International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Thillai Nayaki S et al. Int J Reprod Contracept Obstet Gynecol. 2025 Apr;14(4):1285-1291
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20250876

Original Research Article

Analysis of the status of spot urine albumin creatinine ratio in pregnancy

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Received: 02 February 2025
Accepted: 18 March 2025

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ABSTRACT

Introduction: Urinary albumin-to-creatinine ratio (UACR) has been widely studied as a non-invasive biomarker for detecting and predicting complications in pregnancy.
Methods: A prospective cohort of 170 pregnant women was evaluated for UACR levels in all three trimesters. UACR thresholds were derived using receiver operating characteristic (ROC) curve analysis, with clinical diagnoses as the gold standard. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each threshold.
Results: Mean UACR values increased progressively across trimesters, from 3.6 (±1.9) mg/g in the first trimester to 189.4 (±214.1) mg/g in the third. A UACR threshold of 316 mg/g in the third trimester achieved high diagnostic accuracy for preeclampsia (sensitivity 96.15%, specificity 97.22%, AUC 0.958). Second-trimester thresholds were predictive for preeclampsia (10.6 mg/g; AUC 0.851), GHTN (8 mg/g; AUC 0.5408), and GDM (8.2 mg/g; AUC 0.5409). Fetal complications (8.6 mg/g; AUC 0.6386) and C-sections (8.4 mg/g; AUC 0.5657) were also significantly associated with second-trimester UACR levels.
Conclusion: The study establishes trimester-specific UACR thresholds for identifying and predicting maternal and fetal complications, emphasizing its utility in antenatal care. Incorporating UACR into routine screening could enhance early detection and management of high-risk pregnancies.

Keywords: Urinary albumin-to-creatinine ratio, Pregnancy complications, Preeclampsia, Gestational hypertension, Gestational diabetes mellitus, Fetal outcomes

INTRODUCTION

Maternal health has always been a special area of obstetric research due to its impact on maternal and neonatal outcomes. Increased renal plasma flow, elevated glomerular filtration rate (GFR), and alterations in protein excretion patterns are among the few important renal changes that occur during pregnancy.[1,2] During pregnancy, proteinuria increasingly worsens due to non-selective (proximal tubule) re-absorption and selective glomerular filtration. Although the glomerulus is largely impermeable to albumin, it is known that non-pregnant women filter 500–600 mg of albumin each day (3 mg/l in the filtrate).[3] Normal values are 5 mg/100 ml in the first and second trimesters, 10 mg/100 ml in the third trimester, and 300 mg/day in the third trimester of a healthy pregnancy.[4] Values above 15 mg/100 ml or 300 mg per day are typically indicative of pre-eclampsia or underlying renal illness.[5]

Microalbuminuria is characterised as persistently above-normal albumin excretion in the urine. Since the spot urine albumin-to-creatinine ratio (ACR) offers a trustworthy estimation of albuminuria, it is often a well-known biomarker for evaluating renal health.[6] Unlike 24-hour urine collection, which is labour-intensive and often has compliance issues, spot urine ACR offers a non-invasive, practical, and efficient alternative, making it particularly valuable in antenatal care settings.[7] One of the "cornerstones" of antenatal care is a pre-eclampsia

screening regimen involving routine blood pressure checks and urine checks for proteinuria (often using urinalysis dipsticks). Utilising visual reagent strips, the "dipstick analysis" is quick, portable, and simple. However, several times of the day are used to collect urine samples. This test is confounded by somewhat high false positive and false negative rates. Hence, the "gold standard" test of 24-hour urine collection is nearly always performed after it.[8] In and of itself, this test has issues. The gathering is laborious, time-consuming, inconvenient for patients and hospital staff, and prone to mistakes like inaccurate data due to incomplete collection (in 13-68 percent of collections).[9]

The diagnostic utility of the ACR warrants special attention due to the physiological changes in the renal processing of albumin and creatinine during pregnancy and the pathological perturbations associated with metabolic and hypertensive diseases.[10] However, there is a lack of reliable data establishing normative and pathological ranges for pregnant people, even though numerous research has examined ACR thresholds in non-pregnant populations.[11] Thus, the present study aims to comprehensively analyse the status of spot urine ACR during pregnancy, with a particular focus on its role as a diagnostic tool for renal dysfunction and to estimate spot urine albumin creatinine ratio during the three trimesters of pregnancy

METHODS

Study setting and period

We conducted a prospective follow-up observational study among all pregnant women attending obstetrics outpatient clinic in the Department of Obstetrics and Gynaecology, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur between March 2021 to August 2022

Inclusion criteria

The study participants were recruited with inclusion criteria of all adult pregnant women who provided urine samples in all three trimesters of pregnancy.

