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Demographic Factors, Biochemical Markers, and Obstetric History Associated with the Risk of Preeclampsia in a Sudanese Population Sample

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Preeclampsia significantly contributes to maternal and perinatal illness and death, particularly in low and middle-income countries like Sudan. It is classified by onset timing (early vs. late) and severity (mild vs. severe) and is one of the four hypertensive disorders in pregnancy, including chronic hypertension, gestational hypertension, and chronic hypertension with superimposed preeclampsia. This study aimed to evaluate the demographic, clinical, and biochemical predictors of preeclampsia among Sudanese women.

Methods: This case-control study involved 100 women diagnosed with preeclampsia and 100 healthy pregnant women who acted as the control group at Omdurman Maternity Hospital in Khartoum State, Sudan, from 2019 to 2021. Data on sociodemographic characteristics, obstetric history, and biochemical markers, including platelet counts, were collected using a comprehensive questionnaire and blood sample analysis.

Results: Women with preeclampsia were more frequently over the age of 40 (OR=9.33, 95% CI: 4.54-19.19, $p < 0.001$) and had a longer median duration of marriage (OR=2.9, 95% CI: 1.51-5.58, p=0.001). Lower educational levels (p=0.008) and being housewives (p=0.024) were also more prevalent in the preeclampsia group. Clinically, headache (OR=18.98, 95% CI: 2.44-147.5, p=0.005) and blurring of vision (OR=25.83, 95% CI: 1.17-572.6, p=0.04) were more prevalent in women with preeclampsia. Biochemical markers showed lower platelet counts (p=0.002), higher levels of alanine aminotransferase (ALT) (OR=2.23, 95% CI: 1.51-3.28, $p < 0.001$) and creatinine (OR=16.76, 95% CI: 2.31-121.5, p=0.005), while aspartate aminotransferase (AST) was not significantly associated with preeclampsia.

Conclusion: Family history of preeclampsia was the most significant predictor. Other important risk factors included older age, longer duration of marriage, lower education levels, headache, blurring of vision, and higher levels of alanine aminotransferase (ALT) and creatinine.

Keywords: Preeclampsia; demographic factors; biochemical markers.

1. INTRODUCTION

Women of lower socioeconomic status or living in nations with inadequate healthcare infrastructure are at increased risk for severe preeclampsia outcomes [1]. Preeclampsia is recognized as the second leading cause of maternal mortality globally [2]. It predominantly affects low and middle-income countries, [3]. Studies in Sudan showed that preeclampsia and eclampsia contributed to 4.2% of admissions at a maternity hospital in Kassala, located in eastern Sudan. Additionally, preeclampsia was identified as the primary cause of both maternal and perinatal health complications, leading to 18.1% of maternal fatalities [4,5].

Preeclampsia is a complex condition influenced by various demographic and obstetric factors, including maternal age, duration of marriage, education level, consanguineous marriage, presenting symptoms, and biochemical markers. Studies have shown that women over 35 years of age are at higher risk for preeclampsia [6-9]. Additionally, the duration of marriage has been identified as a factor, with longer durations correlating with increased risks due to age and cumulative health impacts [10]. Education level is crucial for health outcomes, with lower educational attainment linked to higher risks of preeclampsia, reflecting broader socioeconomic disparities. In Sudan, hypertensive disorders in pregnancy, including preeclampsia, are prevalent and significantly associated with lower education levels [11]. It is acknowledged as a crucial factor influencing health outcomes, including pregnancy-related complications [12]. Consanguineous marriage has been observed to increase the risk of preeclampsia due to the potential for genetic predispositions to be expressed more frequently in such unions [11]. Presenting symptoms of preeclampsia are varied and can include urinary tract infection, epigastric pain, headache, blurring of vision, vomiting, and right hypochondrial pain [13]. Blood pressure readings are critical in diagnosing and managing preeclampsia, with elevated levels indicating the severity of the condition [14]. Reproductive history is also significant, with factors such as age of menarche, use of contraceptive pills, gravidity, and parity that affect the risk profile of preeclampsia [15].

