International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 2, February 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.2.2025.191

ORIGINAL RESEARCH

Microalbuminuria as a biomarker of sepsis in admitted patients

[1]Dr. Amit Kumar, [2]Dr. Ramesh Kumar

[1,2]Assistant Professor, Department of Paediatrics, Shri Siddhi Vinayak Medical College & Hospital, Sambhal, Uttar Pradesh, India

Corresponding Author
Dr. Amit Kumar
Assistant Professor, Department of Paediatrics, Shri Siddhi Vinayak Medical College & Hospital, Sambhal, Uttar Pradesh, India
Email: dr.amitkr1@yahoo.in

Received: 12 January, 2025 Revised: 15 January, 2025 Accepted: 25 January, 2025
Published: 15 February, 2025

ABSTRACT

Aim: To evaluate the role of microalbuminuria as a biomarker of sepsis in hospitalized patients. **Materials and methods:** Adult patients (>18 years) with ICU stays exceeding 24 hours were included, while those with anuria, macroscopic hematuria, chronic kidney disease, significant proteinuria, menstruation, or pregnancy were excluded. Ethical approval was obtained with a waiver of informed consent. Patient demographics, medical history, clinical classifications, and laboratory parameters, including cultures and administered antibiotics, were recorded at admission. APACHE II scores were calculated within the first 24 hours, and patients were followed for up to 28 days to assess ICU length of stay and mortality. Patients were classified into two groups: those without sepsis (no SIRS or SIRS due to non-infectious causes) and those with sepsis (SIRS with infection, including severe sepsis and septic shock). Patients who developed infections after 48 hours were not included in the sepsis group, as these were deemed nosocomial. Patients were assessed at admission and 24 hours later for signs of SIRS and infection, using clinical, laboratory, and radiological evidence. Data analysis was done using SSPS software. **Results:** Out of 50 patients, 52% (26) being male and 48% (24) female. The median age of the patients was 52.6 years, ranging from 45 to 70 years. The median APACHE II score was 12 (IQR: 11-21), and the median ICU stay was 5 days (IQR: 3-7). Among the patients, 64% (32) survived, while 36% (18) did not. **Conclusion:** Microalbuminuria is a potential biomarker for distinguishing sepsis and predicting ICU mortality. Elevated levels at admission indicate sepsis, while persistently high levels at 24 hours correlate with increased mortality. Lower APACHE II scores and shorter ICU stays in non-septic patients further support its prognostic value. However, larger studies are needed to confirm these findings and establish standardized cut-off values.

Keywords: sepsis, microalbuminuria**,** inflammation

INTRODUCTION

Sepsis is a severe condition responsible for one in four intensive care unit admissions. It can rapidly progress to septic shock, where hypotension remains unresponsive to fluid resuscitation, leading to organ dysfunction, multi-organ failure, and death. The endothelium plays a crucial role in sepsis-related macro- and microcirculatory disturbances. Its activation results in a pro-coagulant and pro-inflammatory state, disrupted vascular integrity, and abnormal vascular tone. In septic patients, endothelial barrier destruction is evident, with increased levels of circulating endothelial cells observed in cases of septic shock.[1,2,3]

Microalbuminuria, defined as albumin excretion above normal levels (<30 mg/day) but below the detectable threshold of standard dipstick tests (>300 mg/day), is often expressed as the albumin-to-creatinine ratio (ACR) to account for urine flow variations. Sepsis induces uncontrolled systemic inflammation and widespread endothelial damage, increasing vascular permeability to plasma proteins due to inflammatory mediators. This increased permeability contributes to microalbuminuria, reflecting endothelial dysfunction in septic patients.[4,5]

Hence the study aimed to evaluate the role of microalbuminuria as a biomarker of sepsis in hospitalized patients.

MATERIALS AND METHODS

Adult patients (>18 years) with ICU stays exceeding 24 hours were included, while those with anuria, macroscopic hematuria, chronic kidney disease, significant proteinuria, menstruation, or pregnancy

DOI: 10.69605/ijlbpr_14.2.2025.191

were excluded. Ethical approval was obtained with a waiver of informed consent. Patient demographics, medical history, clinical classifications, and laboratory parameters, including cultures and administered antibiotics, were recorded at admission. APACHE II scores were calculated within the first 24 hours, and patients were followed for up to 28 days to assess ICU length of stay and mortality.

