

Urinary Albumin/Creatinine Ratio as an Early Predictor of Outcome in Critically Ill Patients.

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ABSTRACT

Background: In Critical care units, prediction of outcome is of vital importance to the clinician. It allows planning of early therapeutic intervention and appropriate counseling of patient. So sensitive, inexpensive and dynamic prognostic markers which generate rapid and reliable results are therefore desirable in the ICU setting. **Objectives:** 1. "To evaluate microalbumin to creatinine ratio within 6 hours of ICU admission and after 24 hours of ICU admission. 2. To correlate microalbumin to creatinine ratio with APACHE II score to predict outcome in critically ill patients". **Methods:** In this prospective non-interventional study, 98 adult patients admitted to I.C.U. with more than 24 hours of ICU stay were included and Spot urine sample collected at 6, 24 hours of admission to medical ICU ward. Sample will be tested for urine microalbumin by immunoturbidometric method and urinary creatinine was measured by calorimetric method. Albumin: creatinine ratio was measured. For disease prognosis scoring, GCS, SOFA and APACHE II scores were calculated simultaneously. **Results:** Prevalence of ACR at 6 hrs 95.7%, 97.9% at 24 hrs. Out of 98 patients 47 patients died. p value <0.001. Among the survivors there was a significant correlation between decreasing microalbuminuria, microalbumin to creatinine ratio level and decreasing APACHE II and SOFA scores, and increasing GCS score, p- value being 0.0011, 0.002 and 0.0005 respectively. Among the non-survivors there was a significant correlation between increasing microalbuminuria, to creatinine ratio level and increasing APACHE II and SOFA scores, and decreasing GCS score, p value being 0.0001, 0.0001 and 0.0001 respectively. **Conclusion:** This study was carried out to find out the role of microalbuminuria, microalbumin to creatinine ratio as a predictor of prognosis in critically ill patients as compared to standard scoring methods like the Glasgow coma scale, APACHE II and SOFA scores. Hence microalbumin to creatinine ratio at 24 hours may be considered as a predictor of outcome in critically ill patients.

Keywords: ?.

INTRODUCTION

Predicting clinical outcome is an important component of patient care in critical care units:

A number of prognostication tools for ICU patients have been developed to assess the severity of illness and predict prognosis. Though useful, these too are complex. For example, the widely used APACHE II score requires input of a large number of variables derived from the patient's history, physical examination, and initial laboratory data. In addition, scoring systems rely mainly on data obtained early in the course of illness. It is well-known that the physiologic responses of patients to various insults and interventions vary. The strength of initial predictions therefore, may be influenced by numerous factors during the course of hospitalization. These factors may not be accounted for in the initial assessment. Therefore, these prognosis scoring tools, which not only require the

utility of expensive and sophisticated equipments, may also underestimate actual disease outcome in terms of morbidity and mortality.

Multiple system organ failure (MSOF), which is the ultimate hallmark of most critically ill patients, has been described as a sequential failure of the lungs, liver, kidney and other vital organ systems after a variety of acute physiological conditions such as severe infections and sepsis, pancreatitis, hemorrhagic shock, multiple trauma, etc¹. (MacKinnon K.L. et al 2000). Although the mechanism involved in the development of this syndrome is proposed that MSOF after trauma, and severe acute systemic illnesses results from a inflammatory reaction with activation of leucocytes and release of free radicals and other mediators, such as cytokines, from these cells. Other studies have described a rapid increase in microalbumin excretion in acute inflammatory conditions, which related to systemic vascular damage by capillary leak syndrome.

Microalbuminuria, defined as 30-300 mg/day in a 24 hrs collection or 30-300 µg/mg creatinine in a spot collection, is an early marker of glomerular injury. "Microalbuminuria has a rapid onset and typically

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lasts for <48 hrs. The degree of development of microalbuminuria can be proportional to the severity of the illness”.

Microalbuminuria is a simple, less expensive, and prognostic tool for critically ill patients in intensive care units. It has been found to be comparable with the APACHE II and SOFA score.

Hence, considering the large number of critically ill patients admitted to our hospital, it has been proposed to carry out this study on the role of microalbuminuria as a prognostic tool in assessing severity of illness and mortality in critically ill patients admitted to the ICU, Department of Medicine, Shri B. M. Patil Medical College, Vijayapura with the following.

