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The utility of Albumin Creatinine ratio in early assessment of Renal function in Hypertensive Pregnant patients in Benin City, Nigeria

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Abstract

Worldwide, hypertensive conditions via pregnancy (HDP) are a major cause of maternity death. This study explores the potential utility of the Albumin Creatinine Ratio (ACR) in initial renal function assessment for hypertensive pregnant patients in Benin City, Nigeria. The research addresses challenges in accurately measuring the incidence of pregnancy-related hypertension, emphasizing limited access to prenatal care and standardized definitions for pre-eclampsia. Elevated levels of microalbuminuria and ACR in preeclampsia and pregnancy-induced hypertensive cases underscore the link between renal dysfunction and hypertensive disorders. The study reveals a prevalence of microalbuminuria in hypertensive pregnant women and emphasizes the need for early assessment tools. Bivariate correlation analyses show significant associations between ACR and gestational age, microalbuminuria, total cholesterol, and urine creatinine during the 2nd and 3rd trimesters. Receiver Operating Characteristic (ROC) analyses demonstrate promising diagnostic potential for ACR at both trimesters. The distribution of ACR values across age groups provides insights into potential variations in renal function based on maternal age. Notably, severe preeclampsia is associated with higher ACR levels, suggesting its role in indicating the severity of renal involvement. Despite the study's shortcomings, which include its insufficient sampling size, the findings highlight ACR's potential as a valuable marker for renal function and risk stratification in hypertensive pregnant patients.

Keywords: Renal function, abulmin-creatinine-ratio (ACR), microalbumuria, creatinine, preeclampsia pregnancy, hypertention.

Introduction

Among underdeveloped nations, hypertensive problems during pregnancy constitute an important factor of illness as well as mortality among mothers and newborns. The cause of 12% of the maternal deaths globally involves hypertension problems during pregnancy. Throughout Nigeria, Obstetrical care is frequently characterized by high blood pressure during pregnancy as well as related consequences, such as eclampsia, which constitute important contributors to mortality and morbidity among mothers along with newborns[1]. Across medical facilities research conducted throughout Nigeria, cases ranging from 22.6% to 26.2 percent among all births were observed. According to a previous nationwide assessment, eclampsia was a factor across sixteen percent among maternity fatalities throughout healthcare recommendation centers as well as thirteen percent among each pregnancy-related obstetric problems. The inadequate, inaccessible, and underutilized state of the current medical services infrastructure is mostly to blame for this dire situation. Almost significant amount of women of adulthood nevertheless choose conventional childbirth attendant prenatal as well as postpartum healthcare over conventional maternal facilities since it proves better affordable, further widely available, and deemed traditionally suitable[2].

Globally, hypertension due to pregnancy is a major factor in maternal death as well as morbidity[3]. Incidence approximations in less-developed nations have shown a range 4.0 percent to 12.3 percent throughout the period[3,4]. In contrast to statistics from population-level reports, and thus less likely to inflate levels, these figures depend upon facility-centered longitudinal cohort studies. Consequently, the real event continues to be obscure. Overall lack of a common criteria indicating pre-eclampsia, the difficulty in accessing trustworthy pregnancies as well as hypertension tests, and uneven effectiveness and coverage of prevalent healthcare data systems all contribute to assessing challenges. For example, national population health assessments show that 54.4% of pregnant women in Malawi had hypertension tests. This is slightly more than half of all women in the country[5]. In India, although 89% of women receive such measurements, only partial narrative attending at least four pre-birth care sessions[6]. The incidence of pregnancy hypertension was approximately 10%, with variations across countries. Gestational hypertension Chronic hypertension, as well as pre-eclampsia constituted distinct types, revealing unique prevalence patterns. Notably, most diagnoses relied on a broad definition, emphasizing the complexity of accurate measurement.

The predominance of diastolic hypertension, especially in non-severe cases, underscored the inadequacy of palpation for clinical care[7,8].

Renal impairment is a severe side effect of hypertension disorder durng pregnancy which raises the chance of developing renal failure as well as potentially causing irreparable renal damage. In African women experiencing hypertension disorder during pregnancy (HDP), the combined frequency of AKI was 5.9% (95% CI: 3.8-8.7%). The risk factors for AKI included eclampsia, HELLP syndrome, sepsis, and blood transfusion. The outcomes of AKI included maternal mortality (18.4%), fetal mortality (36.8%), and dialysis requirement (23.7%)[9]. Renal dysfunction, particularly acute kidney injury (AKI), frequently arises as a complication of preeclampsia or eclampsia, affecting 15% of all individuals with these conditions[10].

According to WHO[11], there is a 50% increased risk for maternity and infant death associated with this disability. In situations involving chronic renal damage associated with pregnancy, the fetal death rates vary from 23.8% to 38%. On the other hand, a cross-sectional study and comprehensive review revealed that preeclampsia was one of the pregnancy-related variables linked to a 13.3% risk of maternal mortality in women who experienced acute renal damage[12]. Acute kidney injury related to pregnancy is more prevalent in low- and middle-income countries, with reported incidences ranging from 4% to 26%, in contrast to 1% to 2.8% in high-income countries[12].

Nevertheless, there is limited accepting of the epidemiology of severe renal damage, particularly between women with preeclampsia or eclampsia, in low- and middle-income nations. While hypertension, proteinuria, and acute kidney injury typically resolve after childbirth for most women, some may experience persistent or even permanent complications[13,14]. With monitoring durations of up to 17 decades, epidemiologic data shows that pregnancy is related to a higher chance of acquiring cardiac and kidney illnesses, particularly advanced kidney conditions, in the future[15].

Pregnancy-related causes that are most common are severe kidney impairment include obstetric bleeding, hypertension illnesses while pregnant and infections[16]. Additionally, throughout Africa, they are the main causes of mother death and morbidity[17]. Globally, in 2019, approximately 18.1 million women experienced HDP, indicating an 11% rise over the past three decades. In the same year, this disease was linked to almost 28,000 maternal fatalities. With a pooled incidence of 8% in SSA, the prevalence of HDP is noticeably greater in SSA and Asia than in other areas[18].

