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Original Article

Role of Calcium Levels in Pregnant Women with Pre-Eclampsia and Severe Pre-Eclampsia

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ABSTRACT

Objective: To determine the association between hypocalcemia and pre-eclampsia.
Study Design: Case-control study.
Place and Duration of Study: Department of Obstetrics Gynaecology, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jan to Jul 2019.
Methodology: A total of 90 women, (45 with pre-eclampsia and 45 with normotensive) aged 18-40 years, were included. In all patients, 5ml of venous blood was collected and sent to an institutional pathology laboratory for serum calcium level measurement. Hypocalcemia was noted in the patients.
Results: The mean gestational age in the Case-Group was 31.40±1.64 weeks, and in the Control-Group was 31.51±1.69 weeks. The mean BMI in the Case-Group was 24.94±4.39 kg/m2, and in the Control-Group was 24.24±4.61 kg/m2. The mean serum calcium levels in the Case-Group were 5328.73±2638.70 ng/ml, and in the Control-Group were 8630.03±1099.26 ng/ml. In our study, the frequency of hypocalcemia in women with pre-eclampsia (Case Group) was found to be 16(36.56%) compared to only 04(8.89%) in normotensive (Control Group) women with a *p*-value of 005 and Odds ratio of 5.66 which shows a positive association of hypocalcemia with pre-eclampsia.
Conclusion: This study concluded that the frequency of hypocalcemia in pre-eclampsia women is very high, which shows a positive association between hypocalcemia and pre-eclampsia.

Keywords: Calcium association, Hypocalcemia, Pre-eclampsia.

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INTRODUCTION

Gestational hypertension is defined as systolic blood pressure and diastolic blood pressure of 130/90 mmHg 4 hours apart, in the absence of proteinuria in a previously normotensive pregnant woman at or after 20 weeks of gestation.[1] The obstetrical complications of pregnancy include include Pregnancy hypertension and pre-eclampsia with an incidence of 12-22%.[2] It leads to many complications, to name a few are oliguria, HELLP syndrome, fits, blurring of vision, pulmonary edema and fetal growth restriction, including IUGR and SGA.[3,4] For improving maternal and fetal outcomes, detecting raised blood pressure early is imminent, and prompt management is recommended. It is a disease which involves multiple organs, and despite the high prevalence (3-7%) of pre-eclampsia and severity, the pathophysiology is not understood completely, and its cause has not yet been fully elucidated. [5,6]

Calcium levels are important to maintain blood pressure as decreased calcium levels may cause raised blood pressure. The underlying aetiology is the stimulation of parathyroid hormone, which causes renin release, leading to vasoconstriction by increasing its level in vascular smooth muscle.[7,8] There are few studies which showed no effect of serum calcium levels on hypertensive disorders in pregnancy and pre-eclampsia. Intake of Calcium reduces half the risk of pre-eclampsia, which was a significant reduction for women with high-risk factors.[9,10] However, many studies have found hypocalcemia to be an etiological factor for pre-eclampsia. This study aimed to determine the association between hypocalcemia and pre-eclampsia, which will be a very useful addition to the existing literature and will encourage clinicians to prescribe calcium supplements during pregnancy. In addition, our public can be educated about taking proper calcium supplementation as well as proper screening and management of hypocalcemia during pregnancy in order to reduce perinatal morbidity and mortality.

METHODOLOGY

The case-control study was conducted at the Obstetrics & Gynaecology Department, Pak Emirates Military Hospital, Rawalpindi Pakistan, from January to July 2019 after approval from the Institutional Ethical Review Committee (ER/76/C). The sample

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was collected by using an EPI calculator, taking hypocalcemia in women with pre-eclampsia at 25.9% and in women with normal blood pressure at 6.6%.[11]

Inclusion Criteria: Women aged 18-40 years with the gestational age of >28 weeks (assessed on LMP), singleton pregnancy of cephalic presentation (assessed on USG) (both primigravida and multigravida) with pregnancy-induced hypertension were included.

Exclusion Criteria: Women with chronic blood pressure>130/80 mm of Hg, women with chronic renal failure, and women taking calcium supplements were excluded.

Non-probability, consecutive sampling was carried out. A total of 90 pregnant women [45 Cases (Group-A), 45 Controls (Group-B)] presented to the Department of Obstetrics & Gynecology of Military Hospital, Rawalpindi Pakistan, fulfilling the inclusion criteria, were selected. In all patients, 5 ml of blood samples were collected. These samples were sent to the institutional pathology laboratory for serum calcium level measurement. Hypocalcaemia (present/absent) was noted. All data (age, gestational age, parity, BMI, place of living, monthly income, education level and hypocalcaemia were recorded.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Qualitative variables were expressed as frequency and percentages. Hypocalcemia was compared using Chi-Square test, *p*-value of ≤0.05, and Odds ratio of >1 was considered significant.