Exclusion criteria

Women who were diagnosed with mental retardation/other mental disorders or refused to consent to the study were excluded.

Sample size and sampling

We calculated the sample size according to study by Gupta et al at New Delhi, where the prevalence of increased spot urinary protein creatinine ratio was 12%. Taking the prevalence, with 95% confidence interval and 5% absolute precision, sample size was calculated by formula, estimating a minimum sample size to be 163. However, we enrolled a total of 170 individuals who attended during the study period were included. We employed consecutive sampling until the sample size was reached.

Study procedure

The study commenced after obtaining informed consent from all the study participants. Information on sociodemographic details and other relevant clinical details were collected using a pretested semi structured questionnaire. The spot urinary albumin–creatinine ratio (UACR) was determined from three midstream urine samples (in sterile urine containers without preservatives) collected each in the first, second and third trimesters of all pregnant women visiting Obstetrics and Gynaecology OPD of the Medical college hospital. Participants were followed until delivery. The UACR of high-risk pregnancies was compared and correlated. A normal range estimate of the urinary albumin-to-creatinine ratio was established. Urine albumin was measured by the immunoturbidimetric method through a semi-automated biochemistry analyser. Urine creatinine was measured by modified kinetic Jaffe reaction without deproteinization. UACR (mg/g) was calculated using the formula urine albumin/urine creatinine

Statistical analysis

Microsoft Excel was used to code the data. To analyse the data, IBM Corp.'s SPSS v23 programme was employed. For continuous data, descriptive statistics were elaborated as means/standard deviations and medians/IQRs, utilizing a receiver operating curve, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) at various urine albumin creatinine ratio levels are to be computed (ROC). At p 0.05, statistical significance was maintained.

RESULTS

We finally recruited around 170 patients who fitted the inclusion and exclusion criteria. All patients and their relatives agreed to participate in the study thus accounting for a response rate of 100%. Table 1 depicts the sociodemographic characteristics of the study participants. We could see that more than half (53%) of the study participants were belonging to the age group of 25-30 years, with a mean age of 28.4 (8.3) years. Almost half (48%) of the study participants were illiterate or studied up to primary school.

Almost 3/5th of the study participants was belonging to the lower socioeconomic class. Almost everyone (94%) was booked. Almost 2/3rd was multiparous. Around 53% of the study participants had overweight or obese status of BMI. We observed that the mean (sd) distribution of UACR values during 1st, 2nd and 3rd trimester were observed be 3.6 (1.9), 15.4 (22.1) and 189.4 (214.1). Almost 90% children had normal birth weight, more than half had normal delivery and almost 3/4th did not have any comorbidity.

With respect to the comorbidity at presentation, we found that the around 35% did not have any comorbidity i.e., unaffected, while the most common comorbidity was anaemia (18.2%), and GTN (18.2%). We observed that the distribution of mean (sd) UACR values among various comorbidities were observed to be: IUGR-453.5 (124.1), Preeclampsia-548.2 (118.2), GHTN-169.1 (47.5), 145.2 (57.1), Anaemia-113.1 (38.1), No comorbidity- 45.2 (2.1).

