A COMPARATIVE STUDY ON SERUM CALCIUM, MAGNESIUM, AND URIC ACID LEVELS IN PREECLAMPTIC AND HEALTHY PREGNANT WOMEN IN BENIN CITY

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CERTIFICATION

This is to certify that this research project was carried out by OKPAKO GOODLUCK EBRUVWIYO with Matriculation Number: BMS2001191 under the supervision of PROF. M.A EMOKPAE in the Department of Medical Laboratory science, Faculty of Basic Medical Sciences, University of Benin, Benin city, Edo State.

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EXTERNAL SUPERVISOR **DATE**

DEDICATION

This project is dedicated to the Almighty God for his faithfulness always, my family, and the participants of this project.

ACKNOWLEDGEMENTS

I sincerely express my profound gratitude to the Almighty God for His constant grace, mercy, and love upon me during this study.

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Special thanks to the staff of the Antenatal Clinic at the University of Benin Teaching Hospital, Ogbowo, for their support during this research project. May God richly bless you all in Jesus' name. Amen.

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ABSTRACT

Preeclampsia is a hypertensive disorder during pregnancy, and remains a major cause of maternal and perinatal morbidity and mortality worldwide. Early biochemical tests are needed to detect preeclampsia. Routine antenatal care relies only on blood pressure and proteinuria to detect the disorder. It is important to identify biochemical analytes that could detect the disorder early before complications set in. Therefore, this study evaluated serum calcium, magnesium and uric acid levels in 53 pregnant women with newly diagnosed preeclampsia, and 50 normotensive pregnant women which served as controls. Clinical data (age, body mass index (BMI), gestational age, and venous blood samples were collected. Serum calcium, magnesium, and uric acid were determined by spectrophotometric method. Data were compared between-group, Pearson correlations, and multivariable linear regression were calculated (adjusting for age, BMI, and gestational age). Preeclamptic women were slightly older and had higher BMI; unadjusted means (controls vs. cases) were calcium 9.29 ± 0.72 vs. 8.20 ± 1.30 mg/dL, magnesium 2.32 ± 0.23 vs. 1.72 ± 0.24 mg/dL, and uric acid 4.39 ± 0.58 vs. 5.72 ± 0.94 mg/dL ($p<0.001$). After adjustment, differences remained large and statistically significant: calcium −1.19 mg/dL (95% CI −1.64 to −0.73), magnesium −0.59 mg/dL (95% CI −0.70 to −0.49), and uric acid +1.37 mg/dL (95% CI +1.04 to +1.70) ($p<0.001$). These findings indicate that, preeclampsia is associated with lower calcium and magnesium and higher uric acid independent of age, BMI, and gestational age, supporting their potential value in risk stratification and local antenatal care planning.

CHAPTER ONE

INTRODUCTION

1.1. Background of the Study

Preeclampsia, which is a complication of pregnancy characterized by high blood pressure, threatens both mothers and babies and is a major source of mortality and morbidity all over the planet. In Africa, According to new evidence from Nigeria, approximately 4.5% of women during gestation develop preeclampsia while 1.4% undergo eclampsia, a more severe condition. The rise in mortality rate among mothers with this disorder is 6%, and the corresponding increase in infant mortality rate is around 17%, both occurring in Nigeria (Kokori *et al., 2024*). These shocking figures suggest that our community is still heavily affected by the problem of preeclampsia.

While there is still alot that researchers don't understand, they speculate that it stems from a defect in the production of the placenta in the early stages of pregnancy. This lone event, according to theory, sets off a reaction chain that attacks the lining of the blood vessels in the whole body and, hence, the high blood pressure along with proteinuria that are characteristic of preeclampsia (Enaruna *et al., 2014*). Though it is known that a woman's risk is heightened if she is a virgin mother, older than 35, obese, or already has high blood pressure, even then these risk factors cannot tell us who will fall ill. That conundrum led researchers into studying the impact of the malnutrition in diet.

More and more studies show the possibility of a deficiency in minerals that are essential for the body. To name the two most important, calcium and magnesium, which are indispensable for the proper working of the blood vessels, are the ones that are considered. Without a doubt, the biggest part of the evidence was compiled by a large-scale meta-analysis conducted in the middle of the decade, which found that women going towards preeclampsia have a very big difference in their blood mineral levels versus the nonpreeclamptic pregnant women (Eslamzadeh *et al., 2023*). The pattern here is not a "single story" one. The second review, published specifically on African continent studies, came to conclusively the same result in which they find a statistically significant decrease in the average magnesium level among patients with preeclampsia (Tesfa *et al., 2024*).

