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ORIGINAL ARTICLE

Plasma Calcium Levels in Preeclampsia Versus Normotensive Pregnant Women in a Tertiary Hospital: A Comparative Study

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Abstract The role of calcium supplementation in pregnancy to prevent preeclampsia is conflicting. The goal was to determine if there was significant difference between plasma calcium levels in women with preeclampsia and normotensive pregnant women. This was a cross-sectional study of 90 consecutive preeclamptic and 90 normotensive pregnant. Blood samples were taken from them and the plasma isolated from each was analyzed using colorimetric method for calcium and albumin employing calcium kit, albumin kit and spectrum lab 7225 spectrophotometer set (Bran Scientific and Instrument Company, England). The data was analysed using SPSS version 16. Their mean ages were 28.67 ± 5.23 and 28.33 ± 5.06 years respectively (preeclamptic vs. normotensive women respectively; $P = 0.688$). Majority of them were nullipara (48, 53.3% and 46, 51.1% of preeclamptic and normotensive women respectively). The mean gestational age of the preeclamptic women was 36.38 ± 2.54 weeks while that of the normotensive women was 36.24 ± 2.34 years, ($P = 0.715$). The plasma calcium level in preeclamptic women was significantly lower than in normotensive pregnant women (2.07 ± 0.318 mmol/L vs. 2.41 ± 0.224 mmol/L, $P < 0.001$). Preeclamptic women have significantly lower plasma calcium levels than normotensive pregnant women in our community. Routine calcium supplementation for pregnant women at risk of developing preeclampsia is therefore recommended.

Keywords Plasma calcium · Preeclampsia · Normotensive

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Introduction

Preeclampsia is a clinical syndrome of unknown aetiology characterized by the occurrence of hypertension and proteinuria after 20 weeks of gestation, in a formerly normotensive woman [1]. It is a public health issue contributing to significant maternal and perinatal morbidity and mortality globally [2–5]. Preeclampsia and other hypertensive disorders of pregnancy account for nearly 18% of all maternal deaths worldwide, with an estimated 62,000–77,000 deaths per year [6]. The developing countries are more affected by the impact of this disease [7, 8]. In Nigeria, preeclampsia/eclampsia is the leading cause of maternal mortality and is responsible for 28.2% of maternal death [9].

The incidence of preeclampsia worldwide ranges between 2% and 10% [10, 11], while in Nigeria, it ranges between 1.2% and 7.6% [12–16]. Despite many research efforts, the aetiology of preeclampsia remains uncertain [17]. However, origins of the disease process have been

shown to involve a complex interaction of pregnancy specific immunological and vascular adaptation, maternal constitutional factors as well as dysfunctional trophoblastic development and impaired implantation [18, 19]. This eventually leads to endothelial damage, organ ischaemia, widespread inflammation and increased vascular permeability [20]. In recent years, there has been an increasing amount of literature on assessment of calcium intake and risk of preeclampsia [17].

Micronutrients and trace elements play vital roles in metabolism and preservation of tissue functions [21]. Several elemental micronutrient abnormalities like calcium, magnesium, zinc and copper have been suggested to play contributing roles in preeclampsia [22–27].

Previous studies have found reduced calcium levels in patients with preeclampsia [21, 22, 28, 29], whereas Darkwa et al. [31] and Souza et al. [32] observed no significant difference. Despite some controversial findings, it is generally recommended that supplementing high-risk women with calcium during pregnancy, especially in populations with low dietary calcium intake, reduces the risk of preeclampsia [32–34].

The aim of this study, therefore, was to study the serum calcium levels in pregnant women with preeclampsia, compared to normotensive pregnant women at the University of Abuja Teaching hospital, Abuja.

Materials and Methods

Study Design and Location

This was a comparative cross-sectional study between preeclamptic and normotensive pregnant women attending antenatal clinic at the University of Abuja Teaching Hospital, Abuja, Nigeria between January and July 2018. The University of Abuja Teaching Hospital is a 350-bed Federal Government owned tertiary institution situated in Gwagwalada, a high density sub-urb of Abuja, Nigeria's Federal Capital Territory. The study population comprised of 90 preeclamptic women and 90 normotensive pregnant women as controls.

Sample Size Determination

Sample size was calculated using the formula by Kish Leslie for cross-sectional studies [35]:

$$\frac{n = z^2pq}{d^2}$$

where

n = the desired sample size

z = standard normal deviation (1.96 at 95% confidence level)

P = proportion (prevalence) in the target population estimated to have the particular characteristic. In a similar study, Patel et al. [36] found a prevalence of hypocalcaemia in preeclamptic women to be 94%

$q = 1-p$

d = degree of accuracy desired, usually set at 5%.

