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Association between hyperuricemia and adverse perinatal outcomes among women with preeclampsia at a tertiary hospital in Southwestern Uganda: a prospective cohort study

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ABSTRACT

Background: Pre-eclampsia is a major cause of adverse perinatal outcomes, such as preterm birth and perinatal deaths, at Mbarara Regional Referral Hospital (MRRH). While serum uric acid is a crucial marker for predicting adverse outcomes, it is not routinely assessed. This study aimed to compare the incidence of adverse perinatal outcomes between women with and without hyperuricemia and determine the association between hyperuricemia and adverse perinatal outcomes among women with preeclampsia at MRRH.

Methods: We conducted a prospective cohort study from March 2024 to June 2024 at the maternity ward of MRRH. We consecutively enrolled women diagnosed with preeclampsia who were at least 26 weeks gestational age and assessed their serum uric acid levels upon admission. The primary exposure was hyperuricemia ($>6\text{mg/dl}$) while the primary outcome was adverse perinatal outcomes. We compared the incidence of adverse perinatal outcomes among those with and without hyperuricemia using Chi-square and used multivariable modified Poisson regression analysis to determine the association between hyperuricemia and adverse perinatal outcomes among women with preeclampsia.

Results: Among the 111 women enrolled (mean age 28.3 ± 6.5 years), 43 (38.7%) had hyperuricemia. Adverse perinatal outcomes occurred in 55.9% (62/111). Women with hyperuricemia had higher rates of adverse outcomes (88%, $n=38/43$) than those without (35%, $n=24/68$). Specific outcomes were significantly more frequent among hyperuricemic women: fresh stillbirth (21% vs. 0%), low birth weight (49% vs. 26%), Apgar score <7 at 5 min (26% vs. 1%), NICU admission (76% vs. 26%), and early neonatal death (32% vs. 0%), $p < 0.05$. Hyperuricemia was linked to a two-fold increased risk of one or more adverse outcomes (aRR 2.42, 95% CI: 1.54–3.80), fresh stillbirth (aRR 3.14, 95% CI: 1.79–5.48), low Apgar score (aRR 31.5, 95% CI: 3.8–260.9), NICU admission (aRR 2.44, 95% CI: 1.86–4.49), and early neonatal death (aRR 12.1, 95% CI: 4.22–33.98).

Conclusion: Hyperuricemia is common in preeclamptic women at MRRH and is associated with significantly higher rates of complications. Routine serum uric acid testing is recommended for early detection and timely intervention to improve maternal and neonatal health outcomes.

Abbreviations: ALT: Alanine aminotransaminase; AST: Aspartate aminotransaminase; CBC: Complete blood count; ENND: Early neonatal death; FSB: Fresh stillbirth; HMIS: Health Management Information System; IUFD: Intrauterine fetal death; LFTs: Liver function tests; MRRH: Mbarara Regional Referral Hospital; MUST: Mbarara University of Science and Technology; NICU: Neonatal Intensive Care Unit; OBS/GYN: Obstetrics and gynecology; REC: Research Ethics Committee; RFTs: Renal function tests; UA: Uric acid; UNCST: Uganda National Council for Science and Technology

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Introduction

Pre-eclampsia remains one of the leading cause of adverse perinatal outcomes, including preterm birth and perinatal death [1]. Globally, preeclampsia affects approximately four million women annually, resulting in the deaths of over 70,000 women and 500,000 babies [2]. At Mbarara Regional Referral Hospital, pre-eclampsia accounts for more than half (58.9%) of adverse perinatal outcomes, with 20.3% resulting in stillbirth [3].

Preeclampsia as associated with organ dysfunction including the kidneys and may result in raised uric acid levels [4]. The exact mechanism causing hyperuricemia in preeclampsia patients is not well understood but is believed to result from decreased renal excretion and increased production of uric acid by the ischemic placenta due to inadequate implantation [4,5]. Hyperuricemia leads to decreased production of nitric oxide and increased production of inflammatory mediators and vasoconstrictors (TXA and angiotensin II), resulting in reduced fetoplacental circulation [6].