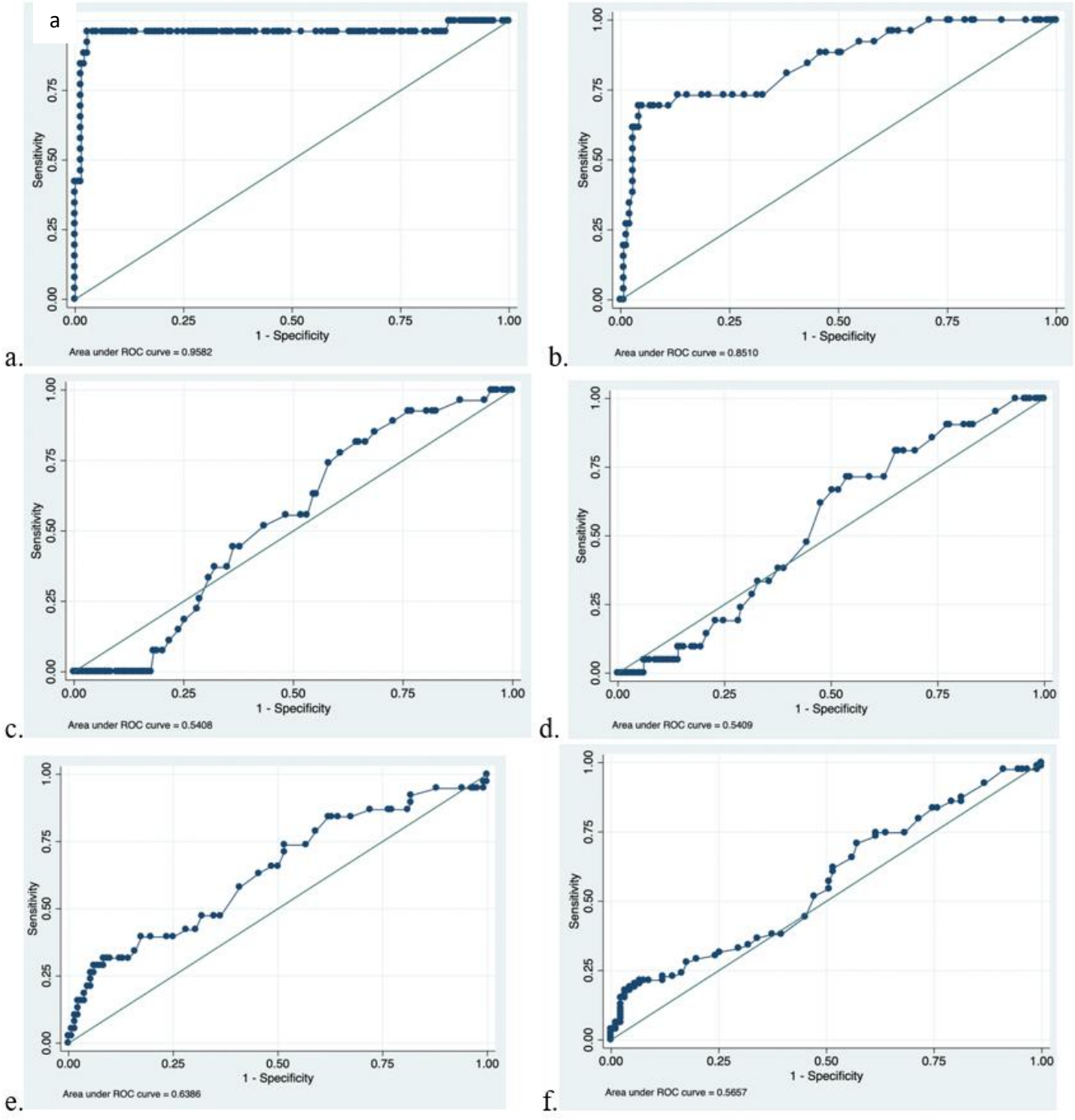

Figure 1: a. Preeclampsia (3rd trimester) b. Preeclampsia (2nd trimester) c. GHTN (3rd trimester) d. GHTN (2nd trimester) e. Fetal complications f. C-section.

The receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic accuracy of spot urinary albumin-creatinine ratio (UACR) across multiple obstetric outcomes. For the detection of preeclampsia in the third trimester, a UACR threshold of 316 mg/g demonstrated the highest diagnostic performance with a sensitivity of 96.15%, specificity of 97.22%, positive predictive value (PPV) of 86.8%, and negative predictive value (NPV) of 96.9%, yielding an exceptional area under the curve (AUC) of 0.958.

Similarly, during the second trimester, a threshold of 10.6 mg/g showed robust accuracy for preeclampsia prediction, with a sensitivity of 73.08%, specificity of 86.81%, PPV of 81.4%, and NPV of 91.2% (AUC=0.851). In contrast, for gestational hypertension (GHTN) and gestational diabetes mellitus (GDM) detection in the third and second trimesters, respectively, the diagnostic thresholds were lower (8.0 mg/g and 8.2 mg/g), with moderate sensitivity (62.48% and 66.08%) and specificity (49.24% and 49.81%). The AUC values for these conditions were 0.5408 and 0.5409, indicating limited discriminatory ability.