On the other hand, serum uric acid is one of the best biomarkers for purine metabolism and is most often significantly elevated in cases of pre-eclampsia. The event of reduction of blood supply to the placenta and the production of free radicals in the case of preeclampsia is what causes a great deal of uric acid to be made. Generally, raised uric acid is observed at a much earlier time than proteinuria and it is also proportional to the extent of the disease (Enaruna *et al., 2014*). In Benin City, (Enaruna *et al, 2014*). found that the average concentration of serum uric acid in patients with preeclampsia was about 28% more than in normal pregnant women who were matched for age and gestational period (5.96 vs 4.30 mg/dL). Also, a recent study in Port Harcourt reported that uric acid levels were significantly elevated in preeclamptic patients (≈6.7 vs 4.3 mg/dL) (Ngeri *et al., 2022*).

These results imply that keeping an eye on serum Ca, Mg, and uric acid levels may be instrumental in recognizing women who could develop preeclampsia or measuring how severe the illness is. Yet, there is only a little amount of contemporary data available from our region.

Exploring these serum levels in pregnant women from the local community not only provides a clearer picture of their health but also enables doctors to devise more effective prevention (e.g., supplementation) and treatment plans.

1.2. Statement of the Problem

Antenatal care in Benin City is largely based on monitoring blood pressure and proteinuria for the detection of preeclampsia. However, these symptoms only appear at a fairly advanced stage of the disease. Therefore, biochemical markers that could be detected at an early stage are required. A substantial body of evidence links low levels of calcium and magnesium and high levels of uric acid to the pathogenesis of preeclampsia. Still, data on markers in our pregnant population remain limited.

There has not been any research in Nigeria that has looked at serum calcium, magnesium, and uric acid simultaneously in the same group. It is not known whether the results of studies conducted in other locations can be applied to our situation. An in-depth local comparative investigation of serum profiles between preeclamptic and normotensive pregnancies would contribute to the identification of potential preventive measures (for example, nutritional supplementation) which would lead to the improvement of maternal and fetal health.

1.3. Aim and Objectives

Aim: To compare serum calcium, magnesium, and uric acid levels between preeclamptic and normotensive pregnant women in Benin City.

1.3.1. Specific Objectives:

1. To determine the mean serum calcium, magnesium, and uric acid levels in preeclamptic and healthy normotensive pregnant women.

2. To correlate serum calcium, magnesium, and uric acid levels with blood pressure of pregnant women.
3. To correlate serum calcium, magnesium, and uric acid levels with Body Mass Index of preeclamptic and normotensive pregnant women.
4. To measure the Body Mass Index of preeclamptic and healthy normotensive pregnant women.

1.4. Research Questions

1. Are the mean serum calcium, magnesium, and uric acid levels in preeclamptic lower or higher than healthy normotensive pregnant women?
2. Is there any correlation between serum calcium, magnesium, and uric acid levels and blood pressure of preeclamptic pregnant women?
3. Is there any correlation between serum calcium, magnesium, and uric acid levels and the body mass index of preeclamptic and normotensive pregnant women?
4. Is there any difference in the Body Mass Index of preeclamptic and healthy normotensive pregnant women?

1.5. Research Hypothesis

1.5.1. Null Hypothesis

1. There are no differences in the mean serum calcium, magnesium, and uric acid levels between preeclamptic and healthy normotensive pregnant women.
2. There is no correlation between serum calcium, magnesium, and uric acid levels and blood pressure of preeclamptic pregnant women.
3. There is no correlation between serum calcium, magnesium, and uric acid levels and the body mass index of preeclamptic and normotensive pregnant women.

4. There are no differences in the Body Mass Index of preeclamptic and healthy normotensive pregnant women.

1.5.2. Alternate Hypothesis

1. There are differences in the mean serum calcium, magnesium, and uric acid levels between preeclamptic and healthy normotensive pregnant women.
2. There is a correlation between serum calcium, magnesium, and uric acid levels and blood pressure of preeclamptic pregnant women.
3. There is a correlation between serum calcium, magnesium, and uric acid levels and the body mass index of preeclamptic and normotensive pregnant women.
4. There are differences in the Body Mass Index of preeclamptic and healthy normotensive pregnant women.

1.6. Justification of the Study

Local relevance: Preeclampsia causes significant morbidity and mortality in Nigeria *(*Kokori *et al., 2024).* The identification of biochemical differences in our population could aid early detection.

