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**Original Research Article**

# Microalbuminuria can predict the development of acute kidney injury in intensive care unit admission

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## ABSTRACT

**Background:** Microalbuminuria, defined as 30–300 mg/day of albumin excretion in urine is a common finding in ICU patients and has shown not only as a predictor of organ failure but prolonged intensive care unit (ICU) stay. Objective of the study was to determine the prediction of acute kidney injury using urine microalbuminuria and to determine the presence of urine microalbuminuria and relationship between ICU length of stay.
**Methods:** The present study is conducted on patients admitted to Medical ICU in SDMCMSH, Dharwad from December 2016 to November 2017. 75 patients who met the inclusion and exclusion criteria were included in the study.
**Results:** The present study included 75 patients, among which 50 were males and 25 were females. The mean age was 60.2years. AKI was developed more in non-diabetics than diabetics and non-hypertensives than hypertensives. The median urine microalbumin at admission in AKI was 80.9 and at 48 hr was130.1 predicted the AKI mean (1.79) in 59 patients with a p value of <0.001 using Mann Whitney test and P value statistically significant.
**Conclusions:** Urine microalbuminuria at 48 hr has predicted AKI in 59 patients with median of 130.1 with statistical significance. Urine microalbuminuria of high value in AKI is directly proportional to prolonged ICU stay. At 48 hours of admission, increased levels of microalbuminuria compared at admission and 48 hour, indicates its prognostic significance among AKI and NON-AKI's in ICU patients.

**Keywords:** Acute kidney injury, ICU prolonged stay, Urine microalbumin

## INTRODUCTION

Acute kidney injury (AKI) is a heterogeneous syndrome defined by a rapid (overhours to days) decline in the glomerular filtration rate (GFR) resulting in the retention of metabolic waste products, including urea and creatinine, and dysregulation of fluid, electrolyte, and acid-base homeostasis.[1] There was difficulty in detecting definite incidence of AKI due to unavailability of standard definition, until recently. Various studies have estimated that 3% to 7% of hospitalized patients and 25% to 30% of patients in the intensive care unit (ICU) develop AKI, with 5% to 6% of the ICU population requiring renal replacement therapy after developing AKI.[2-5]

Albumin is a major serum protein with a size larger than the pores of the glomerular filtration membrane and is generally not filtered in normal kidney. Hence, appearance of albumin in urine is suggestive of glomerular pathology, as its appearance in large amounts in urine represents compromised integrity of the glomerular basement membrane. Albuminuria is

recognized as one the most important risk factors for progression of kidney diseases.[6,7]

Microalbuminuria, defined as 30–300 mg/day of albumin excretion in the urine, occurs rapidly after an acute inflammatory insult such as sepsis and persists in patients with complications. It is a common finding in critically ill patients, where it has shown promise not only as a predictor of organ failure and vasopressor requirement but of mortality, as per few studies.[6] Urine microalbumin estimation is a simple and inexpensive test and it can be used if it helps in management of sepsis, especially in terms of early prediction of organ failure and requirement of inotropic support. This study is done to understand the usefulness of urine microalbuminuria in predicting the mortality and morbidity along with prolonged stay in ICU.

## METHODS

The Prospective, non-interventional study was conducted on patients admitted to Medical ICU in SDMCMSH, tertiary care hospital Dharwad. Period of study was December 2016 to November 2017. Convenience sampling was used.

Method of collection of specimen and processing: spot urine sample collected at the time of ICU Admission and at 48hours of ICU stay to medical ICU. Sample will be tested for urine microalbumin by immune turbidometric method and urine microalbumin:creatinine ratio calculated.

### *Inclusion criteria*

All adult patients admitted to the medical ICU/Medical Emergency ward at SDM MEDICAL COLLEGE AND Hospital with features of SIRS (systemic inflammatory response syndrome) and suspected infection.

### *Exclusion criteria*

Patients receiving nephrotoxic drugs, Patients with preexisting urinary tract infection, Patients with urologic trauma resulting in frank hematuria or urinary infection, Patients with preexisting chronic kidney disease (serum creatinine level ≥2.0 mg/dL), Pregnancy , Pre-existing diabetic neuropathy, Anuria and Patients less than 14 years.

Data will be collected using a pretested performa meeting the objectives of the study. Detailed history, physical examination and necessary investigation will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained.

### *Data analysis and interpretation*

Data was entered into Microsoft excel and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 17.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables were determined. The chi-square test and fisher's exact test (when appropriate) was used to show the associations between predictor and outcome variables. The level of significance was set at 0.05.

