A Comparative Study of Serum Electrolytes and Calcium, Magnesium in Pre-Eclampsia Pregnancy and Healthy Controls at SMS Medical College & Attached Hospital Jaipur (Rajasthan)

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Abstract

Background: Preeclampsia is characterized by the development of hypertension, proteinuria, and edema at 20th weeks of gestation and in its most severe form is associated with thrombocytopenia, disseminated intravascular coagulation, and hepatocellular damage.It is assumed that deficiency of several essential micronutrients may be a predisposing factor in the development of PE. The present study aimed to measure the levels of Calcium, magnesium, and electrolytes in patients with preeclampsia and to evaluate whether these parameters can be used as diagnostic markers of preeclampsia.

Materials & Methods: After taking necessary permissions, a cross sectional study was conducted at Department of Biochemistry and Department of Obstetrics and Gynecology, SMS Hospital, Jaipur. This study includes 34 patients suffering from Pre-eclampsia aged 20-35years compared with 34 matched controls. Serum levels of Calcium, Magnesium and Electrolytes were measured by Spectrophotometryin fully Automated chemistry analyzer AU680 (BECKMEN COULTER).

Results: Results were analyzed statistically by Student's t-test. Mean Calcium for cases was 6.93 ± 0.72 mg/dl and for Controls was 9.55 ± 0.44 mg/dl which was statistically significant (p value < 0.01).The mean Magnesium levels for cases was 1.28 ± 0.16 mg/dl and for Controls was 2.15 ± 0.21 mg/dl. The value was higher for controls and was statistically significant (p value < 0.01).Similarly, Values of Serum electrolytes were found to be lower in Cases as compared to Controls in our study.

Conclusion: The electrolyte and ion profile of 34 pre-eclampsia patients were studied and compared with that of healthy controls. The present study revealed that low serum Ca and Mg levels and electrolyte alterations mainly low sodium and low potassium are associated with pre-eclampsia, which might be attributed to the development and progression of the disease.

Keywords: Pre-Eclampsia (PE), Calcium, Magnesium, Electrolytes.

Introduction

Hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics. These disorders complicate 5 to 10 percent of all pregnancies, and together they are one of the deadly triad-along with hemorrhage and infection that contributes greatly to maternal morbidity and mortality rates.[1] Pregnancies complicated by hypertension are associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction (IUGR), perinatal death, acute renal or hepatic failure, antepartum haemorrhage, postpartum haemorrhage and maternal death.[2]

Preeclampsia, tagged as a syndrome of theories, is a recognized health challenge with devastating foeto-maternal consequences. It has been with numerous postulations suggested to unravel its aetiopathogenesis.[3]Pre-eclampsia is a disorder of pregnancy characterised by high maternal systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg measured on two occasions separated by at least 6 hours with associated proteinuria more than 300 mg or persistent >30 mg/dL (>1+ dipstick) in random urine sample.[4] The disorder usually progresses in the third trimester of pregnancy and worsens over time.[5, 6]

Pre-eclampsia (PE) is an idiopathic multisystem disorder specific to human pregnancy.[1] Preeclampsia is a multisystem disorder and a major cause of morbidity and mortality worldwide.[7] In developing nations, the incidence of the disease has been reported as 4%-18% with hypertensive disorders being the second most common obstetric cause of stillbirths and early neonatal deaths.[8] Its incidence in India is 8-10%. Hypertensive disorder including eclampsia accounts for 13-16% maternal mortality worldwide and 5% in India.[9, 10]

Fluctuations in maternal serum ions may be a precipitating cause of elevated blood pressure in preeclampsia. Imbalances in milieu of serum sodium and potassium that are involved in functioning of vascular smooth muscles may lead to hyper-responsiveness of vasculature to vasoconstrictors like vasopressin, causing vasoconstriction and hypertension in PE.[11] Calcium deficiency stimulates parathyroid hormone and renin release and caused vasoconstriction. It also indirectly affects smooth muscle function by increasing magnesium levels.[12] Magnesium regulates blood pressure by monitoring vascular tone and structure. Magnesium acts as a cofactor for the sodium potassium ATPase activity.[12] Hence all the electrolytes - sodium, potassium, calcium, magnesium is involved in the cardiovascular effects and helps in smooth functioning. Their alteration in pre-eclamptics when compared with normotensive pregnancies is important to study.

Since the electrolytes: calcium, magnesium, sodium and potassium contribute significantly in the functioning of the vascular smooth muscles, the present study was designed to evaluate the role of these electrolytes in pathophysiology and prognostic management of preeclamptic women and to study the associations of these factors in preeclampsia compared to the normal pregnancy group.