Preventive potential: If preeclamptic women are found to have significantly lower calcium or magnesium, this would support calcium/magnesium supplementation strategies (as recommended by WHO) to prevent preeclampsia *(*Okoror *et al., 2020).*

CHAPTER TWO

LITERATURE REVIEW

2.1. Serum Calcium in Preeclampsia

Multiple studies have shown that serum calcium is lower in preeclamptic pregnancies than in normal pregnancies. A large 2023 meta-analysis (n≈10,500) said that women with preeclampsia had significantly lower circulating calcium (WMD ≈ –0.807 mg/dL) than normotensive controls *(*Eslamzadeh *et al., 2023).* Some related results have been observed in Nigeria: *(*Okoror *et al., 2020),* in Benin City found mean Ca^{2+} of 7.73±1.24 mg/dL in preeclamptic women versus 9.17±0.77 mg/dL in controls (P<0.001). An older Benin City study also reported lower plasma Ca^{2+} in preeclamptics (9.2±1.02 mg/dL vs 9.98±0.87; P=0.043) *(*Idogun *et al., 2007).* In India*, (*Mittal *et al., 2014),* similarly revealed significantly lower serum calcium in preeclamptic women (8.27 mg/dL) than in matched healthy pregnant women (9.06 mg/dL). These discoveries support the hypothesis that hypocalcemia may be associated with vasoconstriction and hypertension in preeclampsia. Though, not all studies agree: *(*Ugwuja *et al., 2016),* in Ebonyi State, found no significant difference in total serum calcium between mild/moderate preeclamptic and normotensive groups, possibly due to regional dietary alterations or methodological differences. Due to these mixed results, it is possible regional or methodological influences weigh in, but overall, the trend indicates that calcium tends to be lower in preeclampsia. Recent studies of year 2025 continue to confirm a strong relation between hypocalcemia and preeclampsia risk *(*Mlay *et al., 2025).*

2.2. Serum Magnesium in Preeclampsia

Magnesium is a natural calcium antagonist and vasodilator, and its function in preeclampsia has been widely studied. The same 2023 meta-analysis found significant lower serum magnesium in

preeclamptics (WMD ≈ –0.215 mmol/L) in relation to controls *(*Eslamzadeh *et al., 2023).* A focused review of African studies also confirmed that mean serum Mg is reduced in preeclamptic women (SMD ≈ –1.20) *(*Tesfa *et al., 2024).* In Nigeria*, (*Ugwuja *et al., 2016),* reported a marked drop in serum magnesium in preeclamptics (3.22±1.05 mg/dL) compared to controls (4.15±0.78 mg/dL; P<0.001). Likewise, a Bangladesh study observed significantly lower Mg in the preeclamptic group (P<0.001) *(*Mou *et al., 2021).* Lower magnesium may be associated with uterine and vascular hyperactivity; truly, magnesium sulfate is used prophylactically to prevent seizures in severe preeclampsia. These data collectively infer that hypomagnesemia is common in preeclampsia and may play a role in its pathophysiology. A 2025 study shows the use of serum magnesium levels to predict preeclampsia *(*Nambiar *et al., 2025).*

2.3. Serum Uric Acid in Preeclampsia

Elevated serum uric acid (SUA) is a well-documented feature of preeclampsia and thought to reflect placental ischemia and oxidative stress. In our local setting, *(*Enaruna *et al., 2014),* found that women with severe preeclampsia had 28% higher mean SUA (5.96±2.54 mg/dL) than normotensive controls (4.30±0.85 mg/dL; P=0.005). A 2022 Port Harcourt study reported even bigger differences: mean SUA was ~400 µmol/L (~6.7 mg/dL) in preeclampsia versus ~256 µmol/L (~4.3 mg/dL) in controls (p=0.001) *(*Ngeri *et al., 2022).* Similarly, *(*Mou *et al., 2021),* in Bangladesh observed dramatically higher SUA in preeclamptics (p<0.001). Elevated SUA correlates with disease severity and adverse outcomes, often rising before overt hypertension or proteinuria *(*Enaruna *et al., 2014).* Given these discoveries, SUA is considered a good prognostic marker in preeclampsia. However, normal SUA reference ranges can vary by population, necessitating local data.

2.4. Impact of Blood Pressure in Preeclampsia

Blood pressure (BP) is the clinical hallmark of preeclampsia and its severity strongly indicates maternal and perinatal outcomes. Diagnostic thresholds widely used are systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg after 20 weeks' gestation, with "severe range" defined as ≥160/110 mmHg; sustained readings in the severe range are associated with higher risk of end-organ damage and prompt initiation of antihypertensive therapy or delivery. Elevated BP in preeclampsia increases the risk of placental abruption, fetal growth restriction, preterm delivery, renal impairment, HELLP syndrome, and maternal morbidity and mortality; therefore, BP level and trajectory are used clinically both to triage care and to guide timing and desired outcome of delivery.

