SERUM URIC ACID LEVELS AS PREDICTOR OF PERINATAL OUTCOMES AMONG PATIENTS WITH PRE-ECLAMPSIA ADMITTED AT MUHIMBILI NATIONAL HOSPITAL

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Department of Physiology

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By

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A Dissertation Submitted in Partial Fulfillment of Requirement for the Degree of Master of Science in Physiology

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **"Serum uric acid levels as predictor of perinatal outcome among patients with pre-eclampsia hospitalized at Muhimbili National Hospital"** in partial fulfilment of the requirement for the degree of Master of Science in Physiology Muhimbili University of Health and Allied Sciences.

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……..

Date

DECLARATION AND COPYRIGHT

I, **Calvin Elisante Ulomi**, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature:……Date: ……

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ABSTRACT

Background: Preeclampsia is one of the hypertensive disorders of pregnancy with significantly high morbidity and mortality to both mother and fetus/neonate. Globally it complicates 2%-8% of all pregnancies whereas in Tanzania it accounts for 19.9% of maternal mortality.

Uric acid is a metabolic end product of purines which is commonly found to be elevated in pre-eclamptic patients, but yet its utility in predicting perinatal outcome is still controversial. Serum uric acid is among the routine laboratory investigations done in pre-eclamptic patients admitted at Muhimbili National Hospital (MNH) maternity ward.

Aim of the study: To determine the utility of serum uric acid levels in predicting perinatal outcome among pre-eclamptic patients hospitalized at MNH.

Methodology: This was a hospital based cross-sectional study which involved pre-eclamptic women admitted at MNH maternity ward. The proportion of pre-eclamptic patients with hyperuricemia was determined and then association between serum uric acid and neonatal outcome was assessed. Univariate and multivariate logistic regression was used to identify the association between independent variables (uric acid, Hb, age, parity, pre-eclampsia grade etc) and the perinatal outcomes (birth weight, Apgar score, stillbirth, preterm delivery). P value of <0.05 was considered statistically significant.

Results: Among 268 recruited participants 78.7% had raised serum uric acid, whereas an overall mean serum uric acid level was 0.42±0.09mmol/L. The magnitude of adverse perinatal outcome among pre-eclamptic patients was 19% stillbirth, 68.7% low birth weight, 12.3% Neonatal Intensive Care Unity (NICU) admission, 26.9% low Apgar score and 70.9% for preterm delivery.

In adjusted model raised serum uric acid level (≥0.35mmol/L) once adjusted for pre-eclampsia grade, parity, maternal age, hemoglobin level and delivery mode, it revealed an increased risk in low birth weight (aOR 2.16, 95% CI 1.11-4.20), stillbirth (aOR 11.29, 95%CI 1.49-85.87), low Apgar score (aOR 4.63, 95%CI 1.57-13.71) and preterm delivery (aOR 2.02, 95%CI 1.03-3.95).

Conclusion: Raised serum uric acid is a good predictor of adverse perinatal outcome among hospitalized patients with pre-eclampsia at MNH**.**

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ABBREVIATIONS

ALT	Alanine aminotransferase
ANC	Antenatal Clinic
AST	Aspartate aminotransferase
DM	Diabetes mellitus
FBP	Full blood picture
GA	Gestational age
GFR	Glomerular filtration rate
HTN	Hypertension
IUFD	Intrauterine fetal death
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Heath and Allied Sciences
NICU	Neonatal Intensive Care Unit
sEng	Soluble endoglin
sF1t1	Soluble fms-like tyrosine kinase-1
SUA	Serum uric acid
XO	Xanthine oxidase

DEFINITION OF KEY TERMS

Preeclampsia: pregnancy related hypertensive disorder after 20th week of gestation age, denoted by new onset hypertension (140/90 mmHg measured 6 hours apart) and proteinuria with subsequent renal, hepatic, neurological, cardiovascular and respiratory dysfunction.

Perinatal period: a period immediately before and after delivery or a period between 28 weeks of GA and 7 days post-delivery.

Adverse Perinatal outcome: observed unfavorable fetal and neonatal outcomes during the perinatal period. (i.e. stillbirth, premature delivery, early neonatal death, small for gestation age, low birth weight).

Uric acid: a metabolic waste derived from purine breakdown.

Proteinuria: a condition characterized by presence of greater than normal amounts of protein in the urine **(**i.e. greater than 150mg per day).

Intrauterine fetal death (IUFD): a fetal death that occurs after 20 weeks of gestation but before birth and for unknown GA a fetus that weighs ≥350g.

Stillbirth: a delivery of a baby who has died after 20 weeks of gestation age.

Early neonatal death: death of a live born baby before completing 7 days of extra uterine life.

Premature birth: birth before 37 completed weeks of gestation.

Low birth weight: birth weight below 2500g.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Preeclampsia is a pregnancy related hypertensive disorder after 20th week of gestation and it is denoted by new onset of hypertension and proteinuria. Preeclampsia can affect multiple organ/system with subsequent renal, hepatic, neurological, cardiovascular and respiratory dysfunctions as a result of microangiopathy. Alongside maternal complications, it is also associated with fetal/neonatal complications like preterm birth, IUFD or early neonatal death (1, 2).

The main cause of preeclampsia is not clearly known, though there are some postulations on its pathogenesis. It is thought to result from abnormal trophoblastic invasion of placenta which is later followed by generalized maternal endothelial dysfunction (3). The abnormal placentation may result from mechanisms like genetic factors, immune abnormalities and oxidative stress leading to the upregulation of antiangiogenic factors (sFlt1, sEng) and inflammatory mediators. These circulating factors attributed to placenta, has a role in clinical syndrome sequelae (3, 4).