Biochemical markers, including kidney function, hematological markers, and liver enzymes, are critical for diagnosing and managing

preeclampsia. Studies have shown that the mean plasma uric acid level is significantly higher in Sudanese preeclamptic women compared to normotensive pregnant women. [11,16]. Additionally, levels of ALT and AST are all significantly predictive of adverse maternal outcomes in women with preeclampsia [16]. Assessment of platelet count indices and the morphology of newborns' cord blood among Sudanese preeclamptic mothers also revealed significant differences compared to controls, highlighting preeclampsia's impact on maternal and neonatal health [17]. Furthermore, African studies have emphasized the predictive value of these markers in diagnosing severe forms of the condition [18-20].

2. MATERIALS AND METHODS

This case-control study was carried out at Omdurman Maternity Hospital in Khartoum State, Sudan, between 2019 and 2021. The study involved 200 participants, with 100 preeclamptic women and 100 healthy pregnant women, providing a 95% confidence level within a 0.05 margin of error. Participants in the preeclamptic group were pregnant women diagnosed with preeclampsia (blood pressure ≥140/90 mmHg after 20 weeks gestation, with proteinuria). The control group consisted of age-matched, normotensive pregnant women with uncomplicated pregnancies and no history of chronic illness, thromboembolic diseases, or anticoagulant use. Exclusion criteria included chronic hypertension, diabetes, renal or autoimmune disorders, smoking, thromboembolic events, or anticoagulant therapy. Additional exclusions for the preeclamptic group were preexisting hypertension before 20 weeks, multiple gestations, or confounding systemic conditions.

2.1 Data Collection and Biochemical Assays

Data on demographic, clinical, and biochemical parameters were collected from each participant using a carefully designed and pretested questionnaire. This instrument systematically captured essential information, including sociodemographic characteristics, obstetric history, and biochemical indicators such as AST, ALT, uric acid, creatinine, hemoglobin, platelets, and urine albumin. Blood samples were drawn from the antecubital veins of participants using both K3EDTA and plain tubes for different types of analyses. Levels of liver transaminases (ALT and AST), kidney function markers, and other biomarkers were assessed using an automated (Beckman Coulter AU480, USA) clinical chemistry analyzer according to the manufacturer's protocols.

2.2 Statistical Analysis

The data was analyzed using IBM SPSS Statistics version 29.0. Clinical and biochemical characteristics between the case and control groups were compared using descriptive statistics. For categorical variables, Chi-square tests were utilized, while Mann-Whitney U tests and t-tests were used for analyzing continuous variables. Univariate logistic regression was applied to determine potential predictors of preeclampsia, generating odds ratios (ORs) and 95% confidence intervals (CIs). Predictors with a p-value less than 0.05 were incorporated into a multivariate logistic regression model to account for confounders, using a backward stepwise method to retain significant predictors. The Hosmer-Lemeshow test was used to evaluate the model fit, and the area under the ROC curve (AUC) assessed discrimination. Multicollinearity was examined through variance inflation factors (VIFs), with no significant issues found.

3. RESULTS

The demographic, baseline, gynecologic, obstetric, and biochemical characteristics of women with preeclampsia (N=100) were compared and analyzed against those of the control group (N=100).

Women with preeclampsia exhibited a markedly different age distribution compared to controls, with a higher percentage being over 40 years old. Furthermore, the median length of marriage was notably longer for women with preeclampsia (5 years) compared to controls (3 years) ($p < 0.001$). Education levels differed, with 9% of women with preeclampsia being illiterate or having only primary education, compared to none in the controls ($p=0.008$). A greater percentage of women with preeclampsia were housewives (77% vs. 70%), and none were employed; unlike the 9% observed in the control group ($p=0.024$), the prevalence of consanguineous marriage was similar in both groups.

Presenting symptoms showed significant differences. Headache and blurred vision were more prevalent among women with

preeclampsia. (38% vs. 4%), while 21% of women with preeclampsia had no symptoms compared to 76% of controls. Women in the preeclampsia group showed significantly elevated mean systolic and diastolic blood pressures compared to the control group (153.7 ± 13.8 vs. 117.8 ± 5.2 for systolic and 105.5 ± 13.7 vs. 77.4 ± 5.7 for diastolic, both with $p < 0.001$) (Table 1).

