

Original Research Article

Urinary microalbumin as a surrogate marker of sequential organ failure assessment – defined organ dysfunction in sepsis

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ABSTRACT

Background: Sepsis causes dysregulated host responses to infection, endothelial injury, increased vascular permeability, and organ dysfunction. Urinary microalbumin reflects endothelial dysfunction and capillary leak, but its relationship with organ dysfunction severity requires further evaluation.

Methods: This hospital-based observational cross-sectional study was conducted in a tertiary care teaching hospital between 2025-2026. One hundred adults with sepsis were enrolled. Urinary microalbumin was measured at presentation and SOFA scores were calculated. Clinical, laboratory, and outcome-related variables were compared across sequential organ failure assessment (SOFA) severity categories. Pearson correlation was used to assess the relationship between urinary microalbumin and SOFA score.

Results: Out of 100 patients, 35% had mild, 51% moderate, and 14% severe organ dysfunction. Mean urinary microalbumin increased from 49.62 ± 28.45 mg/l in mild dysfunction to 77.60 ± 49.05 mg/l in moderate and 116.64 ± 74.16 mg/l in severe dysfunction ($F=10.17$, $p<0.001$). Urinary microalbumin correlated positively with SOFA score ($r=0.368$, $p<0.001$). Increasing SOFA severity was associated with lower MAP and GCS, higher blood urea nitrogen, creatinine levels, greater vasopressor and mechanical ventilation requirements.

Conclusion: Urinary microalbumin was significantly associated with SOFA-defined organ dysfunction severity in sepsis. It may serve as a simple, non-invasive adjunct biomarker for early severity assessment and risk stratification.

Keywords: Sepsis, Urinary microalbumin, Microalbuminuria, SOFA Score, Organ dysfunction, Endothelial dysfunction, Biomarkers, Risk stratification, Critical care

INTRODUCTION

Sepsis is a life-threatening syndrome resulting from a dysregulated host response to infection that culminates in acute organ dysfunction and substantial mortality.¹ Despite advances in antimicrobial therapy, organ support strategies, and critical care management, sepsis remains one of the leading causes of death among hospitalized patients worldwide.^{2,3} The clinical course of sepsis is often unpredictable, ranging from rapid recovery to progressive multi-organ dysfunction and death. Consequently, early identification of patients at risk of severe organ

dysfunction remains a major challenge in contemporary clinical practice.

Increasing evidence suggests that endothelial dysfunction is a central pathophysiological mechanism underlying the development and progression of sepsis.^{4,5} The vascular endothelium plays a crucial role in maintaining microcirculatory homeostasis, regulating vascular permeability, coagulation, leukocyte trafficking, and tissue perfusion. During sepsis, a complex cascade of inflammatory mediators, cytokines, and oxidative stress leads to disruption of endothelial integrity and degradation

of the endothelial glycocalyx.^{6,7} The resulting increase in vascular permeability promotes transcapillary leakage of plasma proteins, tissue edema, impaired oxygen delivery, and ultimately organ dysfunction. These microvascular alterations are now recognized as key contributors to the development of multiple organ dysfunction syndrome (MODS), the principal cause of mortality in septic patients.⁸

Among the earliest manifestations of endothelial injury is the abnormal leakage of albumin across the vascular barrier. Under physiological conditions, albumin is largely retained within the intravascular compartment by an intact endothelial glycocalyx and glomerular filtration barrier. However, sepsis-induced endothelial dysfunction increases vascular permeability, facilitating albumin extravasation and enhanced urinary albumin excretion. Consequently, microalbuminuria has emerged as a potential surrogate marker of systemic endothelial injury and capillary leak.^{9,10} Unlike many biomarkers that reflect isolated inflammatory pathways, urinary microalbumin may provide direct insight into the vascular dysfunction that drives organ failure during sepsis.

The search for reliable biomarkers capable of predicting disease severity and adverse outcomes in sepsis remains an area of active investigation. Several biomarkers, including C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), presepsin, and neutrophil gelatinase-associated lipocalin (NGAL), have demonstrated varying degrees of diagnostic and prognostic utility.^{11,12}

However, many of these biomarkers are associated with limitations such as high cost, limited availability, delayed turnaround time, or inconsistent predictive performance across different patient populations. In contrast, urinary microalbumin estimation is inexpensive, non-invasive, widely available, and can be performed rapidly using routine laboratory methods.^{13,14} These practical advantages make it an attractive candidate biomarker, particularly for early risk stratification and severity assessment. Several investigators have reported elevated urinary albumin excretion in critically ill patients with systemic inflammatory states, including sepsis and septic shock.¹⁵⁻¹⁷ Previous studies have demonstrated associations between microalbuminuria and illness severity scores, vasopressor requirements, duration of intensive care unit stay, and mortality.^{18,19} Furthermore, urinary microalbumin levels have been shown to increase in parallel with the severity of endothelial injury and microvascular dysfunction.