The main risk factors related to preeclampsia are previous preeclampsia, multiple pregnancy, nulliparity, preexisting HTN, DM, family history of preeclampsia, obesity, antiphospholipid syndrome and chronic kidney disease (5).

Uric acid as a metabolic byproduct of purine, its serum concentrations can be influenced by diet (i.e. high protein, fructose) alcohol consumption, dysfunctional kidney and high cell turnover. Besides that, experimental and clinical trials have shown a causative role in metabolic, renal and cardiovascular diseases, serum uric acid levels have protective role when acutely elevated (6, 7).

Uric acid is mainly derived from the metabolism of both intrinsic and extrinsic pathways, whereby the last two steps (xanthine and hypoxanthine) are catalyzed by an enzyme xanthine oxidoreductase, i.e. by catalyzing oxidation of hypoxanthine to form xanthine followed by subsequent oxidation of xanthine to form uric acid (7).

In human being the normal serum uric acid levels range from 1.5mg/dL to 6.5mg/dL with a solubility limit of 6.8mg/dL. Unlike other mammals, humans lack the enzyme uricase required for oxidation of uric acid to allantoin which is more soluble (8).

Serum uric acid levels is commonly found elevated among preeclamptic women. The mechanism leading to hyperuricemia in preeclamptic patients is not well known but it is thought to be from decreased excretion by the kidneys and increased generation of uric acid by the ischemic placenta as a sequela of shallow implantation (9).

There is evidence that the ischemic placenta is responsible for an increase in enzyme xanthine oxidase (form of xanthine oxidoreductase) and the metabolism of adenosine triphosphate forming adenosine and xanthine. Xanthine is then acted upon by xanthine oxidase to form uric acid and other oxidants (10).

These metabolites from the ischemic tissue are responsible for glomerular vasoconstriction and endotheliosis, resulting in reduced GFR and raise in uric acid reabsorption by proximal convoluted tubules hence raised serum uric acid concentration (11).

For uncomplicated pregnancies usually there is a decrease in serum uric acid levels by 25%-35% during early pregnancy followed by gradual increase throughout until it returns to its normal levels at term. These pregnancy-related variations in serum uric acid levels are proposed to result from alteration in renal handling of uric acid during pregnancy (12). There is an existing controversy as to whether elevated serum uric acid levels is a strong or poor predictor to perinatal outcome among pre-eclamptic women (13, 14).

1.2 Literature review

Pre-eclampsia is among the global leading threat in maternal health as it poses significant levels of morbidity and mortality to both mother and fetus. Serum uric acid is commonly found elevated in pre-eclamptic patients compared to those with normal pregnancy. A study done India shows a mean serum uric acid levels of 7.65±0.81mg/dl (15). Again a study in India shows a mean serum uric acid among pre-eclamptic women of 6.374±1.43mg/dl (16). Another study done in Iraq shows a mean serum uric acid level among pre-eclamptic women to be7.68±0.79mg/dl (17) .

Uric acid and gestational age

Pre-eclamptic patients tend to have a progressive increase in serum uric acid levels with an increase in gestational age. However, this does not apply to normal pregnancy as they tend to have a decrease in serum uric acid levels in first trimester followed by gradual increase to the normal levels in 3rd trimester. Study done in United States shows a mean serum uric acid concentrations at different GA, whereby the mean serum uric acid concentration of gestational age groups (15 to 24.9weeks), (25 to 34.9weeks) and (35weeks to term) was found to be (4.0±1.2mg/dl), (5.5±1.2mg/dl) and (6.9±1.4mg/dl) respectively (12).

Uric acid and birth weight

Increased low birth weight has been linked with elevated maternal serum uric acid levels. A study done in India shows that an increase in serum uric acid levels has a significant increase in low birth weight babies. However, 6.37mg/dl was found to be the mean serum uric acid concentration in predicting perinatal complications (16). Also, another study in Iraq shows 63.77% of babies with low birth weight were born from preeclamptic women with hyperuricemia (18).

Since serum uric acid is among biochemical markers in pre-eclampsia it can be of great prognostic and diagnostic value, by having its cutoff point mean value. A study in South Korea 2019 found 6.35mg/dl to be an optimal serum uric acid cutoff point in predicting low

birth weight, whereby there is a significant increase in low birth weight with SUA raise above 6.35mg/dl (2).

Serum uric acid and pre-term deliveries

Elevated serum uric acid levels have been generally associated with adverse perinatal outcomes. Study done by Livingstone JR, et al. revealed a significance of maternal serum uric acid in predicting perinatal outcome (19). A study done in Vietnam shows that with a serum uric acid concentration of ≥393 μmol/L there is increased perinatal complications like preterm deliveries and neonatal death (20).

Uric acid and IUFD

For decades now there is inconsistent findings on the significance of maternal serum uric acid level from different studies in predicting perinatal outcomes. One study in India studied two groups of women with SUA levels above and below 6mg/dl and found out those with SUA ≥6mg/dl show adverse perinatal outcomes, with increased risk of IUFD by 20fold, IUGR by 4fold compared to those with SUA <6mg/dl(21) (22).

Serum uric acid is an important biomarker in predicting onset, severity of pre-eclampsia and outcomes. Study in Nigeria shows high serum uric acid has significant high predictive value in pre-eclampsia severity and outcome (14).

