

## Evaluation of Calcium in Preeclamptic Pregnant Women Attending Federal Medical Centre Keffi, North Central Nigeria

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### Abstract:

**Background:** Preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality worldwide, with significant burden in low and middle-income countries such as Nigeria. Hypocalcemia has been implicated in preeclampsia. We aim to evaluate the serum calcium levels in preeclamptic pregnant women to determine its role in preeclampsia. **Methods:** A total of 150 women who consented to be part of the study, were recruited into the study. 50 preeclamptic pregnant women serves as study group and 100 normotensive non-pregnant women serves as the control, following a matching criterion ratio of 1:2. Serum calcium was estimated spectrophotometrically and the blood pressure was measured using a mercury sphygmomanometer. **Results:** The mean and Standard Deviation (SD) of serum calcium levels in preeclamptic pregnant women ( $7.10 \pm 2.10$ ), was statistically significantly lower, ( $p < 0.001$ ) relative to the normotensive non-pregnant women ( $9.60 \pm 0.90$ ). 70% of the preeclamptic women show hypocalcemia; 10% show hypercalcemia; and 20% show a normal serum calcium level. The mean blood pressure in the preeclamptic women was higher than non-pregnant normotensive women, ( $p < 0.001$ ). **Conclusion:** The study demonstrates low serum calcium levels and high blood pressure in preeclamptic women.

**Keywords:** Calcium, Pregnancy, preeclampsia, Hypertension, Normotensive.

### Original Research

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### INTRODUCTION

Preeclampsia is a complication of pregnancy typically characterized by high blood pressure and proteinuria occurring after 20 weeks of gestation [1]. The origin and causes of preeclampsia are multifactorial, involving genetic, immunologic, and environmental factors. Emerging evidence has linked low maternal serum calcium levels with increased risk of preeclampsia, suggesting that calcium plays a role in vascular smooth muscle contractility and endothelial function [1]. In Nigeria, despite efforts to improve antenatal care, preeclampsia remains a common and dangerous complication of pregnancy. Early identification of modifiable risk factors such as hypocalcemia could enhance preventive strategies.

While the exact aetiology remains elusive [2]; several pathophysiological mechanisms, including endothelial dysfunction, abnormal placentation, oxidative stress, and mineral imbalances, have been proposed. Among these, calcium deficiency has been explored as a potential contributing factor. Calcium plays a critical role in vascular smooth muscle function and blood pressure regulation [3].

Calcium is an essential mineral in the human body, playing a vital role in various physiological processes including bone formation, muscle contraction, nerve function, and blood clotting. Calcium, the most abundant mineral in the human body, has several important functions;

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More than 99% of total body Calcium is stored in the bones and teeth supporting their structure [4]. The remaining 1% is found throughout the body in blood, muscle, and the fluid between cells needed for muscle contraction, blood vessel contraction and expansion, secretion of hormones and enzymes, and sending messages through the nervous system so that these vital body processes function efficiently [5]. A constant level of Calcium is maintained in body fluid and tissues within a narrow limit for normal physiological functioning so that when blood Calcium decreases it stimulates the secretion of parathyroid hormone (PTH) which stimulates the conversion of vitamin D to its active form (calcitriol) in the kidneys [6]. Calcitriol increases intestinal Calcium absorption, which in turn stimulates bone Calcium release by activating osteoclasts and decreasing urinary Calcium excretion [6, 7].

Pregnancy is a normal state of increased physiological phenomenon and demand with many biochemical changes including calcium metabolism; and adequate calcium levels are essential to meet the needs of both the mother and the growing fetus. During pregnancy, the demand for calcium increases significantly to support the developing fetus, making the regulation of maternal calcium homeostasis particularly important [3].

The fetus requires a substantial amount of calcium for skeletal development, especially during the third trimester when bone mineralization peaks. Consequently, pregnant women need to ensure sufficient calcium intake to avoid depletion of their own bone calcium stores, which could potentially lead to long-term maternal bone health issues such as osteoporosis [3, 4]. The results of biochemical tests during pregnancy may differ from the normal reference ranges so these may be mistakenly interpreted as abnormal leading to unnecessary and potentially dangerous therapeutic actions [4].