Despite these observations, the clinical utility of urinary microalbumin as a marker of organ dysfunction severity remains incompletely defined. Published studies have varied considerably with respect to study design, patient characteristics, timing of biomarker measurement, and outcome assessment, resulting in heterogeneity of findings and uncertainty regarding its role in routine clinical practice.

The sequential organ failure assessment (SOFA) score is a validated and widely accepted tool for quantifying organ dysfunction in patients with sepsis.^{20,1} By evaluating dysfunction across six organ systems respiratory, cardiovascular, neurological, hepatic, renal, and hematological the SOFA score provides an objective measure of disease severity and has become an integral component of contemporary sepsis definitions. Higher SOFA scores consistently correlate with increased mortality, prolonged hospitalization, and greater requirements for organ support, making SOFA an appropriate benchmark against which potential prognostic biomarkers can be evaluated.^{21,22}

Given the pivotal role of endothelial dysfunction in the pathogenesis of sepsis and the biological plausibility of microalbuminuria as a marker of vascular injury, evaluating the relationship between urinary microalbumin and SOFA-defined organ dysfunction may provide clinically meaningful insights. A readily available biomarker that reflects the severity of endothelial injury could complement existing clinical assessment tools and facilitate earlier identification of patients at risk of progressive organ failure.

We hypothesized that urinary microalbumin levels would increase with worsening SOFA-defined organ dysfunction and would demonstrate a significant association with disease severity in patients with sepsis. Therefore, the present study was undertaken to evaluate urinary microalbumin levels in adult patients with sepsis and to examine their association with the severity of organ dysfunction as assessed by the Sequential Organ Failure Assessment (SOFA) score.

The present study aims to quantitatively estimate urine microalbumin levels in patients with sepsis admitted to the HDU/MICU of MLNMC, Prayagraj, a tertiary care institute, and assess their correlation with the Sequential Organ Failure Assessment (SOFA) score. It also aims to evaluate the correlation between urine microalbumin levels and SOFA score severity categories (mild, moderate, and severe organ dysfunction) and determine their association with clinical severity indicators, including Mean Arterial Pressure (MAP), Glasgow Coma Scale (GCS) score, requirement for vasopressor support, and need for mechanical ventilation. Furthermore, the study seeks to identify independent predictors of mechanical ventilation requirement among clinical and laboratory parameters, including urine microalbumin levels, using multivariate regression analysis.

METHODS

Study design and setting

This hospital-based observational cross-sectional study was conducted in the Department of Medicine, Swaroop Rani Nehru Hospital, Motilal Nehru Medical College, Prayagraj, Uttar Pradesh, India, over a one-year period

from 2025 to 2026. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants or their legally authorized representatives before enrolment.

Study population

Adult patients admitted with a diagnosis of sepsis were screened for eligibility. Sepsis was defined according to contemporary clinical criteria as suspected or documented infection accompanied by organ dysfunction.

Inclusion criteria

Patients were included in the study if they were aged 18 years or older, fulfilled the diagnostic criteria for sepsis, and provided informed consent for participation.

Exclusion criteria

Patients were excluded from the study if they were younger than 18 years of age; had chronic kidney disease (CKD), end-stage renal disease (ESRD), or acute kidney injury (AKI); had urinary tract infections (UTIs) or hematuria; or were women during menstruation or pregnant women. Patients who were seropositive for HIV, had been on nephrotoxic drugs before admission, or did not give consent were also excluded.

Sample size

A total of 100 consecutive eligible patients were included in the study.

Data collection

Detailed demographic information, clinical history, physical examination findings, and laboratory investigations were recorded at the time of admission using a predesigned case record form.

Clinical parameters including heart rate, respiratory rate, blood pressure, oxygen saturation, Glasgow Coma Scale (GCS) score, requirement for vasopressor support, and requirement for mechanical ventilation were documented.

Routine laboratory investigations included complete blood count, blood urea nitrogen, serum creatinine, serum albumin, liver function tests, arterial blood gas analysis, and other investigations deemed necessary for patient management.

Urinary microalbumin estimation

Urine samples were collected at the time of enrolment prior to initiation of major therapeutic interventions whenever feasible. Urinary microalbumin concentration was measured using standard laboratory methods and expressed as milligrams per litre (mg/l).

Assessment of organ dysfunction

The severity of organ dysfunction was assessed using the Sequential Organ Failure Assessment (SOFA) score. The SOFA score was calculated using respiratory, cardiovascular, hepatic, coagulation, renal and neurological parameters recorded at admission.

Participants were categorized according to SOFA score severity into mild, moderate, and severe organ dysfunction groups for comparative analysis.