The median age at menarche was similar between women with preeclampsia and controls. Contraceptive use was slightly higher among preeclamptic group (13% vs. 9%, p=0.370). Women with preeclampsia had higher gravidity and parity compared to controls, with mean gravidity of 3 (range 2-5) versus 2 (range 2-3) (p=0.001) and mean parity of 2 (range 0-4) versus 1 (range 1-2) (p=0.001).

Several risk factors for preeclampsia were more prevalent in women with the condition, including previous history of preeclampsia (12% vs. 0%, p=0.001), chronic hypertension (2% vs. 0%), diabetes mellitus (8% vs. 1%), and family history of preeclampsia (18% vs. 4%). The median time to first conception was shorter for cases compared to the controls (7 months vs. 12 months) (Table 2).

Cases group exhibited significantly higher levels of aspartate transaminase (AST) (33.4 ± 5.1 vs. 19.5 ± 2.9, p=0.001), alanine transaminase (21.7 ± 4.6 vs. 14.3 ± 2.4, p=0.001), creatinine (1.6 ± 0.6 vs. 1.0 ± 0.5, p=0.001), and uric acid (4.8 ± 1.6 vs. 4.1 ± 1.2, p=0.001) compared to the control group. Additionally, platelet counts were significantly lower in women with preeclampsia (242.1 ± 15.3 vs. 269.1 ± 84.7, p=0.002). Hemoglobin levels, however, were similar between the cases and controls, showing no significant difference (Table 3).

Table 1. Sociodemographic and baseline characteristics of the study participants

Variables	Cases group (n=100)	Controls Group (n=100)	*P* value
Age Range			
<25	1%	5%	**<.001**
26-39	82%	94%	
>40	17%	1%	
Duration of marriage in years, median (IQR)	5 (4-10)	3 (2-4)	<.001
Education Level			
Illiterate or Primary	9 %	0%	.008
Secondary	49 %	51%	
University	42 %	49%	
Occupation			
Housewife	77	70	.024
Labourer	1	1	
Employee	0	9	
Other	22	20	
Consanguineous marriage	67%	65%	.765
Presenting symptoms			
Urinary tract Infection	7%	7%	<.001
Vaginal Bleeding	2%	4%	
Epigastric Pain	5%	3%	
Headache	38%	4%	
Vomiting	2%	4%	
Right hypochondrial Pain	5%	1%	
Non	41%	77%	
Presenting Blood Pressure			
Systolic BP mean ±SD	153.7± 13.8	117.8 ± 5.2	<.001
Diastolic BP mean ±SD	105.5± 13.7	77.4 ± 5.7	<.001

Table 2. Gynaecologic and obstetric history among the study population

Variables	Cases group (n=100)	Controls Group (n=100)	*P* value
Age of menarche years, Median (IQR)	13.5 (0.6)	13.7 (0.7)	.163
Using Contraceptive pills	13 %	9%	.370
Gravidity (mean, range)	3 (2-5)	2 (2-3)	.001
Parity (mean, range)	2 (0-4)	1(1-2)	.001
Previous pregnancy Events			
Preterm	2%	1%	.082
Still-birth	4%	13%	
Early Neonatal death	4%	7%	
Abortion	13%	15%	
Pregnancy Termination	3%	0%	
Risk factors for Preeclampsia			
Previous history of Preeclampsia	12%	0%	.001
Chronic Hypertension	2%	0%	
Diabetes Mellitus	8%	1%	
Family history of Preeclampsia	18%	4%	
Connective Tissue Disease	2%	1%	
First Conception After/months, Median (IQR)	7 (5-12)	12 (8-15)	.001

Table 3. Biochemical characteristics between cases (pre-eclampsia) and controls

Variables Mean (±SD)	Cases group (n=100)	Controls Group (n=100)	*P* value
Aspartate Transaminase (AST)	33.4 (5.1)	19.5 (2.9)	.001
Alanine Transaminase (ALT)	21.7 (4.6)	14.3 ((2.4)	.001
Creatinine	1.6 (0.6)	1.0 (0.5)	.001
Uric Acid	4.8 (1.6)	4.1(1.2)	.001
Platelets	242 .1 (15.3)	269.1 (84.7)	.002
Hb mg/dl %	11.7 (3.7)	11.2 (1.9)	.217