A recent study, implicated alterations in calcium metabolism in the pathogenesis of hypertension in pregnancy [8]. In the third trimester, calcium is deposited in the fetal skeleton at the rate of 200mg/day. In addition, urinary excretion of calcium in the third trimester is doubled. Calcium deficiencies have been linked to pre-eclampsia/eclampsia [8]. Further, hypocalcemia, deviations in levels of 1, 25-

dihydroxyvitamin D and parathyroid hormone have been shown in women with pre-eclampsia [9, 10].

Calcium supplementation has been proven to reduce the incidence of pre-eclampsia [11], in a systematic review of twelve studies with 15,528 women, it was reported that calcium supplementation reduced the risk of pre-eclampsia [11].

The study is aimed at evaluating serum calcium levels and blood pressure in preeclamptic women attending FMC Keffi and compare them with the normotensive non- pregnant women to explore a possible link between calcium status and the development of preeclampsia.

## MATERIALS AND METHOD

A hospital-based case-control study was carried out on a total of 150 participants; which were grouped into study group and control group. The study group consist of the preeclamptic pregnant women, 50 in number and the non-pregnant women 100 in number as control. The selection was based on matching criteria adapted for case-control study design. Five milliliters (5mls) of blood sample were collected from the participants into plain container, the samples were allowed to clot, after which, serum was extracted into clean container and kept in the Refrigerator at 26°C till analysis. Serum calcium was estimated Spectrophotometrically using Chem-Well Automated Chemistry Analyzer and Spectrum reagent supplied by Vina Medic (Nig) Limited. Also, the blood pressure of the participants was measured using Mercury Sphygmomanometer.

## Ethical approval

Ethical approval was sought and obtained from the Ethical Clearance Committee of Federal Medical Centre Keffi, Health Research Ethics Committee with reference number: FMC/KF/HREC/02651/24.

## Inclusion and Exclusion Criteria

Pregnant women aged 18-45 years, with a gestational age of 20 weeks or more, who gave their consent were included; while women with pre-existing hypertension, diabetes, or other chronic medical conditions were excluded.

## Data collection

Prior to specimen collection, all participants were administered with structured

questionnaires to obtain demographic information. Each questionnaire had a unique participant identification number (PIDN). The first part of the questionnaires contained the bio data of the participants e.g. sex, age etc. The second part consisted of the duration of the pregnancy. For reasons of privacy, all data were kept confidential in accordance with the World Medical Association Declaration of Helsinki (WMA, 2008). For each participant, only the PIDN was recorded on the laboratory forms (no names). All the filled questionnaires were destroyed after data entry had been completed.

### Statistical analysis

The statistical package of social science (SPSS) window version 20.0 was used for all calculation and data analysis. The Differences in Calcium levels and Blood Pressure between the study group and the control group were tested using a student t-test. P value < 0.001 were considered statistically significant. The demographic characteristics of the participants

were expressed as mean values and standard deviation (SD).

