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BRIEF REPORT

Correlation between maternal variables and the onset and severity of preeclampsia [version 1; peer review: 1 approved with reservations, 1 not approved]

Nafiu Amidu¹, Moses Banyeh ¹, Stephen Justice Adusu²

¹Department of Biomedical Laboratory Science, University for Development Studies, Tamale, Ghana

²Department of Medical Diagnosis, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

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Abstract

Background: The study sought to determine the correlation between the onset and severity of preeclampsia (PE) and maternal sociodemographic variables: age, parity and body mass index (BMI); medical history: systolic blood pressure (SBP), diastolic blood pressure (DBP), and proteinuria; fasting lipids: total cholesterol (TCHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TRIG); liver enzymes: aspartate transaminase (AST), alanine transaminase (ALT) and gamma-glutamyl transferase (GGT), and other variables: serum neutrophil gelatinase associated lipocalin (sNGAL), endothelin-1 (ET-1) and creatinine (CRT).

Methods: This was a case-control study from January-June 2018. The study involved 270 pregnant women aged 18-37 years. Half of the study population (n=135) had PE and were categorized into either early-onset PE (EOPE) or late-onset PE (LOPE) and whether the PE was characterized by severe features (PS) or without severe features (PNS). The cases (PE) were matched by maternal and gestational age to 135 women with normotensive and uncomplicated pregnancies. A single venous blood sample was collected after an overnight fast and analysed using ELISA or routine biochemistry technique.

Results: Maternal blood lipids (except HDL), liver enzymes (except GGT), CRT, sNGAL, ET-1, proteinuria, and BMI were positively correlated while HDL was negatively correlated with the onset and severity of PE ($P < 0.050$).

Conclusion: There are significant correlations between maternal variables and the onset and severity of PE. These findings are useful for the early detection and management of PE, especially in resource-limited settings.

Keywords

Preeclampsia, Correlation, Onset, Severity, Ghana

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1. **Jussara Mayrink**, Federal University of Minas Gerais, Belo Horizonte, Brazil

2. **Johnbosco E Mamah** , Alex Ekwueme
 Federal University Teaching Hospital,
 Abakaliki, Nigeria

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Moses Banyeh (mosesbanyeh@gmail.com)

Author roles: **Amidu N:** Conceptualization, Writing – Review & Editing; **Banyeh M:** Writing – Original Draft Preparation, Writing – Review & Editing; **Adusu Sj:** Data Curation, Investigation, Writing – Review & Editing

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List of abbreviations

ALT, alanine aminotransferase
 AST, aspartate aminotransferase
 CRT, creatinine
 ELISA, enzyme-linked immunosorbent assay
 EOPE, early onset preeclampsia
 ET-1, endothelin-1
 GGT, gamma glutamyl transferase
 HDL, high density lipoprotein
 LDL, low density lipoprotein
 LOPE, late onset preeclampsia
 PE, preeclampsia
 PNS, preeclampsia without severe feature
 PS, preeclampsia with severe features
 TCHOL, total cholesterol
 TRIG, triglycerides
 sNGAL, serum neutrophil gelatinase-associated lipocalin

Introduction

This study sought to determine the correlation between the onset and severity of preeclampsia (PE) and maternal variables in a Ghanaian population. PE is a multi-system disorder of pregnancy with unknown aetiology. It is responsible for about 3–8% of the global burden of maternal and neonatal morbidity and mortality.¹ Hypertension, with or without proteinuria, occurring after 20 weeks of gestation, is the cardinal symptom of PE. The occurrence of PE may be early, happening before 34 weeks (EOPE) or late (LOPE). Preeclampsia may also be characterized by severe features (PS) or without severe features (PNS).²

Although the aetiology of PE is poorly understood, aberrant trophoblastic invasion of the placenta, placental hypoxia and endothelial dysfunction have been suggested. The generalized inflammatory process, angiogenic imbalance, endothelial injury and increased oxidative stress in PE, may cause organ and organ–system dysfunctions including the renal, the hepatic and the cardiovascular systems.^{2,3}

Previous studies have demonstrated that maternal lipids, liver function, renal function, ET-1 and sNGAL are affected by the onset and severity of PE.^{4,5} However, the influence of genetic and environmental factors on PE may lead to population and sub-population variabilities in the correlations between the onset and severity of PE and maternal variables.^{6,7} There is therefore the need for population-specific studies to establish local reference data for the early diagnosis and management of PE.