Patients were classified into two groups: those without sepsis (no SIRS or SIRS due to non-infectious causes) and those with sepsis (SIRS with infection, including severe sepsis and septic shock). Patients who developed infections after 48 hours were not included in the sepsis group, as these were deemed nosocomial. Patients were assessed at admission and 24 hours later for signs of SIRS and infection, using clinical, laboratory, and radiological evidence.

Urinary albumin-to-creatinine ratio (ACR) was measured within 6 hours of admission (ACR1) and at 24 hours (ACR2). Microalbuminuria was defined as an ACR between 30 and 299 mg/g, while values >300 mg/g indicated clinical proteinuria. ACR levels were analyzed using immunoturbidimetric and Jaffe reaction methods. The clinical team and laboratory investigators were blinded to each other's data. The trend of microalbuminuria was assessed by calculating the change in ACR over 24 hours (ΔACR = ACR1 - ACR2) in both patient groups. Data analysis was done using SSPS software.

RESULTS

The study included a total of 50 patients, with 52% (26) being male and 48% (24) female. The median age of the patients was 52.6 years, ranging from 45 to 70 years. The median APACHE II score was 12, with an interquartile range (IQR) of 11 to 21. The median ICU stay was 5 days (IQR: 3–7). Among the patients, 64% (32) survived, while 36% (18) did not survive. (Table 1)

Table 1: Patient Characteristics, Clinical Classification, APACHE II Score, ICU Stay Duration, and Survival Outcomes

No. Of patients	50
Male (%)	26 (52)
Female (%)	24 (48)
Median age (years)	52.6 (45-70)
Median APACHE II (IQR)	12 (11-21)
Median duration of ICU stay, days (IQR)	5 (3-7)
Survivors (%)	32 (64%)
Non-survivors (%)	18 (36%)

Table 2: Comparison of Demographics, Survival Rates, APACHE II Scores, and ICU Stay Duration in Sepsis and Non-Sepsis Patient Groups

	Sepsis group	**Non sepsis group**	**P value**
No. Of patients	15	35	
Males (%)	6 (40)	20 (57.14)	
Females (%)	9 (60)	15 (42.86)	
Median age (years)	50.1 (45-70)	53.6 (45-70)	0.63
Survivors (%)	10 (66.67)	27 (77.14)	0.96
Non-survivors (%)	5 (33.33)	8 (22.86)	0.73
Med APACHE II score (IQR)	16 (13-26)	13 (11-21)	0.03
Median duration of ICU stay, days (IQR)	6 (3-10)	3 (3-7)	0.213

The study included 15 patients in the sepsis group and 35 in the non-sepsis group. Males comprised 40% of the sepsis group and 57.14% of the non-sepsis group, while females accounted for 60% and 42.86%, respectively. The median age was 50.1 years (IQR: 45-70) in the sepsis group and 53.6 years (IQR: 45-70) in the non-sepsis group (p = 0.63). Survival rates were comparable, with 66.67% of sepsis patients and 77.14% of non-sepsis patients surviving (p = 0.96). Non-survivors constituted 33.33% and 22.86% of the sepsis and non-sepsis groups, respectively (p = 0.73). The median APACHE II score was significantly higher in the sepsis group (16, IQR: 13-26) compared to the non-sepsis group (13, IQR: 11-21) (p = 0.03). The median ICU stay duration was longer in the sepsis group (6 days, IQR: 3-10) than in the non-sepsis group (3 days, IQR: 3-7), though the difference was not statistically significant (p = 0.213).