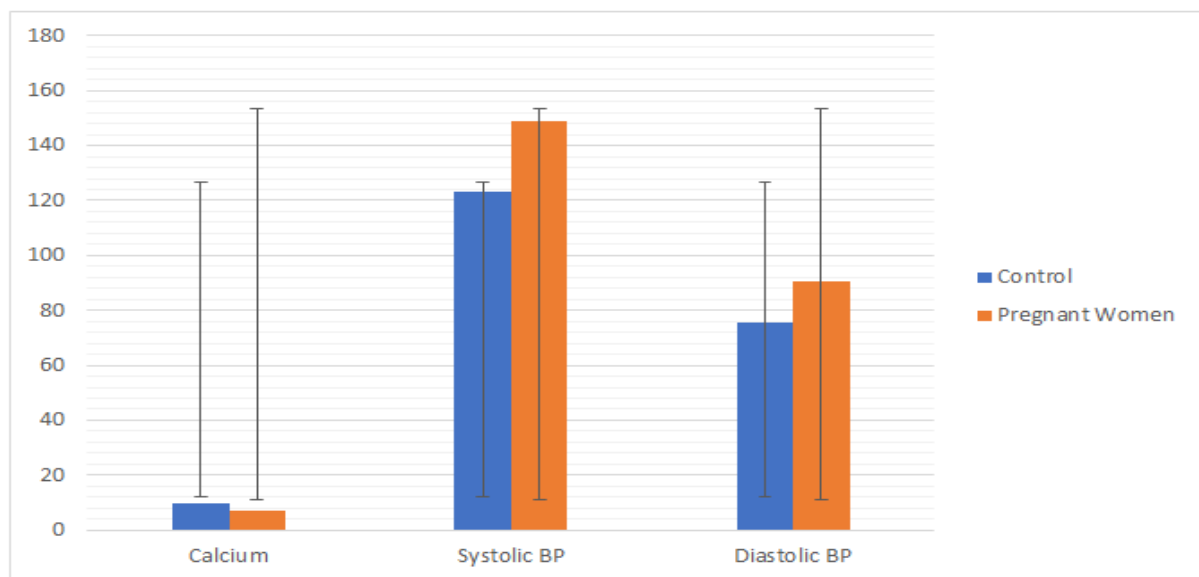
### RESULTS

The mean and SD of serum calcium of the preeclamptic pregnant women shows statistically significant difference relative to the control,  $p < 0.001$ . Equally, the blood pressure were significantly higher in the preeclamptic pregnant women relative to the control,  $p < 0.001$ ; as presented in the Table 1 and Figure 1 below.

**Table 1: Comparison of Mean and SD of the Calcium and Blood Pressure of study participants**

Parameters	Calcium	Systolic BP	Diastolic BP
Control (100)	9.60 $\pm$ 0.90	123.40 $\pm$ 6.30	75.40 $\pm$ 4.70
Pregnant Women (50)	7.10 $\pm$ 2.10	148.80 $\pm$ 11.40	90.5 $\pm$ 9.10
P-value	< 0.001	< 0.001	< 0.001
Remark	SS	SS	SS

**SS = Statistically Significant**



**Fig 1: Comparison of Mean and SD of the Parameters**

The normotensive pregnant women show no statistically significant difference when compared with the control as shown in Table 2 below.

**Table 2: Comparison of Mean and SD of the Normocalaemia**

Parameters	Calcium
Control (100)	9.60 $\pm$ 0.90
Pregnant Women (10)	9.10 $\pm$ 0.80
P-value	0.255
Remark	NSS

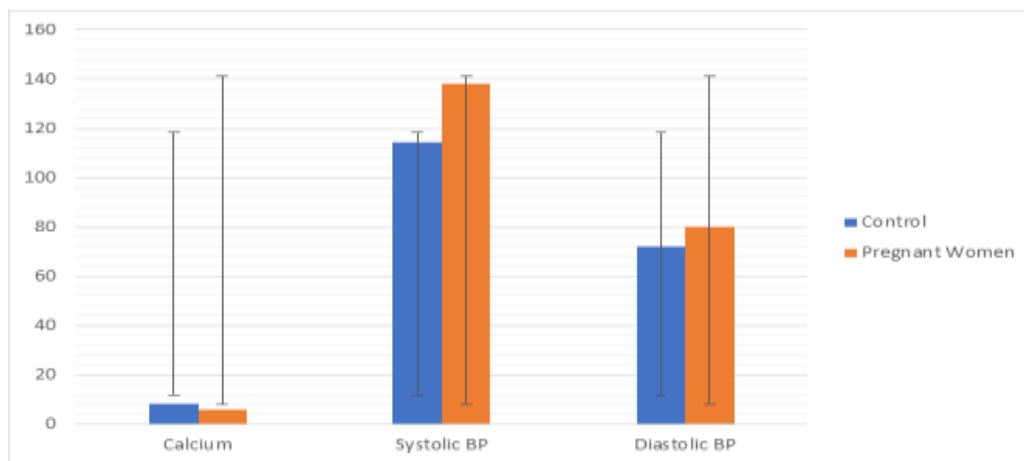
**NSS = Non -Statistically Significant**

The serum calcium and blood pressure of the 35 preeclamptic pregnant women that showed hypocalcemia demonstrated high blood pressure relative to the control,  $p < 0.001$ ; as presented in Table 3 and Figure 2 below.

