Original Article

A Comparative study of Albumin-Creatinine Ratio and APACHE-II in Prediction of Outcome in Critically ill Patients in Intensive Care Units

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Abstract:

Background: *Simple, sensitive, and dynamic markersfor prediction of outcome, which generate rapid and reliable results, are desirable in critical care units.*

Aim: *Evaluation of prediction of outcome in critically ill patients by the Albumin Creatinine Ratio (ACR) on admission (ACR-1) and after 24hours of admission (ACR-2) & making a comparison between Acute Physiology & Chronic Health Evaluation-II(APACHE-II), ACR-1 & ACR-2 in terms of outcome prediction.*

Settings and Study design: *The prospective, observational study was carried out in the 20 bed mixed Medical-Surgical ICU of Dhaka Medical College Hospital.*

Materials and Methods *A total 60 critically ill patient were purposively recruited. Adult patient with ICU stay of more than 24 hours were included &patients with pregnancy, menstruation, a macroscopic hematuria, pre-existing kidney diseases, were excluded in this study. For disease severity scoring, APACHE-II scores & the percentage (%) of prediction of mortality by APACHE-II scores were calculated from data collected during the first 24 hours following ICU admission. Spot urine samples were collected within 6 hrs of admission (ACR1) and again at 24 hrs(ACR2), for quantification of Albumin Creatinine Ratio. Patients were followed up throughout their ICU stay for a maximum of 15 days and the following outcome data were obtained: ICU length of the stay and ICU mortality.*

Results: *There were 32(53.3%) patients were non-survivors and 28(46.7%) patients were survivors. Non-survivors had a significantly higher median Albumin Creatinine Ratio 1(ACR1) =285.00 mg/g & higher median Albumin Creatinine Ratio 2(ACR2) =393.30 mg/g in comparison to the survivors. There were significant differences between the mean and Standard Deviation of the APACHE-II scores, the Albumin Creatinine Ratio 1(ACR1),the Albumin Creatinine Ratio 2(ACR2)&ACR2-ACR1 between the non survivors (p=<0.001,p=<0.001,p=<0.001, p=<0.001 respectively). In, multiplelogistic regressions analysis female sex scored high odds of 361 for mortality compared to males followed by 15% higher mortality by high ACR2.The strength of agreement among APACHEII, ACR1, and ACR2 by kappa statistics revealed a very good agreement (1.000) by the degree of change of ACR2 in comparison to ACR1 and APACHE-II Score in predicting outcome in critical ill patients. A good agreement revealed between ACR1 and the APACHEII Score (0.802), and The APACHEII Score revealed a fair agreement (0.798) in predicting outcome. Results of all the variables were highly significant.* ***Conclusion:*** *The raised Albumin- Creatinine Ratio at 24 hours of ICU admission(ACR2) is a predictor of poor outcome in critically ill patients.*

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Introduction

Predicting of patient outcome is an important component of patient care.Faced challenges, and to allow the planning of early aggressive therapeutic interventions, optimum resource allocation and appropriate counseling of the family and /or patient, they have developed a number of prognostication tools for patients admitted to Intensive Care Units. But the prognostication tools that have employed in ICU though useful are complex. The widely used APACHE (Acute Physiology & Chronic Health Evaluation) II score for example, requires input of a large number of variables derived from the patient's history, physical examinations, and initial laboratory data. This is also true of the APACHE-II score, Sequential Organ Failure Assessment Score, Simplified Acute Physiology Score (SAPS-II) [1,2] and others. In addition, scoring systems rely mainly on obtained early in the course of the illness but the physiologic responses of patient to insults and interventions vary. It is seen that, critical illnesses are more often characterized by the systemic inflammatory response syndrome (SIRS) - the host-response to an acute insult. SIRS is a common finding in the ICU patient which, when severe, can lead to multiple organ failure and finally death[3]. A severe and sustained inflammatory reaction induces rapid and profound changes in the endothelium resulting in loss of barrier integrity leading to systemic capillary leak[4,5]. In the kidneys this manifests as altered glomerular permeability culminating in increased renal albumin excretion in the urine.[6]

The raised Albumin-Creatinine ratio is a reflection of this capillary leak due to endothelial dysfunction. It describes is a clear sign of glomerular injury[7,8] & this can identify very early stages of such insult. Screening for Albumin-creatinine is usually performed by one of three methods[9]. These are: measurement of total urine volume in 12 or 24 hour collection, measurement of the Albumin-Creatinine ratio in morning or random sample,& measurement of urine albumin in morning urine.

