Section: Biochemistry

Original Research Article

MICROALBUMINURIA IN CRITICALLY ILL PATIENTS: A PROGNOSTIC PERSPECTIVE FROM A TERTIARY CARE FACILITY IN KERALA

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Abstract

Background: Microalbuminuria has proven its predictive reliability for morbidity and mortality across various health conditions, including critical illness. The rapid onset of microalbuminuria following acute inflammatory events, such as sepsis or critical illness, suggests its potential as an early indicator of disease severity in acute inflammatory conditions. This study aimed to assess the predictive capabilities of microalbuminuria in critically ill patients admitted to ICUs, exploring its effectiveness at admission and 24 hours post-admission as an outcome predictor. **Materials and Methods:** The study was conducted among 100 critically ill patients admitted to the intensive care units at Government Medical College Kottayam over seven months, from 1st July 2012 to 31st January 2013. The Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2), with Δ ACR calculated by subtracting ACR 1 from ACR 2. **Result:** The median values of the APACHE II score, ACR1, ACR2, and ΔACR were 14.5 (SD-7.735), 208.25 (SD-149.98), 142.89 (SD-76.95), and -65.35 (SD-1.56), respectively. The area under the ROC curves for mortality was highest for ACR2 (0.922), followed by ΔACR (0.912), then APACHE II score (0.848) and ACR1 (0.684). **Conclusion:** The albumin-to-creatinine ratio measured 24 hours after ICU admission (ACR2) is identified as a superior predictor of mortality, potentially surpassing the established APACHE II scores. These findings suggest the promising utility of ACR2 as a timely and effective prognostic tool in intensive care settings, prompting further investigation for potential clinical integration.

INTRODUCTION

The predictive accuracy of microalbuminuria for morbidity and mortality associated with renal and cardiovascular diseases has been verified in type 2 diabetes, arterial hypertension, and the general population. This confirmation underscores its significance across diverse health conditions.[1]

Microalbuminuria, characterized by the excretion of 30–300 mg/day of albumin in the urine, develops rapidly following an acute inflammatory event, such as sepsis or critical illness.[2,3] Microalbuminuria is potentially an early indicator of disease severity in various acute inflammatory conditions. Numerous studies have documented a rapid rise in urine microalbumin excretion during acute inflammatory conditions. This phenomenon seems to be associated with systemic vascular damage, as evidenced by capillary leakage.[4-6]

Despite the development of numerous prognostic tools for patients admitted to the ICU, these tools are inherently complex. The same complexity applies to the APACHE II, Sequential Organ Failure Assessment (SOFA), and Simplified Acute Physiology Score (SAPS). Therefore, there is a need for sensitive, inexpensive, and non-invasive prognostic markers that can yield rapid and reliable results in the ICU setting.[6,7]

This study aimed to assess whether microalbuminuria can predict outcomes in critically ill patients admitted to intensive care units. Additionally, it sought to determine whether microalbuminuria at admission or 24 hours after ICU admission is a more accurate predictor of outcomes.

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MATERIALS AND METHODS

A descriptive study was conducted to assess whether microalbuminuria can predict outcomes in critically ill patients. The research was carried out among 100 critically ill patients admitted to the intensive care units (Medical, Surgical, Neurosurgery, and Trauma ICUs) at Government Medical College Kottayam over seven months, from 1st July 2012 to 31st January 2013. The inclusion criteria for this study comprised all adult patients aged 18 years and older who had spent more than 24 hours in intensive care units (ICUs). Conversely, specific exclusion criteria were defined, which included the presence of anuria, macroscopic hematuria, urinary tract infection, pre-existing chronic kidney diseases, female patients experiencing menstruation, and pregnant individuals. The Institutional Ethics Committee, Govt Medical College, Kottayam approved the study. Verbal consent was taken from all conscious patients. Written informed consent was obtained from their relatives for those not fully conscious and meeting the inclusion criteria. A comprehensive medical history was collected using a standardized proforma. All data, including age, gender, date and time of admission, duration of hospital stay, APACHE II score within 24 hours of ICU admission, history of diabetes, history of hypertension, history of coronary artery disease, and clinical diagnosis, were recorded. Urine samples were collected to assess the presence of microalbumin (Immunoturbidimetric method) and creatinine (Modified Jaffe's method). Additionally, serum levels of sodium, potassium (Ion selective electrode method - Indirect potentiometry), creatinine (Modified Jaffe's method), total white blood cell count (Impedance method), hematocrit (RBC pulse height detection method), and blood pH (Optical fluorescence) were also recorded.

Statistical analysis was performed using SPSS 16.0. The study participants were categorized into survivors and non-survivors based on their outcomes. Quantitative variables were compared using the Independent t-test when the distribution was normal, and the Mann-Whitney U test was employed when the distribution was non-normal. Qualitative variables were analyzed and compared using the Chi-square test. A p-value of 0.05 or less was considered statistically significant. Receiver Operating Characteristic (ROC) curves for APACHE II, ACR1, ACR2, and ΔACR in relation to the outcome variable were generated.

The Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2), with Δ ACR calculated by subtracting ACR 1 from ACR 2. The length of ICU stay was determined in days from the date of admission to the ICU up to the date of discharge from the ICU or death.

RESULTS

The mean age of the study population was 50.64 years (SD-13.712). The majority comprised males (66%). There were 13 cases with medical conditions and 87 with surgical conditions. Of the participants, 52% reported having co-morbidities. Among them, 24% had diabetes, 16% had hypertension, and 12% had coronary artery disease. Additionally, five subjects had both diabetes and hypertension, while two had both diabetes and coronary artery disease. The mean duration of ICU stay was 2.89 days (SD = 1.13). The baseline characteristics of the study population are presented in Table 1, while Table 2 compares different parameters with clinical outcomes.

The median values of the APACHE II score, ACR1, ACR2, and ΔACR were 14.5 (SD-7.735), 208.25 (SD-149.98), 142.89 (SD-76.95), and -65.35 (SD-1.56), respectively [Table 3]. The area under the ROC curves for mortality was highest for ACR2 (0.922), followed by ΔACR (0.912), then APACHE II score (0.848) and ACR1 (0.684) [Table 4].

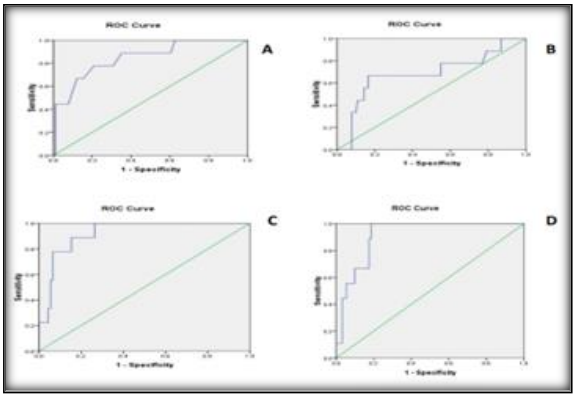

Figure 1: Area under ROC curve for A-APACHE II scores, B- ACR1,C- ACR2 and D- Δ ACR

[APACHE II (Acute Physiology and Chronic Health Evaluation II, Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2), with Δ ACR calculated by subtracting ACR 1 from ACR 2]

Table 1: Baseline characteristics of the study population

Variable	N (%)
Age	
≤ 40	23 (23)
41- 60	56 (56)
≥ 60	21 (21)
Gender	
Male	66(66)

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Female	34(34)
Duration of ICU stay	
≤ 2 Days	44(44)
>2 Days	56(56)
Diagnosis	
Infections and inflammations	12(12)
Trauma	34(12)
Heart diseases	24(24)
Others	30(30)
Diabetes	
Yes	24(24)
No	76(76)
Hypertension	
Yes	12(12)
No	88(88)
CAD	
Yes	12(12)
No	88(88)
ACR1	
<30mg/g	3(3)
30-300mg/g	72(72)
>300mg/g	25(25)
ACR2	
<30mg/g	12(12)
30-300mg/g	74(74)
>300mg/g	14(14)
Outcome	
Non-Survivors	9(9)
Survivors	91(91)

[CAD- Coronary Artery Disease, Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2)]

Table 2: Comparison of various parameters with clinical outcomes

	Non-Survivors N (%)	**Survivors N (%)**	
Age			0.18
≤ 40	1(4.34)	22(95.66)	
41- 60	4(7.14)	52(92.86)	
≥ 60	4(19.04)	17(80.96)	
Gender			0.24
Male	8(12.12)	58(87.88)	
Female	1(2.94)	33(97.06)	
Diagnosis			0.128
Infections and inflammations	1(8.33)	11(91.67)	
Trauma	6(17.64)	28(82.36)	
Heart diseases	0	24(100)	
Others	2(6.67)	28(93.33)	
Diabetes			0.78
Yes	2(8.33)	22(91.67)	
No	7(9.21)	69(90.79)	
Hypertension			0.37
Yes	0	16(100)	
No	9(10.71)	75(89.29)	
CAD			0.532
Yes	0	12(100)	
No	9(10.23)	79(89.77)	
Duration of ICU stay			0.2
≤2 Days	6(13.64)	38(86.36)	
>2 Days	3(5.36)	53(94.64)	
ACR1 albumin creatinine ratio (ACR)			-
<30mg/g	0	3(100)	
30-300mg/g	3(4.17)	69(95.83)	
>300mg/g	6(24)	19(76)	
ACR2 albumin creatinine ratio (ACR)			-
<30mg/g	0	12(100)	
30-300mg/g	2(2.70)	72(97.3)	
>300mg/g	7(50)	7(50)	

[CAD- Coronary Artery Disease, Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2)]