Methods

Study design and settings

This was a case–control study from January to June 2018. The study was conducted at the Richard Novarti Catholic Hospital, located at Sogakope in the South Tongu District of the Volta Region of Ghana.

Study population and selection

The study involved 270 pregnant women aged 18–37 years. The sample size was calculated following the recommendations of Fahim, Negida.⁹ The study population was divided into two groups: 135 women with PE who were further stratified based on the onset of PE as either EOPE (n = 71) or LOPE (n = 64) and also based on the presence or the absence of severe features as either PNS (n = 87) or PS (n = 48). The cases were matched by maternal and gestational age to 135 women with normotensive and uncomplicated pregnancies at sampling (serving as controls). The inclusion criterion was a diagnosis of PE, whether early or late onset, with or without severe features. Exclusion criteria included: all women with twin gestations; those who were previously diagnosed with chronic hypertension, sickle cell anaemia, diabetes mellitus, gestational diabetes, cardiovascular disorder, renal disease and those who were on antihypertensive or magnesium medication before the recruitment. Sociodemographic and clinical information was collected using a structured questionnaire and also from their medical records.

Definitions

The definition of PE, its onset and severity was based on the recommendations of the American College of Obstetricians and Gynecologists.² Preeclampsia was defined as the new-onset of hypertension (systolic ≥ 140 mmHg, diastolic ≥ 90 mmHg, taken 4 hours apart) with proteinuria (2+ on the dipstick at presentation) after 20 weeks of gestation.

Early-onset PE was defined as PE occurring before 34 weeks of gestation and LOPE was defined as PE occurring at/after 34 weeks of gestation. Preeclampsia with severe features was defined as PE characterized by systolic (≥ 160 mmHg) or diastolic (≥ 110 mmHg) blood pressure while PNS was defined as PE without severe features.

Measurements

Blood pressure was measured with the aid of a cuff sphygmomanometer according to the fifth Korotkoff sound. Urine screening for proteinuria was performed using a urine dipstick. A single peripheral venous blood sample was collected from each subject's antecubital vein after an overnight fast (12 h) into an EDTA and a gel-separator tube. The serum samples were allowed to clot for 30 min at 4°C and both tubes were then centrifuged at 1500 rpm for 10 min to separate the serum/plasma. Serum and plasma samples were aliquoted into plastic cryotubes and then frozen at -25°C until analysis. Serum NGAL was analysed in duplicates using the ELISA kit from abcam (152 Grove Street Waltham, MA 02453., USA). The kit had a sensitivity of 14.8 pg/mL, within a linearity range of 46.9 pg/mL - 3000 pg/mL. The intra-assay and inter-assay coefficients of variation were $\leq 3.8\%$ and $\leq 2.7\%$ respectively. Serum ET-1 was analyzed in duplicates using Human ELISA kit (Biomedica Medizinprodukte GmbH, Divischgasse 4, 1210 Vienna, Austria). The sensitivity of the ET-1 ELISA kit was 0.086 pg/mL within a linearity range of 0.00–12.85 pg/mL. The intra-assay and the inter-assay coefficients of variation were $\leq 4\%$ and $\leq 5\%$ respectively. The TCHOL, HDL, LDL, TRIG, AST, ALT, GGT and CRT were assayed using the plasma/serum samples (as appropriate) through routine biochemistry analysis on the BT 1500 automated biochemistry analyzer (Biotechnica Instruments, SPA, Italy) following the manufacturer's instructions and using the recommended reagents. The samples in this study were not previously thawed and refrozen.

