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General Medicine

A STUDY OF MICROALBUMINURIA AS A PROGNOSTC MARKER OF SEPSIS

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ABSTRACT **Background:** Sepsis remains a significant challenge in critical care, with high morbidity and mortality rates globally. Microalbuminuria has been proposed as a potential prognostic marker in sepsis, but its predictive value remains underexplored. **Methods:** This cross-sectional observational study involved 50 patients diagnosed with sepsis at Chigateri General Hospital and Bapuji Hospital. We assessed microalbuminuria levels using nephelometry at 6 and 24 hours post-ICU admission. Data analysis included descriptive statistics and inferential tests to correlate microalbuminuria with sepsis severity and mortality. **Results:** Our findings highlight a strong correlation between elevated microalbuminuria levels and increased sepsis severity. Patients with higher albumin creatinine ratios (ACRs) at 24 hours demonstrated significantly higher ICU mortality rates (p=0.001). These results suggest that microalbuminuria could serve as an effective early prognostic tool. **Conclusion:** Microalbuminuria presents a valuable biomarker for predicting outcomes in septic patients, with potential implications for early therapeutic intervention and resource allocation in critical care settings.

KEYWORDS : Sepsis, Microalbuminuria, Prognostic Marker, ICU Mortality, Critical Care

INTRODUCTION

Sepsis, a complex clinical syndrome characterized by a systemic inflammatory response to infection, continues to be a leading cause of morbidity and mortality worldwide. The early diagnosis and timely management of sepsis are critical, yet the heterogeneity in its clinical presentation often complicates timely identification and treatment. This variability underscores the necessity for reliable biomarkers that can aid in early detection and prognostication. Among potential biomarkers, microalbuminuria emerges as a promising candidate due to its role in indicating endothelial dysfunction, a common pathway in septic progression.[1]

Microalbuminuria, defined as the abnormal excretion of albumin in the urine (30-300 mg/day), has been traditionally associated with cardiovascular diseases and diabetic nephropathy.[2] However, its utility in non-chronic disease settings, particularly in acute systemic inflammatory states like sepsis, has gained attention. The pathophysiological basis for microalbuminuria in sepsis is linked to the disruption of the endothelial barrier under the stress of systemic inflammation, leading to an increase in vascular permeability.[3] This leakage is not limited to the renal glomeruli but is part of a more generalized capillary leakage syndrome seen in sepsis.[4]

The prognostic significance of microalbuminuria in sepsis has been supported by various studies that correlate higher levels of albuminuria with increased severity of sepsis, higher intensive care unit (ICU) admission rates, and increased mortality.[5] In a systematic review of the predictive value of microalbuminuria in critically ill patients, elevated levels were associated with poor outcomes, including death and the development of acute kidney injury.[6] These findings suggest that microalbuminuria could serve as a non-invasive, readily available, and cost-effective biomarker to aid in the risk stratification of patients presenting with sepsis.

Despite its potential, the use of microalbuminuria as a prognostic tool in sepsis is not without challenges. The specificity and sensitivity of microalbuminuria can be influenced by factors such as underlying chronic kidney disease, diabetes, and hypertension, which may also cause elevated urinary albumin independently of septic pathology.[7] Therefore, understanding the context and patient-specific baseline health status is crucial when interpreting microalbuminuria levels in sepsis.

The integration of microalbuminuria into sepsis management protocols could potentially streamline the identification of high-risk patients, enabling targeted therapeutic interventions and more efficient use of healthcare resources. However, further research is necessary to standardize measurement techniques and establish cut-off values that can be reliably used in diverse clinical settings.[8]

Additionally, clinical trials are needed to validate the predictive power of microalbuminuria in sepsis independently and in combination with other biomarkers. Such studies will help to clarify the role of microalbuminuria in the complex interplay of pathophysiological mechanisms in sepsis, which may include not only endothelial dysfunction but also coagulation abnormalities, immune dysregulation, and metabolic disturbances.[9] Furthermore, exploring the temporal dynamics of microalbuminuria during the course of sepsis could provide insights into its utility in monitoring disease progression and response to treatment.[10]

In conclusion, microalbuminuria holds promise as a prognostic marker in sepsis, with the potential to enhance clinical decision-making and improve patient outcomes. As sepsis remains a major challenge in critical care, the identification of reliable biomarkers like microalbuminuria is a crucial area of ongoing research and clinical investigation.

AIMS AND OBJECTIVES

The primary aim of this study was to investigate the relationship between microalbuminuria and the severity of sepsis in hospitalized patients. Specifically, the objectives were twofold: first, to determine the correlation between the degree of microalbuminuria measured upon admission and during the early phase of ICU treatment and the severity of sepsis; second, to evaluate the predictive value of microalbuminuria levels for mortality in patients with sepsis. This study intended to provide critical insights into whether microalbuminuria could serve as a reliable prognostic marker for sepsis, potentially guiding clinical interventions and improving patient outcomes.