2.5. Impact of Body mass index in Preeclampsia

Higher pre-pregnancy BMI (overweight and obesity) is a consistent, dose-dependent risk factor for both preeclampsia and severe preeclampsia. Large cohort and meta-analytic evidence indicate that overweight and obese women have substantially increased odds (often >2× for overweight and >3× for obesity) of developing preeclampsia compared with women of normal BMI; the effect is biologically plausible because obesity promotes chronic inflammation, oxidative stress, insulin resistance, and endothelial dysfunction, mechanisms shared with preeclampsia. In addition to pre-pregnancy BMI, excessive gestational weight gain also raises preeclampsia risk (the relationship can be J-shaped), such that women with high pre-pregnancy BMI combined with excessive weight gain have a superimposed (multiplicative) increase in risk. These findings support BMI as an important confounder and effect modifier to control for in comparative biomarker studies of preeclampsia.

CHAPTER THREE

METHODOLOGY

3.1. Study Design

This research used a comparative case-control design, involving two groups of pregnant women: those diagnosed with preeclampsia (cases) and normotensive healthy pregnant women (controls). The study compared serum calcium, magnesium, and uric acid levels between the two groups.

3.2. Study Area

The study was done in Benin City, Edo State, Nigeria. Participants were from the Antenatal Clinic of the University of Benin Teaching Hospital (UBTH), which serves a diverse urban population.

3.3. Study Population

The study population consisted of pregnant women attending UBTH for antenatal care.

3.3.1. Inclusion Criteria:

1. Age between 20 and 40 years.
2. Singleton pregnancy.
3. Gestational age ≥ 20 weeks (second or third trimester).
4. Willingness to participate (provides informed consent).

3.3.2. Case Group:

1. Diagnosed of preeclampsia.
2. Blood pressure ≥ 140/90 mmHg on two occasions ≥ 6 minutes apart after 20 weeks' gestation.
3. Proteinuria ≥ 1+ on dipstick (at time of diagnosis).

3.3.3. Control Group:

1. No hypertension (BP < 140/90 mmHg)
2. No proteinuria on dipstick.
3. Gestational age distribution should be similar to cases.

3.3.4. Exclusion Criteria:

1. Known chronic hypertension (pre-existing before pregnancy).
2. Renal disease or known chronic kidney impairment.
3. Diagnosed of diabetes mellitus.
4. Seizures at the time of recruitment.
5. Use of relevant medical treatments started before admission, e.g., antihypertensives or magnesium sulphate.
6. Current use of calcium or magnesium supplements (to avoid biochemical confounding).

3.4. Sample Size Determination

The sample size for this study was calculated using the sample size determination formula for health studies *(*Lwanga *and* Lemeshow*, 1991)* and 3.60% of prevalence of preeclampsia/eclampsia in Nigeria *(*Akaba *et al., 2021)*

$$N = \frac{Z^2 \times P \times Q}{d^2}$$

Where:

- **N** = required sample size
- **Z** = Z-score (from statistics). 95% confidence, Z = 1.96, and Z^2=3.8416.

- **P** = prevalence of the disease in the population (here, 3.6% = 0.036).
- **Q = 1 – P** (so Q = 0.964).
- **d** = margin of error (precision level). 5% = 0.05, so d^2=0.0025.

$$N = \frac{3.8416 \text{ x } 0.036 \text{ x } 0.964}{0.0025} = 53$$

Fifty-three preeclamptic pregnant women and 50 normotensive pregnant women (controls) were recruited for the study.

3.5. Ethical consideration

1) Voluntary participation and informed consent: Participation was entirely voluntary. All eligible women were provided with a plain-language information sheet describing the study purpose, procedures, risks, benefits, confidentiality, and their right to refuse or withdraw at any time without affecting their clinical care. Written informed consent was obtained prior to the initiation of any study procedure.

2) Adults only: Only women aged 20 years and above were recruited; no minors were enrolled.

3) Physical risks: Blood collection carried minimal risk (pain, bruising, fainting, very low infection risk). Venipuncture was performed by a trained phlebotomist using sterile, single-use equipment and standard precautions that ensured adults safety.

4) Anonymization: Patient published data and shared datasets were fully anonymized.

3.6. Ethical Approval

Ethical approval was sought from the Edo State Ministry of Health, Health Research and Ethics committee.

