İstanbul Med J 2026; 27(2): 112-5
DOI: 10.4274/imj.galenos.2026.60598

Urine Beta 2 Microglobulin as a Marker of Recovery in Intrinsic Acute Kidney Injury Patients – a Prospective Observational Study

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ABSTRACT

Introduction: Intrinsic acute kidney injury (AKI) is a common and serious syndrome characterized by direct injury to the renal tubules. Although blood creatinine and urea are frequently used to evaluate renal function, they do not sufficiently indicate current tubular damage. Urinary beta 2 microglobulin (β2M) is a lower molecular mass protein reabsorbed via proximal tubules, functions as a possible biomarker for tubular injury and recovery.

Methods: A prospective observational study was carried out over a period of 18 months in the general medicine department of SRM Medical College Hospital and Research Center, enrolling 43 patients over 18 years of age who were diagnosed with AKI. Individuals with chronic kidney disease (CKD) and pre- or post-renal etiologies of AKI were eliminated. Renal parameters such as serum urea, creatinine, urine β2M, electrolytes, complete hemogram, and regular urine analysis, were assessed on admission, 1st, and 3rd months. Ultrasonography was employed to distinguish AKI from CKD. Data were examined to evaluate changes in renal variables over time.

Results: On admission, all patients exhibited elevated levels of urea, creatinine, and urinary β2M. At three months, serum urea and creatinine levels normalized in all patients, although 77.8% still exhibited elevated β2M levels. Notable mean decreases were recorded in urea, creatinine, and β2M of 13.22 mg/dL, 0.74 mg/dL and 11.2 µg/L respectively from starting period to three months. No statistically significant correlation was identified between gender and renal parameters.

Conclusion: Urinary β2M serves as a significant biomarker for identifying ongoing tubular injury in intrinsic AKI, despite the normalization of standard renal indicators.

Keywords: Acute kidney injury, tubular damage, urine β2 microglobulin, renal function

Introduction

Acute kidney injury (AKI) is a term used to describe a heterogeneous group of illnesses that share similar diagnostic characteristics, such as an increase in serum creatinine (SCr) concentration, frequently accompanied by a decrease in urine volume. Up to 30% of intensive care unit (ICU) admissions and 5–7% of acute-care hospital admissions are complicated by AKI (1). The severity of AKI can vary from mild and temporary alterations in glomerular filtration rate laboratory parameters to severe and quickly fatal disruptions in the kidney's capacity to maintain proper circulating volume regulation, eliminate nitrogenous wastes and metabolic toxins, and preserve the electrolyte and acid-base composition of plasma (2).

Because of several factors—including the impact of muscle mass, fluid status, or a delayed rise in creatinine level following the onset of renal injury—SCr is a poor diagnostic marker for AKI, making early intervention difficult (3). Several new biomarkers outperformed SCr in the diagnosis of AKI, and many were strongly correlated with immediate diagnostic results. When tubular damage or inflammation occurs, the majority of biomarkers are increased and stay that way until the injury or inflammation goes away (4).

Numerous proteins, including enzymes and urine beta 2 microglobulin (β2M), are filtered by glomeruli before being reabsorbed in the proximal tubule (5,6). β2M begins to rise early in renal failure and is unaffected by muscle mass. Reduced reabsorption of β2M and tubular enzymes as a result of tubular damage raises urine concentrations (7). These indicators might be useful markers of fibrosis or tubular damage. Serum β2M has been suggested as a potential measure to evaluate kidney function in AKI and chronic kidney disease (CKD) due to these characteristics (8).

Among existing tubular biomarkers, urinary β2M offers several practical advantages over alternatives such as neutrophil gelatinase-associated

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Cite this article as: Srinivas A, Viruthagiri K, David Xavier RJ, Ramkumar P, Thirupathipannaiyam Ananthakrishnan V. Urine beta 2 microglobulin as a marker of recovery in intrinsic acute kidney injury patients – a prospective observational study. İstanbul Med J. 2026; 27(2): 112-5

Received: 23.09.2025
Accepted: 08.03.2026
Publication Date: 12.05.2026

lipocalin, kidney injury molecule-1, and cystatin C. Urinary β2M is a low-molecular-weight protein (11.8 kDa) that is freely filtered at the glomerulus and nearly entirely reabsorbed by proximal tubular cells under normal circumstances; therefore, its rise in urine particularly indicates compromised tubular reabsorptive ability (9,10). Moreover, β2M tests are readily accessible in standard clinical laboratories, necessitate no specialised apparatus, and are significantly more economical than multiplex biomarker panels (11). These attributes render urine β2M a practical and dependable option for assessing tubular integrity in resource-constrained clinical environments.