Pre-eclampsia, eclampsia, chronic hypertension in pregnancy overlaid with high blood pressure, gestational high blood pressure, and chronic hypertension are all included in the broad category of hypertensive diseases during pregnancy (HDP)[7].

A seventeen-fold rise in maternal mortality as well as an 8.2-fold increase in the risk of perinatal death are associated with HDP. Placental separation, renal failure, HELLP syndrome (hemolysis, high liver enzymes, and low platelets), strokes, severe edema of the lungs, heart failure, and widespread coagulopathy are among the maternal problems brought on by HDPs[19]. Moreover, HDP increases the lifetime danger of heart conditions, including arrhythmia, strokes, coronary heart disease, and renal failure[20]. Significantly more acute renal failure attributable to birth-related hypertension conditions than other types of kidney injury occurs when pregnant. This deadly disease is thought to be caused by the antiangiogenic and vasoconstrictive properties of endothelin as well as soluble feline McDonough sarcoma-like tyrosine kinase 1 (sFLT-1), which is released anytime endothelium damage occurs[3,21].

The capacity of the acute urinal albumin-to-creatinine ratio (ACR) to identify minute levels of albumin within urine makes it unique and may replace the requirement for a 24-hour protein level in urine test[22]. Quantitative ACR technique is recommended by the National Kidney Organization, American Diabetic Society, and National Institutes of Health for the assessment of urine albumin[23].

Studies show a correlation between being overweight, diabetes, high blood pressure, overt renal illness, as well as microalbuminuria throughout the overall humanity, as well as a complex prevalence of cardiac disease and early mortality in the decades to come. Despite the usual range of urine albumin, issues might still arise. Whereas prognosis methods have revealed inconsistent findings, prior research has demonstrated that the stage of microscopic albumin precedes a clinical illness, thus serving as a potential indicator for an overt disease[24].

A urine dipstick technique, a rapid although partially quantitative colorimetric assay which can result in inaccurate results and require an additional quantitative assessment is often used for testing proteinuria. Despite being the recognized standard, typical 24-hour protein level in urine measurement might be inaccurate or challenging to utilize due to variations in urine collection techniques[25].

Researchers have lately examined the exact urine protein creatinine ratio and the albumin creatinine ratio (ACR) to detect proteinuria among disorders such as renal failure, blood sugar levels, and pregnancy. Compared to overall proteins excretion, the release of albumin is thought to provide a better realistic picture underlying damage to the renal system and act as a biomarker for dysfunctional central endothelial cells[26].

Since ACR has shown to be a valid marker from proteinuria in preeclamptic women, global bodies are now in favor of spot proteinuria testing in situations of possible hypertension[27]. Urine samples collected from random are used to test each ACR and PC ratio; however, ACR is thought to be higher Sensity and quick compared to PC ratio.

As such, this test can be administered to pregnant patients who visit prenatal clinic[28]. According to the study, women suffering from preeclampsia, preterm birth had mean urine ACRs that were considerably greater compared to those of women who experienced not. Employing receiver operating curve analysis, it further determined its sensitivities and accuracy of urine ACR to forecast these problems. Urine ACR was shown to have high value as a marker for pregnancy and GDM, though not for premature labor[29].

According to previous studies, the albumin creatinine proportion (ACR) is a useful marker of renal microangiopathy that occurs initially. This test is well-known for its ease, quickness, as well sensitivity. Furthermore, conclusions throughout research[30,31], have consistently shown a noteworthy association between albumin creatine and 24-hour amount of urine protein. Prior to this study, we aim to evaluate the medical use of the albumin-creatinine ratio among hypertensive pregnant women in Benin City, Nigeria, as a preemptive measure of renal function.

This study is significant and justified since it addresses the important problem of hypertensive challenges upon pregnancy, especially when it comes to the evaluation of renal function. Pregnancy-related hypertension issues are a major danger to a mother's well-being and a major broad contributor to postpartum morbidity and death. The prevalence of certain conditions, particularly in developing countries, highlights the critical need for efficient diagnostic and prognostic instruments.

The study focuses on how well the Albumin Creatinine Ratio (ACR) in hypertension pregnant women in Benin City, Nigeria, functions as an early indication of renal function. The emphasis of this attention stems from the serious implications of severe renal damage, which can arise as a result of hypertension diseases in pregnant women. AKI greatly raises the risk of maternal and fetal death by causing permanent renal failure, chronic renal failure, and advanced renal disease.

The choice of ACR as a marker for renal function assessment is supported by its unique ability to identify minute levels of albumin within urine, providing a sensitive and quick measure. The study draws on established recommendations from global bodies, including the National Kidney Organization, American Diabetic Society, and National Institutes of Health, advocating for the quantitative ACR technique in assessing urine albumin.

In addition, the study intends to close a knowledge vacuum by providing important insights into the epidemiology of acute kidney damage affecting mothers in low- and middle-income nations who have preeclampsia or eclampsia.

The study's relevance is increased by the possibility that ACR might work as a biomarker for defective central endothelial cells and by its correlation with unfavorable pregnancy results, such as cardiovascular and renal illnesses.

Materials and Methods

Participants and Methods: This research was carried out at the Department of Obstetrics and Gynecology, University of Benin Teaching Hospital and Central Hospital Benin. It involved a prospective case-control study with a total of 190 female participants. The participants were categorized into three groups: preeclamptic group (n=124), Pregnancy-induced hypertensive group (n = 30), and a control group consisting of pregnant women with normal blood pressure (n = 36). The study excluded participants with a history of maternal illnesses such as cardiovascular disease, renal disease, diabetes mellitus, thyroid disease, hepatic disease, or related disorders, including urinary tract infections. Blood pressure measurements were conducted with the participants in a prone position on at least two separate occasions using a mercury sphygmomanometer.