Materials and Methods

After taking Necessary permission from the institute's ethical committee and Department of Obstetrics and Gynecology, the study was conducted at Central Lab, Department of Biochemistry and Obstetrics and Gynecology OPD, SMS Medical College and Hospital, Jaipur. This study was a hospital based comparative Cross sectional study and sampling for the

study was done from the period of May 2021 to December 2022.

Pregnant females in second and third trimester of pregnancy (>20 weeks of gestation) in the age group 20-35 years attending SMS Hospital and having blood pressure >140/90 mm Hg and proteinuria (assessed by dipstick method) were taken as cases. Healthy normotensive pregnant women of matched age and gestational weeks were taken as controls. An informed written consent was obtained from the patients and controls. Patients with the following conditions: Gestational age less than 20 weeks, history of chronic hypertension or use of any hypertensive drugs, endocrine disorder (diabetes mellitus, pheochromocytoma, thyrotoxicosis) /renal disease /hepatic disease /co-arctation of aorta /connective tissue disease (lupus erythematosus) /urinary tract infection and any other chronic medical illness, and patients taking drugs affecting liver and renal function were excluded from the study.

A proforma was used to record relevant information and patient's data.4 mL of venous blood was collected in plain vacutainer and analysed. Serum levels of calcium was measured by Ca+arsenazo III complex-colorimetric method, Magnesium by Calmagite – EGTA-Colorimetric method, and serum electrolytes by Emission spectrophotometry method in fully Automated chemistry analyzer AU680 (BECKMEN COULTER).

All the relevant Demographic, clinical and laboratory data was entered into Microsoft office excel sheet, and thereafter, the data was collected on primer software for Statistical analysis. The association between continuous and categorical variables was assessed by comparisons of means using Student T-test. Statistical significance was set by using p value less than 0.05.

Results

The characteristics of the studied population, including age, the mean levels of serum calcium, serum magnesium and serum electrolytes on comparison between PE patients and Normotensive Pregnant females control group are shown in Table 1.

Table 1: Statistical Indices of the study (*P-value as obtained on applying Student t-test)

Test/ Parameters	Controls(Group 1) (n=34)	CASES(Group 2) (n=34)	P-value
Age (years)	27.91 ± 4.62	27.41 ± 4.27	0.3222 (NS)
Systolic BP (SBP – mm HG)	119.35 ± 3.40	156.53 ± 11.16	< 0.01 (S)
Diastolic BP (DBP – mm Hg)	78.24 ± 3.37	99.41 ± 6.25	< 0.01 (S)
Calcium (mg/dl)	9.55 ± 0.44	6.93 ± 0.72	< 0.01 (S)
Magnesium (mg/dl)	2.15 ± 0.21	1.28 ± 0.16	< 0.01 (S)
Sodium (mMol/L)	139.88 ± 3.00	132.82 ± 3.02	< 0.01 (S)
Potassium (mMol/L)	4.95 ± 0.29	3.48 ± 0.33	< 0.01 (S)
Chloride (mMol/L)	99.23 ± 3.13	98.94 ± 2.92	0.3452 (NS)

Serum Calcium: This table shows mean Calcium for cases was 6.93 ± 0.72 mg/dl and for Controls was 9.55 ± 0.44 mg/dl which was statistically significant (p value

< 0.01). The mean value of Calcium was lower for Cases when compared to controls as shown in Table 1 and Graph 1.
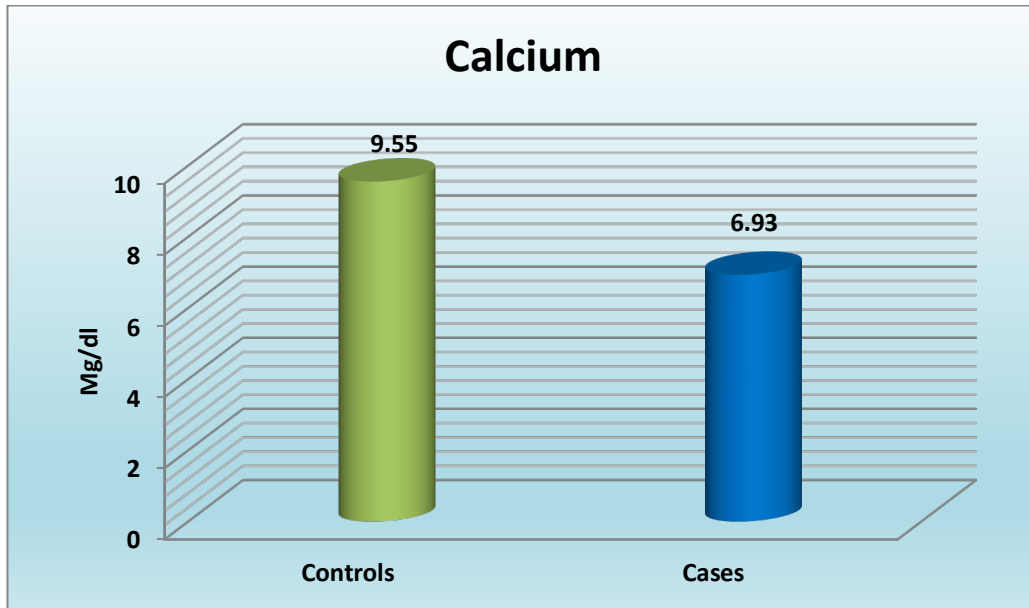
Calcium