Methods

Study Design

This prospective observational study was conducted in the Department of General Medicine at SRM Medical College. Over the course of 18 months, 43 patients participated in this study. The study population was calculated using the given formulas. This study included individuals over the age of 18 who were diagnosed with AKI and sepsis, and who were taking nephrotoxic medications. Individuals receiving chronic renal replacement treatment and those who had pre- and post-renal acute kidney damage (CKD) were not included.

Investigations and Follow-Up

Renal function tests, such as serum urea and creatinine, β2M, urine routine analysis, serum electrolytes, and complete hemogram, were measured at the time of admission. Ultrasonography of the abdomen was performed to differentiate AKI from CKD. These parameters were measured at 1 and 3 months.

Ethics and Consent

The study protocol was approved by the SRM Medical College Hospital and Research Centre Institutional Ethics Committee (registration number: IEC-ST1023-1717, date: 06.11.2023). Written informed consent was obtained from all participants included in the study. The participants were informed about the nature, purpose, and procedures of the study, and their right to withdraw at any time without any consequences. Confidentiality and anonymity of the participants were strictly maintained throughout the study.

Defining Outcomes

AKI Defined by KDIGO

- Increase in SCr by more than or equal to 0.3 mg/dL within 48 hours
- Increase in SCr to more than or equal to 1.55 to 1.9 times baseline, known or presumed to have occurred in the past 7 days
- Urine volume <0.5 mL/kg/hr for 6 hours

Statistical Analysis

The data were examined with SPSS version 22. Continuous variables were expressed as mean ± standard deviation. Renal function markers (urea, creatinine, and β2M), assessed at admission, one month, and three months, were analysed using repeated-measures analysis of variance. A p value less than 0.05 was deemed statistically significant.

Results

The average urea levels considerably declined from admission to three months (48.63±1.3 to 35.42±0.9 mg/dL). Despite a decrease in creatinine (1.86±0.2 to 1.11±0.5 mg/dL) and β2M (388.85±1.7 to 377.65±1.4 µg/L) levels, the alterations were not statistically significant. However, renal function improved during the follow-up period (Table 1).

All patients had abnormal urea, creatinine, and β2M levels when they were evaluated at admission (0 months). After a month of follow-up, 82.2%, 64.4%, and 88.9% of the AKI patients had abnormal urea, creatinine, and β2M readings, respectively. However, after three months' follow-up, all patients had urea and creatinine levels within acceptable ranges. β2M was abnormal in 77.8% of cases (Figures 1-3).

Table 2 displays the analysis of mean renal parameter values over the time frame. The average difference in levels of urea over three months was 13.2±2.3 mg/dL, also indicating a statistically significant decrease. Creatinine levels diminished by 0.74±0.03 mg/dL; however, this alteration was not considered statistically significant. β2M levels demonstrated a notable decrease of 11.2±2.0 µg/L over a period of 3 months.

Table 1. Renal function parameters

Renal function values (mean)	At admission	1 month	3 month	p value
Urea (mg/dL)	48.63±1.3	43.5±2.5	35.42±0.9	0.03
Creatinine (mg/dL)	1.86±0.2	1.57±0.3	1.11±0.5	0.2
β2M (µg/L)	388.85±1.7	382.91±2.8	377.65±1.4	0.4

β2M: Beta 2 microglobulin

Table 2. Mean differences of different parameters

Parameters	Mean difference			p value
	0-1 month	1-3 months	0-3 months	
Urea	5.13±0.9	8.1±1.2	13.2±2.3	0.002
Creatinine	0.28±0.03	0.46±0.06	0.74±0.03	0.1
β2M	5.94±0.8	5.26±1.1	11.2±2.0	0.03