Statistical analysis

Data were entered into a Microsoft Excel (RRID:SCR_016137) spreadsheet (Google Sheets (RRID:SCR_017679) is an open access alternative) and statistical analysis was performed using SPSS (v23) (RRID:SCR_019096), and GraphPad Prism (v8) (RRID:SCR_002798); JASP (RRID:SCR_015823) is an open access alternative. The normality of the data was checked using the Kolmogorov–Smirnov test. Continuous variables were reported as median (IQR) or mean $\pm$ SD (as appropriate) and number (%) for categorical variables. Differences between median and mean values were determined using the Mann–Whitney U test and the student t-test respectively. Spearman rank correlation and linear regression analysis were used to determine the relationship between the independent and the outcome variables. A probability level of $P < 0.050$ was considered statistically significant.

Results

The general characteristics of the study population are summarized in [Table 1](#). This was an observational study with only one stage and as such there were no loss of participants. The controls and the cases (PE) did not differ in maternal and gestational age ($P > 0.050$). The BMI, sNGAL, ET-1, TCHOL, LDL, TRIG, ALT, AST and CRT were significantly elevated while HDL was markedly reduced in PE as compared to the controls ($P < 0.010$). Also, the maternal and gestational age, BMI, GGT and CRT were significantly elevated in LOPE as compared to EOPE ($P < 0.050$). In comparing PNS to PS, maternal age was reduced while sNGAL, ET-1, TRIG, ALT, AST and GGT were considerably increased in PS ($P < 0.050$). The correlation and linear regression analysis between the onset of PE and maternal variables are shown in [Figure 1](#). Aside from maternal age and GGT that showed no significant correlation with the onset of PE, HDL was inversely correlated ($r = -0.125$, $P = 0.048$), while, blood pressure, BMI, parity and proteinuria were all positively correlated with the onset of PE ($P < 0.050$). The correlation and linear regression analysis between the severity of PE and maternal variables are shown in [Figure 2](#). Maternal HDL was inversely correlated ($r = -0.199$, $P = 0.001$), while the rest of the maternal variables (except maternal age, parity and GGT) were all positively correlated with the severity of PE ($P < 0.050$).

Discussion

The study aimed to determine the correlation between the onset and severity of PE and maternal variables. Maternal variables including lipids, liver enzymes (except GGT), creatinine, sNGAL, ET-1 were significantly correlated with the onset and severity of PE. Also, both systolic and diastolic blood pressure, proteinuria, and BMI were positively correlated with the onset and severity of PE.

The increased blood pressure in PE stems from the resistance in the vascular system and decreased intravascular volumes and cardiac output. There is a decrease in conduit artery compliance as well as the obliteration of the fall of nocturnal blood pressure. Hypertension in PE may contribute to organ damage including, acute kidney injury and renal dysfunction.¹⁰ Previous studies have shown that renal blood flow and glomerular filtration rates are decreased in PE as shown by the loss of podocytes, endothelial swelling and glomerular endotheliosis in biopsies from PE patients. Damaged endothelial cells in PE may induce clotting, as well as loss of anticoagulant ability as levels of nitric oxide and prostaglandin, plummet leading to kidney thrombotic microangiopathy.^{11,12} The associated renal dysfunction in PE may

Table 1. General characteristics of the study population stratified by the onset and severity of preeclampsia.