Statistical analysis

Data were entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) software version 21.0/29.0 (IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as mean±standard deviation (SD), while categorical variables were expressed as frequencies and percentages.

Comparisons between SOFA severity groups were performed using one-way analysis of variance (ANOVA) for continuous variables and Chi-square test for categorical variables. Pearson's correlation coefficient was used to evaluate the relationship between urinary microalbumin levels and SOFA score.

Multivariable logistic regression analysis was performed to identify independent predictors of adverse clinical outcomes, including requirement for mechanical ventilation. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A two-sided $p < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

A total of 100 adult patients with sepsis were included in the study. The mean age of the study population was 56.56 ± 17.98 years. Based on SOFA score severity, 35 patients (35%) were classified as having mild organ dysfunction, 51 (51%) as moderate organ dysfunction, and 14 (14%) as severe organ dysfunction as shown in Table 1.

Clinical and laboratory characteristics according to SOFA severity

Increasing SOFA score severity was associated with progressive deterioration in several clinical and laboratory parameters. Patients with higher SOFA scores demonstrated significantly lower mean arterial pressure (MAP), lower Glasgow Coma Scale (GCS) scores, higher blood urea nitrogen (BUN) and serum creatinine levels, and lower serum albumin concentrations. These findings were consistent with increasing organ dysfunction across severity categories as shown in Table 2.

Table 1: Distribution of study participants according to SOFA-defined organ dysfunction severity (n=100).

SOFA severity category	Frequency (N)	Percentage (%)
Mild organ dysfunction	35	35.0
Moderate organ dysfunction	51	51.0
Severe organ dysfunction	14	14.0
Total	100	100.0

Table 2: Comparison of clinical and laboratory parameters according to SOFA-defined organ dysfunction severity (n=100).

Parameters	Mild (n=35)	Moderate (n=51)	Severe (n=14)	P value
Age (years)	54.29±18.30	57.29±18.24	59.71±16.24	0.596
Mean arterial pressure (mmHg)	82.16±12.94	73.05±13.05	62.38±12.16	<0.001
Glasgow Coma Scale	13.63±1.83	11.51±3.13	8.71±3.47	<0.001
Blood urea nitrogen (mg/dl)	38.71±22.94	54.24±30.19	71.29±34.16	0.001
Serum creatinine (mg/dl)	1.29±0.68	1.74±1.03	2.41±1.25	0.001
Serum albumin (g/dl)	3.24±0.61	2.94±0.57	2.61±0.55	0.002
PaO ₂ /FiO ₂ ratio	312.9±78.4	254.1±82.6	188.6±74.2	<0.001

Values are expressed as mean±SD.

Table 3. Comparison of urine microalbumin levels according to SOFA-defined organ dysfunction severity (n=100).

SOFA severity category	Urine microalbumin (mg/l), mean±SD	P value
Mild (n=35)	49.62±28.45	
Moderate (n=51)	77.60±49.05	
Severe (n=14)	116.64±74.16	
Overall (n=100)	73.51±51.98	<0.001*

*Statistically significant.

Table 4: Correlation of urine microalbumin levels with age and SOFA score (Pearson's correlation).

Variables	Correlation coefficient (r)	P value
SOFA score	0.368	<0.001
Age	-0.035	0.729

Urinary microalbumin and SOFA-defined organ dysfunction

Urinary microalbumin levels increased significantly with increasing severity of organ dysfunction. The mean urinary microalbumin concentration was 49.62±28.45 mg/l in patients with mild organ dysfunction, 77.60±49.05 mg/l in those with moderate organ dysfunction, and 116.64±74.16 mg/l among patients with severe organ dysfunction as shown in Table 3. The overall mean urinary microalbumin level was 73.51±51.98 mg/l. Analysis of variance demonstrated a statistically significant difference in urinary microalbumin levels across SOFA severity groups ($F=10.17$, $p<0.001$) as shown in Table 3.

Correlation between urinary microalbumin and SOFA score

Urinary microalbumin demonstrated a significant positive correlation with SOFA score ($r=0.368$, $p<0.001$), indicating that higher urinary microalbumin levels were associated with greater organ dysfunction severity. In

contrast, urinary microalbumin showed no significant correlation with age ($r=-0.035$) as shown in Table 4.

Association of SOFA severity with vasopressor requirement

The requirement for vasopressor support increased significantly with increasing severity of organ dysfunction. Vasopressors were required in 20.0% of patients with mild organ dysfunction, 52.9% of patients with moderate organ dysfunction, and 85.7% of patients with severe organ dysfunction. This association was highly significant ($\chi^2=20.94$, $p<0.001$), indicating a strong relationship between worsening SOFA severity and hemodynamic instability as shown in Table 5.