Graph 1: Comparison of Mean Calcium between Controls (Group 1) and Pre-Eclampsia Cases (Group 2)

Serum Magnesium: This table also shows mean Magnesium for cases was 1.28 ± 0.16 mg/dl and for Controls was 2.15 ± 0.21 mg/dl. The value was higher for controls and was statistically significant (p value < 0.01)as shown in Table 1 and Graph 2.
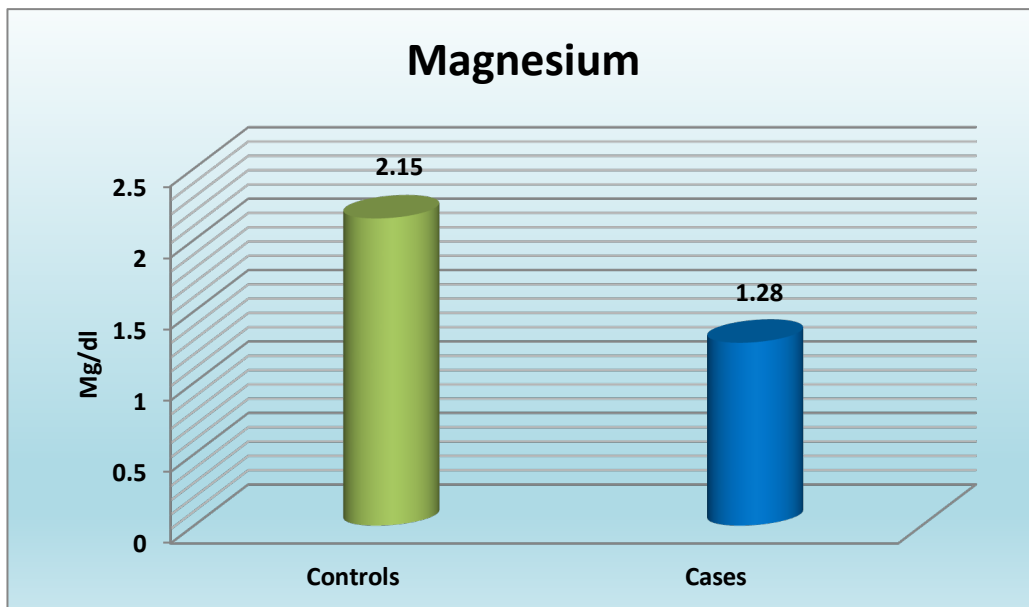
Magnesium

Graph 2: Comparison of Mean Magnesium between Controls (Group 1) and Pre-Eclampsia Cases (Group 2)