**Table 3: Comparison of Mean and SD of Hypocalcemia and Blood Pressure**

Parameters	Calcium	Systolic BP	Diastolic BP
Control (100)	$9.60 \pm 0.90$	$123.40 \pm 6.30$	$75.40 \pm 4.70$
Pregnant Women (35)	$5.60 \pm 1.70$	$148.10 \pm 1.00$	$90.00 \pm 1.10$
P-value	$< 0.001$	$< 0.001$	$< 0.001$
Remark	SS	SS	SS

SS = Statistically Significant



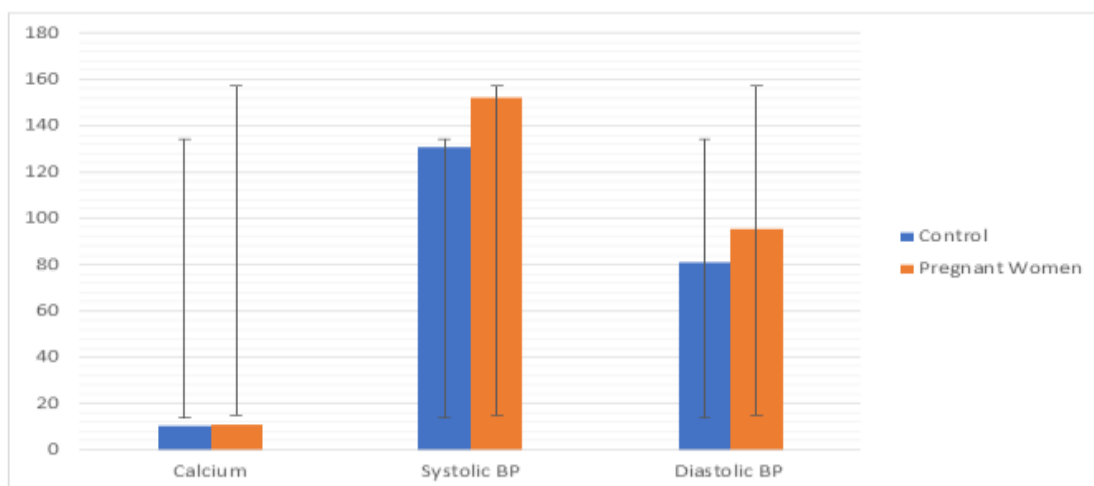
**Fig 2: Comparison of Mean and SD of Hypocalcemia and Blood Pressure**

The blood pressure of the preeclamptic women which showed hypercalcemia 5 in number were statistically higher than the control,  $p < 0.001$  as represented in Table 4 and Figure 3 below.

**Table 4: Comparison of Mean and SD of Hypercalcemia and Blood Pressure**

Parameters	$\text{Ca}^{++}$	Systolic BP	Diastolic BP
Control (100)	$9.60 \pm 0.90$	$123.80 \pm 3.40$	$75.40 \pm 4.70$
Pregnant Women (5)	$10.70 \pm 0.60$	$152.30 \pm 9.40$	$95.4 \pm 8.50$
P-value	0.359	$< 0.001$	$< 0.001$
Remark	NSS	SS	SS

NSS = Non-Statistically Significant; SS = Statistically Significant



**Fig 3: Comparison of Mean and SD of Hypercalcemia and Blood Pressure**

## DISCUSSION

Preeclampsia a pregnancy complication, has been associated with elevated blood pressure and hypocalcemia and is characterized with high morbidity and mortality in pregnant women [1, 9]. Preeclampsia has been known to be common in women with their first pregnancy [1].