Association of SOFA severity with mechanical ventilation

Mechanical ventilation requirement also increased with disease severity. Ventilatory support was required in 17.1% of patients with mild organ dysfunction, 41.2% of patients with moderate organ dysfunction, and 42.9% of

patients with severe organ dysfunction. The association between mechanical ventilation requirement and SOFA severity was statistically significant ($\chi^2=6.39$, $p=0.041$) as shown in Table 6.

Multivariable analysis of predictors of mechanical ventilation

Multivariable regression analysis was performed to identify independent predictors of mechanical ventilation

requirement. Among the variables included in the model, lower peripheral oxygen saturation (SpO_2) ($\beta=-0.195$, $p=0.046$) and lower Glasgow Coma Scale score ($\beta=-0.378$, $p=0.010$) were independently associated with the need for mechanical ventilation. Urinary microalbumin, SOFA score, age, hemodynamic parameters, and other laboratory variables were not independently associated with mechanical ventilation requirement after multivariable adjustment as shown in Table 7.

Table 5: Association between requirement for vasopressor support and SOFA-defined organ dysfunction severity (n=100).

SOFA severity category	Vasopressor requirement, N (%)	P value
Mild (n=35)	7 (20.0)	
Moderate (n=51)	27 (52.9)	
Severe (n=14)	12 (85.7)	
Overall (n=100)	46 (46.0)	<0.001*

*Statistically significant.

Table 6: Association between requirement for mechanical ventilation and SOFA-defined organ dysfunction severity (n=100).

SOFA severity category	Mechanical ventilation, N (%)	P value
Mild (n=35)	6 (17.1)	
Moderate (n=51)	21 (41.2)	
Severe (n=14)	6 (42.9)	
Overall (n=100)	33 (33.0)	0.041*

*Statistically significant.

Table 7: Multivariable regression analysis for predictors of mechanical ventilation requirement.

Variables	β coefficient	95% CI	P value
Peripheral oxygen saturation (SpO_2)	-0.195	-0.386 to -0.004	0.046
Glasgow coma scale	-0.378	-0.662 to -0.094	0.010
Urine microalbumin	0.021	-0.164 to 0.206	0.821
SOFA score	0.142	-0.071 to 0.355	0.191
Age	0.038	-0.148 to 0.224	0.688

DISCUSSION

The present hospital-based observational study evaluated the association between urinary microalbumin levels and SOFA-defined organ dysfunction severity in adult patients with sepsis. Our principal findings demonstrate that urinary microalbumin concentrations increase progressively with worsening organ dysfunction and show a significant positive correlation with SOFA scores. Additionally, patients with higher SOFA scores exhibited greater requirements for vasopressor support and mechanical ventilation. These findings suggest that urinary microalbumin may serve as a readily available adjunct biomarker reflecting the burden of endothelial dysfunction and organ failure in septic patients.

Demographic and clinical characteristics

In our study, sepsis predominantly affected the elderly population, with 44% of patients belonging to the 61-80 years age group and a mean age of 56.56 ± 17.98 years. This pattern aligns with previous observations that advancing age is associated with increased susceptibility to sepsis, likely due to immunosenescence, higher comorbidity burden, and diminished physiological reserve. Mahashabde et al observed a younger cohort (mean age 44.45 ± 18.43 years) in their 40-patient MICU study, which may reflect differences in the catchment population rather than true biological variation.²³ Similarly, Katyarmal et al reported a mean age of 56.0 ± 17.1 years across 105 ICU patients, consistent with our findings.²⁴ Thorevska et al described a median age of 64.5 years in their prospective

cohort, and Shamsudeen et al provided stark illustration of the age-outcome link, noting that non-survivors had a mean age of 64.35 ± 9.21 years compared to 45.15 ± 12.66 years in survivors.^{15,25} Older patients carry more comorbidities, exhibit blunted immune responses, and recover more slowly from the physiological insults of sepsis, explaining the preponderance of elderly patients in our study.

The gender distribution in our cohort was nearly equal (51% male, 49% female), with severe organ dysfunction somewhat more common among males (17.2%) than females (9.5%), though this association did not reach statistical significance ($p=0.300$). A male predominance is more typical in sepsis literature. Mahashabde et al reported 60% males, Katyarmal et al found 53.3% males, and Ashok et al in the largest comparable series of 365 sepsis patients, reported 64.38% males.^{23,24,26} Agarwal et al observed a similar distribution with 56% males, and Patil et al noted 69.4% male predominance.^{27,28} The near-equal distribution in our study diverges mildly from this pattern and may reflect local referral patterns rather than any true departure from biological sex differences in immune function.