**Serum Sodium:** This table also shows that mean Sodium levels for cases 132.82 ± 3.02 mMol/L was lower than that for Controls 139.88 ± 3.00 mMol/L. The value was statistically significant (p value < 0.01) as shown in table 1 and Graph 3.
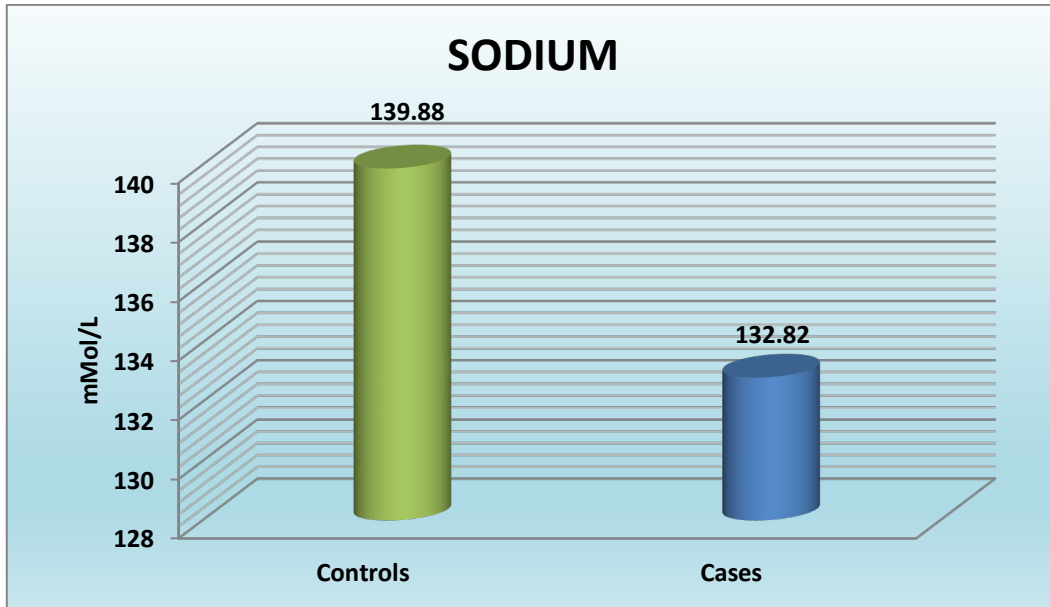
Graph 3: Comparison of Mean Sodium Levels between Controls (Group 1) and Pre-Eclampsia Cases (Group 2)

Serum Potassium: Table 1 also shows that mean Potassium levels for cases 3.48 ± 0.33 mMol/L was lower than that for Controls 4.95 ± 0.29 mMol/L. The value was statistically significant (p value < 0.01). (Graph 4).
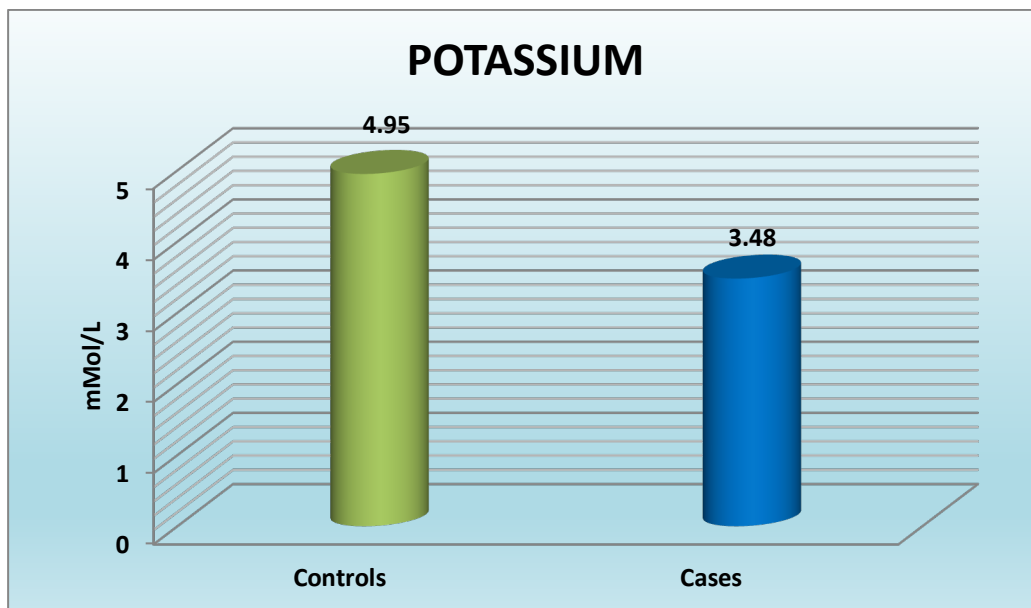
Graph 4: Comparison of Mean Potassium Levels between Controls (Group 1) and Pre-Eclampsia Cases (Group 2)

Discussion

Hypertensive disorders of pregnancy constitute a perplexing and clinically challenging group of pregnancy complications that are responsible for a substantial burden of illness in developed as well as underdeveloped countries of the world. They are a leading cause of maternal and perinatal mortality and morbidity worldwide. Preeclampsia is characterized by the development of

hypertension, proteinuria, and edema at 20th weeks of gestation and in its most severe form is associated with thrombocytopenia, disseminated intravascular coagulation, and hepatocellular damage.