Variable	SI unit	Control n (135)	PE n (135)	Onset EOPE n (71)	LOPE n (64)	Severity PNS n (87)	PS n (48)
Socio-demographics and anthropometrics							
Age	years	27.8 ± 4.63	27.9 ± 4.40	27.0 ± 4.04	29.2 ± 4.12 ^{††}	28.5 ± 3.78	26.7 ± 4.84 [†]
GA	weeks	29.7 ± 3.02	29.9 ± 3.00	28.0 ± 2.10	32.4 ± 2.50 ^{†††}	30.1 ± 3.15	29.7 ± 3.04
BMI	kg/m ²	27.4 ± 5.83	30.2 ± 6.14 ^{**}	28.5 ± 5.03	32.9 ± 6.24 ^{†††}	30.0 ± 6.15	30.6 ± 6.38
SBP	mmHg	105.4(11.91)	151.8 ± 12.24 ^{**}	151.4 ± 9.17	152.3 ± 15.30	146.7 ± 8.39	164.7 ± 11.09 ^{††}
DBP	mmHg	65.0(9.25)	103.6 ± 12.83 ^{**}	105.3 ± 14.04	101.1 ± 10.57	95.6 ± 5.47	115.3 ± 6.77 ^{††}
Proteinuria							
Neg	-	135(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pos (1+)	-	0(0.0)	60(44.4)	32(45.0)	25(38.9)	54(62.1)	0(0.0)
Pos (2+)	-	0(0.0)	27(20.0)	21(30.0)	18(27.8)	30(34.5)	16(33.3)
Pos (3+)	-	0(0.0)	48(35.6)	18(25.0)	21(33.3)	3(3.4)	32(66.7)
Parity							
Nulliparous	-	60(44.4)	48(35.6)	43(60.0)	7(11.1)	33(37.9)	16(33.3)
Primiparous	-	27(20.0)	36(26.7)	11(15.0)	18(27.8)	24(27.6)	13(26.7)
Multiparous	-	48(35.6)	51(37.8)	17(25.0)	39(61.1)	30(34.5)	19(40.0)
Biomarkers							
sNGAL	ng/mL	79.1(72.6-85.4)	95.2(78.6-116.9) ^{**}	84.9(78.6-101.7)	108.8(82.5-119.1)	84.3(77.3-113.0)	132.5(100.2-139.1) ^{††}
ET-1	pg/mL	17.9(10.0-27.8)	60.0(30.0-146.0) ^{**}	59.0(30.0-134.0)	82.0(46.0-148.0)	44.0(24.5-72.0)	136.0(106.0-170.0) ^{††}
TCHOL	mmol/L	3.5(2.8-4.7)	4.6(3.5 ± 5.1) ^{**}	4.2(3.6-5.1)	4.7(3.4-5.6)	4.6(3.3-5.1)	4.7(3.7-5.3)
HDL	mmol/L	1.3(1.0-1.5)	1.0(0.5-1.5) [*]	1.1(0.6-1.6)	1.2(0.5-1.4)	1.1(0.7-1.5)	1.0(0.3-1.4)
LDL	mmol/L	2.1(1.5-2.7)	2.8(1.7-3.9) ^{**}	2.8(2.1-3.9)	3.4(1.7-4.3)	2.8(1.7-3.9)	2.7(1.7-4.7)
TRIG	mmol/L	0.8(0.5-1.1)	0.9(0.7-1.3) ^{**}	1.0(0.7-1.2)	0.9(0.7-1.4)	0.9(0.7-1.2)	1.1(0.7-1.6) [†]
ALT	IU/L	11.1(6.2-22.5)	23.7(16.3-56.1) ^{**}	25.7(14.2-53.8)	21.8(12.2-56.1)	19.3(10.4-25.1)	67.9(35.4-78.5) ^{††}
AST	IU/L	11.2(6.1-23.0)	22.1(10.6-45.0) ^{**}	18.1(9.2-45.1)	25.2(12.5-39.5)	12.7(9.2-35.2)	35.6(23.1-52.3) ^{††}
GGT	IU/L	21.4(11.3-44.0)	16.7(10.6-43.7)	19.5(10.4-71.9)	15.8(7.0-39.2) [†]	14.4(10.9-36.5)	36.2(10.3-56.2) [†]
CRT	μmol/L	48.1(36.6-56.0)	61.3(44.9-91.3) ^{**}	65.0(46.3-92.7)	56.3(44.9-69.5) [†]	60.2(45.1-89.0)	67.4(36.6-102.1)

Results were presented as mean ± SD, median (IQR) and n (%) for parametric, non-parametric and categorical variables respectively. The control group was compared with the preeclamptic (PE) group. The early-onset preeclamptic (EOPE) group was compared to the late-onset preeclamptic (LOPE) group while the preeclamptic with severe features (PS) group was compared to the preeclamptic without severe features (PNS) group. Student t-test (unpaired, 2-tailed) was used for parametric variables while the Mann-Whitney U test (unpaired, 2-tailed) was used for non-parametric variables.