Spot urine samples were collected from the study groups using clean universal bottles and stored at a temperature of minus 4 degrees Celsius until they were ready for analysis of the urinary albumin creatinine ratio. Additionally, the study groups underwent a single antecubital venipuncture, during which 5ml of venous blood was drawn using a sterile disposable syringe. The obtained whole blood was then transferred into a plain bottle, allowed to clot and retract, and subsequently centrifuged at 4000 RPM for 15 minutes. The resulting serum was collected into a 5 ml plain vial using a Pasteur pipette and stored at a temperature of minus 4 degrees Celsius until it was ready for analysis of uric acid, total cholesterol, and creatinine.

For the determination of uric acid, the analyte was was performed colorimetrically following the enzymatic method of Mazumder et al.[32]. The Jaffes method as presented in Allen et al.[33] was adopted in the estimation of both serum and urine creatinine. The colorimetric determination of total cholesterol, using kits from Randox Diagnostics can be referenced to the work of Friedewald et al.[34]. For the microalbumin determination colorimetrically using the Fortress diagnostic kit, the work of Chauhan et al.[35] can be cited. Albumin creatinine ratio was determined as a ratio of urine microalbumin to creatinine, and expressed in mg/g.

Method of data management and statistical analysis: Whereas some demographic data were presented in graphs other were presented in simple frequency Tables. Participants were distributed according to age groups, after having been separated into preeclamptic, normotensive and PIH groups respectively. This distribution was expressed in frequencies and percentage. Comparative results of biochemical analytes in the study participants were separated using single factor ANOVA, having assumed homogeneity of the experimental conditions. The need to establish possible association between ACR and selected biochemical parameters of the study participants at both 2nd and 3rd trimesters amounted to the use of bivariate correlastion analyses at $p<0.05$ and $p<0.01$ (2-tailed) respectively.

In order to estimate possible benchmark for ACR among participants either at 2nd or 3rd trimester, Receiver operator curve was constructed with a concomitant determination of area under the curve as well as sensitivities and specificities.

The SPSS Statistical software version 21 was used to analysed data, whereas GraphPad Prism verion5 was used to present the graphs in the study.

Results and Discussion

The proportion of respondents by gender categories, into the various study groups has been shown on Table-1. About 0.8% of the preeclamptic cases (n=124) were less than 25 years, while no normotensive or PIH individuals were below 25 years. Among the preeclamptic cases, majority (44.4%) were between 31 and 35 years. Whereas 2.4% of the preeclamptic cases were single, 74.2% were married for the first time (Figure-1); while 2.8% of pregnancy induced hypertensive cases were remarried. Majority of the respondents were educated and as such information gathering was not difficult. The obstetric characteristics of the participants showed that average at menarche ranged from 14.29 – 16.09 yrs ($p>0.05$), while parity among the participants also ranged between 2.04 – 3.11 ($p>0.05$) (Table-2). Similarly, the distribution of participants into preeclampsia cases, PIH or normotensive ones did not affect age at confinement (28.15 – 31.09 yrs, $p>0.05$) and gestational age (27.08 – 30.11 wks, $p>0.05$). Table-3 shows the mean values of biochemical analytes in the study participants irrespective of trimester. The incidence of PIH or preeclampsia raised Micro albuminuria when compared with the normotensive cases ($p<0.05$). Whereas microalnuminuria was 11.56mg/dL in the normotensive individuals, it rose to 36.13 – 59.61mg/dL. ACR was 514.34mg/g in preeclampsia and 305.79 mg/g in PIH, compared to 53.56mg/g in the control. Generally, total cholesterol, uric acid as well as plasma and urine creatinine were lower in the control when compared with either preeclampsia or PIH. No differences in these analytes were reported between PIH and preeclampsia.

Table-1: Distribution of participants, according to age groups, into the various study groups.

Age Groups	Preeclampsia cases n (%) (N=124)	Normotensive n (%) (N=36)	PIH n (%) (N=30)	X^2	p-value
18-25 yrs	1 (0.8)	0	0	*5.60* *(p=0.632)*	*6.26* *(p=0.618)*
26-30 yrs	31 (25.0)	11 (30.6)	4 (13.3)		
31-35 yrs	55 (44.4)	15 (41.7)	2 (6.7)		
36-40 yrs	32 (25.8)	7 (19.4)	4 (13.3)		
41-45 yrs	5(4.0)	3 (8.3)	0		

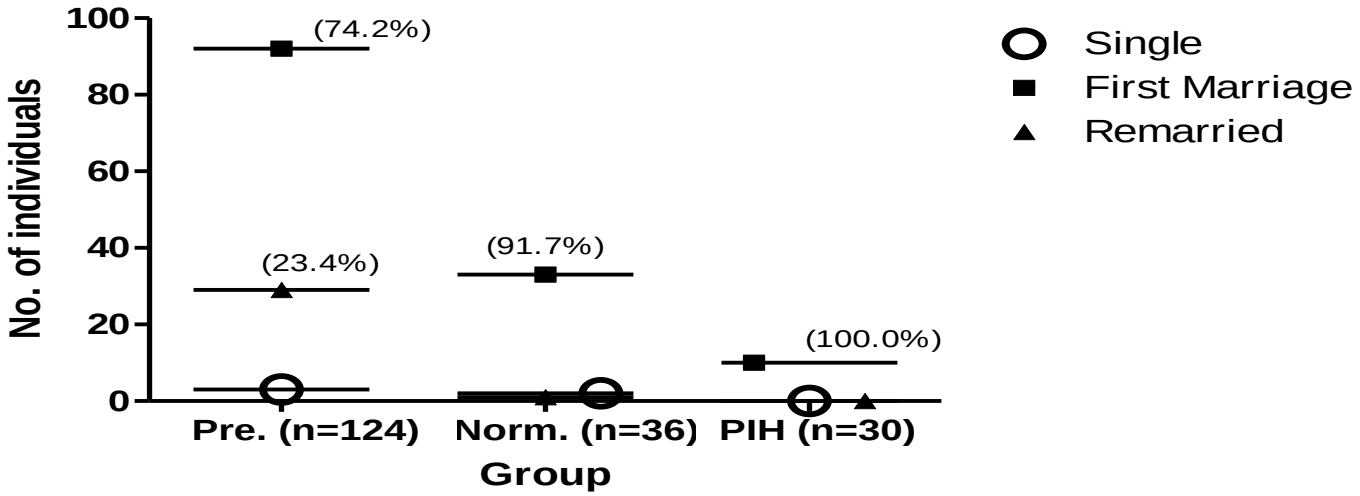


Figure-1: Marital status of the respondents.

