Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 38 (2024) 101155

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Full Length Article

Determining the relationship between severity of proteinuria and adverse maternal and neonatal outcomes in patients with preeclampsia

Elizabeth Jansen van Rensburg *, Louisa B. Seopela, Leon C. Snyman

Department of Obstetrics and Gynaecology, University of Pretoria Faculty of Health Sciences, Kalafong Provincial Tertiary Hospital, 10 Kalafong Road, Atteridgeville, Gauteng 0008, South Africa

ARTICLE INFO

Keywords:
Preeclampsia
Proteinuria
Pregnancy
Hypertension
Maternal outcome
Neonatal outcome

ABSTRACT

Objectives: To investigate the relationship between the severity of proteinuria and adverse maternal and neonatal outcomes in patients with preeclampsia (PE).
Design: Prospective cohort study conducted in Gauteng, South Africa over 12 months. Patients with PE 18 years or older with singleton pregnancies were recruited. We included 248 in the final analysis.
Methods: Proteinuria was quantified using urine protein: creatinine ratio (UPCR). Preeclamptic patients' outcomes were compared according to the UPCR values using regression models and by generating receiver operator characteristic (ROC) curves. Primary maternal outcomes were gestational age (GA) at diagnosis, GA at delivery, development of eclampsia, development of severe features and the need for more than one antihypertensive - agent. Neonatal outcomes were admission to neonatal unit, 5-min APGAR score, need for ventilatory support and early neonatal death.
Results: There was a weak but significant negative correlation between GA at delivery and UPCR (Spearman's correlation coefficient (SCC) −0.191, p = 0.002). Most patients (77 %) required >1 agent to control their blood pressure, however there was no correlation between UPCR and the need for additional agents (SCC −0.014, p = 0.828). There was a statistically significant correlation between UPCR and severe features, especially the development of haemolysis, elevated liver enzymes and low platelet (HELLP) syndrome (p = 0.005). There was no significant correlation between neonatal outcomes and UPCR.
Conclusion: Severity of proteinuria correlated with earlier delivery and development of severe features, specifically HELLP syndrome and pulmonary oedema. There was no correlation between UPCR and requiring additional antihypertensive agents or neonatal outcomes.

1. Introduction

Hypertensive disorders of pregnancy are the 2nd most common cause of maternal deaths in South Africa and account for 18 % of all maternal deaths worldwide [1,2]. Whilst the total number of maternal deaths due to hypertension have decreased over the past 30 years, there has been a 10,8 % increase in the global incidence of these disorders [2].

Preeclampsia is defined as hypertension (blood pressure of >140/90) on at least two occasions four or more hours apart with evidence of proteinuria or organ dysfunction after the 20th week of pregnancy [3,4]. It is associated with increased maternal and perinatal morbidity and mortality [3,5]. Although the incidence seems to vary according to geographical location, preeclampsia is estimated to occur in about 3.2–5.1 % of pregnancies in Sub-Saharan Africa [6].

Severe features may arise in any patient with preeclampsia, which warrants expedited delivery. These severe features are defined by the American College of Obstetricians and Gynaecologists (ACOG) as [7]:

- Severe hypertension (systolic BP ≥ 160 or diastolic ≥110)
  - On two occasions at least 4 h apart while on bed rest (unless already on antihypertensive therapy)
- Thrombocytopenia: Platelets <100 × 10^9/L
- Impaired liver function (without an alternative diagnosis): Elevated liver transaminases greater than twice upper limit of normal or severe persistent right upper quadrant or epigastric pain not responsive to medications
- Progressive renal insufficiency: serum creatinine >97 μmol/l or doubling of serum creatinine in the absence of other renal disease

* Corresponding author.
E-mail address: lisa@jvanrensburg.com (E.J. van Rensburg).

https://doi.org/10.1016/j.preghy.2024.101155
Received 8 April 2024; Received in revised form 6 July 2024; Accepted 30 August 2024
Available online 6 September 2024

- Pulmonary oedema
- Neurological: Unexplained new-onset headache unresponsive to medication (without an alternative diagnosis) or visual symptoms

While the presence of proteinuria has not been necessary for a diagnosis of preeclampsia since 2013, most patients with preeclampsia present with significant proteinuria [3].

Although few, some studies suggest that the severity of proteinuria might be associated with increased risk of developing severe disease and adverse pregnancy outcome [8–10]. Currently, there is no reliable method to accurately predict the likelihood of progression to severe disease in clinical use [5].