Our study demonstrated a relationship between hypocalcemia and pre-eclampsia. In our study the mean serum calcium in pre-eclamptic women was significantly lower at ( $5.60 \pm 1.70$ ) compared to the serum calcium level in normotensive non-pregnant women which was ( $9.60 \pm 0.90$ ); there is a statistically significant difference in serum calcium level of the study group and control group, which is low serum calcium and the development of preeclampsia; this confirmed the hypothesis that hypocalcemia may be an etiological factor in the development of pre-eclampsia; Serum calcium is very important for metabolism at the cellular level and vital for muscle contraction, cell apoptosis and neuronal activity, making it very essential in pregnancy [9, 10].

The disorders of hypertension are the commonest medical complications that develop during pregnancy, characterized by an increase in blood pressure. In accordance with presentation of the condition, the present study showed that systolic and diastolic blood pressure were significantly raised in preeclamptic pregnant women, this is in tandem with other authors [11]. Serum calcium has been reported to be very important for metabolism at the cellular level and is vital for muscle contraction, cell death and neuronal activity [12]. The observation of low Calcium levels is in tandem with other studies on hypertensive disorders in pregnancy [12, 13, 19]. A probable theory to this observation could be that low serum calcium levels as a result of decreases in intracellular calcium, could lead to constriction of smooth muscles in blood vessels and thereby increases vascular resistance [14, 20, 21], leading to a raised systolic and diastolic blood pressure. Furthermore, previous reports suggest that altered calcium homeostasis, as exhibited by increased calcium excretion, is associated with higher blood pressure levels [15, 22, 23]. Low serum calcium levels may also increase blood pressure by stimulating parathyroid hormone and renin release, which in turn increases intracellular calcium in smooth muscle, leading to vasoconstriction [16,

24]. The finding in this study is further supported by the 2011 WHO recommendation, which found a higher risk of pre-eclampsia in pregnant women with low dietary intake of calcium and recommended supplementation for such women [25]. This implies that calcium levels may play a role in hypertensive disorders in pregnancy. Equally, this study aligned with findings of other authors [17, 18, 26], who reported lower serum calcium levels in preeclamptic pregnant women compared to non-pregnant control.

However, Golmohammad Lou *et al.*, have disputed the role of calcium and trace elements in high blood pressure, particularly, in pre-eclampsia [27]. They explained that, although slightly lower, there was no significant difference in calcium and magnesium levels between women with pre-eclampsia and normal, healthy pregnant women [27].

However, the findings highlight the dynamic changes in serum calcium levels during pregnancy, these changes may have important implications for maternal and fetal health, particularly in relation to bone health development and preeclamptic condition. Consistent with previous studies [14], the findings indicate a significant decline in serum calcium levels in pregnancy.

The limitation of this study is that, it only focuses on the gestational pregnancy and preeclampsia, where other confounding conditions like diabetes and lipidemia were not included; these serves as an area of gap which could be explore for further study.

## CONCLUSION

Healthcare providers should be aware of the changes in serum calcium levels during pregnancy and take necessary steps to manage and prevent hypocalcemia. Moreover, pregnant women need calcium supplements to maintain optimal calcium levels. This is crucial for fetal bone development and preventing complications such as preeclampsia and preterm labor.

I recommend the development of novel and clinically relevant tests, that would screen pregnant women to identify women at high risk of developing or already having established preeclamptic conditions at the first trimester of pregnancy. In preeclampsia, such tests could



identify women who may benefit from increased clinical surveillance and carefully timed birth. Conversely, they may identify low risk patients who could safely reduce their antenatal visits.

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**Ethical Consideration:** Approved by the Health Research Ethics Committee, Federal Medical Center, Keffi.

**AUTHORS CONTRIBUTIONS:** ASP was involved in conception of the study, generation of data, writing of the manuscript. BVO was involved in the analysis of data, collation of results. OHB was involved in the proof reading of the manuscript. LMD was involved in proof reading and making of corrections in the manuscript. All authors read and consented to the publication of the manuscript.

**Conflict of Interest:** The authors declare that no conflict of interest exists and agreed to the publication of this article.

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**Data Availability Statement:** Data are available from the corresponding author upon request.

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