*Significant at the 0.010 level.
**Significant at the 0.001 level compared to control.

†Significant at the 0.050 level.

††Significant at the 0.010 level.

†††Significant at the 0.001 level compared to EOPE.

‡Significant at 0.010 level.

‡‡Significant at the 0.001 level compared to PNS.

Figure 1. Correlation between the onset of PE and maternal variables. The control, EOPE and LOPE were dummy coded before linear regression and correlation analysis. *Significant at the 0.010 level, **Significant at the 0.001 level.

account for the elevated serum CRT and sNGAL. Serum NGAL is usually secreted directly into damaged renal tubular cells with the aim of re-epithelialization and has been shown to indicate renal injury much earlier than CRT. Serum NGAL is also involved in immune-system modulation as its levels increase in PE due to the generalized inflammation. The onset and severity of PE are also significantly correlated with proteinuria. Increased proteinuria in PE is due to increased permeability of the renal tubules partly due to the glomerular endotheliosis.¹⁰

PE is also associated with hepatic dysfunction and abnormal lipid metabolism as shown by elevation in some serum liver enzymes and lipids. This may be due to endothelial injury which causes hepatocellular necrosis and hepatic microcirculatory deterioration. Hepatic dysfunction may affect the synthetic functions of the liver including abnormalities in blood coagulation.^{11,13} It has been shown that particles of HDL and LDL are remodelled during normal pregnancy becoming smaller and denser with increased proatherogenic potential and this is worsened by PE.¹⁴ Although the exact mechanism is unknown, the changes in maternal lipid metabolism in PE has been suggested to be a compensatory process to increase energy supply to the developing foetus.¹⁵

Serum levels of ET-1 were elevated in PE as compared to the controls and the levels increased with the severity of the symptoms of the disease.^{4,16–21} Several studies have demonstrated the role of ET-1 in the aetio-pathology of PE including the elevated circulating ET-1, increase in ET-1 converting enzyme (ECE) activity, the differential effect of systemic ECE inhibition and increased localized ET-1 production in tissues of maternal origin.^{16–18,22–24} Further evidence of the role of ET-1 in PE was the increased expression of markers of oxidative stress when placental tissue explant from normal pregnancy were incubated with exogenous ET-1 *in-vitro*. Also, ET-1 reduced JEG-3 cell lines proliferation, evidence of the possible role of ET-1 in preventing trophoblast invasion of the placenta in the early stages of PE.²⁵ In the reduced uterine perfusion pressure (RUPP) model, where blood flow to the uterus was partially restricted, inducing placental

Figure 2. Correlation between the severity of PE and maternal variables. The control, PNS and PS were dummy coded before linear regression and correlation analysis. *Significant at the 0.010 level, **Significant at the 0.001 level.