Similarly, thresholds of 8.6 mg/g and 8.4 mg/g were identified for fetal complications and cesarean section prediction, respectively, with sensitivity and specificity ranging between 54.7% and 63.7%, reflecting moderate diagnostic utility (AUC=0.6386 and 0.5657).

Table 1: Sociodemographic characteristics of the study participants (n=170).

Characteristics	Frequency (%)
Age group (in years)	
<25	36 (21.2)
25-30	90 (52.9)
>30	44 (25.8)
Education	
Illiterate/Primary school	82 (48.2)
Secondary school	52 (30.7)
Graduate	24 (14.1)
Post graduate/Professional	12 (7.1)
Socioeconomic status	
Lower	101 (59.4)
Middle	58 (34.1)
Upper	11 (6.4)
Booking status	
Booked	161 (94.7)
Not booked	9 (5.3)
Parity	
Primi	61 (35.8)
Multiparous	109 (64.2)
Pre pregnancy BMI	
<18.5	25 (14.7)
18.5-24.9	56 (32.9)
25-29.9	70 (41.2)
>30	19 (11.2)
UACR values-Mean (SD)-normal pregnancies	
1st trimester	3.6 (1.9)
2nd trimester	15.4 (22.1)
3rd trimester	189.4 (214.1)
Neonatal complications	
Pre term/ Low birth weight/ IUGR	20 (11.7)
Cord prolapse / CPD in labour	10 (5.8)
Foetal distress	12 (7.1)
Nil	132 (77.6)
Mode of delivery	
Elective LSCS	33 (19.4)
Emergency LSCS	46 (27.1)
Normal delivery	91 (53.4)
Birth weight (in kg)	
<2.5	17 (10.0)
>2.5	153 (90.0)

Table 2: Distribution of comorbidities and the mean UACR values among the study participants (n=170).

Comorbidity	N (%)	UACR-Mean (SD)
Anaemia	31 (18.2)	113.1 (38.1)
GDM	29 (17.1)	145.2 (57.1)
Preeclampsia	16 (9.4)	548.2 (118.2)
GHTN	27 (15.8)	169.1 (47.5)
IUGR	10 (5.8)	453.5 (124.1)
No comorbidity	61 (35.8)	45.2 (2.1)

Table 3: Distribution of ROC cut-off points for UACR thresholds, sensitivity, specificity, PPV and NPV for various diagnostic conditions among the study participants (n=170).

Diagnostic condition	Trimester	UACR threshold (mg/g)	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV, %)	Negative predictive value (NPV, %)	Area under curve (AUC)
Preeclampsia	3rd	316.0	96.15	97.22	86.8	96.9	0.958
Preeclampsia	2nd	10.6	73.08	86.81	81.4	91.2	0.851
Gestational hypertension (GHTN)	3rd	8.0	62.48	49.24	75.4	79.2	0.5408
Gestational diabetes mellitus (GDM)	2nd	8.2	66.08	49.81	81.6	79.2	0.5409
Fetal complications	2nd	8.6	63.7	54.7	79.6	74.2	0.6386
Cesarean section	2nd	8.4	54.7	52.5	71.6	81.2	0.5657

DISCUSSION

We performed this prospective observational study to analyse the spot urine ACR status during pregnancy comprehensively. We noted that during 3rd and 2nd trimesters among preeclampsia patients, UACR cut-off at 316 and 10.6 mg/g had the highest AUC values of 0.958 and 0.851, respectively. However, UACR cut-off values for GHTN during the 3rd and 2nd trimesters showed lower AUC values.

In this study of 170 pregnant women, we found that the majority of participants were aged between 25 and 30 years, with a mean age of 28.4 years, consistent with findings from Gupta et al, though younger than those reported by Baweja et al.[12,13] The mean urinary albumin-creatinine ratio (UACR) values showed significant increases across trimesters, from 3.6 mg/g in the first trimester to 189.4 mg/g in the third trimester, similar to patterns observed in other studies.[12,14] Regarding comorbidities, 35% of participants were unaffected, while anaemia and gestational hypertension (GHTN) were the most common conditions observed in 18.2% each, consistent with national and regional trends.[13-15] UACR levels were notably higher in conditions such as intrauterine growth restriction (IUGR) and preeclampsia than those without comorbidities.