A retrospective cohort study done in Brazil evaluated the maternal and neonatal outcomes of women with preeclampsia. Proteinuria was classified as mild (0.3–2 g/24 h), severe (2–5 g/24 h) and massive (>5g in 24 h). Women with massive proteinuria required earlier delivery and had an increased risk of adverse foetal outcomes [11]. There was an increased risk of composite adverse maternal outcomes in women with massive proteinuria, although eclampsia, HELLP syndrome or abruption were not statistically significant [11].

Another retrospective study done in China showed a positive association between increasing proteinuria and adverse maternal and neonatal outcomes [8]. The authors found that a cut-off of 984.75 mg/24 h had a significantly increased odds ratio.

The gold standard of quantifying proteinuria remains a 24-h urine collection, however this is sometimes impractical. The ISSHP recommends urine dipstick testing and then, if positive, spot urine protein: creatinine ratio sampling to quantify proteinuria [3].

Spot urine protein: creatinine ratio as a tool to diagnose preeclampsia is supported by multiple societies, including the ACOG, ISSHP and NICE [3,12,13]. The use of UPCR in our local population has mostly been extrapolated from the international recommendations. It is based on these recommendations that our hospital uses UPCR as part of the diagnostic evaluation of all preeclamptic patients. While the data in the South African population is limited, there has been a recent case-control study done in Bloemfontein that confirms the high correlation rate between UPCR and 24 h urine protein values in a South African population [14].

It has been well-documented that women with preeclampsia and their neonates are at higher risk of adverse outcomes compared to women without preeclampsia [15]. WHO multinational survey on maternal and neonatal outcomes showed that women with preeclampsia were 4 times more likely to die and 8 times more likely to experience a near miss event or severe adverse outcome than women without preeclampsia [15]. Additionally, women with eclampsia have a pronounced risk and are 60 times more likely to experience one of these events.

Predicting which patients with preeclampsia are at a higher risk of developing severe disease would be useful to determine monitoring strategies, delivery plan and improve patient counselling. Such a strategy might assist with resource allocation to facilities that provide care to women with preeclampsia.

2. Materials and methods

We conducted a prospective cohort study to investigate whether there is a relationship between the severity of proteinuria and adverse maternal and neonatal outcomes in patients with Preeclampsia (PE).

The study took place at the labour ward complex at the Kalafong Provincial Tertiary Hospital (KPTH). KPTH is situated in Atteridgeville, Gauteng, South Africa, and provides a tertiary service to the western region of Tshwane. Patients diagnosed with PE seen in the antenatal clinic and labour ward were enrolled into the study. Ethical approval for the study was granted by the University of Pretoria Faculty of Health Sciences Research Ethics Committee, approval number 461/2022.

The policy for managing preeclamptic patients at KPTH is in line with our national guidelines [4] and involves managing all preeclamptic patients as inpatients. Upon admission, all patients have biochemical testing preformed as outlined below in Section 2.2. If admitted before 34 completed weeks gestational age, routine antenatal corticosteroids are administered. While admitted in the ward, 6 hourly CTG monitoring is preformed, and a minimum of 4 hourly blood pressure monitoring is done. Biochemical testing is repeated at least twice a week unless clinical condition changes. Delivery is planned for 34 weeks unless there is an acute change in maternal or foetal condition. Caesarean sections are reserved for obstetric indications.

2.1. Patient selection

Recruitment of patients was conducted from October 2022 to September 2023 and data collection lasted until the last recruited patients gave birth.

Inclusion Criteria:

1. All patients diagnosed with preeclampsia
2. Patients who are able and willing to provide consent for data collection

Exclusion Criteria:

1. Age <18 years
2. Multiple pregnancy
3. Known chronic renal disease
4. Patients unable or unwilling to provide consent for data collection

2.2. Measurements

According to previous studies conducted on preeclamptic patients, the prevalence of preeclampsia is as low as 6 % of all visits to the antenatal clinic. An average of 2200 pregnant women are seen monthly at the KPTH antenatal clinic, of which about 25 are likely to be diagnosed with PE. The above statistics estimates that the targeted population is about 300 pregnant women diagnosed with preeclampsia per year. To achieve a statistically significant result, a known population sample size estimation method was used with a 95 % confidence interval, 5 % margin of error and a standard deviation of 50 with a population 300 was used to arrive a statistically significant sample size of 168.7 rounded off to 169.

To account for patients that had to be excluded from analysis (see Section 2.1 above), recruitment was done over a year to obtain a statistically significant sample size.