1.3 Conceptual framework

Pre-eclampsia can lead to adverse perinatal outcomes, at the same time risk factors may have an impact in causation of both pre-eclampsia and adverse perinatal outcomes. After developing pre-eclampsia there are several biomarkers which in addition to clinical features, they are used in diagnosing and denoting severity of the disease. These biomarkers are the independent variables and uric acid is the biomarker of interest. Lastly after delivery there will be an assessment of the new born for the perinatal outcomes which are the dependent variables.

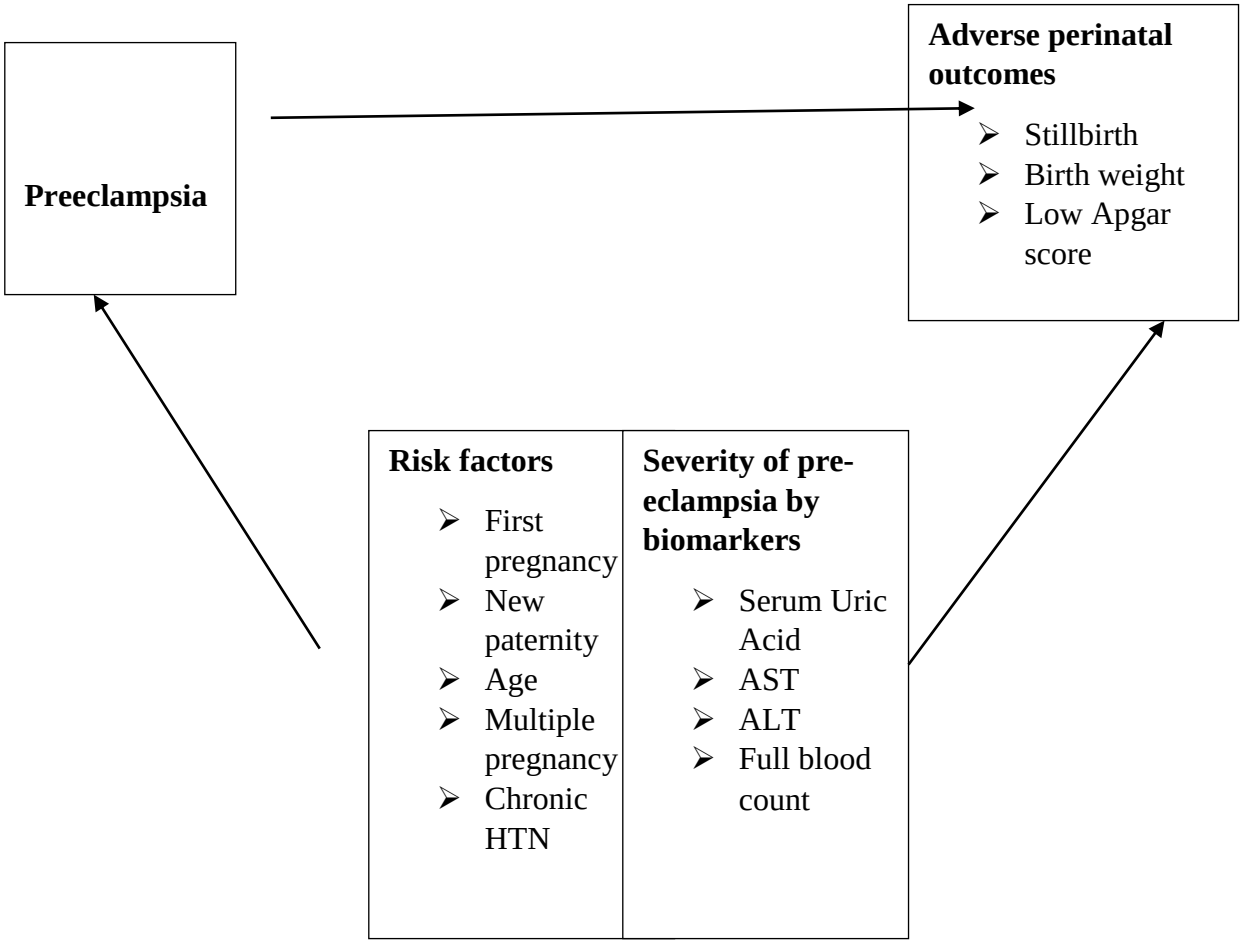


Figure 1: A self-generated conceptual framework showing interrelationship of pre-eclampsia, risk factors, biomarkers and perinatal outcome

1.4 Problem statement

Preeclampsia remains a maternal health concern globally due to its contribution to maternal morbidity and mortality, complicating 2%-8% of all pregnancies (23, 24). In Tanzania it accounts for 19.9% of maternal mortality (23). Elevated serum uric acid levels have been a common finding in preeclampsia (19), yet its utility in predicting adverse perinatal outcome is not reported in our settings.

1.5 Study rationale

Basically, delivery is mainstay treatment for preeclampsia, but some cases can be managed expectantly with increased maternal and fetal monitoring, maternal blood pressure control (19).

Due to variation in genetic make-up metabolism of purines to form uric acid will also vary hence the need to conduct the study at our setting. Maternal biochemical findings including serum uric acid levels are among the predictors of fetal outcome.

The findings of this study will enable identification of pre-eclamptic mothers who may benefit from conservative management vs. immediate delivery hence improvement in intervention plans for proper quality of care among pre-eclamptic patients at MNH and Tanzania in general.

1.6 Research questions

1. What’s the proportion of patients with raised serum uric acid among women with pre-eclampsia?
2. To what extent do pre-eclampsia have impact to adverse perinatal outcome?
3. Do the serum uric acid levels have a role in predicting likelihood to develop adverse fetal/neonatal outcome?

1.7 Objectives

1.7.1 Broad objective:

To determine the utility of serum uric acid levels in predicting perinatal outcome among women with pre-eclampsia hospitalized at Muhimbili National Hospital.