Aims and Objectives

- To evaluate microalbumin to creatinine ratio within 6 hrs of ICU admission and after 24 hrs of ICU admission in critically ill patients.
- To compare microalbuminuria to creatinine ratio with APACHE II score and SOFA score as a predictor for mortality in critically ill patients.

MATERIALS AND METHODS

In this study 98 critically ill patients, admitted in the Intensive Care Unit of BLDE UNIVERSITY Shri B. M. Patil medical college Vijayapur.

Inclusion Criteria

Critically ill patients aged >18 years admitted to the ICU department of Medicine, BLDE UNIVERSITY Shri B. M. Patil medical college Vijayapur.

Exclusion Criteria

- Patients with Anuria, frank hematuria
- Patients with urinary infections
- Patients with Diabetes Mellitus
- Patients with CKD (serum creatinine level ≥ 2.0 mg/dl)
- Patients who are on nephrotoxic drugs
- Patient suffering from chronic organ insufficiency before this hospital admission according to APACHE II guidelines
- Any post-operative patients and patients admitted with Accidents/ trauma.

Urinary samples for microalbuminuria were collected at hospital admission and at 6,24hrs after hospital admission. The level of microalbuminuria, the microalbuminuria:creatinineratio wascalculated.

The severity of illness was assessed by the APACHE II. Similarly the degree of organ dysfunction was assessed using SOFA score, calculated from the time 6 hrs of admission and24 hrs of the hospital stay.

Measurement Of Microalbuminuria:

Collection of sample Urinary samples were collected at hospital admission6, 24, hrs

Method Immunoturbidimetric assay for urinary albumin

AnalyserRandoxautoanalyser

Measurement of Urinary Creatinine:

Sample: The spot sample is diluted 49 times its volume with redistilled water

Method: Colorimetric method

Analyser: Randoxautoanalyser.Albumin Creatinine Ratio: ACR was then calculated.

RESULTS

Table 1: Distribution of Cases According To Clinical Outcome

Clinical Outcome	N	%
Died	47	48
Survived	51	52
Total	98	100

As seen in table,out of 98 patients studied 51 (52%) survived,and47(48%)died during hospital stay.

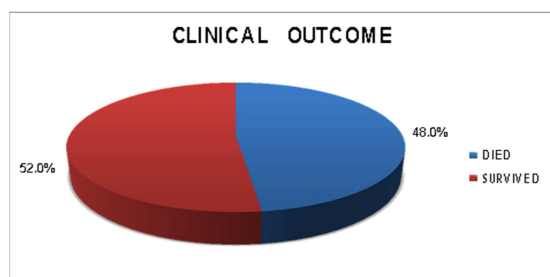


Figure 1: Distribution of Cases According To Clinical Outcome

Table 2: Association of Duration of Stay with Outcome

Duration of Stay	Survived		Died		p Value
	N	%	N	%	
≤5	20	39.2	21	44.7	0.804
6-10	22	43.1	20	42.6	
11-15	6	11.8	3	6.4	
16-20	1	2.0	2	4.3	
>20	2	3.9	1	2.1	
Total	51	100.0	47	100.0	

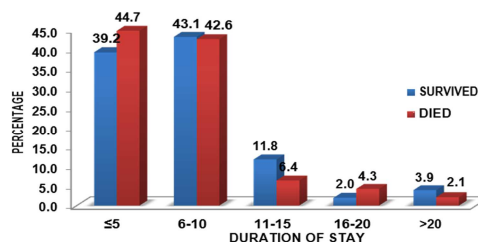


Figure 2: Association of Duration of Stay With outcome

Table 3: Pearson Correlation Of Parameters With Microalbumin According To Outcome

Parameters	Survived		Died	
	R Value	P Value	R Value	P Value
GCS	-0.06	0.677	-0.01	0.949
APACHE	-0.046	0.751	-0.025	0.867
SOFA	-0.015	0.916	0.101	0.499
CRT	0.12	0.402	-0.183	0.218
ACR	-0.231	0.104	0.019	0.897

Table 4: Association of GCS Score with outcome

GCS Score	Survived		Died		Total	p value
	N	%	N	%		
<5	12	34.3	23	65.7	35	0.001*
5-10	29	54.7	24	45.3	53	
>10	10	100.0	0	0.0	10	
Total	51	52.0	47	48.0	98	

Note: * significant at 5% level of significance (p<0.05)

Table 5: Meanges Scoreaccording to Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
GCS score	6 Hrs	7.5	3.4	5.4	2.0	0.001*
	24 Hrs	7.5	3.4	4.7	1.7	<0.001*

Note: * significant at 5% level of significance (p<0.05)among survivors,GCS score gradually increases over the period of time, whereas among the non survivors it has decreasing.