Data was collected using a data sheet that enabled longitudinal data collection with the following sections: antenatal information, a progress update on the development of any adverse outcomes and neonatal data. Antenatal information was collected from patients' files once they consented to participate in the study.

Urinalysis was done on almost all patients with preeclampsia using a spot urine protein:creatinine ratio. A 24-h urine protein excretion was also collected where possible. Biochemical testing for urea, creatinine, alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), haemoglobin and platelets was done according to the established obstetric unit's guidelines for in & outpatients. All laboratory testing was done at the branch of the National Health Laboratory Service (NHLS) situated at KPTH.

The relationship between the following primary maternal outcomes and proteinuria were analysed: (a) gestational age at diagnosis, (b) gestational age at delivery, (c) development of eclampsia, (d) development of severe features, (e) comorbid medical conditions, and (f) the need for more than one agent to control blood pressure.

We also assessed birth weight of the neonate and the following adverse neonatal outcomes: (a) admission to neonatal unit, (b) a 5-min APGAR score, and (c) need for ventilatory support and (d) stillbirth or early neonatal death.

2.3. Data analysis

Data was captured from data sheets into a password protected Microsoft Excel spreadsheet in preparation for statistical analysis. Descriptive data analysis was deployed to describe the characteristics of the variables collected. Discrete data was described using frequencies and percentages, while continuous variables were described using mean, mode, and standard deviations.

Descriptive statistics were followed by distribution analysis (skewness and kurtosis) to test the variables' distribution. Results of the distribution analysis rejected the null hypothesis that the values of UPCR are normally distributed. Nonparametric statistical testing was therefore used to analyse the data. A p-value of <0.05 was considered statistically significant.

Preeclamptic patients' outcomes after delivery were compared according to the severity of proteinuria using a regression model as well as generating a receiver operator characteristics (ROC) curve. All statistical analysis was performed using IBM SPSS Statistics version 26.

3. Results

During the study period, there were 5950 deliveries in total and 340 patients (5.7 %) were diagnosed with preeclampsia. Of the patients diagnosed with preeclampsia, 28 patients were deemed ineligible due to maternal age, multiple pregnancy or did not consent to participation in the study. Sixty-four patients had missing data and were excluded from analysis. A total of 248 patients were included in the final analysis. A summary of patient selection can be found in Fig. 1.

The baseline characteristics of the study population are shown in Table 1. There were 201 HIV negative patients (81 %) and 212 patients who were negative for syphilis (85 %). A large proportion of our population was multiparous (70.2 %). We had 47 patients (19 %) with comorbidities, of which the majority had chronic hypertension. This population's mean BMI was 29.19. The mean gestational age at diagnosis of PE was 33 weeks. Sub-analysis of median UPCR of patients living with HIV and patients without showed no difference. Median UPCR for patients with and without HIV was 0.06 and 0.07, respectively ($p = 0{,}727$).

We found nulliparous patients had a statistically significant higher median UPCR of 0,10 while multiparous patients had a median UPCR of 0,06 (p-value = 0.004).

Twenty-eight (11.3 %) women had chronic hypertension (CHT), 11 (4.4 %) had diabetes and 8 had other medical conditions (mostly asthma and epilepsy). UPCR was significantly *lower* in patients with CHT (median with CHT 0.04, without CHT 0.08, $p = 0.021$). Other comorbidities were evaluated as a composite due to low incidence and had no correlation with UPCR, $p = 0.849$) (Table 4).

In this study, 133 (53.6 %) women delivered via Caesarean section (CS). UPCR was not significantly increased in women that delivered by CS, mean 0,4 (SD = 0,83) and a max 4,16; p-value of 0,14.

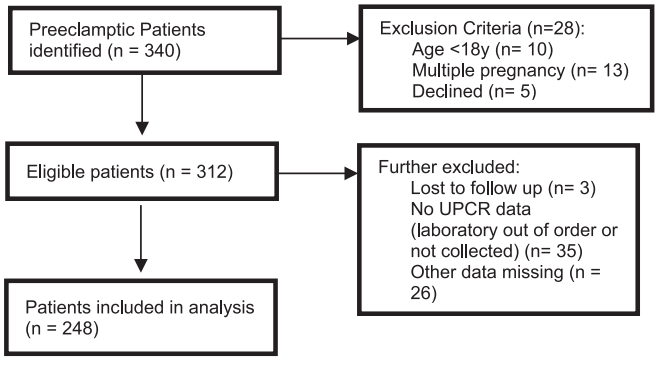


Fig. 1. Flowchart of selected patients.