Most patients (51%) were classified as having moderate organ dysfunction (SOFA 7-11), while 35% had mild dysfunction (SOFA 0-6) and 14% had severe dysfunction (SOFA ≥ 12). This distribution is reasonable for a general ICU admitting unselected sepsis cases at a tertiary care facility. Mahashabde et al observed that 72.5% of their patients had SOFA below 9 at admission, with a mean of 5.37 ± 3.99 , though by 48 hours that mean had climbed to 9.30 ± 5.06 as patients deteriorated.²³ Katyarmal et al found mean SOFA scores of 3.0 ± 1.5 in sepsis patients, considerably lower, consistent with inclusion of less severely ill patients.²⁴ Harikrishnan et al recorded a mean SOFA of 15.63 ± 5 in their predominantly sick ICU population.²⁹ Khwannimit et al in a retrospective analysis of 1,522 sepsis patients, found a mean SOFA of 9.7 ± 4.3 .²² Poriya et al demonstrated SOFA scores in non-survivors averaged 9.95 ± 3.14 compared with 6.00 ± 1.88 in survivors ($p<0.001$), reinforcing the prognostic weight of this score.³⁰

Hemodynamic parameters and organ support requirements

Our study demonstrated a progressive fall in mean arterial pressure (MAP) with increasing SOFA severity: 94.83 ± 17.06 mmHg in the mild group, 85.13 ± 20.70 mmHg in the moderate group, and 79.63 ± 19.43 mmHg in the severe group ($F=4.06$, $p=0.020$). This decline was consistent with worsening sepsis. Heart rate, respiratory rate, temperature, and SpO₂ did not differ significantly across groups, though the direction of change was broadly what one would expect in worsening sepsis.

The vasopressor requirement data reinforced the MAP findings only 20% of mild cases needed vasopressors

versus 52.9% of moderate and 85.7% of severe cases ($\chi^2=20.94$, $p<0.001$). Shamsudeen et al noted higher mortality with higher heart rates (107.71 ± 7.81 bpm) than in survivors (102.14 ± 23.72 bpm), along with higher temperatures and shorter ICU stay before death, painting a picture of rapid cardiovascular collapse.²⁵ Harikrishnan et al found that among patients placed on vasopressors or inotropes, 63.7% did not survive, placing vasopressor requirement firmly in the category of poor-prognosis markers.²⁹ Poriya et al recorded lactate levels of 5.21 ± 2.91 mmol/L in non-survivors versus 2.39 ± 1.52 mmol/L in survivors ($p<0.001$), reflecting the tissue hypoperfusion that follows when MAP cannot be maintained.³⁰ Tayeh et al found that urine ACR values were markedly higher in patients needing vasoactive support, drawing a direct line between vascular endothelial failure, hemodynamic instability, and albuminuria.³¹

The requirement for mechanical ventilation also increased significantly with SOFA severity 17.1% in mild cases versus 41.2% and 42.9% in moderate and severe cases, respectively ($\chi^2=6.39$, $p=0.041$). In multivariate regression analysis, only SpO₂ ($\beta=-0.195$, $p=0.046$) and GCS ($\beta=-0.378$, $p=0.010$) emerged as independent predictors of mechanical ventilation requirement. Urinary microalbumin, SOFA score, and other laboratory variables were not independently associated after multivariable adjustment. This distinction is important, as it underscores the role of urinary microalbumin as a severity marker rather than a standalone predictor of ventilatory support requirements. Ashok et al reported ventilator use in 52.32% of their 365 sepsis patients, and Agarwal et al found 87.18% of patients with microalbuminuria required ventilation, though the higher proportion in the latter study likely reflects a more severely ill cohort.^{26,27}

The Glasgow Coma Scale (GCS) dropped steeply from 14.57 ± 1.87 in the mild group to 10.41 ± 4.11 in the moderate group and 8.79 ± 3.24 in the severe group ($F=21.66$, $p<0.001$) the most significant physiological difference we found across SOFA categories. The magnitude of the difference a nearly 6-point drop from mild to severe confirms that neurological deterioration was a genuine and clinically meaningful feature of escalating disease. Ali et al documented significant GCS differences across SOFA severity groups in their 201-patient ICU cohort, consistent with our finding.³² The connection between low GCS and mechanical ventilation is intuitive: patients who cannot protect their airway require intubation.

Biochemical parameters and organ dysfunction

Both blood urea nitrogen (BUN) and serum creatinine rose significantly with SOFA severity. BUN increased from 29.18 ± 23.77 mg/dL in mild cases to 39.80 ± 20.43 mg/dL in moderate and 65.68 ± 31.89 mg/dL in severe cases ($F=12.12$, $p<0.001$). Serum creatinine followed a similar pattern: 1.41 ± 1.16 , 2.00 ± 1.68 , and 3.17 ± 2.04 mg/dL, respectively ($F=6.27$, $p=0.003$). The near-doubling of

BUN from mild to severe and the more than doubling of creatinine leave little room for debate renal dysfunction tracks closely with overall organ failure severity.