MATERIALS AND METHODS

Study Design and Setting

The research was conducted as a cross-sectional observational study at Chigateri General Hospital and Bapuji Hospital attached to JJM Medical College, Davangere. The hospitals provided a suitable setting due to their high volume of sepsis cases and established intensive care facilities.

Participants

Participants were selected based on predefined inclusion and exclusion criteria. A total of 50 patients diagnosed with sepsis, who were admitted either to the outpatient department or as inpatients during the study period, were enrolled. Inclusion criteria mandated that patients be adults over 18 years of age, who met at least two of the Systemic Inflammatory Response Syndrome (SIRS) criteria: a temperature of

less than 36 degrees Celsius or more than 38 degrees Celsius; a heart rate of more than 90 beats per minute; a respiratory rate of more than 20 breaths per minute; or a white blood cell count of more than 12,000 or less than 4,000 cells/mm³, or more than 10% bands. Exclusion criteria included patients with anuria or hematuria, those with pre-existing chronic kidney disease (evidenced by long-term renal replacement therapy or sonological features of chronic kidney disease), patients with diabetes and hypertension, and those with proteinuria due to renal and post-renal causes.

Data Collection

Data were collected from the medical records of the participants, including demographics, clinical characteristics, and outcomes. Urine samples were collected for microalbuminuria measurement using a CDL nephelometry and dry chemistry method at two time points: at 6 hours and 24 hours after ICU admission. The albumin creatinine ratio (ACR) was calculated at these time points to assess microalbuminuria.

Sample Size

The sample size of 50 patients was determined based on the hospital's average sepsis caseload and the prevalence of microalbuminuria in sepsis patients reported in previous studies. This sample size was considered sufficient to achieve the statistical power needed to detect significant correlations between microalbuminuria levels and sepsis outcomes.

Statistical Analysis

Statistical analyses were performed using the SPSS software version 21.0 for Windows. Descriptive statistics such as mean, standard deviation, frequencies, and percentages were used to summarize the data. Inferential statistical methods, including the t-test for continuous data and the chi-square test for categorical data, were utilized to analyse the differences between groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Results Section

The study encompassed a diverse group of 50 patients admitted with sepsis, stratified into different age groups, gender, and severity levels according to SIRS criteria, APACHE II scores, and urine albumin to creatinine ratio (ACR) measurements.

Patient Demographics and SIRS Criteria

The age distribution of the study cohort showed that the largest group was patients aged 41-60 years, comprising half of the sample (50%, n=25), with 28% (n=7) mortality and a 72% (n=18) survival rate. The 21-40 years age group had a higher mortality rate of 62.5% (n=10) compared to other groups. Patients under 20 and over 60 had the lowest sample sizes and shared similar mortality rates of 20% and 25%, respectively.

Sex distribution analysis revealed a higher number of male patients (62%, n=31) compared to females (38%, n=19), with males experiencing a slightly higher mortality rate (45.16%) than females (26.32%).

Regarding the SIRS criteria, patients who met all four criteria (54%, n=27) demonstrated a lower mortality rate (33.33%) compared to those meeting only three (42.1% mortality, n=19). Patients with the minimum criteria (two SIRS criteria) had the highest mortality rate at 50%, although this group was the smallest (n=4).

APACHE II Scores and Microalbuminuria

The APACHE II score analysis indicated that patients with scores ≥18.5 had a significantly higher mortality rate (55.56%) than those with scores <18.5 (17.39%). The mean APACHE II score for the entire cohort was significantly higher among non-survivors (25.47 ± 6.93) compared to survivors (16.35 ± 6.78), with a significant p-value (<0.0001).

In terms of microalbuminuria, patients with an initial urine ACR (ACR 1) greater than 109.5 had a 100% mortality rate (n=16), whereas those with ACR 1 less than 109.5 showed a considerably lower mortality rate of 8.82% (n=3). A similar pattern was Observed with urine ACR measured at 24 hours (ACR 2), where patients above the cutoff (118.5) also had a 100% mortality rate (n=16). The mean ACR 1 was 108.44 ± 55.05, and ACR 2 was 88.38 ± 60.96 across the study group, indicating significant variability in microalbuminuria levels among patients.

Correlation Analysis

Statistical analysis of the correlation between urine ACR values and APACHE II scores demonstrated strong relationships. The correlation coefficient between ACR 1 and APACHE II was 0.809 ($p<0.0001$), and between ACR 2 and APACHE II was 0.726 ($p<0.0001$). Furthermore, the correlation between ACR 1 and ACR 2 was extremely strong (coefficient 0.912, $p<0.0001$), underscoring the consistency of microalbuminuria as a predictive biomarker over the initial 24 hours of ICU admission.

These findings collectively underscore the significant relationship between higher APACHE II scores, elevated microalbuminuria levels, and increased mortality in sepsis patients. The data confirm that microalbuminuria, particularly when assessed at both admission and 24 hours later, provides critical prognostic information that can aid in anticipating patient outcomes in the context of sepsis.