Table 6: Meanapache Scoreaccording to Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
Apache li Score	6 Hrs	18.2	6.5	18.9	6.4	0.592
	24 Hrs	18.8	6.2	19.5	6.1	0.55

Among the survivors, the mean APACHE II Score is less whereas among non survivors APACHE II score is more at 24 hrs.

Table 7: Meansofa Scoreaccording to Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
SOFA score	6 Hrs	8.4	2.5	9.9	1.9	0.001*
	24 Hrs	8.8	2.5	10.5	1.9	<0.001*

* Significant at 5% level of significance (p<0.05)

Table 8: Meanurinary Microalbuminaccording to Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
Urinary Microalbumin	6 hrs	84.9	73.5	113.7	126.6	0.168
	24 hrs	96.1	81.4	114.9	99.2	0.308

Survivor group has less microalbumin, whereas non survivor group has increased level of microalbumin.

Table 9: Association of Urinary Creatinine With outcome

Urinary creatinine	Survived		Died		Total	p value
	N	%	N	%		
24-50	10	19.6	14	29.8	24	0.262
51-75	18	35.3	15	31.9	33	
76-100	15	29.4	9	19.1	24	
100-125	2	3.9	3	6.4	5	
126-150	0	0.0	3	6.4	3	
>150	6	11.8	3	6.4	9	
Total	51	100.0	47	100.0	98	

Urinarycreatinine between 24-50, out of 24 patients 14 (29.8%) died, 10 (19.6%) survived. Urinarycreatinine >150 out of 9 patients 3 (6.4%) died, 6 (11.8%) survived.

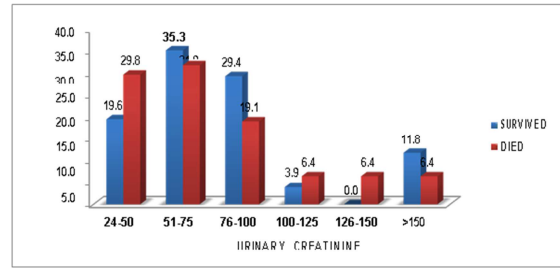


Figure 3: Association of Urinary Creatinine Withoutcome

Table 10: Meanurinary Creatinine According To Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
Urinary creatinine	6 Hrs	76.3	46.1	80.6	54.8	0.674
	24 Hrs	87.1	55.8	81.4	46.8	0.588

Table 11: Association Of Albumin Creatinine Ratio With outcome

Albumin creatinine ratio	Survived		Died		Total	p value
	N	%	N	%		
<30	14	100.0	0	0.0	14	<0.001*
31-50	19	57.6	14	42.4	33	
51-70	11	35.5	20	64.5	31	
71-90	5	29.4	12	70.6	17	
>90	2	66.7	1	33.3	3	
Total	51	52.0	47	48.0	98	

Note: * significant at 5% level of significance (p<0.05)

Albumin to creatinine ratio <30, out of 14 patients all are survived, albumin to creatine ratio between 71-90,out of 17 patients 12(70.6%)died and 5(29.4%)survived.

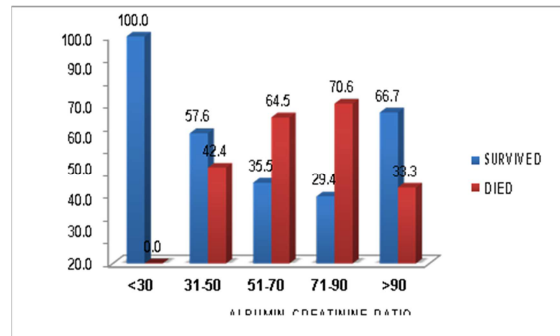


Figure 4: Association of Albumin Creatinine Ratio With outcome

Table 12: Meanalbumin Creatinine Ratioaccording to Outcome

Parameters		Survived		Died		p value
		Mean	SD	Mean	SD	
Albumin creatinine ratio	6 Hrs	46.3	20.1	58.0	15.7	0.002*
	24 Hrs	50.5	21.0	63.8	15.7	0.001*