Therefore, $\frac{n=(1.96)^2(0.94)\,(0.06)}{(0.05)^2} = \frac{0.22}{0.0025} = 88$

This was rounded up to 90 for each arm of the study, bringing the total to 180.

Sampling Method

Convenience sampling method was used to recruit consecutive preeclamptic patients that met the inclusion criteria. Ninety normotensive marching pregnant women were recruited as controls.

Inclusion/Exclusion Criteria

The study population comprised of women that developed preeclampsia in the second half of pregnancy and who were Nigerians, while the control group was made up of 90 normotensive pregnant women. Those who declined consent, or had medical disorders such as renal disease, chronic hypertension or diabetes mellitus were excluded. Those on calcium supplementation or who developed eclampsia were also excluded.

Quantitative Determination of Plasma Calcium

Fasting blood samples from both groups were obtained with vacutainers, with the patients in supine position. Tourniquet was not used. The plasma was immediately separated by centrifugation. Plasma calcium and albumin were estimated by photometric colorimetry in the Chemical Pathology laboratory using calcium kit, albumin kit and spectrum lab 7225 spectro-photometer set (Bran Scientific and Instrument Company, England). Plasma albumin estimation was done in order to get corrected total plasma calcium since plasma calcium is also bound to albumin. The corrected total plasma calcium was calculated using the following formula:

$$\begin{aligned}&\text{Corrected total plasma (mmol/L)}\\&\quad = \text{total calcium measured (mmol/L)}\\&\qquad + 0.2(40 - \text{albumin (mmol/L)}).\end{aligned}$$

Statistical Analysis

Statistical analysis was done using SPSS version 16. The findings were displayed in form of tables and charts. Observed differences were evaluated with Student's t test and $P < 0.05$ was considered significant.

Ethical Approval

Approval for the study was given by the Human Research Ethical Committee of the University of Abuja Teaching Hospital, Abuja.

Results

A total of 180 booked pregnant women (90 preeclamptic and 90 normotensive) were studied. Their socio demographic characteristics are shown in Table 1. The age group 26–30 years accounted for 34 (37%) and 37 (41%) in the preeclamptic and normotensive women respectively, and therefore, constituted the largest number in both groups. The mean ages were 28.67 ± 5.23 years for the preeclamptics and 28.33 ± 5.06 years for the control group. This was not statistically significant ($P = 0.668$). Majority of the participants in both groups had secondary school education as the highest educational level attained (50, 55% and 41, 45.6% for preeclamptics and controls respectively).

Parity distribution shows that 48 (53.3%) of the preeclamptics and 46 (51.1%) of the controls were nullipara. Gestational age distribution revealed that 58 (64.5%) of preeclamptics and 61 (67.8%) of the controls were within the gestational age of 36–42 weeks. The mean gestational age of the preeclamptics was 36.38 ± 2.54 weeks while that of the controls was 36.24 ± 2.34 weeks. This was not statistically significant ($P = 0.715$).

Table 2 shows that the average systolic blood pressure of the preeclamptics and the controls were 159 ± 17.42 and 110 ± 8.73 mm Hg respectively. This was statistically significant ($P < 0.001$). The average diastolic blood pressure of the eclamptics and the controls were 101.11 ± 1.94 and 69.11 ± 8.16 mm Hg respectively. This was statistically significant ($P < 0.001$).

The mean plasma calcium levels in preeclamptic subjects was 2.11 ± 0.034 mmol/L and 2.46 ± 0.241 mmol/L

Table 1 Socio-demographic characteristics

Variable	Preeclamptics			Normotensives		
	Freq.	%	Mean ± SD	Freq.	%	Mean ± SD
Age			28.67 ± 5.24			28.33 ± 5.06
16–20	6	6.7		5	5.6	
21–25	20	22.2		20	22.2	
26–30	34	37.8		37	41.1	
31–35	21	23.3		22	24.4	
36–40	9	10.0		6	6.7	
Total	90	100		90	100	
Educational status						
Tertiary	29	32.2		45	50.0	
Secondary	50	55.5		41	45.6	
Primary	6	6.7		3	3.3	
None	5	5.6		1	1.1	
Total	90	100		90	100	
Parity						
Nullipara	48	53.3		46	51.1	
Primipara	13	14.5		18	20.1	
Multipara	23	25.5		24	26.6	
Grandmultipara	6	6.7		2	2.2	
Total	90	100		90	100	
Gestational age			36.38 ± 2.54			36.24 ± 2.34
29–35	32	35.5		29	32.2	
36–42	58	64.5		61	67.8	
Total	90	100		90	100	