Table 3: Comparison for APACHE II scores, ACR1, ACR2 and ΔACR with clinical outcomes

Variable	**Non-Survivors Median [IQR]**	**Survivors Median [IQR]**	**p value**

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APACHE II score	22[19-29.5]	16[7-19]	0.001
ACR1	363[115-422.5]	155[90.10-271]	0.069
ACR2	400[264.5-549]	63.7[40.90-150]	<0.001
Δ ACR	71.5[0-205]	-59.4[-150.2-Q18 -20.10]	<0.001

[APACHE II (Acute Physiology and Chronic Health Evaluation II, Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2), with Δ ACR calculated by subtracting ACR 1 from ACR 2]

Table 4: Area under ROC curve for APACHE II scores, ACR1, ACR2 and ΔACR

Variable	Area Under the curve (AUC)	p-value	95% Confidence Interval
APACHE II score	0.848	0.001	0.761-0.980
ACR 1	0.684	0.069	0.477-0.891
ACR 2	0.922	<0.001	0.857-0.986
Δ ACR	0.912	<0.001	0.849-0.975

[APACHE II (Acute Physiology and Chronic Health Evaluation II, Albumin-Creatinine Ratio (ACR) was measured within the first 6 hours of ICU admission (ACR 1) and at 24 hours of ICU admission (ACR 2), with Δ ACR calculated by subtracting ACR 1 from ACR 2]

DISCUSSION

This study revealed a high prevalence of microalbuminuria in critically ill patients. Upon ICU admission, 72% had microalbuminuria, shifting to 74% within 24 hours. Basu et al,[8] found similar trends, with 31.9% microalbuminuria upon admission, rising to 53.78% at 24 hours. In contrast, Patel et al,[9] reported lower results, with 71% of ICU-admitted patients having microalbuminuria, persisting in 68% after 24 hours. The high occurrence of microalbuminuria in critically ill patients is likely due to widespread endothelial dysfunction caused by inflammatory mediators released during severe inflammatory responses in critical illnesses. This dysfunction significantly changes vascular and glomerular permeability, increasing albumin escape into the ultra-filtrate. The overwhelmed tubular reabsorptive mechanism exceeds its threshold capacity, causing elevated albumin excretion in urine.[3-5]

The Median ACR1 (urine albumin-creatinine ratio within 6 hours of ICU admission) was higher in non-survivors (363 mg/g, p=0.069) compared to survivors (155 mg/g). Both Bhadade et al,[10] and Patel et al,[9] have reported similar findings. The Median ACR2, recorded 24 hours after ICU admission, exhibited a significant increase among non-survivors (400 mg/g, p=0.000) and a noteworthy decrease among survivors (63 mg/g). The 24-hour sampling was conducted to evaluate goal-directed therapy, and the observed reduction in ACR2 levels among survivors indicates a favourable response to the initial treatment. The ACR2 and APACHE II scores were markedly elevated in non-surviving individuals compared to survivors. This discovery highlights the significant correlation observed between microalbuminuria and APACHE II scores. Both scores quantify the acute physiological response to inflammation and prognosis. A higher median of Δ ACR was observed in non-survivors (71.50) compared to survivors (-59.40). These results align with prior studies by Abid et al,[11] and Gosling et al,[12,13] MacKinnon et al,[14] and Basu et al,[8] all suggesting an association between elevated ACR2 levels and increased mortality.

Thorevska et al,[15] found that patients with ACR > 100 mg/g at ICU admission had a 2.7 times higher risk of death than those with ACR < 100 mg/g. Gosling et al,[12] identified 25.6 mg/g at 6 hours post-ICU admission as an optimal predictor of mortality in a mixed ICU population.

The ROC curves assessed predictive accuracy for mortality using APACHE II score, ACR1, ACR2, and ΔACR. ACR2 demonstrated the highest area under the curve (0.922), outperforming APACHE II (0.848), ΔACR (0.912), and ACR1 (0.684). ACR2, measured at 24 hours post-ICU admission, proved to be a superior mortality predictor, comparable to or better than the traditional APACHE II scores, aligning with findings by Basu et al.[8] In this study, it was discovered that no significant associations existed among age, gender, probable diagnosis, co-morbidities, duration of ICU stay, and outcome.

Byron et al,[16] recent study proposes using point-of-care microalbuminuria to identify sepsis patients in the Emergency Department, especially those without obvious hemodynamic compromise, who may benefit from aggressive monitoring and resuscitation.

CONCLUSION

This study highlights a strong association between microalbuminuria and APACHE II scores in assessing acute physiological responses and prognosis. The measurement of the albumin-to-creatinine ratio at 24 hours of ICU admission (ACR2) emerges as a superior predictor of mortality, rivalling or surpassing the established APACHE II scores. These findings suggest the potential utility of ACR2 as a timely and effective tool for prognostication in intensive care settings, warranting further exploration for clinical integration.

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