1.7.2 Specific objectives:

1. To determine the proportion of women with pre-eclampsia found to have raised serum uric acid levels among patients admitted at MNH.
2. To determine the proportion of adverse neonatal outcomes born to women with pre-eclampsia at MNH.
3. To determine the association between serum uric acid levels and perinatal outcome among women with pre-eclampsia admitted at MNH.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

This was a hospital-based cross-sectional study to determine the utility of serum uric acid levels in predicting perinatal outcome among pre-eclamptic patients at MNH. The study was conducted for a period of four months.

2.2 Study area

This study was conducted at Muhimbili National Hospital (MNH) maternity wards. MNH is the largest tertiary hospital in Tanzania which serves as a referral hospital from lower health facilities in Dar es Salaam, nearby regions and across the country. Maternity department is one among the largest clinical departments with an average of 810 women deliveries per month. The department is composed of two maternity blocks. The first block consists of 5 obstetric wards, one labor ward and one ICU ward. The second block consists of antenatal clinic, post-delivery ward for mothers who have been previously assessed and are stable, mother and babies on Kangaroo care program and mothers with sick babies admitted in neonatal units. Within the department there is a special preeclampsia/eclampsia ward (ward 35) with a 21-bed capacity.

Patients are admitted through labor ward and directed to respective ward depending on the diagnosis, plan of management and delivery. There is always available medical team attending all patients, with a priority to emergency cases followed by stable ones. The on call medical team involves 1 intern, 2-3registrars/residents, one specialist and a consultant. There are also two shifts of nurses, each shift lasting for 12 hours.

Pre-eclamptic patients are usually attended by admitting doctor, reviewed by a specialist, blood sample taken to the laboratory by a nurse attendant and laboratory results will be available within six hours. The routine investigations done to pre-eclamptic patients include uric acid, urea, creatinine, FBP, AST and ALT. After delivery if clinically stable they are transferred from ward 35 to ward 32, 33, 38 and 39.

2.3 Study population

The study involved pregnant women admitted and delivered at MNH maternity ward.

2.4 Inclusion and Exclusion criteria

2.4.1 Inclusion criteria

Pre-eclamptic patients admitted at ≥28 weeks of GA and delivery at MNH maternity ward.

2.4.2 Exclusion criteria

Pre-existing cardiovascular diseases, Diabetes Mellitus or Renal failure

2.5 Variables

2.5.1 Dependent variables: birth weight, Apgar score, NICU admission and stillbirth

2.5.2 Independent variables: uric acid, AST, ALT, Hb, urea, creatinine, age, parity, severe pre-eclampsia

2.6 Sample size calculation

A sample size of 268 was obtained by using Cochran formula, whereby the estimated prevalence of preeclampsia was 19.5% (25) and assumptions being 95% confidence level, 5% margin of error.

$$n = \frac{Z^2 P(1-P)}{e^2}$$

Where;

n=sample size

Z=confidence level 1.96 for 95%

P=estimated prevalence of pre-eclampsia 19.5%(25)

e=0.05

$n=(1.96)^2 x 0.195(1-0.195)/(0.05)^2$

n=241

Taking a non-response rate of 10% into consideration

N= 268

Therefore, this study used a sample size of 268 pre-eclamptic women.

2.7 Sampling procedure and recruitment of participants

All files of patients who were admitted in the obstetric ward were identified from the admission book. The files of patients diagnosed to be pre-eclamptic were taken for data collection. Consecutive sampling technique was used to enroll pre-eclamptic women who have immediately given birth and on admission were admitted as pre-eclamptic patients at ≥28 weeks of GA. The patients who met inclusion criteria were recruited until the sample size of 268 was reached.

2.8 Data collection procedure

Data collection began after obtaining Ethical clearance whereby the Principal Investigator together with two trained research assistants used a well-developed Case Report Forms.

The data collection tool entailed three main parts which are socio-demographic data, perinatal information and laboratory investigations. Socio-demographic details included age, gestational age, parity, education level, occupation, ANC, onset of symptoms, past medical history (HTN, DM, and Preeclampsia) and family history. Information of the newborn involved birth weight, Apgar score, NICU admission, mode of delivery and birth status (dead/alive). Last part included laboratory investigation results which entail serum uric acid level, AST, ALT, Hb, platelets, urea and creatinine.

During data collection a researcher and trained research assistants were going through registry book in ward 35 and other wards to identify pre-eclamptic patients delivered at ≥28 weeks GA, trace the files and record the information to the case report form.

2.9 Data management and analysis

Data was entered and checked for consistency and missing information. Thereafter it was analyzed by using Statistical Package for Social Sciences (SPSS) version 23 computer software**.** Continuous variables like uric acid, birth weight and age were summarized into frequencies, mean and standard deviation. Categorical variables and uric acid were assessed using chi square test(X^2). Univariate logistic regression was used to identify the association

between categorical independent variables and the perinatal outcomes (birth weight, Apgar score, stillbirth); then to control for confounding factors those factors which were significantly associated, were subjected to multivariate logistic regression. P value of <0.05 was considered statistically significant.

2.10 Dissemination plan

Dissertation will be prepared and submitted to MUHAS directorate of postgraduate studies, director of library and posted to MUHAS repositories. Study findings will be presented on local conferences and manuscript will be submitted to peer review journals for publication.

2.11 Ethical considerations

The study was conducted after getting an ethical clearance from the Research and Publication Committee of Muhimbili University of Health and Allied Sciences and permission from Muhimbili National Hospital authorities. There were no major ethical issues since the participants were recruited after delivery and information obtained from their records.