Table 1
Baseline maternal characteristics.

Variable	Mean or number (%)
Age (years)	29.31 ± 6.18
<35	182 (73 %)
≥35	66 (27 %)
Gravidity	
Primigravida	58 (23.4 %)
Multigravida	190 (76.6 %)
Parity	
Nulliparous	74 (29.8 %)
Multiparous	174 (70.2 %)
Gestational age at diagnosis	33.75 ± 4.76 weeks
BMI at booking	29.19 ± 7.09
HIV Status	
Negative	201 (81 %)
Positive	44 (17.8 %)
Unknown	3 (1.2 %)
Syphilis	
Negative	212 (85.5 %)
Positive	4 (1.6 %)
Unknown	32 (12.9 %)
Comorbidities	47 (19 %)
Chronic hypertension	28
Diabetes	11
Other	8

One-hundred and ninety-one of women with PE (77 %) required more than one agent to control their blood pressure (BP). There was no significant difference in the median UPCR of patients that required 1 agent and more than one agent to control BP, ($p = 0.849$). There was still no relationship found when analysed via the ROC curve.

UPCR and gestational age at diagnosis had a weak but statistically significant negative correlation (Spearman's Correlation Coefficient (SCC) −0.14, $p = 0.03$) and at delivery (SCC −0.19, $p = 0.002$). The relationship persisted after grouping patients into gestational age categories as seen in Table 2. The interval between diagnosis and delivery was also slightly shorter in patients with larger UPCR values (SCC −0.134, $p = 0.035$).

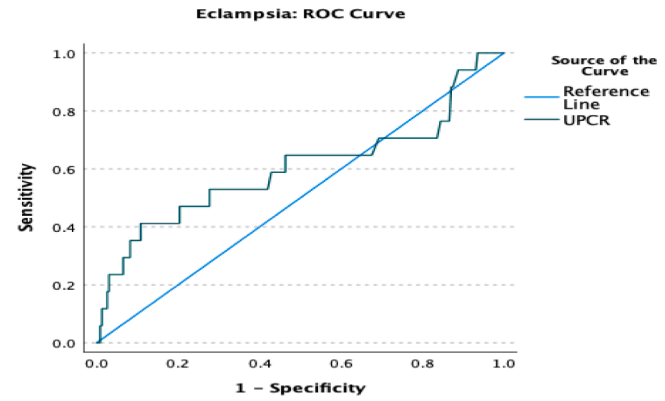
Although not statistically significant ($p = 0.349$), patients who developed eclampsia (n = 17, 7 %) had a higher UPCR median of 0,91 than those without. Plotted on a ROC curve, the model was not better than random prediction (Fig. 2). A large proportion of patients developed severe HT (185, 74.5 %) and the ROC curve indicated a strong correlation between severe BP and UPCR (Fig. 3).

A large but nonsignificant difference was noted in UPCR medians of patients with and without acute kidney injury (AKI). These findings were confirmed when analysing their respective ROC curves. Four patients developed pulmonary oedema during the study period. Although their UPCR median did not differ to those who did not develop pulmonary oedema, the ROC curve showed a strong correlation between larger UPCR and the development of pulmonary oedema (Fig. 4). This finding should be interpreted with caution due to a low number of patients.

Forty-four (17.7 %) patients developed HELLP syndrome and had a significantly higher median UPCR values ($p = 0.005$). The ROC curve also demonstrated a strong association between higher UPCR and the development of HELLP syndrome (Fig. 5).

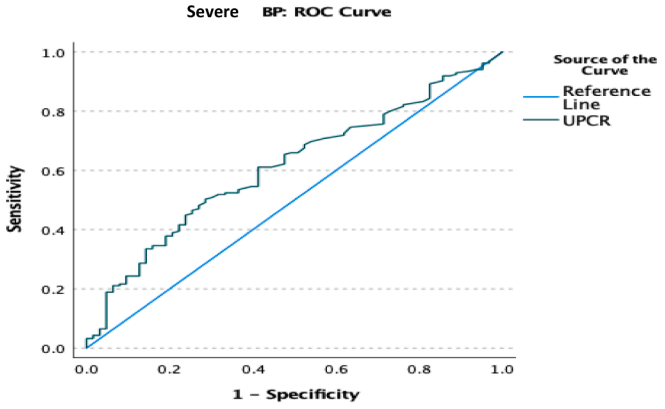
Table 2
UPCR and Gestational Age (GA).