Note: * significant at 5% level of significance (p<0.05)

Table 13: Roc Analysis of Parameters In Detecting Death

Test Variable(s)	Area Under the Curve	SE	p value	95% Confidence Interval	
GCS score	0.564	0.058	0.275	0.45	0.678
Apache ii score	0.525	0.059	0.67	0.41	0.64
Sofa score	0.498	0.059	0.972	0.382	0.614
Urinary Microalbumin	0.571	0.058	0.224	0.457	0.686
Urinary creatinine	0.479	0.059	0.725	0.363	0.595
Albumin creatinine Ratio	0.722	0.052	<0.001*	0.62	0.825

Table 14:

Test Variable(s)	Positive if Greater Than or Equal to	Sensitivity	Specificity
GCS Score	7.8	55.3%	52.9%
Apache ii score	17.3	53.2%	51.0%
Sofa score	7.8	61.7%	41.2%
Urinary microalbumin	77.0	57.4%	56.9%
Urinary creatinine	68.8	46.8%	45.1%
Albumin creatinine Ratio	51.0	68.1%	64.7%

As seen in table,albumin to creatinine ratio had p value <0.001 statistically significant compared with other parameters.

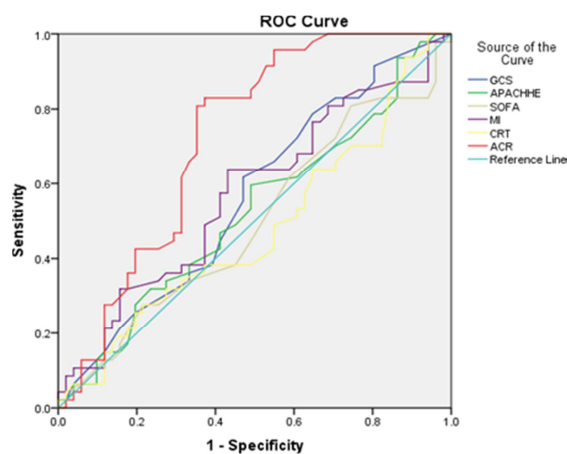


Figure 5: Roc Curve Of Parameters In Detecting Death

Table 15: Prevalence (%) Of Microalbuminuria And Albumin Creatinine Ratio By Major Diagnosis

Major diagnosis	Urinary microalbumin (>30)		Albumin creatinine ratio (>30)	
	No of Patients	Prevalence (%)	No of Patients	Prevalence (%)
CVA	17	94.4	17	94.4
MI	16	94.1	15	88.2
SEPSIS	9	75.0	12	100.0
OP POISON	11	100.0	6	54.5
COPD	11	84.6	10	76.9
Organ Disfunction	42	89.4	44	93.6

Table 16: Prevalence (%) Of Microalbuminuria and Albumin Creatinine Ratio By Mortality At 6 And 24 Hrs

Parameter		Died (n=47)		Survived (n=51)		Total		P value
		No of Patients	Prevalence (%)	No of Patients	Prevalence (%)	No of Patient s	Prevalence (%)	
Urinary microalb umin (>30)	6 Hrs	44	93.6	47	92.2	91	92.9	0.779
	24 Hrs	46	97.9	50	98.0	96	98.0	0.953
	Overall	41	87.2	46	90.2	87	88.8	0.643
Albumin creatinin e ratio (>30)	6 Hrs	45	95.7	41	80.4	86	87.8	<0.001*
	24 Hrs	46	97.9	47	92.2	93	94.9	0.028*
	Overall	46	97.9	38	74.5	84	85.7	<0.001*
Total		47	100.0	51	100.0	98	100.0	

Note: * significant at 5% level of significance (p<0.05)