β2M: Beta 2 microglobulin

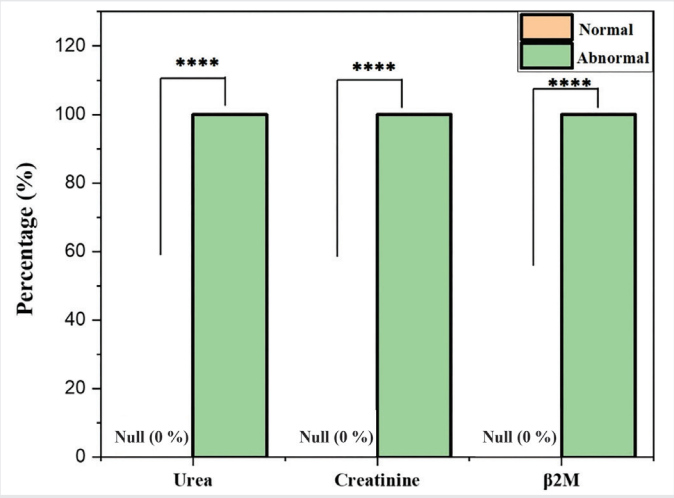

Figure 1. Renal values at admission. **** indicates the renal values are extremly significant

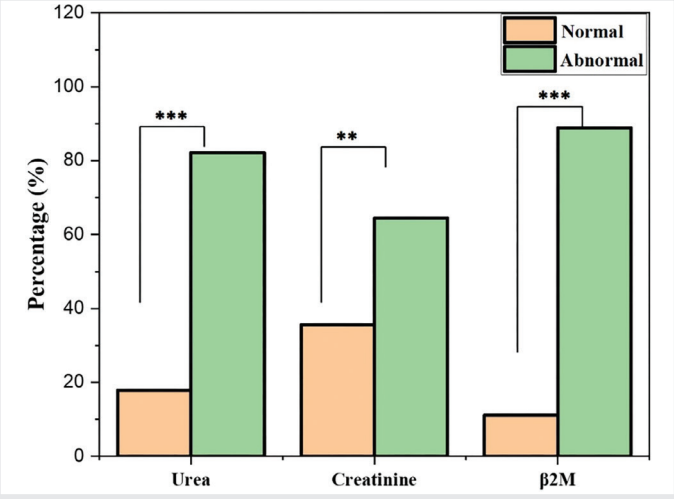

Figure 2. Renal values after 1 month of follow up. Values marked with asterisks indicate levels of statistical significance: **: indicates moderately significant differences, and *** indicates highly statistically significant differences in renal values

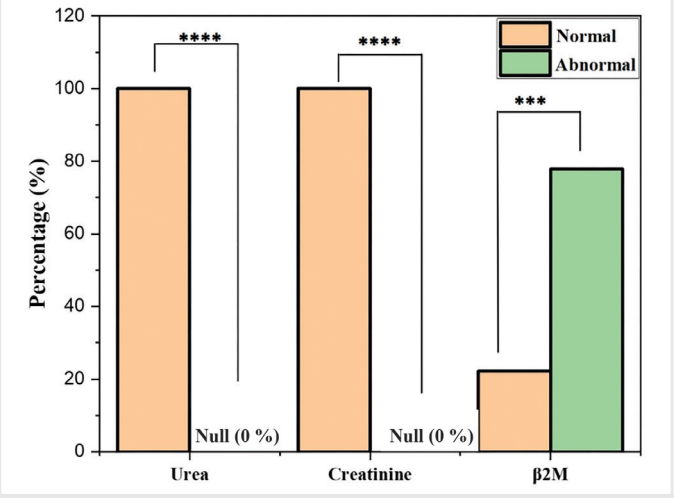

Figure 3. Renal values after 3 months of follow-up. Values marked with asterisks indicate levels of statistical significance: *** indicates highly significant differences, and **** indicates extremely significant differences in renal values

Discussion

In this study, patients with AKI exhibited a gradual enhancement in renal function indicators over a 3-month follow-up period. The study findings align with other finding, who documented substantial enhancements in renal function subsequent to proper intervention in intrinsic AKI (12).

SCr levels exhibited a reduction from period of admission to three months, although the alteration was not statistically significant. The average difference over 0-3 months was 0.74±0.03 mg/dL, indicating a progressive enhancement in glomerular filtration performance. Chapman et al. (13) observed analogous results, indicating that SCr may normalize at a slower rate and is affected by variables such as muscle mass and hydration condition, hence constraining its sensitivity to early tubular injury.