UPCR	GA in Weeks			
	20–28	29–34	34–37	>37
Mean	0,905	0,456	0,251	0,224
95 % CI (L;H)	0,09; 1,72	0,27; 0,64	0,16; 0,34	0,1; 0,35
Median	0,146	0,094	0,054	0,067
Std. Deviation	1,527	0,819	0,394	0,559
Minimum	0,026	0,002	0,010	0,008
Maximum	4,041	3,526	1,580	4,160



Area	Std. Error	P-Value	95% CI	Model Quality
0.601	0.088	0.247	0.430-0.773	43%

Fig. 2. ROC curve eclampsia.



Area	Std. Error	P-Value	95% CI	Model Quality
0.612	0.039	0.004	0.536-0.689	54%

Fig. 3. ROC curve severe BP.

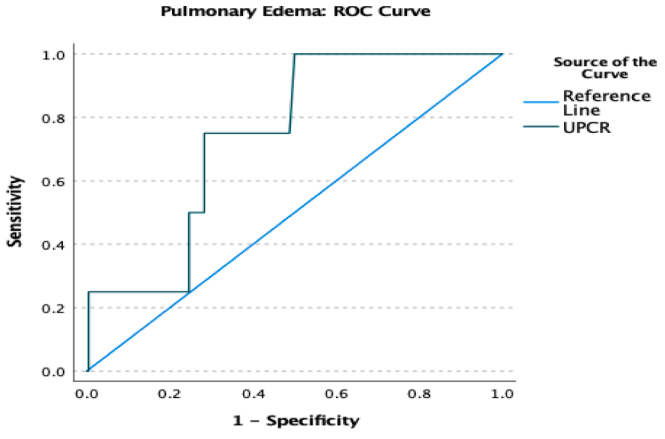
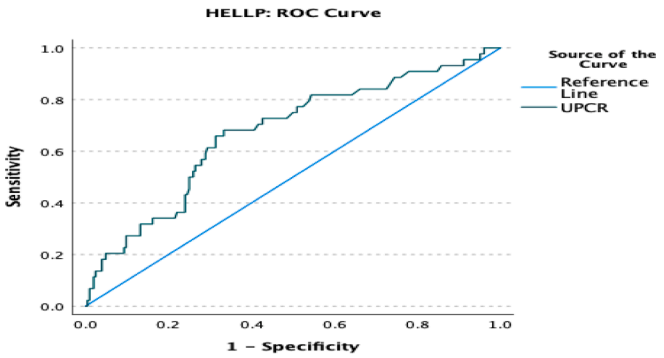


Fig. 4. ROC curve pulmonary oedema.

When analysing the occurrence of severe features as a composite outcome, the UPCR was significantly higher (p = 0,006) (Table 3).

One-hundred and twelve babies (45.2 %) were admitted to the neonatal unit, and 55 babies required some form of ventilatory support. Seventy-six (30 %) babies were small for gestational age (SGA), 23 (9 %) were stillbirths, and there were no early neonatal deaths. There was no significant relationship between UPCR median and neonatal admission, SGA, or death, (p-values, 0.098, 0.106, 0.109 respectively).



Area	Std. Error	P-Value	95% CI	Model Quality
0.672	0.046	<0.001	0.582-0.761	58%

Fig. 5. ROC curve HELLP syndrome.

Birth weight correlated negatively with UPCR (SCC −0.22, p < 0.001), which is expected considering the relationship between UPCR and earlier gestational age at delivery. There was a very weak negative association between UPCR and 5 min AGPAR score, (SCC −0.13, p = 0.05). A summary of neonatal outcomes can be found in Table 4.

4. Discussion

The incidence of preeclampsia (5.7 %) during the study period was slightly higher than that reported in other Sub-Saharan countries [6]. A large systematic review and *meta*-analysis found the pooled prevalence of preeclampsia in Sub-Saharan Africa to be 4.1 % (95 % CI 3.2–5.1 %) [6].

Compared to other studies, the study findings had similarities in a few areas. A secondary analysis of the Vitamins in Pre-Eclampsia trial (VIP trial) similarly found that women with higher levels of proteinuria had an increased rate of severe hypertension [9]. However, in contrast to our study, high UPCR levels were also found to be associated with higher rate of caesarean section and magnesium sulphate therapy [9].