DISCUSSION

Sepsis is a life-threatening condition characterized by a dysregulated immune response to infection, leading to widespread inflammation, endothelial dysfunction, and organ damage. Early detection and prognosis assessment are crucial for improving patient outcomes. Microalbuminuria, defined as an elevated level of albumin in urine beyond the normal range but below the detection limit of standard dipstick tests, has emerged as a potential biomarker for sepsis. It reflects increased vascular permeability and

DOI: 10.69605/ijlbpr_14.2.2025.191

endothelial injury, both hallmark features of sepsis. As a rapid, non-invasive, and cost-effective test, microalbuminuria may serve as an early indicator of sepsis severity and progression in hospitalized patients, aiding in timely intervention and management.[6,7,8]

Our study included a total of 50 patients, with 52% (26) being male and 48% (24) female. The median age of the patients was 52.6 years, ranging from 45 to 70 years. The median APACHE II score was 12 (IQR: 11-21), and the median ICU stay was 5 days (IQR: 3-7). Among the patients, 64% (32) survived, while 36% (18) did not. The study population was divided into a sepsis group (15 patients) and a non-sepsis group (35 patients). Males accounted for 40% of the sepsis group and 57.14% of the non-sepsis group, while females constituted 60% and 42.86%, respectively. The median age was 50.1 years (IQR: 45-70) in the sepsis group and 53.6 years (IQR: 45-70) in the non-sepsis group ($p = 0.63$). Survival rates were similar, with 66.67% of sepsis patients and 77.14% of non-sepsis patients surviving ($p = 0.96$). Non-survivors comprised 33.33% of the sepsis group and 22.86% of the non-sepsis group ($p = 0.73$). The median APACHE II score was significantly higher in the sepsis group (16, IQR: 13-26) compared to the non-sepsis group (13, IQR: 11-21) ($p = 0.03$). The median ICU stay was longer in the sepsis group (6 days, IQR: 3-10) than in the non-sepsis group (3 days, IQR: 3-7), though the difference was not statistically significant ($p = 0.213$).

In the study conducted by Basu S et al.[9], the role of microalbuminuria in differentiating sepsis from non-sepsis and predicting mortality in critically ill patients was evaluated through a prospective, non-interventional study in a 20-bed ICU. Among 94 eligible adult patients, the albumin-creatinine ratio (ACR) was measured at admission (ACR1) and after 24 hours (ACR2). Patients with sepsis, severe sepsis, or septic shock ($n = 30$) had significantly higher median ACR1 levels compared to non-septic. ROC analysis indicated that an ACR1 cut-off of 124 mg/g could differentiate sepsis with 80% sensitivity and 64.1% specificity. Additionally, median ACR2 levels were significantly higher in non-survivors than survivors An ACR2 cut-off of 99.6 mg/g predicted ICU mortality with 85% sensitivity and 68% specificity. The study concluded that low microalbuminuria on ICU admission is unlikely to indicate sepsis; while persistently low levels at 24 hours strongly predict ICU survival, comparable to APACHE II scores.

Bhadade RR et al.[10], in his study, microalbuminuria levels were observed in 125 sepsis patients and 38 non-sepsis patients admitted to the medical ICU of a tertiary referral center. Results showed significantly higher microalbuminuria levels in sepsis patients compared to non-sepsis patients. In sepsis survivors, levels decreased after 24 hours, while they remained nearly unchanged in non-sepsis patients. The study found that changes in microalbuminuria over 24 hours could indicate therapy effectiveness, while persistently high or increasing levels were predictors of poor outcomes. Additionally, elevated microalbuminuria at 24 hours and an increasing trend over time predicted mortality more accurately than APACHE II and SOFA scores.

In another study conducted by Gosling P et al.,[11] urine albumin levels within the first six hours of ICU admission were compared with patient demographics, clinical classification, outcomes, inotrope/vasopressor requirements, and mortality risk assessments, including SOFA and APACHE II scores. Median ACR1 was significantly higher in medical patients compared to surgical patients with ACR2 showing a similar trend. For all patients, ACR decreased significantly within six hours of ICU admission, except in those who did not survive, where the median ACR remained elevated. Higher ACR1 and ACR2 values were observed in non-survivors compared to survivors and were also elevated in patients requiring inotropic or vasopressor support. ACR1 and ACR2 were inversely correlated with the Po2/Fio2 ratio at 48 hours and positively correlated with mechanical ventilation duration and ICU stay. ACR2 independently predicted mortality, while ACR1 was associated with inotrope requirements, outperforming APACHE II and SOFA scores in these predictions. The study concluded that urine albumin levels changed rapidly within the first six hours of ICU admission and served as a reliable predictor of ICU mortality and inotrope requirement, suggesting that serial urine albumin measurements could effectively monitor the microvascular effects of systemic inflammation.