## RESULTS

In this study population the age varied from 16-90 years and mean age was 60.2 years with standard deviation of 18.3 years. Majority (56%, n=42) were above 60 years of age suggesting higher incidence of AKI in elderly population. Majority of participants (67%, n=50) belonged male gender and rest belonged to female gender.

Prevalence of diabetes, hypertension was 28% (n=21), 27% (n=20) of study population respectively. Majority of the patients (41.3%, n=31) had respiratory system involvement leading to AKI, followed by Cardiovascular and gastrointestinal system involvement (10.7%, n =8).

Among the patients who presented to medical ICU, 59 of them had AKI giving prevalence of 78%. There was higher mean creatinine value after 48 hours with mean increase in 0.65 mg/dl compared to admission. There was increase in 24.4 mg/dl in median urine albumin levels after 48 hours of admission when compared to baseline values.

When assessed at baseline, mean serum creatinine was higher among patients with non-AKI group (1.22mg/dl, SD-0.24) compared to AKI group. But when same was compared after 48 hours, patients with AKI group had higher mean serum creatinine levels (1.79mg/dl, SD-0.49) compared to non-AKI group and this was statistically significant when assessed using student test. The difference in rise of serum creatinine value in 48 hours in AKI group was 0.77mg/dl and 0.19mg/dl in non-AKI group showing significant difference among the two groups.

Urine albumin levels among AKI and non-AKI group at the time of admission and after 48 hours of admission respectively. At the time of admission, median urine albumin was higher among AKI group (80.9mg/dl), than non-AKI group, but this difference was not statistically significant. But when urine albumin was compared again after 48 hours, the difference had increased significantly and median urine albumin in AKI group was 130.1mg/dl. When compared between AKI and non-AKI groups, there was increase in 49.2mg/dl after 48 hours in AKI group, but in contrast, there was decreasing trend in non-AKI group with decrease in 7.6mg/dl in 48 hours and this difference was statistically significant ($P<0.05$). Comparison of urine albumin levels among AKI and non-

AKI group was again compared among patients with and without diabetes (Table 1 and Table 2).

**Table 1: Comparison of urine albumin at the time of admission among AKI and non AKI group (n=75).**

| | Difference in urine albumin at admission | | P value |
|---|---|---|---|
| | Median | Min-Max (range) | |
| **AKI** | 80.9 | 3 to >300 | 0.64 |
| **No AKI** | 61.1 | 19.4 to >300 | |

Mann Whitney test and P value statistically not significant

**Table 2: Comparison of urine albumin after 48 hours of admission among AKI and non AKI group (n=75)**

| | Difference in urine albumin at 48 hours | | P value |
|---|---|---|---|
| | Median | Min-Max (range) | |
| **AKI** | 130.1 | 11.2 to >300 | <0.001 |
| **No AKI** | 53.5 | 21.7 to >300 | |

Mann Whitney test and P value highly statistically significant

**Table 3: Comparison of median urine micro-albumin in AKI and non-AKI groups among patients with diabetes and no diabetes (n=75).**

| Difference in urine albumin at 48 hrs. | Diabetes patients | | Non-diabetes patients | |
|---|---|---|---|---|
| | Median | Min-Max (range) | Median | Min-Max (range) |
| **AKI** | 132.6 (n=20) | 26.2 to >300 | 130(n=39) | 11.2 to >300 |
| **No AKI** | 52.6 (n=1) | 23.7 to >300 | 54.3(n=15) | 21.7 to >300 |
| **P value** | 0.136 | | 0.002* | |

*Mann Whitney test and P value statistically significant

There was increase in median urine albumin levels in both diabetes and non-diabetes population but the difference was significant in non-diabetes group (P-0.002). Non-hypertensive's had higher incidence (73.3%,n=55) when compared to patients with hypertension(26.7%,n=20) (Table 3).

**Table 4: Comparison of duration of hospital stay to development of AKI (n=75).**

| ICU stay | Number | No AKI | AKI | P value |
|---|---|---|---|---|
| **<5 days** | 29 | 13 (45) | 16 (55) | |
| **5-8 days** | 30 | 2 (7) | 28 (93) | <0.001 |
| **>8 days** | 16 | 1 (7) | 15 (93) | |
| **Total** | 75 | 16 (21.4) | 59 (78.6) | 100 |

With ICU stay <5 days duration, incidence of AKI was 55% (n=16/30) and incidence of AKI increased to 93% (n=28/30). There was progressive increase noted with development of AKI with duration of ICU stay and this was found to be statistically significant. Incidence of AKI for the study population was 78.6% (n=59) and the incidence of AKI after 5 days of hospital stay was 93% and is higher when compared to the overall incidence of AKI (Table 4).

There was increase in median urine albumin levels when compared to ICU duration of <5 days (87.4), 5-8 days (109.8) and >8 days (117.6). There was increase in urine albumin levels with duration of ICU stay but this was not statistically significant.