Table-2: Obstetric characteristics of the study participants.

Queries	Preeclampsia cases (A) n (%) (N=124)	Normotensive (B) n (%) (N=36)	PIH(C) n (%) (N=30)	p-value		
				A+B	A+C	B+C
Age at menarche (yrs)	14.29 ± 2.52	16.09 ± 5.13	14.38 ± 2.41	0.092	0.327	0.073
Parity	2.67 ± 1.29	2.04 ± 1.16	3.11 ± 1.87	0.613	0.066	0.105
Age at last confinement (yrs)	28.15 ± 5.38	31.09 ± 5.66	29.0 ± 3.38	0.114	0.313	0.252
Gestational age (wks)	27.08 ± 4.05	27.94 ± 8.24	30.11 ± 7.24	0.302	0.421	0.092

Table-3: Mean values of biochemical analytes in the study participants irrespective of trimester.

Group	Micro alb. (mg/dL)	ACR (mg/g)	Total cholesterol (mg/dL)	Uric acid (mg/dL)	Plasma Creatinine (mg/dL)	Urine Creatinine (mg/dL)
Preeclampsia	59.61a ± 12.08	514.34a ± 108.70	208.45a ± 3.40	5.58a ± 0.15	1.41a ± 0.04	126.12a ± 10.35
Normotensive	11.56b ± 0.67	53.56a ± 5.23	132.46c ± 4.90	2.68c ± 0.21	0.78b ± 0.03	271.29b ± 24.34
PIH	36.13a ± 11.06	305.79a ± 155.64	169.79b ± 7.43	4.19b ± 0.40	1.22a ± 0.05	163.86a ± 16.18
F-statistic	2.450	2.758	65.396	48.373	29.431	20.433
p-value	0.049	0.066	<0.001	<0.001	<0.001	<0.001

Means on same columns with similar superscript do not differ from one another (p>0.05).

Table-4: Bivariate correlation between ACR and selected biochemical parameters of the study participants at both 2nd and 3rd trimesters.

Parameters		2nd trimester				3rd trimester	
		AG	GA	ACR		ACR	TC
Age of participants (AG)	R	1	0.092	0.111		NA	NA
	p-value		0.406	0.318		-	-
Gestational age (GA)	R	0.092	1	-0.290**		NA	NA
	p-value	0.406		0.008		-	-
MicroAlbumin	R	0.047	-0.459**	0.819**		0.954**	0.212*
	p-value	0.671	0	0		0	0.027
ACR	R	0.111	-0.290**	1		1	0.216*
	p-value	0.318	0.008				0.024
Total cholesterol (TC)	R	0.254*	0.108	0.263*		0.216*	1
	p-value	0.021	0.332	0.016		0.024	
Uric Acid	R	0.107	0.202	0.133		0.155	0.543**
	p-value	0.334	0.067	0.23		0.107	0
Plasma creatinine	R	0.108	0.049	0.09		0.006	0.442**
	p-value	0.331	0.66	0.416		0.952	0
Urine creatinine	R	-0.260*	-0.163	-0.380**		-0.175	-0.232*
	p-value	0.018	0.14	0		0.069	0.015

*. Correlation is significant at the 0.05 level (2-tailed); **. Correlation is significant at the 0.01 level (2-tailed).

The need to establish possible association between ACR and selected biochemical parameters of the study participants at both 2nd and 3rd trimesters was established (Table-4). Association between ACR and gestational age (R= -0.290 p<0.01), microalbuminuria (R= 0.819 p<0.01), total cholersterol (R= 0.263 p<0.01), and urine creatinine (R= -0.380 p<0.01) have been reported during the second semester. Apart from ACR versus microalbuminuria, the associations were week. During third trimester, association between ACR and microalbuminuria was higher, compared to the second trimester (R= 0.954 p<0.01).

Table-5 shows the bivariate correlation between ACR and selected biochemical parameters of the study participants irrespective of trimester. Aprt from the strong association between ACR and microalbuminuria (R= 0.955, p<0.01), relationship among ACR and other selected parameters (Table-5) were weak.

Distribution of ACR according to age and within the 2nd and 3rd trimesters have been presented on Figure-2. Results showed that during 2nd trimester, a higher ACR value of 150.7 mg/g was obtained within the 36 – 40 yrs age category, compared to 101.1 mg/g in the 41-45yrs gap. During the 3rd trimester however, ACR ranged from 157.7 mg/g within the 18 – 25 yrs gap to 928 mg/g in the 36 – 40 yrs age category. This generally showed a higher ACR range at 3rd trimester than at 2nd trimester according to the age distribution.

Table-5: Bivariate correlation between ACR and selected biochemical parameters of the study participants irrespective of trimester**.**

Parameters		GA	ACR	TC
Gestational age (GA)	R	1	0.019	0.009
	p-value		0.807	0.904
MicroAlbumin	R	0.018	0.955**	0.118
	p-value	0.816	0	0.125
ACR	R	0.019	1	0.132
	p-value	0.807		0.086
Total cholesterol (TC)	R	0.009	0.132	1
	p-value	0.904	0.086	
Uric Acid	R	0.101	0.140	0.444**
	p-value	0.191	0.068	0
Plasma creatinine	R	-0.038	-0.077	0.317**
	p-value	0.625	0.317	0
Urine creatinine	R	0.084	-0.117	-0.241**
	p-value	0.277	0.13	0.002

*. Correlation is significant at the 0.05 level (2-tailed); **. Correlation is significant at the 0.01 level (2-tailed).