The 24hrs collection of urine is time consuming and thus expensive and requires highly motivated patients, careful information and it is often difficult to perform. But the measurement of the Albumin-Creatinine ratio in morning or random sample is more convenient and easier. The level of the Albumin-Creatinine ratio values between 3-30 mg /mmol (30-300microgram/mg)[9].

We conjectured that, the Albumin-Creatinine ratio(ACR) would reflect the degree of ongoing endothelial dysfunction .The level of micro albumin in urine also reflect the status of endothelial function after effective protocol directed therapeutic intervention like fluid resuscitation, antibiotics, inotrope & vasopressor use, tight glycemic control. Thus, the Albumin-Creatinine ratio(ACR) could predict the outcome better in a comparison to APACHE-II score.

Materials and Method:

This prospective, observational study was carried out in Department of Anesthesia, Analgesia and Intensive Care Unit of Dhaka Medical College Hospital, Dhaka over a period of 24 months starting from January 2012 to December 2013. Prior to the commencement of this study, the research protocol was submitted to the Ethical Review Committee of Dhaka Medical College Hospital and was approved. Study population was the patients who were admitted in ICU, DMCH. A total 60 critically ill patient were purposively recruited for the study. All adult critically ill patients aged 18 years or more admitted in ICU having any one of the criteria of critically ill patients & patients of ICU who stayed for more than 24 hours were included in this study.On the other hand patient staying in ICU <24hours, patients with anuria ,female patients with pregnancy and menstruation,, patients with hematuria &pre-existing Kidney Disease (Serum creatinine ³ 2.0 mg/dl)were excluded in this study.

Study Procedure: For disease severity scoring, APACHE-II scores & the percentage (%) of prediction of mortality by APACHE-II scores were calculated from data collected during the first 24 hours following ICU admission. Spot urine samples were collected by ICU nurses within 6 hrs of admission and again at 24 hrs, for quantification of Albumin Creatinine Ratio, which were referred to as ACR1, ACR2 respectively. Patients were followed up throughout their ICU stay for a maximum of 15 days and the following outcome data were obtained: ICU length of the stay and ICU mortality. Data were collected using

a structured questionnaire containing all the variables interest. The questionnaire included age, sex, diagnosis, co-morbid conditions, clinical classification, Glasgow Coma Scale, Blood Pressure, Temperature, Heart rate, Respiratory rate and some relevant investigations, the Albumin- Creatinine ratio from urine sample were done. Materials and instruments required to perform the study were arterial blood gas analyzer, blood sample and urine sample. Spot urine samples were received in the biochemistry lab and stored at 20 degree centigrade till analysis.Urinary Albumin- Creatinine ratio was measured using the immune-turbidimetric method & urinary creatinine was measured using a modified kinetic Jaffe reaction.

Statistical analysis: Collected data were analyzed using SPSS (Statistical Package for Social Sciences) for windows, version 21.0 (SPSS, Team Eqx, 1337).The test statistic was used to analyze data were descriptive statistics. T-test was done and data were presented as Mean±SD, and Median.Multiple logistic regression analysis was done for prediction of outcome among the APACHE-II scores, ACR1 and ACR2.The strength of agreement were calculated among APACHEII, ACR1, and ACR2 by kappa statistics.

Results:

Table 1 demonstrates that the incidence of Albumin-creatinine ratio which occurred mostly between the age group of 19-30 (40%) followed by the age group 41-50 (23.3%); the age group 31-40 years and 51-60 years shared 13.3% each while the rest (10%)fell into the age group > 60 years.

Table I *Incidence of raised Albumin- Creatinine ratio between the different age groups:*

Age	Frequency	Percent
19-30 yrs	24	40.0
31-40 yrs	8	13.3
41-50 yrs	14	23.3
51-60 yrs	8	13.3
>60 yrs	6	10.0
Total	60	100.0

Table II : it was observed that there were 40 males and 20 females with raised ACR

Table-II. *Incidence of raised ACR between male and female*

Sex	Frequency	Percent
Male	40	66.7
Female	20	33.3

Table-III : demonstrates the survivors (28) and non-survivors(32) among the patients.