CHAPTER THREE

3.0 RESULTS

During the study period there were 4505 admissions, whereby 437 patients were pre-eclamptic. Among the admitted pre-eclamptic patients, 169 participants did not fulfil the eligibility criteria due to missing information. Therefore, 268 participants were recruited, data analysed and the results presented in response to objectives.

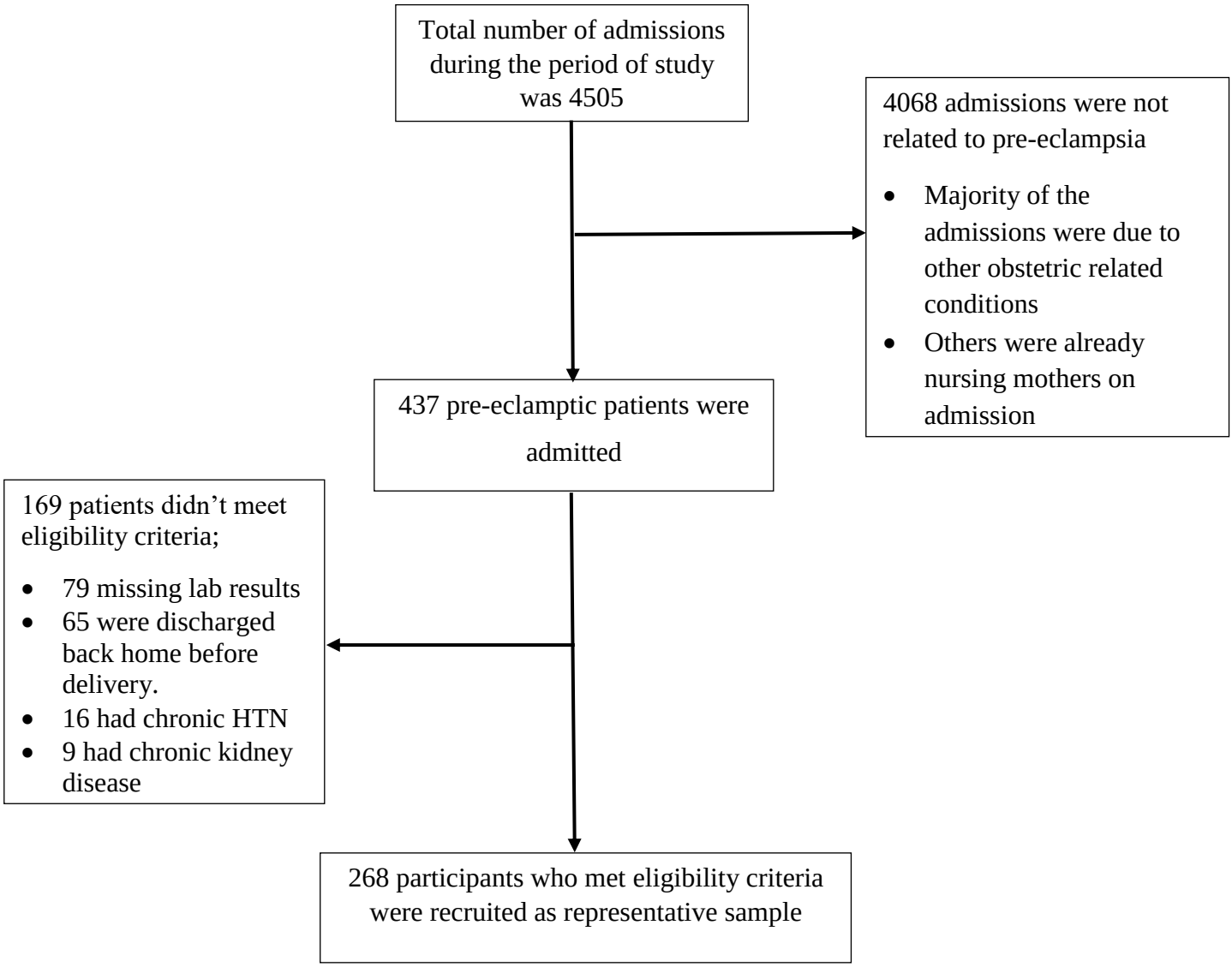


Figure 2: Consort diagram showing a schematic recruitment of study participants.

3.1 Social demographic characteristics

Majority of the study participants 196(73.13%) were of the age ranging between 20 and 34 years, with an overall mean age of 28.88±6.28years. A large proportion of patients 124(46.27%) had secondary education. Most participants 236(88.1%) had regular antenatal clinic attendance, 190(70.9%) participants had preterm deliveries. 184(68.7%) participants delivered underweight babies, 196 babies had an Apgar score of ≥7 in the 5^{th} minute of life and of all deliveries 33(12.3%) neonates were admitted in the neonatal ICU. 61.6% of the patients had no severe features of pre-eclampsia. Table 1

Table 1: General characteristics of study participants (n=268)

Variables	Attribute	Frequency (%)
Age	<20	11(4.1)
	20 -34	196(73.1)
	≥35	61(22.8)
	Informal	4 (1.5)
	Primary	94(33.6)
	Secondary	124(46.3)
Education	High education	50(18.6)
ANC visits	Regular	236(88.1)
	Irregular	32(11.9)
GA at delivery	<37	190(70.9)
	≥37	78(29.1)
Delivery mode	SVD	132(49.3)
	CS	136(50.7)
Pre-eclampsia	Mild	165(61.6)
	Severe	103(38.4)
Apgar score	≥7	196(73.1)
	<7	72(26.9)
NICU admission	Admitted	33(12.3)
	Not admitted	235(87.7)
Parity	Prime	98(36.6%)
	Multipara	170(63.4%)