A significant correlation between proteinuria and severe features of preeclampsia was found in this study, specifically the development of HELLP syndrome, which is in contrast to the previously mentioned Brazilian study which found that although there was an increased risk of composite adverse maternal outcomes in women with massive proteinuria, eclampsia, HELLP syndrome or abruption were not statistically significant [11]. Most patients with severe features presented from home or referral institutions and only rarely developed them while being managed expectantly as inpatients. This indicates that suitable patients were appropriately selected for expectant management.

Significantly lower UPCR in patients with CHT could be due to the lower threshold of diagnosing PE in patients with CHT, rather than CHT being protective against proteinuria. UPCR was not always repeated in patients with a baseline value. A retrospective cohort study done by Morgan et al. found that 47 % of patients with chronic hypertension and no proteinuria developed preeclampsia, although having significant proteinuria at baseline (i.e. before 20 weeks gestation) was associated with a higher risk of developing superimposed preeclampsia, preterm birth and foetal growth restriction [16].

A recently published study done in India evaluated the relationship between proteinuria and adverse maternal and neonatal outcomes in women with severe preeclampsia [17]. No relationship was found between proteinuria and composite adverse maternal outcomes, which

Table 3
UPCR and maternal outcomes.

		Count (248)	Mean UPCR	95 % Confidence Interval for Mean	Median UPCR	Std. Deviation	Minimum	Maximum
Mode of delivery	Unknown	6	0,73	−0,61:2,06	0,04	1,27	0	3,18
	CS	133	0,40	0,26:0,55	0,09	0,83	0	4,16
	NVD	109	0,24	0,14:0,33	0,06	0,49	0	3,53
	The medians of UPCR are the same across categories of Mode of delivery. P-value = 0,140							
Eclampsia	Unknown	17	0,32	−0,07:0,71	0,05	0,76	0	3,18
	No	214	0,29	0,21:0,38	0,07	0,64	0	4,16
	Yes	17	0,91	0,26:1,58	0,17	1,28	0,014	3,98
	The medians of UPCR are the same across categories of Eclampsia. P-value = 0,349							
Pulmonary oedema	Unknown	11	0,42	−0,21:1,04	0,05	0,93	0	3,18
	No	233	0,32	0,23:0,41	0,07	0,67	0	4,16
	Yes	4	1,12	−1,97:4,22	0,20	1,94	0,067	4,041
	The medians of UPCR are the same across categories of Pulmonary Oedema. P-value = 0,408							
Severe BP after presentation	Unknown	13	0,29	−0,24:0,81	0,05	0,87	0	3,18
	No	50	0,17	0,07:0,27	0,05	0,35	0,01	1,98
	Yes	185	0,39	0,28:0,5	0,08	0,77	0,00	4,16
	The medians of UPCR are the same across categories of Severe BP after presentation. P-value = 0,059							
HELLP Syndrome	No	204	0,27	0,19:0,35	0,06	0,60	0	4,16
	Yes	44	0,66	0,33:0,98	0,17	1,06	0,00	4,04
	The medians of UPCR are not the same across categories of Delivery-HELLP Syndrome. P-value = 0,005							
AKI	No	226	0,28	0,2:0,36	0,06	0,59	0	3,85
	Yes	22	0,96	0,33:1,58	0,18	1,40	0,00	4,16
	The medians of UPCR are the same across categories of AKI. P-value = 0.232							
COSF	No	181	0,22	0,15:0,29	0,06	0,48	–	3,50
	Yes	67	0,65	0,39:0,92	0,13	1,09	0,00	4,16
	The medians of UPCR are not the same across categories of COSF. P-value = 0,006							

UPCR and maternal outcomes.
CS – Caesarean section, NVD – normal vaginal delivery, BP – blood pressure, HELLP – haemolysis, elevated liver enzymes and low platelets, AKI – acute kidney injury, COSF – composite of severe features.

does not echo the findings of the present study. Additionally, a statistically significant association with composite adverse neonatal outcomes was found, which is in contrast to our study findings [17]. It is important to note that they only included women with preeclampsia who had severe features, which may limit the comparison to the current study.

A prospective study specifically looked at UPCR in relation to adverse maternal and neonatal outcomes and found a positive relationship between increasing UPCR and adverse maternal outcomes [18]. While they found a similar relationship between UPCR and neonatal outcomes, this relationship did not persist when plotted on an ROC curve. These findings were reiterated by another retrospective study conducted in China that showed UPCR was an independent predictor of adverse maternal and neonatal outcomes [19].