Preeclampsia complicated by hyperuricemia has been associated with increased adverse maternal, fetal and perinatal outcomes [6]. Prior research shows that women with elevated serum uric acid levels ($>6\text{mg}/100\text{ml}$) are 4 times more likely to develop severe preeclampsia, 66 times more likely to have neonates with Apgar scores below 7, and 3 times more likely to deliver low birth weight babies compared to those with normal uric acid levels [7]. However, some studies argue that elevated uric acid levels are poor predictors of fetal outcomes [8].

Despite the substantial burden of preeclampsia and adverse perinatal outcomes in sub-Saharan Africa, there is still a lack of data on the relationship between hyperuricemia and these adverse outcomes in women with preeclampsia [9]. Therefore, this study set out to compare the incidence of adverse perinatal outcomes between women with and without hyperuricemia and to determine the association between hyperuricemia and adverse perinatal outcomes among women with preeclampsia at Mbarara Regional Referral Hospital.

Materials and methods

Study setting and design

We conducted a hospital-based prospective cohort study among pregnant women with preeclampsia from March 2024 to June 2024 at Mbarara Regional Referral Hospital (MRRH), a government-funded public referral and teaching hospital affiliated with Mbarara

University of Science and Technology in southwestern Uganda. The maternity department manages approximately 8,000 to 10,000 deliveries annually [10,11]. MRRH provides specialized care for mothers with high-risk pregnancies and newborns with complications, with a reported preeclampsia prevalence of 11.3% [11]. The hospital is equipped with an adult intensive care unit, operating theater, 24-h clinical laboratory, and a neonatal intensive care unit (NICU). These facilities ensure that patients receive the critical care they need [10,12].

Study population and eligibility criteria

We included all women diagnosed with preeclampsia at a gestational age of 26 weeks or more admitted to the High-risk Obstetrics unit of MRRH. Participants were enrolled at the time of admission. Preeclampsia was defined as new-onset hypertension accompanied by proteinuria ($\geq 2+$ protein on dipstick) without features of end-organ dysfunction [2,10]. Severe preeclampsia was defined as preeclampsia with or without proteinuria, associated with features of end-organ dysfunction such as severe hypertension (blood pressure $\geq 160/110\text{mmHg}$), persistent epigastric pain, persistent headache, visual disturbances, elevated creatinine levels, and elevated liver transaminases [10,13,14]. Eclampsia was defined by the occurrence of generalized tonic-clonic convulsions in individuals showing signs and symptoms of preeclampsia [10,15]. Women with intrauterine fetal death and those with multiple pregnancies were excluded from the study.

Sample size calculation and sampling

The sample size for this study was determined using the OpenEpi online software, taking into account the following assumptions: a confidence level of 95%, a power of 80%, an equal ratio of participants with hyperuricemia (exposed) to those with normal serum uric acid levels (non-exposed) at 1:1, and a projected threefold increase in the odds of adverse perinatal outcomes for the exposed group. These assumptions were informed by a previous study conducted in Umuahia, Nigeria [7]. With these parameters, the final minimum sample size required was determined to be 111 participants, following accounting for a 10% attrition rate ($100/1-0.1$) of the required sample size calculated to be 100 participants. Pregnant women with preeclampsia were consecutively sampled until the desired sample size was achieved.

Data collection procedure

Upon obtaining written informed consent from eligible participants, we used a pretested questionnaire to gather baseline sociodemographic, obstetric, medical, and clinical data. The collected data comprised demographic characteristics (such as age, marital status, residence, employment status, and referral history), obstetric characteristics (including gestational age, parity, number of antenatal visits, clinical features, and previous history of pre-eclampsia/eclampsia). Blood samples were then obtained from the study participants to assess serum uric acid levels and conduct additional laboratory tests (haemoglobin estimation, platelet count, creatinine level, and serum aspartate and alanine transaminases) upon their admission to the High-Risk Obstetrics ward. Participants were subsequently followed up for outcomes at the time of delivery and up to seven days postpartum. This information was entered into Research Electronic Data Capture (REDCap) tools [16].

Study variables

Data were collected by two research assistants using an interviewer-administered structured questionnaire. The primary exposure variable was hyperuricemia; defined as serum uric acid levels > 6.0 mg/dl [4,7,17,18].