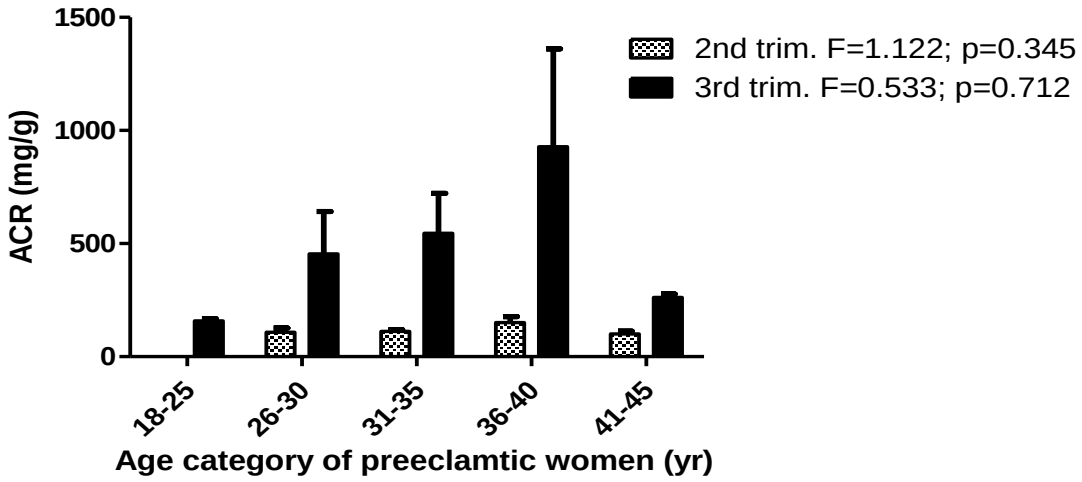
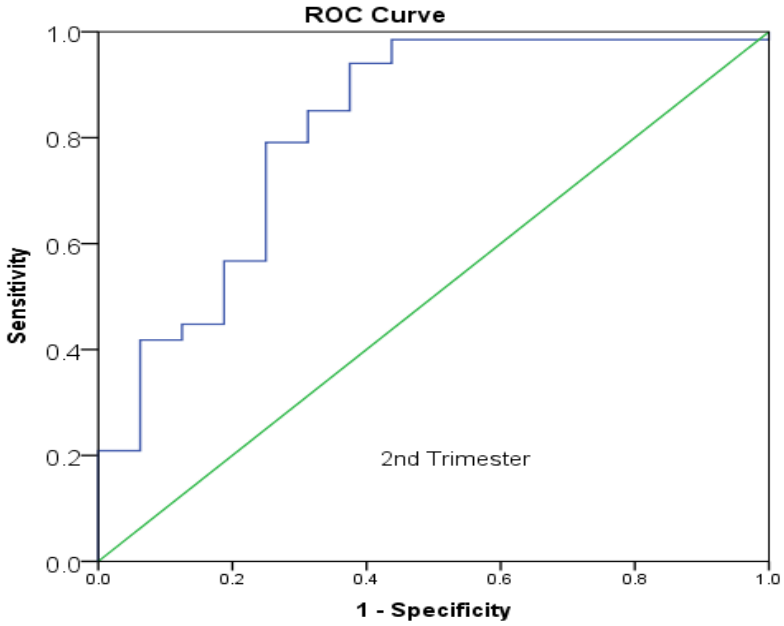


Figure-2: Pattern of ACR distribution by age in the trimesters.

Receiver operator curve at 2nd trimester (Figure-3) showed an range below the curve of 0.818 (p<0.001). From the coordinates of the curve (Table 6), the benchmark ACR was set at 82.9177 mg/g following a sensitivity of 0.821 and a precision of 0.313 (Table-6). Following cross tabulation in a 2-by-2 contingency using ACR at 2nd trimester, determinations showed a sensitivity of 91.67%, specificity of 47.83%, and a prevalence of 72.28% respectively (Table-7).

Figure-4 showed an ROC with an AUC of 0.951 (p<0.001) and a benchmark value determined from the Coordinates of the Curve at 3rd trimester (Table-8) at 52.0317mg/g. This indicated that pregnant women with ACR at 52.03mg/g at above were likely to have preeclampsia during the third trimester. Sensitivity was 89.04%, with an accuracy of 85.71%. Table-9 shows a poor Linear-by-Linear Association of 45.05 and a strong predicting value of 95.59.



Area under the curve				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% C.I.	
			Lower Bound	Upper Bound
0.818	0.066	<0.001	0.688	0.948

Figure-3: Receiver operator curve at 2nd trimester.

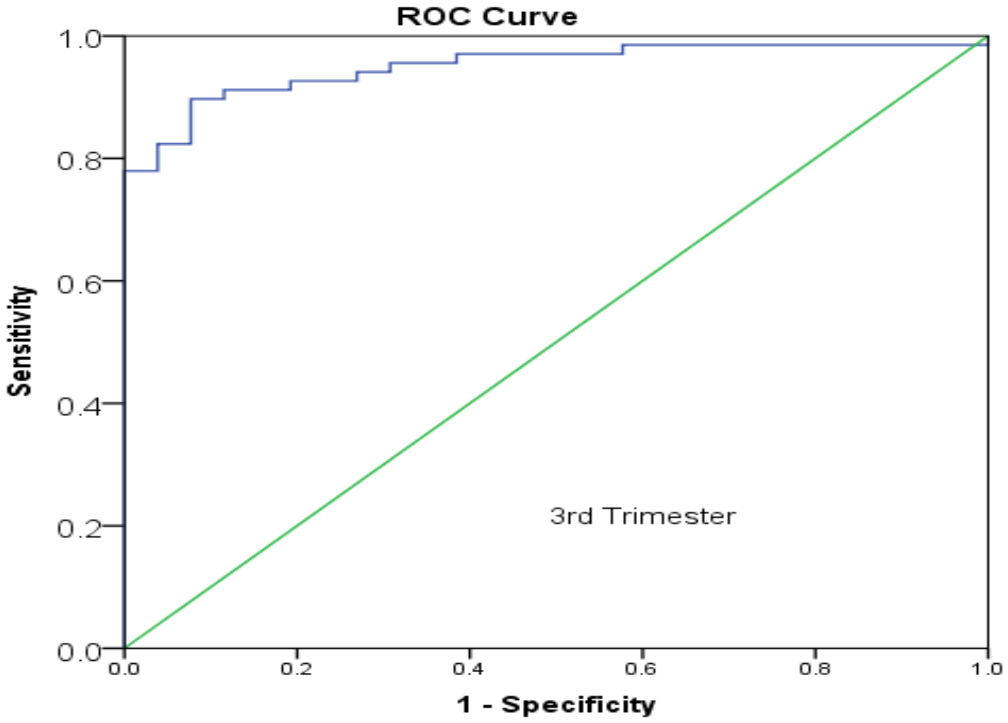
Table-6: Coordinates of the Curve at 2nd trimester.