hypoxia and ischemia, there was increased expression of preproendothelin mRNA, with the associated proteinuria, renal injury and endothelial dysfunction.^{26,27} However, issues have been raised regarding the interpretation of serum ET-1 results; firstly, ET-1 from syncytiotrophoblastic cells in the placenta would have been diluted by the time blood reaches the antecubital area for sampling, secondly, ET-1 is an autocrine/paracrine product whose serum levels does not reflect local tissue production. It has been suggested that an ET-1 receptor saturation study be performed, in addition to serum ET-1 estimation, to measure ET-1 receptor activation since a prolonged steady-state of ET-1 receptor saturation may be reached in PE through the continuous infusion of ET-1 from the uterine veins.²⁸ This study is among a few studies coming from Ghana to have simultaneously determined the correlation between the onset and severity of PE with multiple maternal variables, including sNGAL and ET-1. However, the authors acknowledge some limitations; blood samples were collected after the manifestation of symptoms and diagnosis of preeclampsia. It is recommended that sampling is done in each trimester through to the post-partum period to determine the exact period changes in maternal variables begin to occur due to PE. Also, quantitative 24-hour urine protein or creatinine-to-protein ratio is preferred to the dipstick method in screening for proteinuria.

In conclusion, the onset and severity of PE are significantly correlated with maternal variables such as parity, proteinuria, blood pressure, lipids, liver enzymes, sNGAL, ET-1 and creatinine. There is therefore the need for regular monitoring of these maternal variables for the early detection and management of PE in the Ghanaian population.

Data availability

Underlying data

OSF: Underlying data for 'Correlation between maternal variables and the onset and severity of preeclampsia'.

<https://doi.org/10.17605/OSF.IO/CF8XB>.

The project contains the following underlying data: maternal socio-demographics and anthropometric variables as well as serum/plasma fasting lipids, liver enzymes, creatinine, neutrophil gelatinase-associated lipocalin, and endothelin-1. The cases were grouped by the onset of PE and also by its severity.

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

Authors' contributions

NA conceived the idea and designed the experiment, SJA performed the experiment and collected the data, MB analysed the data and wrote the manuscript. All authors provided critical feedback, read and approved the final manuscript.

Ethics approval and consent to participate

All procedures performed in this study involving human participants were done following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board of the University for Development Studies (UDS), Tamale.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Consent for publication was granted.

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[PubMed Abstract](#) | [Publisher Full Text](#)

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Johnbosco E Mamah

Obstetrics and Gynaecology Department, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Nigeria

This article is a short communication, this would guide the intensity of my review.

Overall, the study is relevant in contemporary Obstetrics especially in sub-saharan Africa where the burden of preeclampsia is still quite high and there is limited resources for its investigation and treatment. With some improvement suggested below, the study would be a valuable addition to the body of knowledge regarding what is known about preeclampsia.

The authors need to review the article to improve the grammar and readability.

Abstract: The abstract was well written. It was structured and concise. The methodology section of the abstract should include a summary of the statistical analysis performed. It is good practice to list the keywords in alphabetical order.

Introduction: As cited by the authors, preeclampsia affects about 3-8% of pregnancies globally but the incidence in sub-Saharan Africa including Ghana is even higher based on available studies. The authors should comment on the local burden of the disease.

Methodology: This needs significant improvement to make the work reproducible elsewhere. I acknowledge that the authors were thorough in the methodology for the biochemical analysis of the blood sample taken and in describing the data analysis performed but that is as far as it goes.

The work could be improved upon by describing how the participants were recruited (sampling method), how the diagnosis of preeclampsia was made and at what point, what is the minimum and maximum gestational age for recruitment into the study, and how the sample size was calculated or arrived at. I note that the reference quoted in the methodology for the sample size calculation (ref 9) does not correspond to the listed citation in the list of references. Moreover, reference number 8 is missing in the body of the text.

In the definition of terms, the authors failed to list out the severe features of preeclampsia apart from severe hypertension. Severe hypertension ($\geq 160/110$ mmHg) alone in the absence of proteinuria or other features of severe preeclampsia is not the same as severe preeclampsia (See ACOG practice bulletin number 222, December 2018).¹ Listing out the clinical and biochemical features of severe preeclampsia would also validate the authors statement in the introduction that preeclampsia could be diagnosed as new onset hypertension after 20 weeks gestation with or without proteinuria.

The authors report there was no attrition in the study, were all the patients admitted overnight to collect the fasting sample? If some went home after the initial diagnosis, did they all return the next morning for a fasting sample to be taken? Were they medicated at the time of sample collection and was there repeat blood pressure check at this time? These need to be clarified.