Similar to the study finding, the secondary analysis of the VIP trial also found an increased incidence of preterm delivery in women with greater amounts of proteinuria, however in contrast the incidence of small for gestational age (SGA) infants was increased. Since proteinuria was found to have an inverse relationship with both gestational age at diagnosis and delivery in the current study, a similar relationship was expected for lower birth weight SGA as well. It was interesting to note that there was no significant relationship between proteinuria and SGA in this study, contradicting the findings of Murali et al. [17] Inaccurate pregnancy dating especially in women who seek antenatal care late could be a contributing factor, or that women with preeclampsia in our population group, even those with severe features, were less likely to have placental disease resulting foetal growth restriction and SGA.

As with any research, this study had some limitations. During the study, there was a short period when laboratory urinalysis was not working and as a result some data could not be retrieved. This limitation resulted in some patients being excluded from final analysis. There was not universal collection of 24-h urine protein, which limit the comparison of spot UPCR and 24-h urine protein in this specific study.

As the data sheets did not allow collection of certain subjective symptoms of imminent eclampsia, for example headache or epigastric pain, some data on severe features may have been missed. However, we are of the opinion that by only using objectively measurable outcomes we could more reliably report on the association of UPCR to these outcomes.

Strengths of this study include its relatively large sample size and prospective data collection.

In conclusion, our study found that a larger amount of proteinuria correlated with earlier delivery and the development of severe features, specifically HELLP syndrome and pulmonary oedema. There was no correlation between UPCR and the need for additional agents to control blood pressure. We did not find a significant relationship between UPCR and neonatal outcomes.

Based on these findings, patients with a higher UPCR may require more frequent biochemical testing to facilitate the early detection of HELLP syndrome. UPCR values may aid in patient counselling regarding the risk of development of severe features and the risk of earlier delivery. More research is needed before making definitive recommendations.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 4
UPCR and neonatal outcomes.

		Number	Mean UPCR	95 % Confidence Interval for Mean	Median UPCR	Std. Deviation	Minimum	Maximum
SGA (Y/N)	No	168	0,28	0,17:0,38	0,06	0,68	0	4,16
	Yes	76	0,47	0,29:0,66	0,10	0,81	0	4,04
	The medians of UPCR are the same across categories of SGA (Y/N). p-value = 0,106							
Admission	Unknown	4	0,12	−0,05:0,28	0,11	0,10	0,03	0,23
	No	128	0,27	0,15:0,4	0,06	0,71	0	4,16
	Yes	112	0,42	0,28:0,56	0,09	0,75	0	3,99
	The medians of UPCR are the same across categories of Admission (Y/N). p-value = 0,098							
Ventilatory support	Unknown	25	0,43	0,11:0,75	0,09	0,78	0	3,53
	No	164	0,30	0,19:0,41	0,06	0,71	0	4,16
	Yes	55	0,40	0,2:0,61	0,10	0,76	0	3,99
	The medians of UPCR are the same across categories of Ventilatory support (Y/N). p-value = 0,088							
Nasal prongs	No	222	0,33	0,24:0,43	0,06	0,74	0	4,16
	Yes	22	0,39	0,11:0,66	0,10	0,62	0,02	2,20
	The medians of UPCR are the same across categories of Nasal prongs (Y/N). p-value = 0,467							
CPAP	No	217	0,33	0,23:0,42	0,06	0,70	0	4,16
	Yes	27	0,43	0,07:0,79	0,09	0,92	0	3,99
	The medians of UPCR are the same across categories of CPAP (Y/N). p-value = 0,366							
Intubation	No	242	0,34	0,25:0,43	0,07	0,73	0	4,16
	Yes	2	0,18	0,07:0,3	0,18	0,01	0,18	0,19
	The medians of UPCR are the same across categories of Intubation (Y/N). p-value = 0,464							
Early neonatal death	Unknown	17	0,42	−0,08:0,92	0,05	0,97	0,02	4,04
	No	227	0,33	0,24:0,43	0,07	0,71	0	4,16
	The medians of UPCR are the same across categories of Early neonatal death (Y/N). p-value = 0,862							
Stillbirth	No	219	0,30	0,21:0,38	0,06	0,64	0	4,16
	Yes	23	0,76	0,21:1,3	0,18	1,27	0,01	4,04
	The medians of UPCR are the same across categories of Stillbirth (Y/N). p-value = 0,109							