Positive if greater than or equal to[a]	Sensitivity	1 - Specificity
22.3838	1.000	1.000
24.0196	0.985	1.000
24.7729	0.985	0.938
26.4125	0.985	0.875
71.3830	0.881	0.375
73.9125	0.866	0.375
77.4631	0.851	0.375
79.4939	0.851	0.313
81.3708	0.836	0.313
82.9177	***0.821***	***0.313***
83.3007	0.806	0.313
260.1358	0.075	0.000
276.0875	0.060	0.000
290.7420	0.045	0.000
387.5376	0.030	0.000
632.3271	0.015	0.000
782.2183	0.000	0.000

Table-10 shows analyte composition of preeclamptic subjects separated on the basis of severity of disease. At mild preeclampsia, Micro Albuminuria was 52.90mg/dL; this was minimally different from ACR value (63.32mg/dL) at severe preeclampsia (p>0.05). Althogh severity of preeclampsia did not affect composition of plasma and urine creatinine in preeclamptic subjects, ACR levels were elevated at severe preeclampsia.

Table-7: Results of Two-by-two contingency Table for 2nd trimester data.

	Value	p-value
Sensitivity (%)	91.67	Na
Specificity (%)	47.83	Na
Positive predicitive value (PPV)	82.09	Na
NPV	68.75	Na
Prevalence	72.28	Na
Pearson Chi-Square	16.67	<0.001
Likelihood Ratio	15.114	<0.001
Linear-by-Linear Association	16.464	<0.001



Area Under the Curve (AUC)				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% C.I.	
			Lower Bound	Upper Bound
0.951	0.021	<0.001	0.909	0.992

Figure-4: Receiver operator curve at 3rd trimester.

Table-8: Coordinates of the Curve at 3rd trimester.

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
7.8688	1.000	1.000
10.4117	0.985	1.000
45.9171	0.971	0.385
48.4280	0.956	0.385
51.1619	0.956	0.346
52.0317	***0.956***	***0.308***
53.2215	0.941	0.308
54.4399	0.941	0.269
3889.9279	0.088	0.000
4144.7092	0.074	0.000
4440.2257	0.059	0.000
4660.4981	0.044	0.000
5167.4868	0.029	0.000
6022.3866	0.015	0.000
6546.7692	0.000	0.000

Table-9: Results of Two-by-two contingency Table for 3rd trimester data.

	Value	p-value
Sensitivity (%)	89.04	na
Specificity (%)	85.71	na
Positive Predicitive value (PPV)	95.59	na
NPV	69.23	na
Prevalence	87.95	na
Pearson Chi-Square	45.55	<0.001
Likelihood Ratio	43.18	<0.001
Linear-by-Linear Association	45.06	<0.001

Table-10: Analyte composition of preeclamptic subjects separated on the basis of severity of disease.

Groups	Mild (n, 39)	Severe (n, 85)	p-value
Micro Albuminuria (mg/dL)	52.90±20.89	63.32±15.02	0.592
ACR (mg/g)	113.14±9.21	201.31±13.42	0.046
Plasma – Creatinine (mg/dL)	1.62±0.58	1.44±0.14	0.053
Urine – Creatinine (mg/dL)	141.13±27.03	118.81±18.66	0.102

Discussion: The results of this research provide insight into the possible use of the Albumin Creatinine Ratio (ACR) in hypertensive pregnant patients in Benin City, Nigeria, as a prenatal indication of renal function. The study sought to address the important problem of hypertensive conditions prior to conception, which contributes significantly to the morbidity and death of mothers worldwide. The findings of the study are consistent with other research, such as studies by Berhe et al.[4], which found that hypertension throughout pregnancy is a significant determinant in postpartum morbidity and death. The challenges in accurately measuring the incidence of pregnancy-related hypertension, as discussed in the literature review, are reaffirmed by the study's acknowledgment of limited accessibility to reliable prenatal care and standardized definitions for pre-eclampsia.

The elevated levels of microalbuminuria and ACR in preeclampsia and pregnancy-induced hypertensive (PIH) cases compared to normotensive individuals underscore the relationship among renal dysfunction as well as hypertension during gestation. Microalbuminuria was found among 46.7% of the pregnant hypertension group, 6.7% of the pregnant normotensive group, and 3.3% of the non-pregnant control group. This aligns with previous research highlighting the link between albuminuria and adverse maternal outcomes, emphasizing the need for early assessment tools. The bivariate correlation analysis revealed significant associations between ACR and gestational age, microalbuminuria, total cholesterol, and urine creatinine during both the 2nd and 3rd trimesters. These associations recommend that ACR can function as a valuable marker used for renal function besides may provide insights into the progression of hypertensive disorders throughout pregnancy.

Furthermore, the ROC analysis demonstrated promising diagnostic potential for ACR at both the 2nd and 3rd trimesters. The ACR threshold of 15 mg/g showed an accuracy of 86.7% and a precision of 90% in detecting microalbuminuria in the hypertensive pregnant group. The determined benchmark values and associated sensitivities and specificities offer clinicians a quantitative measure for identifying pregnant patients at risk of preeclampsia. The robust sensitivity observed in our research is particularly noteworthy, as it indicates a high likelihood of correctly identifying true positive cases.