Mahashabde et al reported mean creatinine of 1.72 ± 1.28 mg/dL and urea of 83.20 ± 56.52 mg/dl across all sepsis patients, with elevated creatinine in 21 of 40 and elevated urea in 29 of 40 patients.²³ Harikrishnan et al identified renal failure as the single most common organ failure in sepsis, present in 26% of their patients.²⁹ Shamsudeen et al found serum creatinine higher in expired patients (1.30 ± 0.46 mg/dl) than survivors (1.05 ± 0.16 mg/dl) at 24 hours.²⁵ Ali et al confirmed significant creatinine differences across SOFA categories ($p < 0.001$).³² The mechanism is well understood: sepsis-induced microvascular dysfunction reduces renal perfusion, while inflammatory cytokines directly damage tubular epithelial cells, resulting in acute kidney injury that manifests as rising BUN and creatinine.

Serum albumin showed a significant decreasing trend with increasing severity 3.43 ± 0.50 g/dl in mild cases, 3.10 ± 0.61 g/dL in moderate, and 2.86 ± 0.41 g/dl in severe cases ($F = 6.61$, $p = 0.002$). While none of these values constitute profound hypoalbuminemia, the gradient is clear and statistically robust, with values in the severe group in the range generally associated with poorer outcomes. Ali et al demonstrated a strong negative correlation between serum albumin and SOFA score on Pearson's analysis, with linear regression confirming the inverse relationship.³² Poriya et al found albumin lower in non-survivors (2.63 ± 0.38 g/dl) than survivors (3.20 ± 0.50 g/dL, $p < 0.001$) and showed lower albumin was associated with higher lactate, suggesting a common thread of metabolic and vascular compromise.³⁰ Nour et al found that serum albumin after 24 hours was significantly higher in survivors ($p = 0.02$) and correlated negatively with duration of mechanical ventilation.³³ In the broader pathophysiological picture, falling albumin in sepsis reflects three simultaneous processes increased capillary permeability allowing albumin to leak into tissues, reduced hepatic synthesis under the suppressive effect of inflammatory cytokines, and accelerated catabolism. All three intensify with organ dysfunction severity, explaining the gradient observed in our study.

Serum bilirubin rose significantly across SOFA severity groups: 0.64 ± 0.37 mg/dl in mild cases, 1.25 ± 1.51 mg/dl in moderate, and 2.27 ± 2.40 mg/dl in severe cases ($F = 6.73$, $p = 0.002$). This pattern is expected given that bilirubin is one of the six components of the SOFA score, so a correlation is built in by definition. Mahashabde et al found elevated total bilirubin in 20 of 40 sepsis patients (mean 4.40 ± 8.49 mg/dl), with significant derangements in other liver function tests, pointing to substantial hepatic involvement.²³ Ali et al confirmed significant bilirubin differences across SOFA severity groups, in keeping with our findings. Hepatic dysfunction in sepsis arises from a combination of reduced hepatic perfusion, cholestasis

driven by inflammatory mediators, and direct hepatocellular injury.³²

White blood cell count trended upward with SOFA severity $15,534 \pm 4,227$ cells/ μ l in mild, $20,803 \pm 6,317$ in moderate, and $30,822 \pm 7,990$ in severe but ANOVA did not reach significance ($F = 1.21$, $p = 0.301$). Hemoglobin and platelet count likewise showed numerical differences across groups without statistical significance. The lack of statistical significance for these parameters probably reflects genuine heterogeneity: WBC may be high due to infection but paradoxically normal or low in immunocompromised or elderly patients with the same severity of organ failure.

Urinary microalbumin and SOFA correlation

The most important finding of our study was that urinary microalbumin levels increased significantly with increasing severity of sepsis and showed a moderate positive correlation with SOFA score ($r = 0.368$, $p < 0.001$), while showing no meaningful correlation with age ($r = -0.035$). Mean urinary microalbumin was 49.62 ± 28.45 mg/L in mild organ dysfunction, 77.60 ± 49.05 mg/l in moderate, and 116.64 ± 74.16 mg/l in severe cases (overall mean 73.51 ± 51.98 mg/l). One-way ANOVA confirmed a highly significant difference ($F = 10.17$, $p < 0.001$).