The independent variables for this study encompassed maternal age, parity, employment, marital status, referral history, education, HIV serostatus, chronic hypertension, diabetes mellitus, severity of preeclampsia, gestational age, antenatal care attendance visits, previous history of preeclampsia, labor induction, delivery mode, and duration from admission to delivery.

The outcome variable was defined as one or more adverse perinatal outcomes, including fresh stillbirth, low birth weight (<2500 grams), low Apgar score (<7 at 5 min), NICU admission, and early neonatal death (within 7 days after birth).

Data management and analysis

The data were exported to STATA 17 (StataCorp, College Station, Texas, USA), cleaned and analyzed. Baseline characteristics were summarized as frequencies (percentages) for categorical variables, as means ($\pm$ standard deviations) for continuous variables. The proportion of hyperuricemia was reported as a percentage of the total study participants with preeclampsia.

The overall incidence of adverse perinatal outcomes was reported as a percentage of the total study participants with pre-eclampsia. We compared the incidence of adverse perinatal outcomes among women with

and without hyperuricemia using a chi-square test or Fisher's Exact test, as appropriate. The comparison was done for a composite outcome of 1 or more adverse perinatal outcomes and each adverse perinatal outcome. We performed multivariable modified Poisson regression analysis to assess the associations of hyperuricemia and adverse perinatal outcomes. We determined the association of hyperuricemia and composite adverse perinatal outcomes and separately determined the association between hyperuricemia and each adverse perinatal outcome. Each model was adjusted for maternal age, referral status, parity, gestational age, antenatal care attendance, mode of delivery, labor induction, duration from admission to delivery, sex of the baby, serum creatinine, thrombocytopenia, ALT and AST levels. We reported both crude and adjusted risk ratios and the corresponding 95% confidence intervals. Variables with a p-value of less than 0.05 were reported as significant.

Results

During the study period (March 2024 to June 2024), we screened 1580 women for inclusion in our study. Of these, 126 women were admitted with preeclampsia, and 111 were recruited into the study, while 15 mothers were excluded because they had intrauterine fetal death at admission.

Socio-demographic characteristics of study participants

The mean age of study participants was 28.3 ± 6.5 years, with the majority being married (84.7%), employed (66.7%) and referred from other facilities (57.7%) as shown in Table 1.

Obstetric and clinical characteristics of the study participants

The majority were multiparous (52.3%), had gestational ages between 37-42 weeks (61.3%), and delivered vaginally (58.6%). Most (68.5%) had attended at least 4 ANC visits, and 15.3% had a prior history of preeclampsia from the previous pregnancy (Table 2).

Proportion of hyperuricemia among women with pre-eclampsia

The proportion of hyperuricemia among women with pre-eclampsia at MRRH was 38.7% ($n=43$) (95% Confidence Interval: 30.1%-48.2%).

Table 1. Socio-demographic and medical characteristics.

Characteristics	Hyperuricemia			P value
	Total (N=111)	Yes (N=43)	No (N=68)	
Age (years) mean (SD)	28.29 (6.47)	29.28 (6.95)	27.68 (6.12)	0.200
Maternal age category				0.260
<20	11 (9.9%)	4 (9%)	7 (10%)	
20-34	80 (72.1%)	28 (65%)	52 (76%)	
>34	20 (18.0%)	11 (26%)	9 (13%)	
Residence				0.800
Urban area	61 (55.0%)	23 (53%)	38 (56%)	
Rural area	50 (45.0%)	20 (47%)	30 (44%)	
Marital status				0.820
Unmarried	17 (15.3%)	7 (16%)	10 (15%)	
Married	94 (84.7%)	36 (84%)	58 (85%)	
Employed				0.490
No	37 (33.3%)	16 (37%)	21 (31%)	
Yes	74 (66.7%)	27 (63%)	47 (69%)	
Education level				0.280
None	2 (1.8%)	2 (5%)	0 (0%)	
Primary	54 (48.6%)	20 (47%)	34 (50%)	
Secondary	35 (31.5%)	12 (28%)	23 (34%)	
Tertiary	20 (18.0%)	9 (21%)	11 (16%)	
Religion				0.070
Catholic	47 (42.3%)	17 (40%)	30 (44%)	
Anglican	58 (52.3%)	21 (49%)	37 (54%)	
Moslem	6 (5.4%)	5 (12%)	1 (1%)	
Referral status				0.210
No	47 (42.3%)	15 (35%)	32 (47%)	
Yes	64 (57.7%)	28 (65%)	36 (53%)	
Chronic hypertension				0.160
No	91 (82.0%)	38 (88%)	53 (78%)	
Yes	20 (18.0%)	5 (12%)	15 (22%)	
Diabetes mellitus				0.640
No	107 (96.4%)	41 (95%)	66 (97%)	
Yes	4 (3.6%)	2 (5%)	2 (3%)	