Table 1: Patient Distribution By Age And Outcomes

Age Group (Years)	Number of Patients	Death	Survived	Total
<20	5	1 (20%)	4 (80%)	5 (10%)
21-40	16	10 (62.5%)	6 (37.5%)	16 (32%)
41-60	25	7 (28%)	18 (72%)	25 (50%)
>60	4	1 (25%)	3 (75%)	4 (8%)
Total	50	19 (38%)	31 (62%)	50 (100%)

Table 2: Patient Distribution By Sex And Outcomes

Sex	Number of Patients	Death	Survived	Total
Male	31 (62%)	14 (45.16%)	17 (54.84%)	31 (62%)
Female	19 (38%)	5 (26.32%)	14 (73.68%)	19 (38%)
Total	50	19 (38%)	31 (62%)	50 (100%)

Table 3: Patient Distribution By Number Of SIRS Criteria And Outcomes

SIRS Criteria Met	Number of Patients	Death	Survived	Total
2	4 (8%)	2 (50%)	2 (50%)	4 (8%)
3	19 (38%)	8 (42.1%)	11 (57.9%)	19 (38%)
4	27 (54%)	9 (33.33%)	18 (66.67%)	27 (54%)
Total	50	19 (38%)	31 (62%)	50 (100%)

Table 4: Overall Patient Outcomes

Outcome	Number of Patients	Percentage
Death	19	38%
Survived	31	62%
Total	50	100%

Table 5: APACHE II Score and Patient Outcomes

APACHE II Score	Death	Survived	Total	Mean Score	P-value
<18.5	4 (17.39%)	19 (82.61%)	23 (46%)	16.35 ±6.78	<0.0001
≥18.5	15 (55.56%)	12 (44.44%)	27 (54%)	25.47 ±6.93	

Table 6: Distribution Of Urine ACR 1 And ACR 2 With Patient Outcomes

Measurement	< Cutoff	>Cutoff	Total	Mean SD	P-value
ACR 1	3 (8.82%)	16 (100%)	34 (68%)	108.44 ±55.05	<0.0001
ACR 2	3 (8.82%)	16 (100%)	34 (68%)	88.38 ±60.96	<0.0001

Table 7: Correlation Between Micro-albuminuria And APACHE II Score

Variable	Correlation Coefficient	P-value
ACR 1 & APACHE II	0.809	<0.0001
ACR 2 & APACHE II	0.726	<0.0001
ACR 1 & ACR 2	0.912	<0.0001

DISCUSSION

The relationship between microalbuminuria and patient outcomes in sepsis has been a subject of research interest due to its potential implications in early detection and management strategies. In our study, microalbuminuria showed a significant correlation with mortality rates, with 100% of patients exhibiting an ACR greater than 109.5 at admission, subsequently succumbing to their condition. This finding is consistent with other studies that have identified microalbuminuria as a marker of endothelial dysfunction and a predictor of mortality in critically ill patients, emphasizing its role in prognostic assessments in sepsis.

A study by Gosling et al. reported similar findings where elevated microalbuminuria was associated with increased mortality and

severity of disease in ICU patients.[11] They found that an ACR threshold similar to our study provided a significant predictive value for poor outcomes. Conversely, in a study by Donadello et al., while an association between microalbuminuria and sepsis severity was observed, the ACR thresholds differed slightly, suggesting variability in cutoff points that may be influenced by demographic or clinical characteristics of the study population.[12]

The significant correlation coefficients between ACR levels and APACHE II scores in our study (ACR 1 and APACHE II, r=0.809; ACR 2 and APACHE II, r=0.726) underline the reliability of microalbuminuria as a marker reflective of overall disease severity. This is in alignment with findings from Anand et al., who noted that integrating microalbuminuria with other clinical scores enhances the predictive accuracy for patient outcomes in sepsis.[13]

However, it's important to acknowledge studies like the one by Shaw et al., which presented contrasting results where microalbuminuria did not significantly predict mortality beyond conventional scoring systems in a diverse ICU population.[14] This discrepancy could be attributed to differences in patient selection, underlying health conditions, or the timing of microalbuminuria measurement, suggesting that while useful, microalbuminuria should not be the sole marker relied upon for prognostic evaluations in sepsis.

CONCLUSION

The findings from this study reinforce the prognostic value of microalbuminuria in patients with sepsis, demonstrating a strong association with increased mortality and disease severity as indicated by APACHE II scores. Microalbuminuria could serve as a valuable addition to existing clinical assessment tools, providing critical information that can guide therapeutic strategies and potentially improve patient outcomes. However, the variability noted in different studies calls for standardized approaches in the use of microalbuminuria as a prognostic marker in clinical practice. Further research is needed to establish standardized thresholds and to validate the utility of microalbuminuria across different healthcare settings and populations.

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