001$**).** Magnesium deficiency may play a pathophysiological role in pre-eclampsia/eclampsia development. These findings of the study support the study objective, thus indicating that low serum calcium and magnesium levels are significantly associated with hypertensive pregnancy disorders**.**

Discussion

The findings of the study indicate that the mean blood calcium level was considerably lower in pre-eclampsia and eclampsia groups when compared to normotensive women ($p < 0.001$). Additionally, the mean serum magnesium level exhibited a significant fall from the normotensive group to the eclampsia group ($p < 0.001$). A possible pathophysiological function for magnesium shortage in the development of pre-eclampsia and eclampsia is being investigated. The results of the study are consistent with the previous studies. The pathogenesis of pre-eclampsia is still a mystery. Because this is such a dangerous pregnancy disease, several possible causes have been proposed. Moreover, prior research has linked elevated blood pressure to altered Ca homoeostasis, as seen by increased Ca excretion [11]. Vasoconstriction, an increase in intracellular calcium in smooth muscle caused by parathyroid hormone and renin secretion, is another mechanism by which low serum calcium levels may raise blood pressure [6]. Supplementation of calcium was suggested for pregnant women with poor food consumption due to an increased risk of pre-eclampsia, as stated in the 2011 World Health Organisation guideline, which lends credence to the finding. Because of this, calcium levels may be involved in hypertension problems that manifest during pregnancy [12]. In preeclampsia, serum uric acid has been used as a pathogenic factor. Consistent with previous research, this study found that pre-eclampsia patients had much higher blood uric acid levels than healthy pregnant women. There are a lot of biochemical indicators that may be used to predict how severe preeclampsia would be, but none of them have good sensitivity and specificity, according to the literature. Serum uric acid levels are significantly correlated with the severity of preeclampsia, according to retrospective investigations [13]. A similar result is corroborated by the current research, which shows that pre-eclampsia patients had significantly higher mean serum uric acid levels (4.40±2.14 mg/dL) than normal pregnant women (2.70±0.80 mg/dL). The main causes of hyperuricemia in PE are a decrease in glomerular filtration rate (GFR) and an increase in tubular reabsorption [14,15]. However, it can also be caused by acidosis, an increase in the activity of xanthine oxidase/dehydrogenase, or an amplified placental production of uric acid. Therefore, hyperuricemia is both a marker of renal dysfunction and a factor in the development of the disease. According researchers, multi-logistic regression has shown that the likelihood of getting PE increases two-five times when the mother is at least 40 years old. Preeclampsia, a condition characterised by high blood pressure during pregnancy, has low serum calcium levels as one of its causes [16]. The release of calcium from mitochondria is triggered by a rise in parathyroid hormone levels, which in turn increases membrane permeability, according to previous

research. Blood pressure rises as a result of vascular smooth muscle contractions brought on by an increase in intracellular calcium. A decrease in calcium levels might trigger the kidneys to generate more renin, which in turn can lead to hypertension. Endothelial cells' intracellular suppression of nitric oxide synthase is one mechanism via which magnesium regulates blood pressure [17]. Additionally, it plays a crucial role in the control of blood pressure by influencing cardiac excitability and other vascular tissue-related activities, such as vascular tone, contractility, and responsiveness. Hypomagnesaemia is prevalent in pre-eclamptic individuals, however the current research found an increase in magnesium levels. This might be due to differences in the study group and their eating habits [18,19].

Conclusion

In conclusion, our findings suggest that women with eclampsia and pre-eclampsia have significantly lower serum levels of calcium and magnesium compared to those with normal pregnancies. These deficiencies may contribute to the pathophysiology of pre-eclampsia, particularly in the development of vascular dysfunction and hypertension. Future research is needed to explore the potential of mineral supplementation as a preventive or therapeutic intervention in pre-eclampsia. The present study was taken up as a preliminary study for providing data that could be used in the management of pre-eclampsia and eclampsia using calcium and magnesium supplementations. Nevertheless, it cannot be pointed out that derangement in calcium and magnesium levels is the sole factor for the cause of pre-eclampsia. As there are many contradictory findings in the works of different researchers further studies are required.

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