*P value < 0.05.

Abbreviations. SD, standard deviation.

Comparison of adverse perinatal outcomes among women with or without hyperuricemia in women with preeclampsia

The overall incidence of adverse perinatal outcomes was 55.9% (62/111) of all study participants. Adverse perinatal outcomes were more common among women with hyperuricemia (88%, 38/43) compared to those without hyperuricemia (35%, 24/68). This was similar for fresh stillbirth (21% versus 0%), low birth weight (49% versus 26%), low Apgar score < 7 at 5 min (26% versus 1%), NICU admission (76% versus 26%) and early neonatal death (32% versus 0%), $p < 0.05$ (Table 3).

Association of hyperuricemia with adverse perinatal outcomes

Women with hyperuricemia had an increased risk of having 1 or more adverse perinatal outcomes (adjusted risk ratio [aRR] 2.42, 95% CI: 1.54-3.80), fresh stillbirth (aRR 3.14, 95% CI: 1.79-5.48), 5 min Apgar score < 7 (aRR 31.5, 95% CI: 3.8-260.9), admission to NICU (aRR 2.44, 95% CI: 1.86-4.49) and early neonatal death (aRR 12.1, 95% CI: 4.22-33.98),

Table 2. Obstetric and clinical characteristics.

Characteristics	Hyperuricemia			P value
	Total (N=111)	Yes (N=43)	No (N=68)	
Gravidity				0.540
Primigravida (1)	32 (28.8%)	10 (23%)	22 (32%)	
Multigravida (2-4)	58 (52.3%)	25 (58%)	33 (49%)	
Grand multipara (>5)	21 (18.9%)	8 (19%)	13 (19%)	
Gestational age (weeks)				0.002*
<34	18 (16.2%)	16 (25.8%)	2 (4.1%)	
≥34	93 (83.8%)	46 (74.2%)	47 (95.9%)	
ANC visits				0.023*
<4	35 (31.5%)	19 (44%)	16 (24%)	
≥4	76 (68.5%)	24 (56%)	52 (76%)	
Mode of delivery				0.390
Vaginal	65 (58.6%)	23 (53%)	42 (62%)	
Cesarean	46 (41.4%)	20 (47%)	26 (38%)	
Fetal heart rate at enrollment (bpm)				0.170
<120	7 (6.3%)	5 (12%)	2 (3%)	
120-160	102 (91.9%)	37 (86%)	65 (96%)	
>160	2 (1.8%)	1 (2%)	1 (1%)	
Prior history of preeclampsia				0.160
No	94 (84.7%)	39 (91%)	55 (81%)	
Yes	17 (15.3%)	4 (9%)	13 (19%)	
Malaria in current pregnancy				0.800
No	89 (80.2%)	35 (81%)	54 (79%)	
Yes	22 (19.8%)	8 (19%)	14 (21%)	
Proteinuria				0.013*
≤1+	17 (15.3%)	2 (5%)	15 (22%)	
≥2+	94 (84.7%)	41 (95%)	53 (78%)	
AST (u/l) mean (SD)	48.0 (67.5)	70.4 (103.3)	33.9 (16.5)	0.005*
ALT (u/l) mean (SD)	39.6 (34.6)	50.9 (51.4)	32.4 (13.2)	0.006*
Creatinine (mg/dl) mean (SD)	1.60 (6.3)	2.77 (10.1)	0.86 (0.4)	0.021
Urea (mg/dl) mean (SD)	20.39 (14.6)	26.80 (17.2)	16.35 (11.0)	<0.001*
Hemoglobin (g/dl) mean (SD)	12.33 (1.56)	12.33 (2.06)	12.34 (1.15)	0.990
Platelet count (x10 ³ cells/uL) mean (SD)	223.63(86.23)	202.62(103.15)	236.91(71.23)	0.041*

*P value < 0.05.