3.2 Proportion of raised serum uric acid level among pre-eclamptic patients. (n=268)

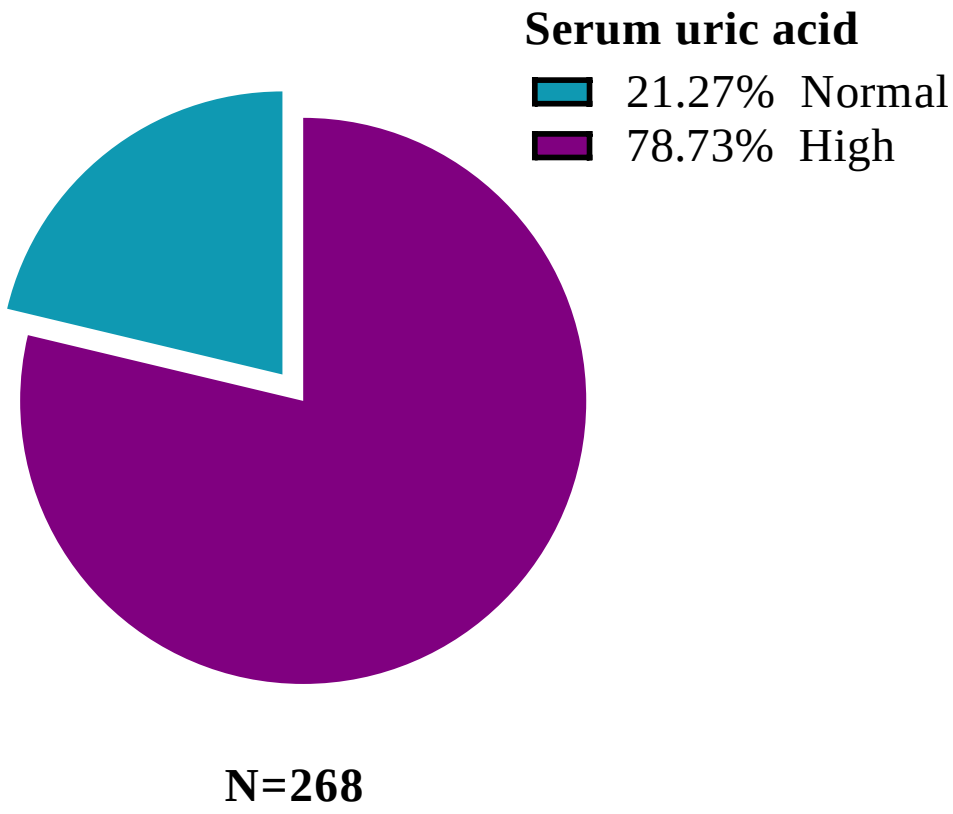


Figure 3: From the chart above, it shows that out of 268 participants 211(78.7%) were having high serum uric acid levels(>0.35mmol/L).

3.3 Proportions of adverse perinatal outcome among pre-eclamptic patients.

Among 268 pre-eclamptic mothers 70.9% gave birth before 37weeks of gestation age. A total of 184(68.7%) patients out of 268 pre-eclamptic patients delivered babies with less than 2500grams. 26.9% of babies delivered to pre-eclamptic patients had an Apgar score of less than 7 in their fifth minute of life. A total 51(19%) patients out of 268 pre-eclamptic patients had stillbirth deliveries. Among all neonates delivered by these pre-eclamptic patients 33(12.3%) neonates were admitted in Neonatal Intensive Care Unit. However of all neonates born to women with pre-eclampsia 47(17.5%) neonates had no any adverse perinatal outcome**.** Figure 4.

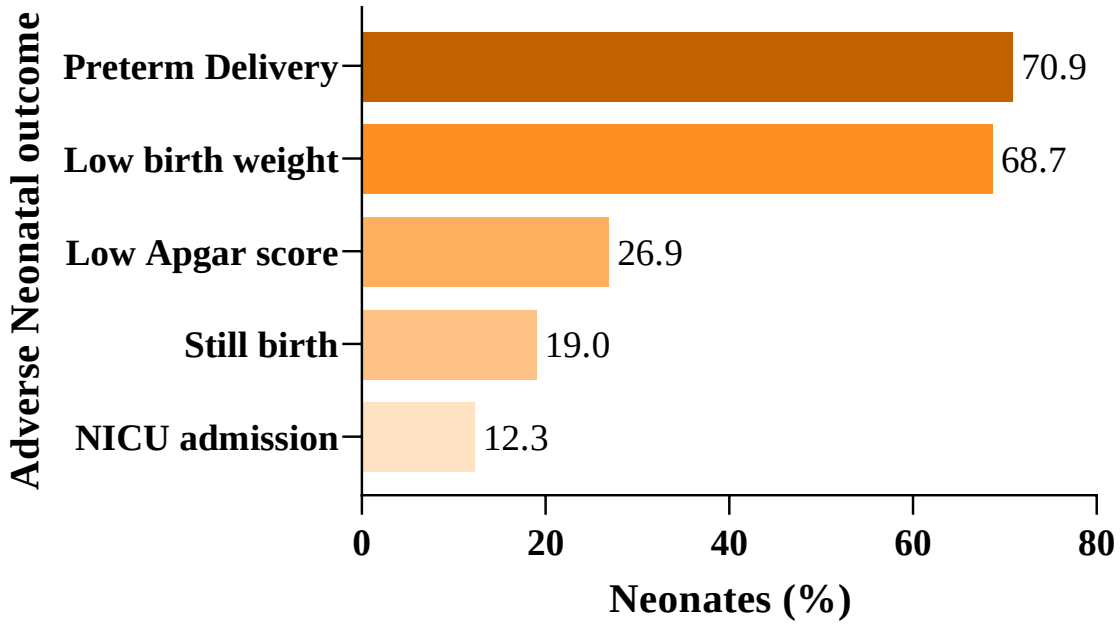


Figure 4: Bar chart showing prevalence of adverse perinatal outcome among pre-eclamptic patients.