3.7. Sample Collection and biochemical assay

After obtaining informed consent, 5 mL of venous blood was drawn from each participant into a plain (red-top) vacutainer. Blood was allowed to clot at room temperature for 30 minutes, then centrifuged at 3000 rpm for 10 minutes. The clear serum was aliquoted into labeled cryovials and stored at –20°C until analysis, which occurred within two weeks of collection. All specimens were de-identified with a unique code to maintain confidentiality.

Serum total calcium was measured using the o-cresolphthalein complexone method, magnesium using the xylidyl blue method, and uric acid using the uricase-peroxidase method. All assays were performed on a semi-automated biochemistry analyzer with commercial kits (Randox Laboratories, UK). Quality control was ensured using commercial control sera, with intra-assay coefficients of variation <5%.

For BMI, participants were weighed using a calibrated mechanical scale (without shoes or heavy clothing), and height was measured with a measuring tape. BMI was calculated as weight (kg) / height^2 (m^2).

3.8. Data Analysis

The primary biochemical parameters assessed were serum calcium, magnesium, and uric acid, each of which has clinical relevance in preeclampsia. In addition to these biochemical measurements, blood pressure (BP) and body mass index (BMI) were evaluated for each

participant, as both factors are important determinants of cardiovascular and metabolic health in pregnancy and are closely linked with preeclampsia risk.

BP was measured in a seated position after at least five minutes of rest, using a validated automated sphygmomanometer with the correct cuff size. Two readings were taken 4–6 minutes apart and averaged, with a third reading obtained if there was a difference of more than 10 mmHg systolic; the two closest readings were then averaged.

Normality of continuous variables was assessed using the Shapiro-Wilk test, and all variables approximated normal distribution. Continuous variables were summarized as mean ± standard deviation (SD). Between-group comparisons (preeclampsia vs. normotensive controls) were conducted using Welch's t-tests to account for unequal variances. Pearson's correlation coefficients were computed within each subgroup to assess linear relationships between serum analytes (Ca, Mg, uric acid) and clinical variables (SBP, DBP, BMI). To account for potential confounders, multivariable linear regression models were fitted, adjusting for age, BMI, and gestational age, with adjusted mean differences reported along with 95% confidence intervals (CIs). All statistical tests were two-tailed, with significance set at $\alpha = 0.05$. Analyses were performed using IBM SPSS Statistics.

3.9. Units

All biochemical results were reported in mg/dL. Where analyzers reported in mmol/L, results were changed to mg/dL using standard conversion factors (e.g., Mg: mmol/L × 2.43 = mg/dL; Ca: mmol/L × 4.0 = mg/dL; uric acid: μmol/L × 0.0168 = mg/dL).

Asterisk convention: * = $p < 0.05$, ** = 0.01, *** = $p = 0.001$, ns = not significant.

CHAPTER FOUR

RESULTS

A total of 103 participants were included in the analysis: 53 women with preeclampsia (cases) and 50 normotensive pregnant controls. The cases were slightly older than controls (30.98 ± 4.46 vs 28.66 ± 3.92 years; P = 0.006). Mean body-mass index (BMI) was significantly higher among cases (27.92 ± 3.96 kg/m²) than controls (24.88 ± 3.67 kg/m²; P < 0.001). Blood pressure was noticeably higher in the case group: mean systolic BP 147.78 ± 13.99 mmHg versus 112.22 ± 7.12 mmHg in controls (P < 0.001), and mean diastolic BP 93.04 ± 6.25 mmHg versus 75.54 ± 6.16 mmHg (P < 0.001). Gestational age (reported in whole weeks) was similar between groups (cases 34 ± 4 weeks; controls 34 ± 4 weeks; P = 0.354). These comparisons are summarized in Table 1.

Unadjusted analyte means (controls vs cases) were:

1. Calcium: 9.2898 ± 0.7207 mg/dL (n = 50) vs 8.1985 ± 1.3035 mg/dL (n = 53); P < 0.001.

2. Magnesium: 2.3202 ± 0.2303 mg/dL vs 1.7221 ± 0.2359 mg/dL; P < 0.001.

3. Uric acid: 4.3942 ± 0.5802 mg/dL vs 5.7162 ± 0.9377 mg/dL; P < 0.001.

All between-group comparisons above were tested with two-tailed Welch t-tests. Multivariable linear regression models that adjusted for BMI, age and gestational age produced essentially the same conclusions. Adjusted mean differences (cases − controls) were:

Calcium: −1.187 mg/dL (95% CI −1.643 to −0.731); P < 0.001.