The distribution of ACR values across age groups in both trimesters provides additional insights into the potential variations in renal function based on maternal age. These observations could inform personalized approaches to monitoring and managing hypertension accuracy while pregnant. The severity of preeclampsia must be taken into account in our study. ACR levels were considerably higher in severe preeclampsia, even though microalbuminuria levels did not differ between moderate and severe instances. The normotensive pregnant group (9.4 ± 3.2mg/g) and the non-pregnant control group (7.8 ± 2.4mg/g) had considerably lower mean ACR values than the hypertensive pregnant group (24.8 ± 9.6mg/g). This implies that ACR may play a part in providing doctors with important information for risk stratification by showing the degree of renal involvement in hypertensive diseases. Our study is not without limits, though. The study's single-center design and somewhat small sample size may have limited how far the results may be applied. Additionally, it is difficult to attribute observed alterations to hypertensive illnesses alone because there is no control group with other renal problems.

Conclusion

Finally, this work sheds important light on the renal effects of hypertensive diseases during pregnancy, with a particular emphasis on preeclampsia and pregnancy-related hypertension. The meticulous examination of urinary biomarkers, particularly the Albumin Creatinine Ratio (ACR), elucidates the potential of these markers in assessing renal function among pregnant women with hypertensive disorders. The significance of proactive monitoring and early diagnosis of renal failure in this susceptible group is highlighted by our findings. The observed correlations between ACR and various clinical parameters emphasize the utility of this non-invasive tool in predicting and managing renal complications associated with hypertensive disorders during pregnancy. Even while our findings add to the body of information already in existence, it is critical to recognize the limitations of the study, such as the small sample size and the single-center design.

To confirm and expand on our findings, future studies with bigger and more varied sample sizes are necessary. In the end, improving mother and fetal health outcomes is the main objective of this study. We intend to improve clinical procedures, risk assessment, and targeted therapies that might lessen the negative effects of hypertension problems while pregnant affecting renal function by clarifying the complex interactions between hypertensive diseases and renal function.

Abbreviations: Acute kidney injury (AKI), Albumin Creatinine Ratio (ACR), Albumin-creatinine ratio – (ACR), Analysis of varance (ANOVA), Area Under the Curve (AUC), Gestational age (GA); Hypertensive conditions via pregnancy (HDP), Plasma creatinine (PC), Pregnancy-indeed hypertension (PIH), Receiver Operating Characteristic (ROC), sarcoma-like tyrosine kinase 1 (sFLT-1), Total cholesterol (TC)

Ethics Approval and Consent to Participate: For every research participant, informed permission was acquired. The research's purpose and nature were thoroughly explained to the participants, who also had the option to leave the study at any time without losing the medical care they were receiving. University of Benin Teaching Hospital's ethical permission (Protocol. No. ADM/E.22/A/VOL.VII/1469) dated April 24, 2017, was also acquired.

References

1. Salako, B. L., Odukogbe, A. T. A., Olayemi, O., Adedapo, K. S., Aimakhu, C. O., Alu, F. E., & Ola, B. (2003). Serum albumin, creatinine, uric acid and hypertensive disorders of pregnancy. *East African medical journal*, 80(8), 424-428.

2. Buga, G. A., & Lumu, S. B. (1999). Hypertensive disorders of pregnancy at Umtata General Hospital: perinatal and maternal outcomes. *East African medical journal*, 76(4), 217-222.

3. Payne, B., Hanson, C., Sharma, S., Magee, L., & Von Dadelszen, P. (2016). Epidemiology of the hypertensive disorders of pregnancy. *Pregnancy Hypertension*, 57(3), 63-74.

4. Berhe, A. K., Kassa, G. M., Fekadu, G. A., & Muche, A. A. (2018). Prevalence of hypertensive disorders of pregnancy in Ethiopia: a systemic review and meta-analysis. *BMC pregnancy and childbirth*, 18, 1-11.

5. Ministerio da Saude - MISAU/Moçambique, Instituto Nacional de Estatística - INE/Moçambique, and ICF International (2013). MoçambiqueInquéritoDemográfico e de Saúde 2011. Calverton, Maryland, USA: MISA/Moçambique, INE/Moçambique and ICF International. Available at http://dhsprogram.com/ pubs/pdf/FR266/FR266.pdf.

6. International Institute for Population Sciences (IIPS) and ICF (2017). National Family Health Survey (NFHS-4), 2015-16: India. Mumbai: IIPS. 637p. Available online at https://dhsprogram.com/pubs/pdf/fr339/fr339.pdf

7. Magee, L. A., Brown, M. A., Hall, D. R., Gupte, S., Hennessy, A., Karumanchi, S. A., ... & von Dadelszen, P. (2022). The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. *Pregnancy hypertension*, *27*, 148-169.

8. Magee, L. A., Sharma, S., Nathan, H. L., Adetoro, O. O., Bellad, M. B., Goudar, S., ... & CLIP Study Group (2019). The incidence of pregnancy hypertension in India, Pakistan, Mozambique, and Nigeria: a prospective population-level analysis. *PLoS medicine*, *16*(4), e1002783.

9. Ekrikpo UE, Adejumo OA, Akpan EE, Udo AI, Nelson UAU, Umoh IO, Okpechi IG (2023). The prevalence of acute kidney injury in women with hypertensive disorders of pregnancy in Africa: a systematic review and meta-analysis. *African Journal of Nephrology*, 26(1), 95-105. URL: https://www.journals.ac.za/ajn/article/view/5868

10. Szczepanski, J., Griffin, A., Novotny, S., & Wallace, K. (2020). Acute kidney injury in pregnancies complicated with preeclampsia or HELLP syndrome. *Frontiers in medicine*, 7, 22.

11. World Health Organization (2010). Causes of maternal and child deaths. Taking Stock of Maternal, Newborn and Child Survival 2000–2010 Decade Report, 11-21. Available online at https://iris.who.int/bitstream/handle/10665/44346/ 9789241599573_eng.pdf?sequence=1

12. Liu, Y., Ma, X., Zheng, J., Liu, X., & Yan, T. (2017). Pregnancy outcomes in patients with acute kidney injury during pregnancy: a systematic review and meta-analysis. *BMC pregnancy and childbirth*, 17, 1-9.