3.4 Proportions of adverse neonatal outcome among pre-eclamptic mothers with hyperuricemia

A total 50(23.7%) out of 211 pre-eclamptic mothers with hyperuricemia had stillbirth deliveries. Among pre-eclamptic mothers with hyperuricemia 72.5% gave birth to babies with less than 2500gram. 28(13.3%) neonates who were delivered from mothers with hyperuricemia were admitted in Neonatal Intensive Care Unit. Among 211 pre-eclamptic patients with hyperuricemia 74.4% gave birth before 37 weeks of gestation age. 68(32.2%) babies were delivered with an Apgar score of less than 7 in the fifth minute of life. Table 2.

Table 2: Proportions of adverse neonatal outcomes born to pre-eclamptic mothers who had raised serum uric acid

Outcome	Uric acid <0.35mmol/L (%) n=57	Uric acid ≥0.35mmol/L (%) n=211	Total	P-Value
Birth status				
Stillbirth	1(1.8)	50(23.7)	51	0.001
Live birth	56(98.2)	161(76.3)	217	
Birth weight				
≥2500	26(45.6)	58(27.5)	84	0.009
<2500	31(54.4)	153(72.5)	184	
NICU				
Admitted	5(8.8)	28(13.3)	33	0.359
Not admitted	52(91.2)	183(86.7)	235	
Gestation at delivery				
Preterm	33(57.9)	157(74.4)	190	0.015
Term	24(42.1)	54(25.6)	78	
Apgar score				
≥7	53(93)	143(67.8)	196	0.001
< 7	4(7.0)	68(32.2)	72	

3.5 Factors associated with raised serum uric acid level

Logistic regression analysis results based on a uric acid threshold of more than 0.35mmol/L. In univariate logistic regression analysis, participants who had raised serum uric acid level

were found to have increased risk of low birth weight (OR 2.1, 95% CI 1.21-4.04; P<0.01); stillbirth (OR 17.4, 95% CI 2.35-128.85; P<0.005); low Apgar score (OR 6.3, 95% CI 2.19-18.12; P<0.001) and preterm delivery (OR 2.11, 95% CI 1.15-3.89; P<0.016). However, the NICU admission had no association which was statistical significant.

In adjusted model, the following association was revealed; low birth weight (aOR 2.16, 95% CI 1.11-4.20; P<0.024) when uric acid was adjusted for pre-eclampsia grade, hemoglobin level and gestation age; stillbirth (aOR 11.29, 95%CI 1.49-85.87; P<0.019) once uric acid was adjusted for pre-eclampsia grade and hemoglobin level; low Apgar score (aOR 4.63, 95%CI 1.57-13.71; P<0.006) when uric acid was adjusted for delivery mode, pre-eclampsia grade and gestation age; preterm delivery (aOR 2.02, 95%CI 1.03-3.95; P<0.041)once uric acid was adjusted for pre-eclampsia grade. Table 3.

Table 3: Factors associated with raised serum uric acid.

Outcome	cOR	95% CI	P - value	aOR	95%CI	P - value
Low birth weight	2.12	1.21 – 4.04	0.01	2.16	1.11 – 4.20	0.024
Stillbirth	17.39	2.35 – 128.85	0.005	11.29	1.49 – 85.87	0.019
Low Apgar score	6.3	2.19 – 18.12	0.001	4.63	1.57 – 13.71	0.006
Preterm delivery	2.11	1.15 – 3.89	0.016	2.02	1.03 – 3.95	0.041
NICU admission	1.59	0.59 – 4.38	0.363			

CHAPTER FOUR

4.0 DISCUSSIONS

This hospital based cross-sectional study involved 268 pre-eclamptic patients, who were admitted in maternity ward at MNH with the objective of determining the utility of maternal serum uric acid in predicting perinatal outcome.

4.1 Magnitude of hyperuricemia among pre-eclamptic patients

The findings of this study show that the proportion of patients with hyperuricemia among pre-eclamptic patients was 78.7%. This was almost consistent with the previous study by Zangana *et al* which reported 63.5% (18). The mean serum uric acid level from the recruited subjects was 0.42±0.09mmol/L, which is in line with other studies (15, 16). The high levels of serum uric acid seen in these pre-eclamptic patients is probably due to delayed proper intervention as majority of the patients are admitted as referrals hence having deranged uric acid (2).

4.2Prevalence of adverse perinatal outcome among pre-eclamptic patients

Low birth weight: In our study 68.7% neonates with less than 2500grams were delivered from pre-eclamptic patients, which was consistent with other studies (61.5%) and (63.7%) from South Korea and Iraq respectively (2, 18). The high proportion of low birth weight seen in our study can possibly be explained by the fact that, in our study the participants were recruited at a gestation age of 28weeks and above compared to those at 34weeks.

Stillbirth: 19% of the study subjects had stillbirth deliveries which almost matched the study findings in China 17% by Liu D *et al* (26). The high proportion of stillbirth observed in this study is likely a result of preeclampsia complication like placental insufficiency (27).