In our study, the mean age in control group 27.91 ± 4.62 years was almost similar to the cases group (27.41 ± 4.27 years). This difference was statistically not significant (p value =0.3222). Controls were matched in this respect. Age has an important influence on the incidence of hypertensive disorders of pregnancy. Young primigravidae under 20 years and all patients over 30 years have an increased chance of hypertension. Findings of a study by Luo J et al[13] in 2020 suggested that women of advanced maternal age should be regarded as at high risk for pregnancy complications, including HDP. A large cohort of Japanese women with singleton pregnancies also indicated that advanced maternal age was a risk factor for HDP.[14]Our results were in also in agreement with results of Agu and Okeudo[15], they also observed that there was no significant difference in the age of women with normal pregnancy and PE.

The mean Calcium for cases was 6.93 ± 0.72 mg/dl and for Controls was 9.55 ± 0.44 mg/dl which was statistically significant (p value < 0.01). The mean value of Calcium was lower for Cases when compared to controls. The mean Magnesium for cases was 1.28 ± 0.16 mg/dl and for Controls was 2.15 ± 0.21 mg/dl. The value was higher for controls and was statistically significant (p value < 0.01).The present study depicts lower serum Ca and Mg in preeclapmsia compared to normal pregnant women. Similarly, A study conducted by Dwivedi et al[16] showed a reduced level of serum calcium and magnesium among women with preeclampsia in third trimester. The findings of lower levels of serum calcium and magnesium in women with pre-eclampsia is in tandem with previous

studies such as by Kanagal et al., 2014[17]; Olusanya et al., 2015[18]; Aslam et al., 2020[19] and Okoror et al., 2020[20. Serum calcium and magnesium are very important for metabolism at the cellular level and are vital for muscle contraction, cell death and neuronal activity, making it very essential in pregnancy. Serum calcium and magnesium are important cofactor for various enzymatic processes and water balance in cells.[21] These trace element plays an essential role in vascular smooth muscle tone and contraction, and hence are vital in blood pressure regulation.[21]

Calcium and magnesium both act on smooth muscle and regulates blood pressure. Variety of calcium binding sites (eg. Troponin, parvalbumin, myosin and calmodulin) that plays a role in regulation of muscle contraction. Major effect of magnesium is to reduce the rate of calcium binding sites that bind magnesium and calcium competitively.[22] Lowering of serum calcium and increase of cellular calcium led to constriction of smooth muscle in blood vessel and increase of vascular resistance.[22]

The mean Sodium levels for cases 132.82 ± 3.02 mMol/L was lower than that for Controls 139.88 ± 3.00 mMol/L. The mean Potassium levels for cases 3.48 ± 0.33 mMol/L was lower than that for Controls 4.95 ± 0.29 mMol/L. Alterations in serum electrolytes levels indicate the underlying physiological and pathological changes of pregnancy. We found the serum sodium levels to be significantly decreased in the PIH cases as compared to that in controls. Our findings are in accordance with those reported by other authors, as Searcy R.L[23] and Pitkin R.M. et al[24]. Indumati et al[25] documented that sodium levels decreased significantly in pre-eclamptics than normal pregnancies and potassium levels were shown no much significant difference between them. In the present study serum, potassium levels were found to decrease in pre-eclamptic

patients as compared to normal pregnant women

The intrarenal production of cyclic GMP, endothelin and PGE2 are all decreased in preeclampsia and this may have implications in the sodium retention, hypertension, intrarenal thrombosis and the vasospasm of preeclamptic pregnancy.[26]The "peripheral arterial vasodilation hypothesis" of sodium and water retention in pregnancy and its implications for the pathogenesis of preeclampsia-eclampsia explain that with increased endothelial damage, sodium retention and increased sensitivity to angiotensin lead to hypertension, oedema and proteinuria, the diagnostic triad of preeclampsia-eclampsia.[27]Potassium decreases vascular responsiveness to vasopressors, like norepinephrine. Leads to vasodilatation and decreases platelet aggregation, which could both decrease blood pressure and protect against hypertension-induced endothelial injury, all of which are responsible for the pathogenesis of symptoms of preeclampsia.

Conclusion

The present study revealed that low serum Calcium and Magnesium levels and electrolyte alterations mainly low sodium and low potassium are associated with pre-eclampsia, which might be attributed to the development and progression of the disease. In preeclampsia water and electrolyte imbalances occur that lead to peripheral vascular resistance and hypertension. Also, hypomagnesemia, hypocalcemiais found to be significantly associated with preeclampsia. Hence, studying these electrolytes help us to understand the pathogenesis of pre-eclampsia, aid in the treatment of pre-eclampsia and may be used to predict the onset and severity of PEalong with help in early detection and prompt treatment of preeclampsia and also can prevent the adverse outcomes of pregnancies.

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