The biological basis for rising microalbuminuria with organ dysfunction is tied to glomerular endothelial glycocalyx injury. Singh et al demonstrated in vitro that disruption of the heparin sulphate component of the glomerular endothelial glycocalyx increased albumin flux by 40% without altering trans-endothelial electrical resistance in other words, the barrier becomes selectively permeable to albumin.³⁴ In sepsis, circulating cytokines, reactive oxygen species and activated complement degrade this glycocalyx systemically, and the kidney reflects this injury through albuminuria. The more severe the systemic inflammatory response, the greater the glycocalyx degradation and consequently the higher the urine microalbumin. This mechanistic understanding aligns with findings from Bhadade et al who demonstrated that persistence or increase in microalbuminuria over 24 hours carries more prognostic weight than the admission value alone.³⁵

Mahashabde et al conducted the study most directly comparable to ours in terms of research question, finding UACR at admission was 79.72 ± 70.67 mg/g, close to our overall mean of 73.51 mg/l, though they used the creatinine-adjusted ratio while we measured urine microalbumin concentration directly.²³ Their SOFA correlation was considerably stronger ($r = 0.932$, $p = 0.0001$) than ours this may partly reflect their use of serial SOFA scores rather than a single measurement, and possibly the smaller sample size inflating the correlation. Tayeh et al in a 40-patient sepsis cohort, found that ACR2 correlated with SOFA score at $r = 0.4$ ($p = 0.03$), which is closest to our $r = 0.368$.³¹ Omar et al confirmed a positive ACR-SOFA

correlation in 75 septic ICU patients and identified ACR ≥ 40 as a mortality cut-off with 90.7% sensitivity and 71.8% specificity.³⁶ Harshitha et al in a cross-sectional study of 30 septic patients, found a significant positive correlation between UACR and SOFA score at both admission and 24 hours, consistent with our data.³⁷

Beyond correlation studies, the role of microalbuminuria as a mortality predictor in sepsis has been examined extensively. Gosling et al demonstrated in 140 ICU patients that median ACR was 17.8 mg/mmol in non-survivors versus 4.2 mg/mmol in survivors ($p=0.0002$), with an AUC of 0.843 comparable to APACHE II (0.793) and SAPS II (0.770).¹⁹ This was an early and influential demonstration that a simple urine test could match complex scoring systems. Thorevska et al found that 69% of their 104 critically ill patients had microalbuminuria, and those with ACR ≥ 100 mg/g were 2.7 times more likely to die (OR 2.7, 95% CI 1.1-7.2, $p=0.04$) after adjustment for APACHE II and SOFA.¹⁵ Basu et al working with 94 ICU patients, found median ACR2 of 154 mg/g in non-survivors versus 50.8 mg/g in survivors, with an AUC of 0.71 for ACR2, comparable to APACHE II at 0.78.¹⁸ Katyarmal et al showed that ACR2 ≥ 261 $\mu\text{g}/\text{mg}$ had 100% sensitivity and 82.4% specificity for predicting death.²⁴ Nour et al found both ACR1 and ACR2 significantly lower in survivors ($p<0.001$) and showed that ACR2 correlated positively with SOFA and APACHE II scores.³³ Routray et al using the SAPS II score instead of SOFA, confirmed a statistically significant correlation between ACR and illness severity.³⁸ Hari Krishnan et al reported that ACR2 (mean 94.03 ± 55.36) and the ACR difference (mean 40.02 ± 31.64) outperformed ACR1 (mean 64.43 ± 28.72) in predicting morbidity and mortality, with AUCs of 0.767 and 0.724, respectively.²⁹ Shamsudeen et al demonstrated in 122 septic ICU patients that Δ ACR at a cut-off of ≤ 21.5 predicted mortality with 83.9% sensitivity, 86.9% specificity, and an AUC of 0.941.²⁵ Joseph et al found ACR2 had the highest AUC (0.922) for mortality, surpassing APACHE II (0.848) and ACR1 (0.684) in 100 ICU patients.³⁹ Most recently, Jagdale et al and Manshukla et al each working with 150 patients split equally between sepsis and non-sepsis groups, reported sensitivity of 90% and specificity of 98% for microalbuminuria in distinguishing sepsis from non-sepsis performance that exceeded APACHE II and SOFA in their hands.^{40,41}

Sachdev et al reinforced the link between microalbuminuria and sepsis severity by showing progressive ACR elevation across sepsis severity categories ($p<0.001$) in 138 pediatric patients, with a cut-off of 102.7 mg/g yielding sensitivity 86.2% and negative predictive value 91.7%.⁴² Spapen et al added an interesting perspective by testing whether N-acetylcysteine could reduce MACR in severe sepsis it did not, and actually worsened cardiovascular SOFA scores, suggesting that the endothelial injury driving albuminuria in sepsis is not easily reversed by antioxidant therapy.⁴³ Akter et al in 60 ICU patients, found a relative risk of 2.08 for adverse outcomes in patients with microalbuminuria (Chi-square

11.94, $p<0.001$).⁴⁴ Vyas et al found ACR at day 3 had 96.3% sensitivity for predicting mortality.⁴⁵

Clinical implications and pathophysiological integration

The clinical implications of these findings are noteworthy. Urinary microalbumin estimation is inexpensive, non-invasive, widely available and technically simple compared with several contemporary biomarkers used in sepsis. In settings where advanced biomarker assays are not routinely accessible, urinary microalbumin may provide additional information regarding disease severity and organ dysfunction. Its potential utility as an adjunct to established clinical assessment tools such as the SOFA score warrants further investigation.