RESULTS

The study included women with a mean age of 25.44±4.33 years. The mean gestational age was 31.53±1.67 weeks. The mean gestational age in Group-A was 31.40±1.64 weeks, and in Group-B, it was 31.51±1.69 weeks. The distribution of patients according to parity is shown in Table-I.

Table-I: Distribution of Parity among Study Participants (n=90)

Parity	Cases	Controls
0-2	27(60%)	29(64.4%)
3-4	18(40%)	16(35.5%)

The mean BMI in Group-A was 24.94±4.39 kg/m_2, and in Group-B was 24.24±4.61 kg/m_2. The mean height and weight in Group-A was 5.31±0.23 m and 66.07±7.93 kg, and in Group-B was 5.19±0.30 m and 69.30±7.53 kg. The mean serum calcium levels in Group-A were 5328.73±2638.70 ng/ml, and in Group-B were 8630.03±1099.26 ng/ml. Stratification of Hypocalcemia for age, gestational age, parity, body mass index, place of living, socioeconomic status and educational level was done. In this study, the frequency of hypocalcemia in women with pre-eclampsia (Group-A) was found to be 16 (36.56%) compared to only 04(8.89%) in normotensive (Group-B) women with a *p*-value of 0.05 and Odds ratio of 5.66 which showed a positive association of hypocalcemia with pre-eclampsia as shown in Table-II.

Table-II: Association of Calcium Levels and pre-eclampsia (n=90)

	Cases	Controls			*p*-value	Odds Ratio
Hypocalcemia	Present	Absent	Present	Absent	0.005	5.66
	16(35.5%)	29(64.4%)	04(8.8%)	41(91.1%)		

DISCUSSION

Decreased micronutrients in the diet lead to poor maternal and fetal outcomes as well as associated complications of pregnancy. The effect of low-dose Calcium is important since even modest blood pressure reductions at a population level may have important benefits in reducing major hypertension complications. Emphasis shall be on preventing the development of complications rather than treating these later. Empirical evidence derived from already documented studies revealed the role of micronutrient supplementation in preventing some pregnancy disorders through increased intake of Calcium and magnesium, besides moderating the risk of hypertensive disorders in pregnancy.[12] Moreover, intake of Calcium increases magnesium levels, which has an indirect effect on smooth muscle functioning.[13,14] This study reflected significant interlinkages of hypocalcemia with pre-eclampsia (36.56%) as compared to women with normotensive (8.89%). In one study, hypocalcemia in pre-eclampsia was found to be 48% as compared to 0.0% in normotensive women.[15] In comparison, another study highlights incidences of 56.67% in women having hypocalcemia with pre-eclampsia as compared to only 20.0% in normotensive women.[16]

Contrary to the above, Herrera *et al*. showed no significant differences in the levels of magnesium and Calcium in women having pre-eclampsia and normotensives.[17] Moreover, a study undertaken by Lopez-Jamiloo *et a*l. demonstrated that women with

pre-eclampsia have significantly low levels of serum ionized calcium, which is linked to low calcium intake.[18] Kisters *et al*. [19] showed correspondence among changes in intracellular Calcium, magnesium concentration and pre-eclampsia, while the effect of cell membranes with the above association has not been deliberated further. Around the world, multiple studies were conducted to explore the impact and association of plasma calcium and magnesium metabolism, intracellular and membrane calcium and magnesium concentrations in women with normal pregnancy as against having pre-eclampsia. These studies concluded a significant increase in membranous calcium content in women with pre-eclampsia compared to healthy pregnant women. At the same time, an inverse correlation exists with membranous magnesium content, which is relevant to the present study. Kanagal *et al*. [20] studies on calcium supplementation in pregnancy concluded reduced maternal morbidity and mortality by prevention of pre-eclampsia in pregnant women with low blood pressure who are on daily calcium supplementation of 1.5–2 g; the same finding was supported by Hofmeyr *et al*. in their systematic review on calcium intake in pregnancy at the community level, which is similar to our study results.

On the contrary, one of the studies by Steegers *et al*. determined that supplementation of calcium levels has no linkages in the fall of risk of pre-eclampsia. Rather, a decrease may be ascertained to an extent in deficient populations.[21] Most of the above-mentioned studies supported the hypothesis that hypocalcemia and hypomagnesemia are possible etiologies of hypertensive disorders in pregnancy. In contrast, few studies concluded that measuring these elements may be useful for early diagnosis of pre-eclampsia.

CONCLUSION

This study concluded that the frequency of hypocalcemia in pregnant hypertensive women was very high. Therefore, clinicians should prescribe their patients calcium supplements during antenatal visits in order to prevent pre-eclampsia. In addition, it is important to create public awareness so that the general public can be educated on the proper screening and management of hypocalcemia during pregnancy in order to reduce perinatal morbidity and mortality.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

SK & NN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

RA & UU: Study design, concept, drafting the manuscript, critical review, approval of the final version to be published.

SZ & TK: Data acquisition, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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