Abbreviations. ANC, antenatal care; AST, aspartate transaminase; ALT, alanine transaminase; SD, standard deviation.

Table 3. Comparison of adverse perinatal outcomes among women with or without hyperuricemia in women with preeclampsia at MRRH.

Adverse perinatal outcome	Hyperuricemia			P value
	Total (N=111)	Yes (N=43)	No (N=68)	
Composite adverse perinatal outcome (≥1)	62 (55.9%)	38 (88%)	24 (35%)	<0.001*
Fresh stillbirth	9 (8.1%)	9 (21%)	0 (0%)	<0.001*
Low birth weight	39 (35.1%)	21 (49%)	18 (26%)	0.016*
Low 5-minute Apgar score (<7)*	10 (9.8%)	9/34 (26%)	1/68 (1%)	<0.001*
Admitted to NICU [#]	44 (43.1%)	26/34 (76%)	18/68 (26%)	<0.001*
Early neonatal death [#]	11 (10.8%)	11/34 (32%)	0 (0%)	<0.001*

*P value < 0.05.

Abbreviations. NICU, neonatal intensive care unit.

[#]n=102 (less of fresh still births).

compared to those without hyperuricemia. Only low birth weight was not independently associated with hyperuricemia (Table 4).

Table 4. Association of hyperuricemia with adverse perinatal outcomes among women with preeclampsia.

Variables	≥1 adverse perinatal outcome		Unadjusted analysis		Adjusted analysis	
	Yes (N=62)	No (N=49)	Crude RR (95% CI)	P value	Adjusted RR (95% CI)	P value
Hyperuricemia						
No	24 (39%)	44 (90%)	Ref.		Ref.	
Yes	38 (61%)	5 (10%)	2.50[1.78,3.52]	<0.001*	2.21[1.51,3.23]	<0.001*
Maternal age category						
<20	6 (10%)	5 (10%)	1.01[0.56,1.81]	0.960	0.96[0.54,1.69]	0.898
20-34	43 (69%)	37 (76%)	Ref.		Ref.	
>34	13 (21%)	7 (14%)	1.21[0.83,1.77]	0.330	1.03[0.60,1.78]	0.893
Referred						
No	21 (34%)	26 (53%)	Ref.		Ref.	
Yes	41 (66%)	23 (47%)	1.43[0.99,2.07]	0.056	1.20[0.79,1.83]	0.383
Gestational age (weeks)						
<34	16 (26%)	2 (4%)	1.80[1.38,2.34]	<0.001*	1.33[0.86,2.05]	0.198
≥34	46 (74%)	47 (96%)	Ref.		Ref.	
ANC visits						
<4	25 (40%)	10 (20%)	1.47[1.07,2.01]	0.016*	0.99[0.66,1.49]	0.967
≥4	37 (60%)	39 (80%)	Ref.		Ref.	
Mode of delivery						
Vaginal	39 (63%)	26 (53%)	Ref.		Ref.	
Caesarean	23 (37%)	23 (47%)	0.83[0.58,1.19]	0.310	0.82[0.54,1.18]	0.276
Labor induction						
No	53 (85%)	42 (86%)	Ref.		Ref.	
Yes	9 (15%)	7 (14%)	1.01[0.63,1.61]	0.973	0.94[0.59,1.63]	0.744
Time from admission to delivery						
Within 24 h	37 (60%)	35 (71%)	Ref.		Ref.	
24-48 h	20 (32%)	12 (25%)	0.72[0.43,1.21]	0.216	0.88[0.45,1.72]	0.714
>7 days	5 (8%)	2 (4%)	0.88[0.51,1.51]	0.629	0.98[0.51,1.87]	0.949
Creatinine (mg/dl)						
<1.1	42 (68%)	44 (90%)	Ref.		Ref.	
≥1.1	20 (32%)	5 (10%)	1.64[1.22,2.19]	0.001*	1.24[0.78,1.97]	0.359
Urea (mg/dl)						
<50	59 (95%)	47 (96%)	Ref.		Ref.	
≥50	3 (5%)	2 (4%)	1.08[0.51,2.26]	0.842	0.68[0.32,1.42]	0.301
AST (u/l)						
<70	53 (85%)	47 (96%)	Ref.		Ref.	
≥70	9 (15%)	2 (4%)	1.54[1.10,2.15]	0.011*	1.30[0.49,3.50]	0.593
ALT (u/l)						
<70	54 (87%)	48 (98%)	Ref.		Ref.	
≥70	8 (13%)	1 (2%)	1.68[1.24,2.25]	0.001*	0.86[0.30,2.46]	0.775
Hemoglobin (g/dl)						
<11	9 (15%)	2 (4%)	1.54[1.10,2.15]	0.011*	0.77[0.46,1.28]	0.318
≥11	53 (85%)	47 (96%)	Ref.		Ref.	
Platelet count (x10 ³ /ul)						
≥100	56 (90%)	49 (100%)	Ref.		Ref.	
<100	6 (10%)	0 (0%)	1.88[1.57,2.24]	<0.001*	0.7[0.28,1.78]	0.459