A limitation of our study is the small sample size, which may affect the generalizability of the findings. Variability in results could also occur due to individual patient differences, necessitating larger studies to validate our conclusions.

CONCLUSION

Microalbuminuria appears to be a valuable biomarker for distinguishing sepsis from non-sepsis in critically ill patients and may serve as an early predictor of disease severity and ICU mortality. Elevated microalbuminuria levels at ICU admission were associated with sepsis, while persistently high levels at 24 hours correlated with increased mortality risk. Additionally, lower APACHE II scores and shorter ICU stays in non-septic patients reinforce the prognostic value of microalbuminuria. However, given the study's small sample size, further large-scale studies are needed to validate these findings and establish standardized cut-off values for clinical use.

REFERENCES

1. Bone RC, Spiung CL, Sibbaki WS. Definitions for sepsis and organ failure Crit. Care Med. 1992;19:973–6. doi: 10.1097/00003246-199206000-00002.

DOI: 10.69605/ijlbpr_14.2.2025.191

https://doi.org/10.1097/00003246-199107000-00024 PMid:1824030.

2. Aird WC. The role of the endothelium in severe sepsis and multiple organ dysfunction syndrome. Blood, J Am Soc Hematol. 2003;101(10):3765–77. doi: 10.1182/blood-2002-06-1887. https://doi.org/10.1182/blood-2002-06-1887 PMid:12543869.
3. Ait-Oufella H, Maury E, Lehoux S, Guidet B, Offenstadt G. The endothelium:physiological functions and role in microcirculatory failure during severe sepsis. Intensive Care Med. 2010;36(8):1286–98. doi: 10.1007/s00134-010-1893-6. https://doi.org/10.1007/s00134-010-1893-6 PMid:20443110.
4. Mutunga M, Fulton B, Bullock R, Batchelor A, Gascoigne A, Gillespie JI, et al. Circulating endothelial cells in patients with septic shock. Am J Respir Crit Care Med. 2001;163(1):195–200. doi: 10.1164/ajrccm.163.1.9912036. https://doi.org/10.1164/ajrccm.163.1.9912036 PMid: 11208646.
5. Zhou J, Schmidt M, Johnston B, Wilfart F, Whynot S, Hung O, et al. Experimental endotoxemia induces leukocyte adherence and plasma extravasation within the rat pial microcirculation. Physiol Res. 2011;60(6):853. doi: 10.33549/physiolres.932054.
6. Angus DC, Linde-Zwirble WT, Lidicker J. Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29:1303–10. doi: 10.1097/00003246-200107000-00002.
7. Todi S, Chatterjee S, Bhattacharyya M. Epidemiology of severe sepsis in India. Crit Care. 2007;11:65.
8. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345:1368–77. doi: 10.1056/NEJMoa010307.
9. Basu S, Bhattacharya M, Chatterjee TK, Chaudhuri S, Todi SK, Majumdar A. Microalbuminuria: A novel biomarker of sepsis. Indian J Crit Care Med. 2010 Jan;14(1):22-8. doi: 10.4103/0972-5229.63034. PMID: 20606905; PMCID: PMC2888326.
10. Bhadade RR, deSouza R, Harde MJ, Sridhar B. Microalbuminuria: a biomarker of sepsis and efficacy of treatment in patients admitted to a medical intensive care unit of a tertiary referral center. J Postgrad Med. 2014 Apr-Jun;60(2):145-50. doi: 10.4103/0022-3859.132320. PMID: 24823513.
11. Gosling P, Czyz J, Nightingale P, Manji M. Microalbuminuria in the intensive care unit: Clinical correlates and association with outcomes in 431 patients. Crit Care Med. 2006 Aug;34(8):2158-66. doi: 10.1097/01.CCM.0000228914.73550.BD. PMID: 16775565.