Table 4. Adjusted and unadjusted odds ratios for predictors of preeclampsia

Variable	Univariate Analyses		Multivariate Analyses	
	Unadjusted OR	*P* value	Adjusted OR	*P* value
Age	9.33 (4.54-19.19)	<.001	8.31 (1.29-53.31)	.026
Parity	24.75 (3.25-188.3)	.002	0.78 (0.32-1.9)	.585
Duration of Marriage	1.59 (1.35-1.87)	<.001	2.9 (1.51-5.58)	.001
Family History of Preeclampsia	8.61 (1.06-70.17)	.044	96.8 (5.52-1696.3)	.002
DM	2.01 (1.47-2.74)	<.001	3.17 (0.01-1599.1)	.716
Headache	5.27 (1.72-16.19)	.004	18.98 (2.44-147.5)	.005
Blurring of Vision	14.71 (5.00-43.25)	<.001	25.83 (1.17-572.6)	.04
AST	2.25 (0–Inf)	.997		
ALT	1.92 (1.6-2.31)	<.001	2.23 (1.51-3.28)	<.001
Uric acid	5.01 (0–Inf)	.986		
Creatinine	10.02 (5.01-20.07)	<.001	16.76 (2.31-121.5)	.005
Platelets	5.81 (0–Inf)	.983		

Our study analysis examined the association of various predictors with the occurrence of preeclampsia using both odds ratios (OR) unadjusted and adjusted with their 95% confidence intervals (CI) and p-values (Table 4). Women older than 35 years demonstrated a higher risk of developing preeclampsia. Parity initially showed a strong unadjusted association

with preeclampsia, but this association did not remain significant after adjustment. The duration of marriage was significantly linked to an increased risk of preeclampsia in unadjusted and adjusted models. A family history of preeclampsia emerged as a robust independent predictor in both unadjusted and adjusted models. Although diabetes mellitus (DM) initially showed a significant unadjusted association, it was not significant after adjustment. Headache and blurring of vision were significantly associated with preeclampsia in both unadjusted and adjusted models. Liver enzyme levels showed mixed results; aspartate aminotransferase (AST) was not significantly associated with preeclampsia, while alanine aminotransferase (ALT) was significantly associated in both unadjusted and adjusted models. Creatinine levels were significantly associated with preeclampsia in both models. Neither uric acid nor platelet count showed significant associations with preeclampsia.

4. DISCUSSION

This study aimed to identify key preeclampsia (PE) predictors among Sudanese women, focusing on demographic, clinical, and biochemical factors.

Among the various factors analyzed, family history of preeclampsia emerged as the most significant predictor in our regression analysis, with a strong independent association with preeclampsia, highlighting the importance of taking a comprehensive family history during prenatal visits to identify high-risk women. Women with a maternal history of Preeclampsia have a 3- to 3.5-fold higher risk, and those with an affected sister have a 1.5- to 2-fold increased risk. Furthermore, the risk nearly doubles if both mother and sister had Preeclampsia [21,22]. Women who have mothers, sisters, grandmothers, or aunts who have experienced preeclampsia are at an elevated risk of developing the condition themselves [23]. Our finding also aligns with several studies, emphasizing the significance of family history as a preeclampsia risk factor [10,15,24,25].

In the current study, women with preeclampsia had a significantly different age distribution compared to controls, with a higher proportion over 35 years old. This age difference, coupled with a longer median duration of marriage in the preeclampsia group, suggests that older age and extended marital duration may contribute to the risk of developing preeclampsia. The logistic regression analysis supported these findings. This correlation is supported by Meazaw et al., who emphasized the importance of reproductive history in Preeclampsia risk [15] And numerous other studies have identified an advanced maternal age as a contributing preeclampsia risk factor [10,14,25]. Women with longer marriages and advanced age are at higher risk due to immune and physiological factors. [26]. Advanced maternal age contributes to Preeclampsia due to blood vessel problems caused by reduced nitric oxide and increased oxidative stress, leading to poor placental blood flow. [26,27]. Women of advanced age are more prone to developing atherosclerosis, which impacts small arteries, including those in the kidneys and uterus, and leads to hypertension. Consequently, older pregnant women are at an elevated risk of developing preeclampsia [23].