Receiver operating characteristic curve for urine albumin levels after 48 hours in comparison to development to AKI was studied. Area under the curve was 0.81. 95% confidence interval is in between 0.69-0.94 (Table 5).

**Table 5: Comparison of urine albumin levels after 48 hours of admission to duration of ICU stay (n=75).**

| ICU stay | Difference in urine albumin at 48 hours | | P value |
|---|---|---|---|
| | Median | Min-Max (range) | |
| <5 days | 87.4 | 21.2 to >300 | 0.334 |
| 5-8 days | 109.8 | 11.2 to >300 | |
| >8 days | 117.6 | 23.1 to >300 | |

Kruskal Wallis test and P value statistically significant

## DISCUSSION

Patients were distributed from age 16-90 with age >60 constituting 56%. Mean age (SD) of study participants was 60.2 (18.3) years. A study conducted by Basu et al showed mean age of 63.5 years and a study done by Todi et al showed a mean age of 58.17years.[6,8] A study conducted in United states of America by Angus DC et al showed mean age of 57 years.[9] A study conducted by Rodriguez et al showed mean age as 45 years.[10] Mean age detected in above mentioned studies were similar to the findings in our study with mean age in elderly age group and higher incidence of AKI in geriatric patients. Patients with age >60years constituted 56% of the study population and is in consistency with infections being most common cause in elder age group.

In this present study done showed male being more common with 50 patients being male (66.7%) and 25 patients being females (33.3%). This is consistent with study conducted by Todi et al epidemiology of sepsis in India with male patients constituting 57.71%, study done by Angus et al which showed male patients constituted 51.9% and another study done by Basu et al showed male patients were high in number 62.8%.[8,9,6] Findings from above mentioned studies were consistent with our findings with higher incidence of AKI among male patients. In this present study AKI was developed more in nondiabetics than diabetics (54 patients 72% non-

diabetics vs 21 diabetics 28%) and non-hypertensives than hypertensives (55 patients 73.3% non hypertensive's vs 20 hypertensives 26.7%).

Among the ICU admission majority of cases being respiratory cases 31(41.3%), miscellaneous up-to 12 cases (16.0%), CVS 8 cases(10.7), GIT 8 cases (10.7), CNS 7cases (9.3), VHF 6 cases (8.0%) and genito-urinary system 3 cases(4.0%). This study is in consistent with Basu S et al study which showed majority cases of respiratory illness (n= 18).[8]

The median urine microalbumin at admission in AKI was 80.9 and at 48hr was130.1 predicted the AKI mean (1.79) in 59 patients (78.7) with a p value of <0.001 using Mann Whitney test and p value statistically significant. A study conducted by Zhang et al in Chinese population in 2013 showed higher incidence of AKI among patients who had increased urine albumin and cut off to predict AKI was set at 143 mg/g with specificity of 91.7% and sensitivity of 79.2% with area under the curve being 0.86, which was higher when compared to our study as our cut off for predicting AKI was urine albumin creatinine value of 82 mg/g with sensitivity of 76.27% and specificity of 81.25% as area under ROC curve was 0.81.[11] The decrease in the cut off for urine albumin to creatinine ratio to predict in our study can be explained by difference in ethnicity, etiology and higher incidence of AKI in our study.

In this present study done, the length of ICU stay for <5 days was seen in 29 patients among which AKI was present in 16 (55%) patients and between 5-8 days stay was seen in 30 patients and among them AKI was present in 28 patients (93%), for >8 days stay was seen in 16 patients and AKI was seen in 15 patients (93%). Among these patients stay of <5 days urine microalbumin median was 87.4, for stay in between 5-8days median was 109.8 and for stay >8 days urine microalbumin was 117.6 suggesting that urine microalbuminuria can predict the prolonged stay in ICU and AKI. But when statistical analysis was applied, association of AKI and duration of hospital stay was statistically significant and association with urine albumin and ICU duration was positive, but the association was not statistically significant.

## CONCLUSION

At 48 hours of admission, increased levels of Microalbuminuria compared to Microalbuminuria levels at admission and 48 hours, indicates it's prognostic significance among survivors and non-survivors in critically ill patients. Microalbuminuria is an inexpensive and rapid diagnostic bedside tool, could be efficiently utilized for identification of patient survival in ICU. Early institution of intensive therapy to these patients can improve survival rates. Microalbuminuria is an inexpensive and rapid diagnostic tool, serial measurements may prove a useful aid in the clinical assessment of critically ill patients at risk of worse prognosis, even in resource poor areas. Hence Microalbuminuria can be used as a dynamic marker of prediction of AKI in ICU admission.

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