Table-III. *The survivors and non-survivors among the patients*

Patient Status	Frequency	Percent
Non-survivors	32	53.3
Survivors	28	46.7

Table IV demonstrates that there were medical 42 &18 surgical cases

Table IV. *Incidence of raised ACR between the medical and surgical cases:*

Patient status	Frequency	Percent
Medical	42	70
Surgical	18	30

Table V : showed that 16 patients had Hypertension, 12 patients had Diabetes, 6 patients had others & 26 patients had no history of any co-morbidity.

Table V: *Co-morbid conditions among the patients:*

Co-morbid conditions	Frequency	Percent
Hypertension	16	20
Diabetes	12	28.9
Others	6	10
None	26	41.1

Table VI : demonstrates the Mean±SD , Median and Minimum-Maximum values of variables in terms of Age of the patients, Length of the ICU stay ,APACHEII score, Albumin Creatinine Ratio1, Albumin Creatinine Ratio 2.

Table VII : demonstrates that the Median of variables between the non survivors and survivors in terms of APACHEII scores, the Albumin Creatinine Ratio 1(ACR1 , the Albumin Creatinine Ratio 2(ACR2), the Length of ICU stayand the age of the patients.

Table 8 : demonstrates that the Mean and the Standard Deviation of the variables in the terms of the age of the patient, the APACHEII scores, the Albumin Creatinine Ratio 1(ACR1), the Albumin Creatinine Ratio 2(ACR2), the Length of ICU stay, theACR2-ACR1 between the non survivors and the survivors.

Table VI *The Mean±SD, Median and Minimum-Maximum values of variables in terms of Age of the patients, Length of the ICU stay, APACHE-IIscore, Albumin Creatinine Ratio1, Albumin Creatinine Ratio 2*:

Variables	Mean±SD	Median	Minimum-maximum
Age of patients	40.67±17.92	35.5	19-78
Iength of ICU stay	6.7±3.48	6	2-15
APACHE II score	26.1±8.72	27.5	7-40
Albumin Creatinine Ratio 1	166.97±135.14	110.5	25-410
Albumin Creatinine Ratio 2	249.73±191.43	315.9	15-560
ACR2 - ACR1	82.76±77.58	71.5	-15.30-272.80

Table VII *The Median of variables between the non survivors and survivors*

Patient Status	APACHE II score	Albumin Creatinine Ratio 1	Albumin Creatinine Ratio 2	Lengh of ICU stay	Age of patients
Non survivor N=32					
Median	32.00	285.00	393.30	7.50	45.00
Survivor N=28					
Median	20.50	32.40	62.15	5.5	30.50

Table VIII: *a)The Mean and the Standard Deviation of the age of the patient between the non survivors and the survivors:*

	Patient Status	N	Mean	Std. Deviation	P
Age of patients	Non survivor	32	40.88	14.91	0.95
	Survivor	28	40.43	21.44	

Table VIII: *b) The Mean and the Standard Deviation of the APACHEII Scores between the non survivors and the survivors:*

	Patient Status	N	Mean	Std. Deviation	P
APACHE II score	Non survivor	32	31.75	4.68	<0.001
	Survivor	28	19.64	7.74	

Table VIII: *c) Mean and the Standard Deviation of the % of prediction of mortality by the APACHEII score between the non survivors and the survivors*:

	Patient Status	N	Mean	Std. Deviation	P
% prediction of	Non survivor	32	66.88	16.19	<0.001
mortality	Survivor	28	31.72	21.15	

Table VIII: *d) The mean and Standard Deviation of the Albumin Creatinine Ratio 1(ACR1) among the non survivors and the survivors.*

	Patient Status	N	Mean	Std. Deviation	P
Albumin	Non survivor	32	2.75	90.09	<0.001
Creatinine Ratio 1	Survivor	28	43.57	25.03	

Table VIII: *e) The mean and Standard Deviation of the Albumin Creatinine Ratio 2(ACR2) among the non survivors and the survivors:*

	Patient Status	N	Mean	Std. Deviation	P
Albumin	Non survivor	32	4.17	81.28	<0.001
Creatinine Ratio 2	Survivor	28	59.12	27.61	

Table VIII: *f) The Mean and the Standard Deviation of the Length of ICU stay between the non survivors and the survivors:*

	Patient Status	N	Mean	Std. Deviation	P
Length of	Non survivor	32	7.69	4.29	0.09
ICU stay	Survivor	28	5.57	1.79	

Table VIII: *g)* The mean and Standard Deviation of theACR2-ACR1 among non survivors and the survivors:

	Patient Status	N	Mean	Std. Deviation	P
ACR2-ACR1	Non survivor	32	1.42	56.48	<0.001
	Survivor	28	15.55	25.03	

Table IX: demonstrates that the Mean and the Standard Deviation of the variables in the terms of the age of the patient, the APACHEII scores, the Albumin Creatinine Ratio 1(ACR1), the Albumin Creatinine Ratio 2(ACR2), the Length of ICU stay, theACR2-ACR1 between the between the male and female.