Furthermore, our study found a higher prevalence of illiteracy or only primary education and a greater percentage of housewives among the preeclampsia group, indicating that lower socioeconomic status might be linked to a higher risk. This result is in agreement with many earlier research, such as Mekie et al. study, which found that women with no formal education had less knowledge about Preeclampsia, leading to poor health-seeking behaviors, delayed diagnosis, and inadequate management. Still, Women with higher education are more likely to attend regular antenatal care, receive counseling on pregnancy complications, and adopt preventive measures vital for the early detection and management of Preeclampsia [28].

In this study, significant clinical differences in presenting symptoms were observed in the presenting symptoms, such as headache and blurring of vision, which were markedly more common in women with preeclampsia, which aligns with the known symptoms of the condition. Logistic regression analysis confirmed that these symptoms were significant predictors of preeclampsia even after adjusting for other variables. These findings align with studies by Adam et al. indicating that pregnant women with a history of migraine have increased odds of developing preeclampsia [29]. This may be because the brain requires about 20% of the body's oxygen to function properly. Cerebral blood flow (CBF) can normally be controlled to meet this demand. Insufficient CBF can cause brain injury and stroke, while hyperperfusion can damage the blood-brain barrier (BBB) and cause

swelling, which is common in pre-eclampsia and eclampsia. Severe symptoms include headache, vision problems, altered consciousness, and seizures [30].

Reproductive history significantly influences the risk of preeclampsia. In our study, compared to controls, women with preeclampsia had higher gravidity and parity and a shorter median time to first conception. These factors may contribute to the physiological stress experienced during pregnancy, potentially increasing the risk of preeclampsia. Multiple pregnancies cause repeated physiological stress, leading to cumulative vascular damage, endothelial dysfunction, and increased vascular resistance, which are all risk factors for Preeclampsia. Consequently, women with higher gravidity and parity are at greater risk for Preeclampsia [31]. However, both primigravida and multigravida women are at risk, indicating a complex interplay of factors [32].

In the present study, biochemical markers revealed significant differences between women with preeclampsia and controls. Higher levels of alanine aminotransferase (ALT) were significantly associated with preeclampsia, while aspartate aminotransferase (AST) did not show a significant association. The regression model verified that ALT was a significant predictor of preeclampsia. These results align with numerous studies that reported significantly higher ALT levels in preeclamptic women [13,16,33]. Preeclampsia-related liver disease, typically observed in the third trimester, is uncommon but signifies a severe form of the condition, with HELLP syndrome being an extreme variant of preeclampsia [30].

Our study found that creatinine levels were notably higher in women with preeclampsia, and this association remained significant after adjusting for other factors, making creatinine a strong predictor of preeclampsia according to logistic regression analysis. While uric acid levels were higher in preeclampsia cases during univariate analysis, they did not remain significant in the multivariate model. Physiological changes during pregnancy, such as hemodilution, increased vascular volume, and changes in renal function, influence both serum uric acid and creatinine levels. Even though the relationship between serum uric acid and preeclampsia has been recognized for over 50 years, its predictive role for preeclampsia and adverse pregnancy outcomes remains inconsistent and not strong enough to be included in current risk scores [34]. Studies have also indicated that high uric acid levels are unreliable maternal and fetal outcome predictors [35].

5. CONCLUSION

The most significant predictor of preeclampsia was a family history of the condition. Demographic factors such as older age, longer duration of marriage, and lower education levels were also linked to a higher risk. Clinically, headache and blurred vision were more frequently observed in women with preeclampsia. Biochemical markers, including higher alanine aminotransferase (ALT) and creatinine levels, were significantly associated with preeclampsia.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

DATA AVAILABILITY

The data supporting this study's findings are available from the corresponding author, Dr. Faris Abdon, upon reasonable request. However, the data are not publicly available due to privacy or ethical restrictions. For any inquiries or requests, please contact farismabdon@gmail.com.

CONSENT AND ETHICS APPROVAL

The study adhered to ethical guidelines, ensuring confidentiality and informed consent. The Ethics Committee of Al-Neelain University granted ethical approval (IRB Serial No: NU-IRB-18-8-8-41).

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COMPETING INTERESTS

The authors state that they have no conflicts of interest related to this article and have no personal or financial relationships with any individuals or organizations that could inappropriately influence (bias) their work.

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