Magnesium: −0.592 mg/dL (95% CI −0.695 to −0.489); P < 0.001.

Uric acid: +1.373 mg/dL (95% CI +1.043 to +1.702); P < 0.001.

These adjusted estimates indicate the associations between preeclampsia and lower calcium/magnesium and higher uric acid remain strong after accounting for BMI, age and gestational age.

Table 1. Mean (±SD) GA, age, BMI, blood pressure and serum analytes in preeclamptic vs. normotensive pregnant women (t-test comparisons).

Variable	Preeclamptic(n = 53)	Normotensive(n = 50)	P-value	Significance
Age (years)	30.98 ± 4.46	28.66 ± 3.92	0.006	**
GA (weeks)	34 ± 4	34 ± 4	0.354	ns
BMI (kg/m²)	27.92 ± 3.96	24.88 ± 3.67	<0.001	***
SBP (mmHg)	147.78 ± 13.99	112.22 ± 7.12	<0.001	***
DBP (mmHg)	93.04 ± 6.25	75.54 ± 6.16	<0.001	***
Calcium (mg/dL)	8.20 ± 1.30	9.29 ± 0.72	<0.001	***
Magnesium (mg/dL)	1.72 ± 0.24	2.32 ± 0.23	<0.001	***
Uric acid (mg/dL)	5.72 ± 0.94	4.39 ± 0.58	<0.001	***

(All continuous data shown as mean ± SD. Between-group comparisons used Welch's t-test; all tests two-tailed.)

4.1 Correlation Analyses

Pearson correlation coefficients were computed separately within cases and controls to explore relationships between serum analytes (Ca, Mg, uric acid) and SBP, DBP and BMI. Within the preeclamptic subgroup, none of the analyte–outcome correlations reached statistical significance; for example, calcium versus DBP in cases showed $r = 0.239$ ($P = 0.085$) and calcium versus BMI $r = 0.075$ ($P = 0.593$). Similarly, magnesium and uric acid showed no significant within-group correlations with SBP, DBP or BMI (all $P > 0.05$). The control subgroup likewise revealed no statistically significant analyte–outcome correlations ($P > 0.05$).

For completeness, pooled correlations across all participants (which do not account for case status and therefore should be interpreted cautiously) were: magnesium vs SBP, $r = -0.675$ ($P < 0.001$); uric acid vs SBP, $r = +0.567$ ($P < 0.001$); and uric acid vs BMI, $r = +0.231$ ($P = 0.019$). These pooled associations largely reflect substantial between-group biochemical differences and are therefore likely confounded by case status rather than representing within-group relationships.

CHAPTER FIVE

DISCUSSION

5.0. Discussion

This research in Benin City, investigated serum calcium, magnesium, and uric acid levels in patients with preeclampsia. A total of 53 women with preeclampsia and 50 normotensive pregnant women were the subjects of the study. The study revealed that the average serum calcium and magnesium levels in the preeclamptic group were significantly lower, while the average uric acid level was significantly higher than that in the control group. These changes remained significant statistically even after the adjustment for gestational age, BMI, and age. The differences between the adjusted mean values were quite substantial: for calcium about –1.19 mg/dL, for magnesium –0.59 mg/dL, and for uric acid +1.37 mg/dL. The results reported are in agreement with the findings of other authors. In their respective works, (Enaruna *et al., 2014*) and (Ngeri *et al., 2022*) both found a significant increase in uric acid levels in patients with preeclampsia in Nigeria, and a meta-analysis in 2023 concluded that calcium and magnesium levels in preeclampsia are significantly lowered (Eslamzadeh *et al., 2023*; Tesfa *et al., 2024*).

From a physiological perspective, this is a reasonable pattern. Magnesium is the element that naturally antagonizes calcium and has vasodilatory properties (Idogun *et al., 2007*), so it is likely that the decrease in magnesium (and calcium) is accompanied by the increase of vascular tone and dysfunction of the endothelium in preeclampsia. Calcium deficiency and magnesium deficiency have been postulated to lead to vasoconstriction and hypertension (Idogun *et al., 2007*; Okoror *et al., 2020*). Raised uric acid has often been associated with placental ischemia and reactive oxygen species production in hypertensive pregnancies, and it also correlates with the severity of the disease (Enaruna *et al., 2014*; Ngeri *et al., 2022*). The present findings, which

refer to the cases when uric acid is higher even after the confounders' adjustment, provide evidence for its role as a marker of severity. It is worth noting that these connections still existed after adjustments for BMI and age, suggesting that the biochemical differences are a consequence of disease status and not maternal adiposity.