*P value < 0.05.

Abbreviations. RR, risk ratio; ANC, antenatal care; AST, aspartate transaminases; ALT, alanine transaminases.

Discussion

This prospective cohort study evaluated the impact of hyperuricemia on neonatal outcomes among women with preeclampsia at Mbarara Regional Referral Hospital (MRRH). Women with elevated uric acid levels experienced significantly higher rates of adverse perinatal outcomes, such as fresh stillbirths, low Apgar scores, NICU admissions, and early neonatal deaths. These results emphasize the importance of routine serum uric acid testing for early detection and timely intervention, which could improve neonatal health in low-resource settings.

The incidence of adverse perinatal outcomes among women with preeclampsia in our study was substantial at 55.9%. This finding aligns with evidence from other

studies conducted in comparable settings [3,19]. For instance, a study conducted at the same hospital half a decade ago, showed an incidence of 58% [3], and in southern Ethiopia found that adverse perinatal outcomes occurred in 61.8% of women with preeclampsia [19]. Similarly, research from Zimbabwe reported a high incidence of adverse outcomes in women with severe preeclampsia and eclampsia [20]. These studies collectively underscore the significant risk that preeclampsia poses to both maternal and neonatal health, particularly in low-resource settings where access to comprehensive prenatal care is often limited. The high incidence of adverse outcomes highlights the urgent need for improved monitoring, early detection, and intervention strategies to mitigate these risks. Routine

serum uric acid testing emerges as a potential intervention.

Our study revealed that women with hyperuricemia had a higher likelihood of encountering multiple adverse perinatal outcomes, such as fresh stillbirths, early neonatal deaths, NICU admissions, and low Apgar scores, in comparison to those without hyperuricemia. The rate of fresh stillbirth was consistent with similar studies conducted in Nigeria and Tanzania [5,7], respectively. This could be attributed to the fact that these studies were conducted in similar settings—tertiary institutions in low-income countries—with comparable standards of perinatal care and among a similar population of women with preeclampsia. Hyperuricemia reduces nitric oxide production while increasing advanced inflammatory mediators, such as cytokines, interleukins, fractalkine and MIP-1 β , alongside vasoconstrictors like TXA & angiotensin II. These changes impair fetoplacental circulation, contributing to intrauterine growth restriction [6,21].

The rate of neonatal intensive care unit (NICU) admission was consistent with similar studies conducted in Iraq and Tanzania [5,22], respectively. This could be related to obstetric complications such as severe preeclampsia, which may result in preterm termination of pregnancy. These preterm deliveries often lead to complications of prematurity, such as low Apgar scores, necessitating NICU admission.

Low birth weight was similar to studies done in India and Korea [23,24], respectively. This can be related to the early termination of pregnancy due to preeclampsia or impaired placental function. Nevertheless, Apgar score < 7 at 5 min was similar to another study done in Vietnam and Nepal [17,25] respectively. However, the reason could be that elevated uric acid levels can lead to a reduction in nitric oxide, causing vasoconstriction [6].