Table 2 Comparison of different variables

Parameters (coefficients)	Pet (90) mean ± SD	Norm (90) mean ± SD	*P* value (decision criteria)
Age (years)	28.67 ± 5.237	28.33 ± 5.064	t = 0.430; $P = 0.668$
GA (week)	36.38 ± 2.54	36.24 ± 2.34	t = 0.366; $P = 0.715$
Parity	1.16 ± 1.59	1.01 ± 1.370	t = 0.664; $P = 0.507$
Systolic BP	159 ± 17.42	110.44 ± 8.73	t = 23.64; $P < 0.001$
Diastolic BP	101.11 ± 1.94	69.11 ± 8.16	t = 20.99; $P < 0.001$
Corrected plasma cal.	2.07 ± 0.318	2.41 ± 0.224	t = 8.21; $P < 0.001$
Plasma albumin (g/L)	42.67 ± 0.259	42.92 ± 0.28	t = 0.665; $P = 0.507$
Plasma calcium (mmol/L)	2.11 ± 0.034	2.46 ± 0.241	t = 8.43; $P < 0.001$
Education	3.16 ± 0.086	3.41 ± 0.069	t = 2.315; $P = 0.022$

in normotensives. This was statistically significant ($P < 0.001$) as shown on Table 2.

The mean corrected plasma calcium levels for the preeclamptics and the controls were 2.07 ± 0.318 mmol/L and 2.41 ± 0.224 mmol/L respectively. This was statistically significant ($P < 0.001$). The corresponding mean serum albumin levels were 42.67 ± 0.259 g/L and 42.92 ± 0.28 g/L respectively. This was not statistically significant ($P = 0.507$).

Table 3 shows the frequency of those who had hypocalcaemia, normal plasma calcium and hypercalcaemia among the 2 groups. Fifty-five (61.1%) of the study group had hypocalcaemia (corrected calcium level below 2.25 mmol/L) while 16 (17.8%) of the controls had hypocalcaemia. Five (5.6%) of the control group had hypercalcaemia (corrected serum calcium levels > 2.75 mmol/L), while none among the preeclamptic group had hypercalcaemia.

Discussion

This study evaluated the plasma calcium levels in preeclamptics and normotensive pregnant women with similar socio-demographic parameters. The age group of 26–30 years that constituted the highest number of the preeclamptics was similar to the findings by Kooffreh et al. [12] in Calabar, Nigeria. Majority of the preeclamptics were nulliparous. This is similar to findings from other studies from Calabar, Sokoto and Shagamu in Nigeria respectively [12, 14, 15].

This study has shown that the plasma calcium level among the preeclamptic was significantly lower than in the normotensive patients. This finding was similar to that by Elmugabil et al. [21] and Patrelli et al. [29]. Other authors, however, did not find any significant difference in the serum levels between preeclamptic and normotensive women [30, 31, 37].

Belizan et al. [38] first described the inverse relationship between calcium intake and hypertensive disorders of pregnancy based on the observation that Mayan Indians in Guatemala, who used to soak their corn in lime before cooking, had a high calcium intake and low incidence of preeclampsia and eclampsia. Similar findings from Ethiopia showed a very low prevalence of preeclampsia where the diet contained high levels of calcium [39]. Low calcium intake may cause high blood pressure by stimulating either parathyroid hormone or renin release, thereby increasing intracellular calcium in vascular smooth muscle, leading to vasoconstriction [40].

It is in the light of this that several randomized controlled trials (RCT) have tested the significance of routine calcium supplementation in preventing pregnancy induced hypertension [41, 42]. Inadequate calcium intake, defined as daily intake < 600 mg, has been shown to be associated with an increased incidence of hypertensive disease in pregnancy [43].

A lot of controversies have trailed the use of calcium supplementation in prevention of pregnancy induced hypertension. Whereas some authors did not find any benefit [32, 41], others demonstrated its benefit in reducing incidence of pregnancy induced hypertension in women at

Table 3 Frequency of hypo-, normo-, and hyper-calcaemia

Corrected plasma calcium (mmol/L)	Preeclamptics		Normotensives	
	Frequency	Percentage	Frequency	Percentage
< 2.25	55	61.1	16	17.8
2.25–2.75	35	38.9	69	76.6
> 2.75	0	0	5	5.6
Total	90	100	90	100

risk of developing the disease [1, 21, 33]. The World Health Organization, however, recommended that in a population with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of preeclampsia [34].

One of the limitations of this study was the fact that the dietary intake of the participants was not assessed. It was therefore not possible to ascertain the effect of dietary calcium on plasma levels in the two groups.

This study has shown significant lower levels of plasma calcium in preeclamptic women compared to normotensive pregnant women. We therefore recommend routine calcium supplementation to women at high risk of developing preeclampsia in our community.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

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