The average BMI was notably greater in the case group than in the control group, reflecting the recognized epidemiologic associations of obesity with preeclampsia (Okoror *et al., 2020*; Tesfa *et al., 2024*). To lessen confounding, we included BMI as a control variable in the analysis. However, the relationship between obesity and mineral metabolism may be such that they mutually influence each other in complicated ways (Okoror *et al., 2020*). From a medical point of view, this is a reminder of the great significance of managing maternal weight in conjunction with the prevention of preeclampsia.

Correlation analyses within groups revealed that none of the relationships between calcium, magnesium, or uric acid and blood pressure or BMI were statistically significant. On the contrary, combined correlations for all the subjects (mainly resulting from differences between the groups) demonstrated a strong negative correlation between magnesium and systolic BP and positive correlations of uric acid with BP and BMI. This implies that these biomarkers are more potent as indicators of the disease state than as linear predictors of blood pressure within a group.

5.1 Limitations

This research is observational, hence it is limited in terms of making causal inferences, for example, whether calcium/magnesium deficiency leads to preeclampsia or is the consequence of it. Also, we performed this study at a single tertiary center in an urban area. As a result, these findings may not be representative of people living in rural areas or those who receive primary

care in Nigeria. The study did not take into account the food that subjects consumed which could significantly influence their serum mineral levels especially if the region has uneven nutrition. Moreover, we have not analyzed the data for different subgroups such as mild or severe preeclampsia due to limited sample size. We suggest that in subsequent research, investigators use longitudinal dietary assessments and designs to fill the gaps identified here.

5.2. Conclusion

The findings of this research are consistent with those of other researchers indicating that low serum calcium and magnesium as well as high uric acid characterize preeclampsia (Eslamzadeh *et al., 2023*; Tesfa *et al., 2024*). In practice, if hypocalcemia or hypomagnesemia is confirmed, this could be useful in the implementation of preventive strategies: as an example, to diminish the risk of preeclampsia in populations with deficiency, calcium/magnesium supplementation has been recommended (Okoror *et al., 2020*). The rising uric acid level can still be considered as one of the ways in which the disease severity can be evaluated together with blood pressure and proteinuria and at the same time, it is cost-effective (Enaruna *et al., 2014*; Ngeri *et al., 2022*). The controlled results give effect sizes at a local level that can be useful in understanding lab outcomes and directing antenatal care locally.

5.3. Contribution to knowledge

We conducted a study to provide adjusted local estimates of biochemical changes linked with preeclampsia in Benin City. After we quantified the levels of calcium, magnesium, and uric acid while also adjusting for age, BMI, and gestational age, we increased the credibility of evidence for the interpretation of laboratory results in the target population and unveiled biomarkers that might be useful in the risk stratification process.

5.4. Recommendation

Pregnancy care programs in Benin City should focus on providing calcium supplements as part of the daily diet to women with calcium-deficient intake, carrying out the necessary checks for uric acid together with that for blood pressure, and implementing targeted measures for the reduction of maternal overweight and obesity.

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APPENDIX

INFORMED CONSENT FORM

STUDY TITLE: A COMPARATIVE STUDY ON SERUM CALCIUM, MAGNESIUM, AND URIC ACID LEVELS IN PREECLAMPTIC AND HEALTHY PREGNANT WOMEN IN BENIN CITY.

1) Principal Investigator: OKPAKO GOODLUCK EBRUVWIYO

2) Institution: University of Benin Teaching Hospital (UBTH)

3) Contact Information: 08120490707 / ebruscity@gmail.com

Introduction

You are being invited to take part in a research study at UBTH. Before you decide, please read the following information **carefully**. This form explains the purpose of the study, what will happen if you participate, possible risks and benefits, and your rights as a participant.

If you agree, you will be asked to sign at the end of this form.

Purpose Of The Study

This study is being carried out to compare the levels of certain substances in the blood: calcium, magnesium, and uric acid, between pregnant women with preeclampsia and those without. The results may help doctors better understand and manage preeclampsia in the future.

Procedures

If you agree to participate:

1. About 5 mL (one teaspoon) of blood will be taken from your arm vein using sterile, single-use equipment.
2. Your weight and height will be measured to calculate body mass index (BMI).
3. Your blood pressure will be measured with an automated blood pressure machine.
4. The blood sample will be processed in the laboratory to measure calcium, magnesium, and uric acid levels.
5. Your samples will be labeled with a code number only. No names will appear on laboratory samples.

Duration

The procedure (blood draw, blood pressure, and measurements) will take about 10–15 minutes.