Preterm delivery: The proportion of deliveries before 37weeks of gestation in our study was found to be 70.9% among the subjects with hyperuricemia. This finding seem to be quite comparable with the proportion of preterm delivery 75.6% found in Maternity teaching hospital in Erbil, but was contrary to 43.2% which was obtained from the study

done in Vietnam (18, 21). The observed high proportions are probably due to the fact that delivery is the absolute management of pre-eclampsia, therefore majority of the subjects with severe features of pre-eclampsia being delivered before term, whereas the big variation might be due to the differences in study design.

Low Apgar score: 26.9% of neonates born to pre-eclamptic patients had an Apgar score of less than seven in the fifth minute of life. This proportion was much lower than those of previous studies done in India, Iraq and Iran which reported 39.2%, 55% and 66% respectively (18, 22, 28). The relatively low proportion of low Apgar score neonates in our study may be due to timely intervention of obstetric complications and the differences in study design and sample size.

NICU admission: In our study 12.3% of neonates were admitted in the neonatal intensive care unit. These findings did not match with other studies done by Meena *et al*, India and Zangana *et al*, Iraq reporting a proportion of 34% and 57.48% NICU admissions respectively (15, 18)

4.3 Factors associated with high serum uric acid

Outcome factors that were found to be significantly associated with elevated serum uric acid levels were low birth weight, stillbirth, low Apgar score and preterm delivery. However, there was no statistical significant association with NICU admission. In this study we found that low birth weight was significantly associated with hyperuricemia, whereby the P-value was 0.024 when odds are adjusted (OR 2.12, 95% CI 1.21-4.04). This finding concurs with studies by Hawkins *et al* and Ryu *et al* whose odds almost matched with ours (2, 29).

Also the study shows that pre-eclamptic patients with hyperuricemia had increased risk in stillbirth deliveries (OR 17.39, 95% CI 2.35-128.85). The odds in our study was almost in line with the odds reported by Tejal *et al* (OR 20, 95% CI 1.13-360.29) a study done in India (22).

Raised serum uric acid was found to have 6.3 times increased risk in low Apgar score (95% CI 2.19-18.12). These finding were quite comparable to (OR 5.514, 95%CI 1.877-16.198) which was reported by Tam M *et al*, Vietnam(21)

In our study hyperuricemia was also a good predictive factor for preterm deliveries (OR 2.11, 95% CI 1.15-3.89). The odds in our study was lower than the findings reported by Tejal *et al* (OR 6.0, 95% CI 1.24-28.98) and Tam *et al.* (OR 6.36, 95% CI 3.01-13.08)(21, 22).

In adjusted model raised serum uric acid it revealed an increased risk in low birth weight (aOR 2.16, 95% CI 1.11-4.20), stillbirth (aOR 11.29, 95%CI 1.49-85.87), low Apgar score (aOR 4.63, 95%CI 1.57-13.71) and preterm delivery (aOR 2.02, 95%CI 1.03-3.95).

CHAPTER FIVE

5.0 STRENGTHS AND LIMITATIONS

5.1 Study strengths

This was the first study conducted at Muhimbili National Hospital in Tanzania which revealed the utility of raised serum uric acid in predicting adverse neonatal outcome and highlighted the magnitude of adverse perinatal outcome among pre-eclamptic patients in our setting.

5.2 Study Limitations

Since our study was done in a single center tertiary hospital, it might overestimate the magnitude of the adverse perinatal outcome. Also during data collection some details were missing from patient's records and therefore they were not recruited as they did not meet eligibility criteria.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Raised serum uric acid levels are a good prognostic factor of adverse fetal/neonatal outcomes among women with pre-eclampsia. There was a relationship between raised serum uric acid and the stillbirth, low birth weight, low apgar score and preterm delivery.

6.2 Recommendations

Based on our study findings raised serum uric acid is of good prognostic value in predicting adverse neonatal outcome, hence it can be utilized in the intervention plans to improve quality of care among pre-eclamptic patients.

This study calls upon for a large prospective and multicenter study to explore temporal relation of serum uric acid versus maternal and perinatal outcome, which will involve recruitment of participants at 20weeks of gestation age.

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APPENDICES

Appendix I: Clinical Research Form

Utility of SUA in predicting perinatal outcome among pre-eclamptic patients admitted at MNH

Study number …….

Hospital number …….

Date ……..

Gestational age……

Residence …….

LNMP……..

EDD……..

BP…….

PART 1: SOCIO-DEMOGRAPHIC DATA

Age

Less than 20years	
20-35years	
Above 35years	

Marital status

Married	
Single	
Divorced	
Widowed	
Cohabiting	

Education level

Informal/None	
Primary education	
Secondary education	
College/University	

Occupation status

Employed	
Entrepreneur	
Not working	
Others	

Parity

Gravida 1	
Gravida 2	
Gravida 3	
Gravida 4	
Gravida 5 and above	

ANC visits

No	
Regular	
Irregular	

Past Medical History

Hypertension	Yes	
	No	
Diabetes Mellitus	Yes	
	No	
Renal failure	Yes	
	No	
Heart failure	Yes	
	No	

PART 2: PERINATAL OUTCOME

Birth weight	<2.5kg	
	≥2.5kg	
Gestational age	<37 weeks	
	≥37 weeks	
Mode of delivery	SVD	
	C/S	
Apgar score	1^{st} minute	
	5^{th} minute	
NICU admission	Yes	
	No	
Stillbirth	Yes	
	No	

PART 3: LABORATORY INVESTIGATION

Serum Uric Acid	
Serum Creatinine	
Serum Urea	
AST	
ALT	
HB	
Platelets	