DISCUSSION

Assessing the severity of illness of patients is one of the important aspect of management of critically ill patients in high dependency care areas like ICUs. This is done both for the benefit of the patients and also in determining the optimum plan of management these patients. Hence many severity assessment scores have been developed including the APACHE, SOFA, score etc. These assessment scoring methods are objective, quite expensive. Multiple system organ failure (MSOF), which is the ultimate hallmark of most critically ill patients, has been described as a sequential failure of the lungs, liver, kidney and other vital organ systems after a

variety of acute physiological conditions such as severe infections and sepsis, pancreatitis, hemorrhagic shock, multiple trauma, etc. Although the mechanism involved in the development of this syndrome are not clear, it is proposed that MSOF after trauma, and severe acute systemic illnesses results from inflammatory reaction with activation of leucocytes and release of free radicals and other mediators, such as cytokines, from these cells which causes a rapid increase in urine albumin due to systemic vascular damage exemplified by capillary leak syndrome. Hence, microalbuminuria has been considered a marker of vascular damage. "It is now considered that

microalbuminuria is an important predictor for the development of diabetic nephropathy, characterized by proteinuria, increase BP, and decrease glomerular filtration rate". Microalbuminuria associated with Many acute inflammatory conditions. The rapid increase in renal permeability to plasma protein after trauma⁵, ischemia², proportional to the severity of the insult, which led to the increased renal and vascular permeability occurs simultaneously. Microalbuminuria, defined as 30-300 mg/day in a 24 hr collection or 30-300 µg/mg creatinine in a spot collection. It lasts for <2 days and has a rapid onset. "The level of microalbuminuria can be proportional to the severity of the illness".

Microalbuminuria has been found to be is comparable with the other parameters like APACHE and SOFA. Microalbuminuria may be a simple, important and complementary method in assessing the severity and prognosis of patients admitted in the hospital and help in aggressively managing patients. We collected the urinary samples from the patients at hospital admission, 6 hrs, and 24 hrs, after hospital admission. We also calculated the GCS score, APACHE II score and SOFA score at same interval of time.

"So it is important to evaluate the mean rather than a single value". The results and observations of our study are discussed below

1) **Mortality rate:**

Out of the 98 patients studied, there was a mortality rate of 48%.

2) **Duration of stay and mortality:**

The mean duration of stay in the ICU was 8.8 days with a standard deviation of 4.98.

41 patients whose duration of stay was less than 5 days mortality rate 44.7%.

42.6% of the patient whose duration of stay was between 6-10 days and 6.4% of the patients who stay was between 11-15 days and 2.1% of the patients who stayed for more than 20 days died.

3) **Diagnosis of the patients and mortality:**

In this study we observed that, Cerebrovascular accidents (18.4%), followed by MI (17.3%), COPD (13.3%), Sepsis (12.2%), op poison (11.2%), LRTI (7.1%), Chronic liver disease with HE (7.1%), Seizure (7.1%), TBM (5.1%) and cerebral malaria (1%).

25.5% of Sepsis, 19.1% of CVA, 17.1% of COPD, 12.8% of MI and 8.5% of CLD, 6.4% of OP POISON did not survive.

4) **Organ dysfunction at the time of presentation:**

In our study, 42% presented with multiorgan failure, 30% had acute respiratory failure and 25.5% had sepsis at the time of presentation.

5) **Prevalence of Microalbuminuria**

In our study we found the prevalence of microalbuminuria in critically ill patients to be 92.9% at 6 hrs, 98% at 24 hrs of time of admission. Out of the 98 patients with microalbuminuria 91

(92.9%) had microalbuminuria at the 6 hrs of admission and 96(98%) at 24 hrs of admission. Prevalence of albumin to creatinine ratio; Prevalence of ACR at 6 hrs 95.7%, 97.9% at 24 hrs. Out of 98 patients 47 patients died. p value <0.001

6) **GCS score and mortality**

In our study we found that mortality was significantly higher in patients with a lower GCS score. For example, in the patients with a GCS score below 5, the mortality was 65.7%, in the patients with GCS score of 5-10 had a mortality of 45.3% and patients with a GCS score >10 had a mortality of 0% (p<0.05) There was an increasing trend of mean GCS score in the patients who survived and a decreasing amongst those who did not.

7) **APACHE II Score and Mortality**

In our study we found that with increasing APACHE II score there was an increase in mortality. 4 patients with APACHE II less than 10, 75% patients survived, 25% patient died. while 60 patients who had an APACHE II score of 11-20, 29 (48.3%) patients died. 29 patients who had APACHE II score of 21-30, 14 (48.3%) patients died. with an APACHE II score between >3ie0 ,3 (60%) patients died. Furthermore, the survivors had a decreasing score and non-survivors had a rising score of the APACHE II scores.