In this study, hyperuricemia was independently associated with adverse perinatal outcomes. Women with hyperuricemia had a 2.5 times increased risk of one or more adverse perinatal outcomes compared to those without hyperuricemia.

Our finding is similar to what was found in a cohort study done in India that showed that hyperuricemia was 1.5 times more likely to be associated with adverse perinatal outcomes. Similarly, findings from a study conducted in Nigeria showed that hyperuricemia increased the likelihood of fresh stillbirth by 20.8 times, low Apgar score (<7) at 5 min by 10.4 times and admission to NICU by 66 times [7].

This was similar to another study in Nigeria that reported a 2.9 times higher risk of NICU admission

among women with hyperuricemia [26]. Another study conducted in Vietnam also reported a 1.8 times higher likelihood of fresh stillbirth and 7.8 times higher risk of early neonatal death [17]. While the study in Ghana reported that women with hyperuricemia were 3.2 times more likely to have low birth weight neonates [26].

The association of hyperuricemia and adverse perinatal outcomes noted in our study and the other comparable studies is as a result of uric acid being a potent mediator of inflammation in vascular smooth muscle and, increased serum uric acid directly promotes oxidative stress with the production of reactive oxygen radicals and also increases the concentration of monocytes which then produce pro-inflammatory cytokines such as interleukins, tumor necrosis factor-alpha (TNF-alpha) and thromboxane A2 [27]. The pro-inflammatory factors then lead to endothelial dysfunction and contribute to ischemia-reperfusion injury, compromising blood and nutrient supply to the fetus [4]. This leads to placental insufficiency, fetal hypoxia, intrauterine growth restriction which ultimately contributes to intrauterine fetal death [28]. The placental insufficiency may also be associated with fetal distress, low Apgar scores and ultimately increased rates of NICU admissions and early neonatal deaths [5,26].

This study's strengths lie in its focus on a critical high-risk group of preeclamptic women, who face significant adverse perinatal outcomes in low-resource settings. It provides valuable insights into the impact of hyperuricemia on perinatal outcomes and proposes actionable solutions, such as routine serum uric acid testing, to enhance early detection and intervention efforts.

Our study, however, was not without limitations. It was conducted at a single tertiary referral hospital, which may limit the generalizability of the findings to other settings. Additionally, we excluded women with intrauterine fetal death, potentially underestimating the burden of hyperuricemia and limiting the understanding of the full spectrum of outcomes related to hyperuricemia in preeclamptic women. Another limitation was the lack of evaluation of serum inflammatory markers, complete blood cell-based indices (such as eosinophil counts), and Doppler ultrasound parameters which could have provided valuable insights into the mechanisms linking hyperuricemia to adverse perinatal outcomes. Finally, our focus on seven-day perinatal outcomes without long-term follow-up misses potential impact of hyperuricemia on neonatal health over-time. Future research should aim to address these gaps.

Conclusion

The incidence of adverse perinatal outcomes among women with preeclampsia was notably high. Women with preeclampsia and hyperuricemia experienced a higher incidence of adverse perinatal outcomes compared to those without hyperuricemia. This association highlights the importance of hyperuricemia as a significant risk factor for adverse perinatal outcomes in preeclampsia. We recommend routine testing of serum uric acid levels in preeclamptic patients, along with consistent neonatologist assessment of all neonates born to women with hyperuricemia. We additionally recommend a longer prospective study to investigate their long-term outcomes.

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Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of Mbarara University of Science and Technology (Reference number: MUST REC-2024-1347) and the Uganda National Council for Science and Technology (UNCST) (HS4536ES). Written informed consent was obtained from all study participants. All principles of data transfer and protection of human research participants outlined in the Declaration of Helsinki were observed.

Authors' contributions

CRedit: **Hani Omar Wehlie**: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft; **Yarine Fajardo Tornos**: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – review & editing; **Julius Businge**: Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing; **Onesmus Byamukama**: Conceptualization, Investigation, Methodology, Validation, Writing – review & editing; **Musa Kayondo**: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing; **Paul Kato Kalyebara**: Conceptualization, Investigation, Methodology, Validation,

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Availability of data and materials

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