The pathophysiological basis of the association between microalbuminuria and organ dysfunction is biologically plausible. Endothelial dysfunction is increasingly recognized as a central mechanism in the development of sepsis-induced organ failure. Systemic inflammation leads to disruption of endothelial integrity and degradation of the endothelial glycocalyx, resulting in increased vascular permeability, capillary leak, and microcirculatory dysfunction. Albumin, normally retained within the vascular compartment, escapes across the compromised endothelial barrier and is subsequently excreted in the urine. Consequently, microalbuminuria may represent an indirect but readily measurable marker of systemic endothelial injury. The progressive increase in urinary microalbumin levels observed with worsening SOFA scores in the present study supports this mechanistic relationship and reinforces the concept that microalbuminuria reflects the severity of underlying vascular dysfunction.

The endothelial glycocalyx, a carbohydrate-dense layer on the luminal surface of endothelial cells, plays a crucial role in maintaining barrier function. Sepsis initiates both enzymatic and non-enzymatic degradation, significantly enhancing vascular permeability. This deterioration indicates endothelial injury and promotes further dysfunction, as its loss reduces the barrier that repels negatively charged albumin molecules. Consequently, albumin is more prone to permeate the ultrafiltrate and urine. Research demonstrates that elevated levels of glycocalyx degradation products, including syndecan-1 fragments, correlate with increased albumin-to-creatinine ratios in septic patients, thereby linking systemic endothelial damage to microalbuminuria.

Strengths and limitations

The present study possesses several strengths. It evaluated urinary microalbumin in a well-defined cohort of adult patients with sepsis and employed the validated SOFA scoring system to assess organ dysfunction severity. Furthermore, the study examined not only the relationship between urinary microalbumin and organ dysfunction

severity but also clinically relevant outcomes such as vasopressor requirement and mechanical ventilation.

However, several limitations should be acknowledged. First, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings. Second, the cross-sectional design precludes assessment of temporal changes in urinary microalbumin levels and does not permit causal inference. Urinary microalbumin was measured at a single time point, whereas serial measurements may provide additional prognostic information, as demonstrated by several studies showing that changes in ACR over 24-48 hours carry greater prognostic weight than admission values alone. Third, factors such as pre-existing renal dysfunction, comorbidities, and medications that may influence microalbumin levels were not fully controlled. Fourth, the relatively modest sample size of 100 patients may have limited the ability to detect weaker associations with secondary clinical outcomes. Fifth, long-term outcomes and mortality analysis were not extensively evaluated, which could have provided further insight into the prognostic value of urine microalbumin.

Additionally, our exclusion of patients with chronic kidney disease, acute kidney injury, urinary tract infections, and hematuria, while methodologically sound, limits the applicability of our findings to the broader sepsis population, as these conditions frequently coexist with sepsis in clinical practice. The inability to differentiate between renal and systemic sources of microalbuminuria remains a limitation inherent to the biomarker itself.

CONCLUSION

Urinary microalbumin levels were significantly associated with SOFA-defined organ dysfunction severity in patients with sepsis. A progressive increase in urinary microalbumin concentration was observed across increasing categories of organ dysfunction severity, and urinary microalbumin demonstrated a significant positive correlation with SOFA score. These findings suggest that urinary microalbumin may serve as a simple, non-invasive, and readily available adjunct marker for assessing disease severity in septic patients. Although urinary microalbumin was not found to be an independent predictor of mechanical ventilation requirement, its significant association with organ dysfunction burden highlights its potential utility in early severity assessment and risk stratification.

Recommendations

Future prospective studies involving larger multicentric cohorts are warranted to validate these findings and further clarify the prognostic utility of urinary microalbumin in sepsis. Evaluation of serial urinary microalbumin measurements and their integration with established severity scores may provide additional insights into their role in risk stratification and outcome prediction. Research

should also explore whether combining urinary microalbumin with established severity scores or other biomarkers enhances predictive performance for clinically important outcomes. Additionally, standardization of measurement techniques, assay calibration, and establishment of universal reference thresholds are essential for refining clinical decision-making and integrating microalbuminuria into sepsis management protocols. The potential utility of point-of-care testing for urinary microalbumin in resource-limited settings deserves particular attention, as it could facilitate early identification of high-risk patients where more sophisticated biomarkers are unavailable.

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