These findings correlated with the findings of other authors. Omar Abidet al,^[3] (2001) found that increase "APACHE II" score was significantly associated with increasing microalbuminuria level. R. Martynoga et al,^[7] (2009) found that APACHE II score and age behaved as independent predictors of mortality, p-values being less than 0.0001 and less than 0.002 respectively.

8) **SOFA Score and mortality**

In our study we found that out of the 98 patients with SOFA score less than 5,

2 (100%) survived, p-value of which is <0.001 which is statistically significant. 19 (33.3%) of 57 patient died who had a SOFA score between 5-10 the p-value being <0.001 which was statistically significant. Out of 39 patients, 28 (71.8%) with SOFA score between >10 did not survive. Furthermore with increasing SOFA score the mortality of the patients increased. Similar findings have been observed by various other authors. Other study found that independent of the initial SOFA score and increase in SOFA score predicts mortality of atleast 50% A mean SOFA average above 5 as well as SOFA variation within the first 72 hrs proved to be a good predictive marker in early patients with septic shock and severe sepsis.

9) **Microalbuminuria, albumin to creatinine ratio and mortality**

"Our study showed that the rise in microalbuminuria level and microalbumin to creatinine ratio at 6 hrs, 24 hrs of time in the patients was inversely

proportional with survival and directly proportional to mortality”.

11 patients had urinary microalbumin level between 21-30 or less. Four out of these 6 patients (54.5%) died, 5 (45.5%) patients survived. On the other hand the mortality of the patients rose proportionately with higher level of urine microalbumin; out of 32 patients 17(53.1%) patients who had microalbumin level ≥ 100 $\mu\text{g}/\text{mg}$ did not survive.

14 patients had albumin to creatinine ratio <30 , all are survived. those who had albumin to creatinine ratio 51-70, out of 31 patients 20 (64.5%) died. albumin to creatinine ratio >90 who had ,mortality rate 33.3%.

Moreover probably cut-off values may vary among ICU patients. The trend during the first day of ICU stay is probably more important than any specific cut-off value (Abid O et al 2001)^[3].

In 2001 Abidet al,^[3] didn't use any cut-off value, but they considered the trend of MACR over 48 h. Gosling et al,^[4] used a cut-off of 5.9 mg/mmol. A key feature of microalbuminuria is its low specificity and low positive predictive value. Using a lower cut-off value further decreases specificity and positive predictive value, whereas a higher cutoff value balances sensitivity and specificity increasing the positive predictive value.^[9]

“In clinical ICU practice the trend of microalbuminuria is more important.”^[3]

The introduction of time as a variable poses problems as the timing of measurement is subject to debate”.^[4,8]

The performance of microalbuminuria as a measurement varies with time. Eight hours after ICU admission sensitivity was 63% and specificity 73%, while at 18h after ICU admission they were, respectively 73% and 85%^[5,9]

The outcome derives from the mean of MACR over the first few hours of intensive care. This will be condition and patient specific. These considerations have been recently confirmed by Gosling et al,^[6] (2006). They measured MACR in 450 critically ill patients within 15 min of ICU admission and after 4–6 h.

10) ROC and correlation between GCS score, APACHE II score, SOFA score and microalbuminuria, microalbumin to creatinine ratio;

These analyses show that severity of the illness of both survivors and non- survivors. In the non-survivors, an increasing level of microalbuminuria, microalbumin to creatinine ratio had a direct correlation with decreasing GCS scores and increasing APACHE II score and SOFA score respectively. Similarly, in the survivors, a decreasing level of microalbuminuria, microalbumin to creatinine ratio had a direct correlation with an increasing GCS score and decreasing APACHE II score and SOFA score respectively

CONCLUSION

There was significant correlation between microalbuminuria levels and microalbumin to urine creatinine ratio and the Glasgow Coma Scale, APACHE II and SOFA scores in predicting clinical outcome of the critically ill patients studied.

Hence microalbumin to creatinine ratio at 24 hours may be considered as a predictor of outcome in critically ill patients.

Patient without significant microalbuminuria, albumin to creatinine ratio during first 6 hrs of ICU admission are less likely to have sepsis. At 24 hours, absence of elevated levels of microalbuminuria, albumin to creatinine ratio is strongly predictive of ICU survival, equivalent to APACHE II, SOFA scores.

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