13. Berks, D., Steegers, E. A., Molas, M., & Visser, W. (2009). Resolution of hypertension and proteinuria after preeclampsia. *Obstetrics & Gynecology*, 114(6), 1307-1314.

14. Stepan, H., Nordmeyer, A. K., & Faber, R. (2006). Proteinuria in hypertensive pregnancy diseases is associated with a longer persistence of hypertension postpartum. *Journal of human hypertension*, 20(2), 125-128.

15. Vikse, B. E., Irgens, L. M., Leivestad, T., Skjærven, R., & Iversen, B. M. (2008). Preeclampsia and the risk of end-stage renal disease. *New England Journal of Medicine*, *359*(8), 800-809.

16. Shalaby, A. S., & Shemies, R. S. (2022). Pregnancy-related acute kidney injury in the African continent: where do we stand? A systematic review. *Journal of nephrology*, *35*(9), 2175-2189.

17. Musarandega, R., Nyakura, M., Machekano, R., Pattinson, R., & Munjanja, S. P. (2021). Causes of maternal mortality in Sub-Saharan Africa: a systematic review of studies published from 2015 to 2020. *Journal of Global Health*, *11*.

18. Gemechu, K. S., Assefa, N., & Mengistie, B. (2020). Prevalence of hypertensive disorders of pregnancy and pregnancy outcomes in Sub-Saharan Africa: A systematic review and meta-analysis. *Women's Health*, *16*, 1745506520973105.

19. Ye, C., Ruan, Y., Zou, L., Li, G., Li, C., Chen, Y., ... & Zhang, W. (2014). The 2011 survey on hypertensive disorders of pregnancy (HDP) in China: prevalence, risk factors, complications, pregnancy and perinatal outcomes. *PloS one*, 9(6), e100180.

20. Malek, A. M., Wilson, D. A., Turan, T. N., Mateus, J., Lackland, D. T., & Hunt, K. J. (2021). Maternal coronary heart disease, stroke, and mortality within 1, 3, and 5 years of delivery among women with hypertensive disorders of pregnancy and pre- pregnancy hypertension. *Journal of the American Heart Association*, 10(5), e018155.

21. Sani, H. M., Vahed, S. Z., & Ardalan, M. (2019). Preeclampsia: a close look at renal dysfunction. *Biomedicine & Pharmacotherapy*, *109*, 408-416.

22. American Diabetes Association (2003). Standards of medical care for patients with diabetes mellitus *Diabetes care*, *26 Suppl 1*, S33–S50. https://doi.org/ 10.2337/diacare.26.2007.s33

23. Eknoyan, G., Hostetter, T., Bakris, G. L., Hebert, L., Levey, A. S., Parving, H. H., ... & Toto, R. (2003). Proteinuria and other markers of chronic kidney disease: a position statement of the national kidney foundation (NKF) and the national institute of diabetes and digestive and kidney diseases (NIDDK) 1. *American Journal of Kidney Diseases*, 42(4), 617-622.

24. Shaarawy, M., & Salem, M. E. (2001). The clinical value of microtransferrinuria and microalbuminuria in the prediction of pre-eclampsia.

25. Côté, A. M., Firoz, T., Mattman, A., Lam, E. M., von Dadelszen, P., & Magee, L. A. (2008). The 24-hour urine collection: gold standard or historical practice?. *American journal of obstetrics and gynecology*, 199(6), 625-e1.

26. Maynard, S. E., Min, J. Y., Merchan, J., Lim, K. H., Li, J., Mondal, S., ... & Karumanchi, S. A. (2003). Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. *The Journal of clinical investigation*, 111(5), 649-658.

27. Cade, T. J., de Crespigny, P. C., Nguyen, T., Cade, J. R., & Umstad, M. P. (2015). Should the spot albumin-to-creatinine ratio replace the spot protein-to-creatinine ratio as the primary screening tool for proteinuria in pregnancy?. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health*, 5(4), 298-302.

28. Wilkinson, C., Lappin, D., Vellinga, A., Heneghan, H. M., O'Hara, R., & Monaghan, J. (2013). Spot urinary protein analysis for excluding significant proteinuria in pregnancy. *Journal of Obstetrics and Gynaecology*, 33(1), 24-27.

29. Singh, B., Pushpalatha, K., & Patel, S. (2023). Correlation of Mid-Trimester Spot Urinary Albumin: Creatinine Ratio With the Adverse Pregnancy Outcome. *Cureus*, 15(3).

30. Yu, G., Cheng, J., Li, H., Li, X., & Chen, J. (2022). Comparison of 24-h urine protein, urine albumin-to-creatinine ratio, and protein-to-creatinine ratio in IgA nephropathy. *Frontiers in Medicine*, *9*, 809245.

31. Chang, C. C., Su, M. J., Ho, J. L., Tsai, Y. H., Tsai, W. T., Lee, S. J., ... & Chu, F. Y. (2016). The efficacy of semi-quantitative urine protein-to-creatinine (P/C) ratio for the detection of significant proteinuria in urine specimens in health screening settings. *Springer Plus*, 5, 1-5.

32. Mazumder, T., Mamun, I. P., Zaman, M. S., Islam, A. K., Chowdhury, S., Reza, M. S., & Hussain, M. S. (2021). Comparative lipid and uric acid suppressing properties of four common herbs in high fat-induced obese mice with their total phenolic and flavonoid index. *Biochemistry and Biophysics Reports*, 26, 100990.

33. Richmond, W. (1973). Enzymatic determination of total serum cholesterol. *Clin. Chem.*, 20, 470-475.

34. Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, 18(6), 499-502.

35. Chauhan, N., & Pundir, C. S. (2014). Covalent immobilization of uricase inside a plastic vial for uric acid determination in serum and urine. *Analytical Sciences*, 30(4), 501-506.