SGA – small for gestational age.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] South African National Department of Health (NDoH), in: The 2017 Annual Saving Mothers Report, NDoH, Pretoria, 2017, p. 5.
[2] W. Wang, X. Xie, T. Yuan, Y. Wang, F. Zhao, Z. Zhou, et al., Epidemiological trends of maternal hypertensive disorders of pregnancy at the global, regional, and national levels: a population-based study, BMC Pregnancy Childbirth 21 (1) (2021) 364.
[3] M.A. Brown, L.A. Magee, L.C. Kenny, S.A. Karumanchi, F.P. McCarthy, S. Saito, et al., Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice, Hypertension 72 (1) (2018) 24–43.
[4] J. Moodley, P. Soma-Pillay, E. Buchmann, R.C. Pattinson, Hypertensive disorders in pregnancy: 2019 National guideline, S. Afr. Med. J. 109 (9) (2019) 12723.
[5] R.G. Sinkey, A.N. Battarbee, N.A. Bello, C.W. Ives, S. Oparil, A.T.N. Tita, Prevention, diagnosis, and management of hypertensive disorders of pregnancy: a comparison of international guidelines, Curr. Hypertens. Rep. 22 (9) (2020) 66.
[6] K.S. Gemechu, N. Assefa, B. Mengistie, Prevalence of hypertensive disorders of pregnancy and pregnancy outcomes in Sub-Saharan Africa: A systematic review and meta-analysis, Womens Health (Lond. Engl.) 16 (2020), 1745506520973105.
[7] The American College of O and G, Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy, Obstet. Gynecol. 122 (5) (2013) 1122–1131.
[8] T. Lei, T. Qiu, W. Liao, K. Li, X. Lai, H. Huang, et al., Proteinuria may be an indicator of adverse pregnancy outcomes in patients with preeclampsia: a retrospective study, Reprod. Biol. Endocrinol. 19 (1) (2021) 71.
[9] L. Poston, A.L. Briley, P.T. Seed, F.J. Kelly, A.H. Shennan, Vitamins in pre-eclampsia (VIP) Trial Consortium. Vitamin C and vitamin E in pregnant women at risk for pre-eclampsia (VIP trial): randomised placebo-controlled trial, Lancet 367 (9517) (2006) 1145–1154.
[10] K. Bramham, C.E. Poli-de-Figueiredo, P.T. Seed, A.L. Briley, L. Poston, A. H. Shennan, et al., Association of proteinuria threshold in pre-eclampsia with maternal and perinatal outcomes: a nested case control cohort of high risk women, PLoS ONE 8 (10) (2013) e76083.
[11] J.P. Guida, M.A. Parpinelli, F.G. Surita, M.L. Costa, The impact of proteinuria on maternal and perinatal outcomes among women with pre-eclampsia, Int. J. Gynaecol. Obstet. 143 (1) (2018) 101–107.
[12] Hypertension in pregnancy: diagnosis and management. London: National Institute for Health and Care Excellence (NICE); 2019.
[13] ACOG, Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222, Obstet. Gynecol. 135 (6) (2020) e237–e260.
[14] A. Berthet, S. Bartolo, D. Subtil, E. Clouqueur, C. Garabedian, H. Azaïs, Spot urine protein-to-creatinine ratio as a diagnostic test in pre-eclampsia: a gold standard? Int. J. Gynaecol. Obstet. 149 (1) (2020) 76–81.
[15] E. Abalos, C. Cuesta, G. Carroli, Z. Qureshi, M. Widmer, J.P. Vogel, et al., Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health, BJOG 121 (Suppl 1) (2014) 14–24.
[16] J. Kadlec, K. Bartkiewicz, A. Černoch, K. Lemr, A. Miranowicz, Experimental hierarchy of the nonclassicality of single-qubit states via potentials for entanglement, steering, and Bell nonlocality, Opt. Express 32 (2) (2024) 2333–2346.
[17] A. Murali, S. Rengaraj, P.S. Priyamvada, S. Sivanandan, K.R. Udayakumar, Proteinuria in predicting adverse outcomes in women with severe features of pre-eclampsia from a developing country: a prospective cohort study, Int. J. Gynaecol. Obstet. (2023).
[18] A. Chadha, S. Tayade, Urinary protein-to-creatinine ratio: an indicator of adverse clinical outcomes in preeclampsia with proteinuria, Cureus 14 (3) (2022) e23341.
[19] J. Xiao, W. Fan, Q. Zhu, Z. Shi, Diagnosis of proteinuria using a random urine protein-creatinine ratio and its correlation with adverse outcomes in pregnancy with preeclampsia characterized by renal damage, J. Clin. Hypertens. (Greenwich) 24 (5) (2022) 652–659.