The authors matched for gestational age and maternal age, did they correct for other confounders such as BMI, autoimmune diseases or parity which were not matched during recruitment? If not, then I suppose this a weakness and should be mentioned.

Discussion: The authors have written a robust discussion but there was little to no discussion of how this study compares with similar studies elsewhere. There was an objective acknowledgement of weaknesses and limitations of the study.

Conclusion: The authors have concluded as rightly found in the study that there was a significant correlation between maternal variable and preeclampsia. The results do not support their recommendation for regular monitoring of these variables for early detection of preeclampsia. They performed only a one off analysis with no follow-up to confirm consistency in their initial findings. The subjects on the case arm of the study already have the disease, I don't see how the variables predict preeclampsia in this case. It would have been good to know if any body in the control developed preeclampsia down the line and how this related to their initial biochemical findings. At best it can be concluded that the maternal variable correlated with the severity of the disease at the time of assessment.

The authors have recommended for these variables to checked regularly for early detection of preeclampsia, I would assume that these are expensive investigations which may not be affordable to the average patient in sub-Saharan Africa due to widespread poverty.[ref-2# I would recommend the authors perform a sub analysis of the data to determine which of the variable had the best correlation with preeclampsia and make a case for its wider use or more studies to confirm its utility. Performing all the assays listed in this study which might be difficult to afford and may not add much in terms of actual clinical practice.

References: The references are well written but ref 8 is missing in the body of the text.

References

1. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. *Obstet Gynecol* . 2020; **135** (6): e237-e260 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Saleh, Mariam: Number of people living below the extreme poverty line in Africa from 2016 to 2027. *Statista: CTHS*. 2022. [Reference Source](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Maternal medicine

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 01 November 2022

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Jussara Mayrink

Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

Introduction:

The third paragraph is really confused. Please, try to rewrite it, with some more data about the relationship between variables and preeclampsia, as well as, being very clear regarding the objective of this study. Reading all the text it is clear that the objective of the study is to establish the relationship between variables and preeclampsia, however, it must be clear in the introduction.

Definitions:

Considering this is a scientific article, which has many functions, as being instructive to readers, more than just inform the results, I think it would be interesting to add a sentence like “in this study, we consider **the** sign of severity present the arterial blood pressure above 160X110 mmHg”. This is not the only sign of severity, as the authors already know. This must be considered in the text. The same should be considered to the concept of preeclampsia. The authors choose a “partial” concept of preeclampsia in the reference applied (ACOG, 2019). However, the concept should be cited in the text in its totality.

Discussion:

The relationship between onset of preeclampsia and variables

- BMI: authors should add a sentence or a paragraph about this. The relationship of late-onset preeclampsia and higher BMIs has been already established and it is particularly interesting (see Roberts JM, Hubel CA, 2008).¹

The relationship between severity of preeclampsia and variables

- Serum liver enzymes: at this point, authors should point the concept of HELLP syndrome, which is a validated sign of severity of preeclampsia.
- Proteinuria: at this point, authors must be very careful with this result, in order to avoid the misunderstanding of consider high levels of proteinuria and severity of preeclampsia, which is not totally true, as demonstrated in the literature. I know this is a result of this study and of course, authors should point it out. However, consider adding a sentence pondering on this important discussion.

Conclusion:

“There is therefore the need for regular monitoring of these maternal variables for the early detection and management of PE in the Ghanaian population.”

Is it feasible to the Ghanaian context?

Maybe the relevance of the findings should be considered in the light of the etiology of preeclampsia, in a treatment axis, in a prevention action, etc.

Proposing the measure of variables throughout the prenatal care in order to diagnose preeclampsia doesn't seem to be a reasonable conclusion.

References

1. Roberts JM, Hubel CA: The two stage model of preeclampsia: variations on the theme. *Placenta*. 2009; **30 Suppl A**: S32-7 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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