Receiver operating characteristic (ROC) analysis was used to establish UACR cut-offs for predicting various pregnancy complications. A UACR value of 316 mg/g in the third trimester was optimal for detecting preeclampsia, achieving a sensitivity of 96.15%, specificity of 97.22%, and an AUC of 0.958, corroborating Gupta et al.'s findings.[12] For the second trimester, UACR thresholds of 10.6 mg/g and 8 mg/g were identified for preeclampsia and GHTN, respectively, with moderate sensitivity and specificity. UACR values of 8.2 mg/g predicted gestational diabetes mellitus (GDM) with comparable performance.

Secondary analysis showed UACR thresholds of 8.6 mg/g and 8.4 mg/g for predicting fetal complications and cesarean delivery, respectively. While sensitivity and specificity were lower for these outcomes, findings aligned with previous studies, underscoring the potential of UACR as a useful biomarker for antenatal risk stratification and early intervention.[7,10]

The association between creatinine excretion, a proxy for renal filtration efficiency, and albumin excretion, a measure of glomerular permeability, is reflected in the spot urine ACR. Increased filtration of plasma proteins, including albumin, is the result of a 50–80% rise in renal plasma flow and GFR during pregnancy, especially in the second trimester.[17] Even though this adaptive hyperfiltration is usually harmless, it can cause temporary increases in ACR, hence correct interpretation requires reference values unique to gestation.[18] Through mechanisms like endothelial failure, increased vascular permeability, and inflammatory mediators, pathophysiological alterations in situations like preeclampsia and gestational diabetes mellitus (GDM) worsen albuminuria despite physiological adaptations.[12,19]

ACR elevations seen under these circumstances offer a useful diagnostic window into the severity and course of the disease.

Compared to conventional proteinuria assessments, spot urine ACR screening during pregnancy has several benefits, such as time savings and a less patient load. Research has shown a clear correlation between high ACR levels and negative outcomes such fetal growth restriction and premature birth, especially when preeclampsia is present.[20] An ACR threshold of >30 mg/g, for example, was found to be strongly linked to severe preeclampsia and newborn morbidity in a recent meta-analysis.[21]

Although spot urine ACR is useful, there are difficulties in interpreting it during pregnancy. Pregnancy-related physiological albuminuria may overlap with pathological thresholds, increasing the risk of false-positive results.[19] ACR measures are further complicated by the fact that creatinine excretion fluctuates according on maternal muscle mass, hydration status, and dietary protein intake.[20] This diversity highlights the need for reference ranges that are particular to the population and gestational age, which are currently understudied in clinical guidelines. Furthermore, regular procedures for sample collection and analysis are required due to concerns about diurnal fluctuations in albuminuria and sample integrity, even if spot ACR assessments are convenient.[21,22] To maximize the practical relevance of ACR as a screening tool during pregnancy, future research must overcome these limitations.

Our study was one among the very few studies that has evaluated the spot UACR for various diagnosis and trimesters among pregnant women. Our study had a few limitations. First, our sample size was small to capture all the evaluate the effect outcome on all independent variables. Secondly, due to the observational nature of this study we were not able to establish causal relationships between the exposure and outcome. Finally, the findings are generalisable only to similar study settings, as the study was conducted only from one single centre in south India.

CONCLUSION

The use of the spot UACR as a reliable biomarker for predicting preeclampsia, gestational hypertension (GHTN), gestational diabetes mellitus (GDM), fetal complications, and cesarean delivery are highlighted in this study. The results show that UACR levels progressively rise across trimesters, highlighting its dynamic link with pathological and physiological changes during pregnancy. The UACR cut-off values determined by receiver operating characteristic (ROC) analysis showed moderate predictive potential for other conditions such GHTN, GDM, and fetal problems, and high sensitivity and specificity for identifying preeclampsia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Thillai Nayaki S, Punithavathi J, Zeba N. Analysis of the status of spot urine albumin creatinine ratio in pregnancy. Int J Reprod Contracept Obstet Gynecol 2025;14:1285-91.