Table IX : *a) Mean and the Standard Deviation of the age of the patients between the male&female*

	Sex	N	Mean	Std. Deviation	P
Age of patients	Male	40	36.80	18.69	0.09
	Female	20	48.40	14.06	

Table IX : *b) The Mean and the Standard Deviation of the APACHEII scores*

	Sex of Patients	N	Mean	Std. Deviation	P
APACHE II score	Male	40	25.45	8.98	0.57
	Female	20	27.40	8.48	

Table IX : *c) Mean and the Standard Deviation of the % of prediction of mortality by APACHEII scores:*

	Sex of Patients	N	Mean	Std. Deviation	P
Albumin 1	Male	40	1.69	135.75	0.90
	Female	20	1.62	141.10	

Table IX : *d) The Mean and the Standard Deviation of the Albumin Creatinine Ratio 1(ACR1) between the male and female:*

	Sex of Patients	N	Mean	Std. Deviation	P
% prediction	Male	40	50.0500	26.94	0.90
of mortality	Female	20	51.3000	23.97	

Table IX : *e) The Mean and the Standard Deviation of the Albumin Creatinine Ratio 2(ACR2) between the male and female*:

	Sex of Patients	N	Mean	Std. Deviation	P
Albumin	Male	40	2.44	190.97	0.81
Creatinine Ratio 2	Female	20	2.62	202.09	

Table IX : *f) The Mean and the Standard Deviation of the Length of ICU stay between the male and female:*

	Sex of Patients	N	Mean	Std. Deviation	P
Length of	Male	40	6.250	3.04	0.32
ICU stay	Female	20	7.600	4.25	

Table IX : *g) The Mean and the Standard Deviation of the ACR2-ACR1 between the male and female:*

	Sex of Patients	N	Mean	Std. Deviation	P
ACR2-ACR1	Male	40	74.6150	63.57	0.43
	Female	20	99.0400	102.09	

*T-test was done to analyze the data and data were presented as Mean and ±SD.

Table X Multiple logistic regressions were done to assess the effect of different factors on mortality. Female sex scored high odds of 361 for mortality compared to males followed by 15% higher mortality by high ACR2.

Table X: *The interpretation of the multiple regressionsanalysis for prediction analysis:*

Variables	OR	95.0% C.I.for EXP(B)		P
		Lower	Upper	
Age	1.013	.000	.	1.00
Female sex	361.36	.000	.	1.00
APACHEII	.64	.000	.	1.00
ACR1	1.05	.000	8.50	1.00
ACR2	1.15	.000	6.03	0.99
Length of ICU stay	1.80	.000	.	1.00

Table XI: Strength of agreement among APACHEII, ACR1, ACR2:

The strength of agreement among APACHEII, ACR1, and ACR2 was calculated using kappa statistics. The test revealed a very good agreement (1.000) by the degree of change of ACR2 in comparison to ACR1 and APACHEII Score in predicting outcome in critical ill patients. A good agreement revealed between ACR1 and the APACHEII Score (0.802), and The APACHEII Score revealed a fair agreement (0.798) in predicting outcome. Results of all the variables were highly significant [APACHEII ($p<0.001$), ACR 1($p<0.001$), ACR2 ($p<0.001$)].

Table XI: demonstrates the strength of agreement among APACHE-II, ACR1,ACR-2 which was calculated using kappa statistics. The test revealed a very good agreement (1.000) by the degree of change of ACR2 in comparison to ACR1 and APACHE-II Score in predicting outcome in critical ill patients.