Conversely, β2M exhibited a more gradual decrease from admission to three months. The average difference during 0-3 months was 11.2±2.0 µg/L. This signifies that, although glomerular function improved, tubular recovery remained delayed. The results align with those of Argyropoulos et al. (7), who highlighted β2M as a sensitive indicator of ongoing tubular dysfunction despite the normalization of SCr levels.

The sustained increase in β2M after three months, as demonstrated in our study, underscores the continuous tubular damage that may elude detection by standard markers. Other researches claimed that enduring tubular dysfunction following AKI may facilitate the progression to CKD, despite corrected serum urea and creatinine levels (13-15).

Numerous investigations have confirmed β2M as an early prognostic biomarker for the severity and course of AKI. Shahjahan et al. (16) indicated that β2M provides enhanced sensitivity relative to creatinine for identifying renal impairment at multiple stages.

Our data indicate that whereas glomerular markers such as urea and creatinine may return to normal within three months post-AKI, tubular markers like β2M could stay at elevated levels, signifying subclinical injury and an increased CKD risk progression. This highlights the need to integrate tubular biomarkers into standard monitoring regimens for patients with AKI, enabling earlier management and preservation of long-term renal function.

Current research indicates that urine β2M levels over 300 µg/L may signify considerable proximal tubular dysfunction, necessitating further clinical monitoring. In the setting of AKI-to-CKD progression, consistently elevated β2M levels—especially those over 200 µg/L beyond 90 days post-AKI—are linked to inadequate tubular healing and an increased risk of long-term renal decline (17-19). Subsequent prospective research involving larger cohorts should validate specific cut-off values across diverse AKI patient populations to establish standardised clinical criteria for risk classification.

Study Limitations

The current study has a limited sample size, perhaps constraining the generalisability of the results. Although the sample size was determined to satisfy the minimum statistical criteria for this single-centre observational study, a larger multi-centre cohort would enhance the generalisability and statistical power of the results and is recommended

for future investigations. The follow-up duration was restricted to three months, precluding the assessment of long-term outcomes such as the progression to chronic renal disease. Urine β2M levels are influenced by urine pH, collection techniques, and storage conditions, which were not entirely standardised. Furthermore, since this was a single-center observational study, the findings may have limited generalisability to other demographic groups or clinical settings.

Conclusion

This study demonstrated a considerable improvement in urea and creatinine levels within three months post-AKI, indicating successful glomerular recovery. Nonetheless, sustained elevation of β2-microglobulin indicates continued tubular damage despite adjusted conventional indicators. β2M may function as a sensitive marker for assessing subclinical renal impairment. The integration of tubular biomarkers may improve the long-term care and prognosis of patients with AKI.

Ethics

Ethics Committee Approval: The study protocol was approved by the SRM Medical College Hospital and Research Centre Institutional Ethics Committee (registration number: IEC-ST1023-1717, date: 06.11.2023).

Informed Consent: Written informed consent was obtained from all participants included in the study. The participants were informed about the nature, purpose, and procedures of the study, and their right to withdraw at any time without any consequences. Confidentiality and anonymity of the participants were strictly maintained throughout the study.

Acknowledgments

We would like to thank SRM Medical College Hospital and Research Centre, Faculty of Medicine and Health Sciences, SRMIST, Kattankulathur, for their cordial support of this study. We also extend our gratitude to Dr. Vishnupriya Subramaniyan, Ph.D., Research Writer, SRM Medical College Hospital and Research Centre, SRMIST, for her valuable assistance in the preparation of this manuscript.

Footnotes

Authorship Contributions: Surgical and Medical Practices - A.S., R.J.D.X., P.R.; Concept - A.S., K.V., V.T.A.; Design - R.J.D.X., P.R., V.T.A.; Data Collection or Processing - A.S., K.V., R.J.D.X., P.R., V.T.A.; Analysis or Interpretation - A.S., R.J.D.X., P.R., V.T.A.; Literature Search - A.S., K.V., R.J.D.X., V.T.A.; Writing - A.S., P.R., V.T.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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