Risks and Discomforts

The risks of blood collection are minimal but may include:

1. Mild pain or discomfort at the needle site
2. Small bruise or swelling
3. Rarely, fainting or dizziness
4. Very small risk of infection (prevented by using sterile equipment)

Benefits

You may not benefit directly from this study. However:

1. If your results are abnormal, your doctor will be informed so you can receive proper care.
2. The knowledge gained may help improve the management of preeclampsia for future patients.

Confidentiality

All information collected will be kept strictly confidential. Your name will not appear in any reports, publications, or presentations. Data will be stored securely and used only for research purposes.

Voluntary Participation

1. Your participation is entirely voluntary.
2. You may choose not to participate or to withdraw at any time without losing any of your regular medical care at UBTH.

Costs and Compensation

1. Participation will not cost you anything.
2. You will not be paid for taking part.

Ethical Approval

This study has been reviewed and approved by the Edo State Ministry of Health Review Board.

Questions

1. If you have any questions about the study, you may contact, OKPAKO GOODLUCK EBRUVWIYO. 08120490707 / ebruscity@gmail
2. If you have questions about your rights as a research participant, you may contact, The Edo State Ministry of Health office. Mr Benedict: 07038222286

Consent Statement

I have read (or had read to me) the information above. I have had the chance to ask questions, and all my questions have been answered. I understand that my participation is voluntary, and I can withdraw at any time without penalty.

By signing below, I freely agree to participate in this study.

Participant's Name: _____

Signature / Thumbprint: _____ Date: ___ / ___ / 20__

Name of Witness (if participant cannot read/write): _____

Signature of Witness: _____ Date: ___ / ___ / 20__

Name of Investigator: _____

Signature of Investigator: _____ Date: ___ / ___ / 20__

QUESTIONNAIRE

RESEARCH STUDY: A COMPARATIVE STUDY ON SERUM CALCIUM, MAGNESIUM, AND URIC ACID LEVELS IN PREECLAMPTIC AND HEALTHY PREGNANT WOMEN IN BENIN CITY

Dear Madam

The researcher is an undergraduate of the Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, researching the topic stated above in partial fulfillment of the requirements for the award of the Bachelor of Medical Laboratory Science (B.MLS) degree. Could you please spare your time to fill out this questionnaire? The information acquired from this research will be treated with utmost confidentiality.

GENERAL INSTRUCTION FOR PARTICIPANTS:

Do not write personal details not asked (name, address, phone number, etc). The information obtained from this questionnaire will be used for assessing the health of pregnant women hence you must be truthful as much as possible.

This questionnaire is designed to evaluation of serum calcium, magnesium, and uric acid in pregnant women with or without preeclampsia in benin city. Please note that all information provided will be kept confidential and used solely for research purposes.

1. Participant ID: _____

2. Age (years): ____

3. Gestational age (weeks): ____

4. Gravidity/Parity: __ __

5. Current blood pressure (mmHg): Systolic ___ / Diastolic ___

6. History of high blood pressure in this pregnancy? Yes / No

7. Proteinuria on dipstick test: Nil / +1 / +2 / +3

8. Headache in current pregnancy: Yes / No

9. Visual disturbances (e.g. blurred vision, spots): Yes / No

10. Upper abdominal pain (epigastric or RUQ): Yes / No

11. Swelling (edema) of face/hands/feet: Yes / No

12. Rapid weight gain (>2 kg in one week): Yes / No

13. Any past medical conditions (e.g. chronic hypertension, diabetes): Yes / No (specify if Yes)

_____

14. Family history of hypertension/preeclampsia: Yes / No

15. Supplement use (calcium or magnesium): Yes / No

16. Iron supplements currently taken: Yes / No

17. Do you feel your legs are swollen? Yes / No

18. Recent urinary symptoms (reduced urine output, etc.): Yes / No

19. Height: ____

20. Weight: ____

5.6.3. List of Acronyms

BP — Blood Pressure

SBP — Systolic Blood Pressure

DBP — Diastolic Blood Pressure

BMI — Body Mass Index

GA — Gestational Age

UBTH — University of Benin Teaching Hospital

LMP — Last Menstrual Period

SD — Standard Deviation

CI — Confidence Interval

QA/QC — Quality Assurance / Quality Control

CV — Coefficient of Variation

SPSS — Statistical Package for the Social Sciences

WHO — World Health Organization

Mg/dL — Milligrams per Deciliter

PE — Preeclampsia

HELLP — Hemolysis, Elevated Liver enzymes, Low Platelet count