Table-XI *Kappa analysis*

Patient Status	APACHEII	ACR1	ACR2
Alive (14)	2 (14.3)	0	0
Dead (16)	15 (93.8)	13 (81.2)	16 (100)
Total	17	13	16
Kappa	0.798	0.802	1.000
P	<0.001	<0.001	<0.001

Discussion:

In the present study, total 60 criticallyill was purposively allocated&for disease severity scoring APACHE-II scores were calculated from data collected during the first 24 hours following ICU admission. The trend of Albumin-creatinine ratio was assessed from the change of ACR value within 6 hrs of admission (ACR1) to the ACR value at 24 hours (ACR2) of patients. The difference of ACR2 from ACR1 (ACR2-ACR1) was calculated. In this study, it was showed that the incidence of Albumin-creatinine ratio was high mostly between the age group of 19-30 (40%) followed by the age group 41-50 (23.3%); the age group 31-40 years and 51-60 years shared 13.3% each while the rest (10%)fell into the age group > 60 years which correlates the findings of the study of MacKinon et al[13].Incidence of Albumin-creatinine ratio among the sex of the patients was asked and it was observed that there were 40 (66.7%) males and 20(33.3) in females in this study.The comparison of the patient status was showed in the terms of survivors and non-survivors among the patients. There were 32(53.3%) patients were survivors and 28(46.7%) patients were non-survivors among the patients. The incidence of Albumin-creatinine ratio was showed in this study between the medical and surgical cases. There were 42(70%) cases medical and remaining 18(30%) were surgical.The co-morbid conditions were also observed. There were 16 patients had history of Hypertension, 12 patients had history of Diabetes, 6 patients had history of COPD, Bronchial asthma and others were26 in number which correlates the findings of the study of Thorevskaet al[12].The Median of variables between the non survivors and survivors in terms of APACHE-II scores,the Albumin Creatinine Ratio 1(ACR1), the Albumin- Creatinine Ratio 2(ACR2).The median of the Length of ICU stay and the age of the patients were observed in this study.The Median of APACHE-II score was 32.00 in non survivors which was significantly higher in the patients who died on the ICU in comparison to those who survived which was 20.50 in survivors. These APACHE-II scores were higher than the other studies (Basu, S.et al[14] and Thorevska,N.et al)[11,12]. The Median of Albumin Creatinine Ratio 1(ACR1) which was also significantly higher in the patients who died on the ICU in comparison to those who survived (Median=285.00 in non survivors and 32.40 in survivors).These results were similar to the study of Basu, S. et al[14]. The Median of Albumin Creatinine Ratio 2(ACR2) which were significantly higher in the patients who died on the ICU in comparison to those who survived (Median=393.30 in non survivors and 62.15 in survivors).These results were also similar to those of Basu S et al[12].The median of the Length of ICU stay is more in non-survivors (Median=7.5 in non survivors and 5.5 in survivors).The median age of the patients are 45.00 in non survivors and 30.50 in survivors.In this study, the Mean and the Standard Deviation of the variables between the non survivors and the survivors were showed .There were significant differences between the mean and Standard Deviation of the APACHE-II scores between the non survivors and the survivors

(p=<0.001). The mean and Standard Deviation of the % of prediction of mortality by the APACHE-II score also shows significant differences between the non survivors and the survivors (p=<0.001). There were significant differences between the mean and Standard Deviation of the Albumin Creatinine Ratio 1(ACR1) among the non survivors and the survivors (p=<0.001). The mean and Standard Deviation of the Albumin Creatinine Ratio 2(ACR2) among the non survivors and the survivors also shows significant differences (p=<0.001). The Mean and the Standard Deviation of the Length of ICU stay between the non survivors and the survivors fails to show significant differences(p=0.09). The Mean and the Standard Deviation of the age of the patients between non survivors and the survivors also fails to show significant differences (p=0.95). There were significant differences between the mean and Standard Deviation of theACR2-ACR1 among non survivors and the survivors (p=<0.001). There were no significant differences between the male and female in terms of age of the patients (p=0.09), APACHE-II scores (p=0.57), % of prediction of mortality by APACHE-II scores (p=0.90), the Albumin Creatinine Ratio 1(ACR1)(p=0.90) , the Albumin- Creatinine Ratio 2(ACR2)(p=0.81), the Length of ICU stay(p=0.32) and theACR2-ACR1(p=0.43) showed in this study.In contrast to our study results,Surupa et al[14] conducted a study and they showed in the sepsis group, median ACR1 was 206.5, which was significantly higher compared to non-sepsis group (ACR176.4,p=0.0016).The Receiver Operating Curve(ROC) analysis showed that a cut off value 124mg/g ,ACR1 may be able to discriminate between patients with and without sepsis with a sensitivity of 80%, specificity of 64.1%, positive predictive value(PPV) of 51.1% and negative predictive value (NPV)of 87.3%. The Median ACR2 (154) was significantly higher (p=0.004) in sepsis group as compared to non-sepsis group (50.8).The ROC curve analysis revealed that ACR2 at a cut off value 99.9mg/g could predict mortality with a sensitivity of 85%,specificity of 68% with a NPV of 97% and PPV of 30%.

In our study, it was observed that by the variable age, the outcome could be predicted. By the variable sex, the outcome could be predicted more than that of age. But the well known APACHE-II Score failed to predict outcome as like as age, sex ACR1, ACR2 and the length of the ICU stay.ACR1 could predict outcome but not more than ACR2.It was observed that ACR2 could predict outcome more significantly but the length of ICU stay predicted outcome most significantly. It was observed that the more the length of ICU stays the more the mortality. Multiplelogistic regressions were done to assess the effect of different factors on mortality. Though none of the variables became significant to be associated with the mortality, female sex scored high odds of 361 for mortality compared to males followed by 15% higher mortality by high ACR2.

Limitations:

As the sample size was small, the findings derived from study cannot be generalized to reference population and the data should be interpreted with utmost caution. This study was carried out in an adult Intensive Care Unit (ICU).So pediatric group of population was not included in the study. This was a single centre study.

Conclusion:

The results of present study indicated that the degree of change of Albumin -Creatinine Ratio at admission and after 24hrs of ICU admission could predict the outcome in critically ill patients than that of APACHE-II. The raised Albumin Creatinine Ratio at 24 hours of ICU admission is a predictor of poor outcome in critically ill patients. So, the Albumin Creatinine Ratio would provide a rapid, simple, inexpensive bedside test to identify patients who may benefit from appropriate early therapeutic strategies, which may prevent further capillary leak and hence the onset of multi organ failure and death.

Recommendation:

The speed and magnitude of the renal permeability response to indirect injury and its association with outcome suggest that measurement of Microalbuminuria can play an important role in the early identification of patients at increased risk of developing Multi system organ failure. As the number of patients studied was small, further studies in larger numbers of heterogeneous patients are recommended.

References:

1. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: Aseverity of disease classification system. Crit Care Med 1985; 13:818-29.

2. Lemeshow S, Teres D, Avrunin JS, Pastides H: A comparision of methods to predict mortality of intensive care unit patients. CritCareMed 1987: 8: 715-22.

3. Davies MG, Hagen PO: Systemic inflammatory response syndrome.Br J Surg 1997; 84: 920-35.

4 Willium YS, Pal SK: Correlation of microalbuminuria and outcome in patients with extensive burns. Br J Anaesth 2006; 97(4): 499-502.

5. Fishel RS, Are C, Barbul A. Vessel injury and capillary leak. Crit Care Med 2003; 31:S502-S511.

6. Jensen JS, Borch-Johnsen K, Jensen G ,Feldt-Rasmussen B.Microalbuminuria reflects generalized transvascular albuminLeakiness in clinically healthy subjects:ClinSci 1995; 88: 629-33.

7. Shearman CP, Gosling P, Walker KJ; is low proteinuria a nearly predictor of severity of acute pancreatitis? J ClinPathol1989 :42:1132-5.

8. Gosling P. Microalbuminuria: a marker of systemic disease. BrJHosp Med 1995; 54:285-90.

9. Gosling P, Hughes EA, Reynolds TM, Fox JP: Microalbuminuria is an early response following acute myocardial infarction. Eur Heart J 1991: 12:508-13.

10. Gosling P, Sanghera K, Dickson G. Generalized vascular permeability and pulmonary function in patients following serious trauma : J Trauma 1994; 36:477-81.

11. Gopal S, Carr C, Nelson P: Does micro-albuminuria predict illness severity in critically ill patients on the intensive care unit? A systematic review: Crit Care Med 2006; 34(6): 1805-10

12. MacKinnon KL, Molnar Z, Lowe D, Watson ID, Shearer E. Use of microalbuminuria as a predictor of outcome in critically ill patients. Br J Anaesth 2000; 84:239-41.

13. Thorevska N, Sabahi R, Upadya A, Manthous C, Amoateng-Adjepong Y. Microalbuminuria in critically ill medical patients: Prevalence , predictors, and prognostic significance. Crit Care Med 2013; 31: 1075-81

14. Basu S, Chaudhuri S, Battacharrya M, ChaterjeeTK, TodiS, Majumder A: Microalbuminuria: An inexpensive, non-invasive bedside tool to predict outcome in critically ill patients. Indian Journal of Clinical Biochemistry, April 2010,Volume 25, Issue2,pp146-152.