SERUM LACTATE ALBUMIN RATIO AS A PREDICTOR OF MORTALITY IN SEVERE SEPSIS AND SEPTIC SHOCK AT TRIBHUWAN UNIVERSITY TEACHING HOSPITAL, KATHMANDU

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ABSTRACT

Introduction

Severe sepsis and septic shock, is a common cause of emergency room admission and is associated with high morbidity and mortality worldwide. This study inspects the prediction of mortality in severe sepsis and septic shock with increased lactate/albumin ratio.

Objective

The objective of the study was to predict the serum lactate albumin ratio as an indicator of mortality in severe sepsis and septic shock.

Methodology

It was a hospital based cross sectional study done at Tribhuvan University Teaching Hospital, Kathmandu from November 2015 to October 2016. The consent was taken from patients. Acute Physiology and Chronic Health Evaluation II score, serum lactate and serum albumin levels on first day of arrival in emergency room were calculated. Patients were classified as severe sepsis and septic shock and treated according to Surviving Sepsis Campaign 2012 guideline. The patient were follow up at 28 day, The associations of 28-day outcome with Acute Physiology and Chronic Health Evaluation II score, serum lactate value, serum albumin value and serum lactate albumin ratio value were derived.

Results

Out of total 240 severe sepsis and septic shock patients it is found that increased serum lactate/albumin ratio was an independent predictor of the mortality with cut off value of 0.07. Furthermore serum lactate albumin ratio shows strong correlation with APACHE 2 score in predicting mortality in severe sepsis and septic shock.

Conclusion

Increased lactate/albumin ratio predicts mortality in patients with severe sepsis and septic shock.

KEY WORDS

Severe sepsis, septic shock, serum lactate albumin ratiow

INTRODUCTION

Severe sepsis and septic shock, are the major cause of emergency room admission and are associated with high morbidity and mortality worldwide.[1] Severe sepsis and septic shock has been recognized to have a high risk of death with high mortality rate of 20–30% with overall hospital death of 30–50%.[2-4] Similarly mortality rate of sepsis in Nepal found to be 40%, so sepsis is still the leading cause of death.[5,6] Furthermore majority of those who survives after the diagnosis of severe sepsis have poor quality of life who frequently develop cognitive and functional disability require substantial ongoing acute and long-term care.[7-9] Similar to polytrauma, acute myocardial infarction or stroke, early administered resuscitation in the initial hours after severe sepsis and septic shock develops are likely to influence outcome.[2] Delayed identification and inadequate resuscitation in severe sepsis and septic shock leads to the high mortality.[10]

As the incidences of severe sepsis and septic shock are increasing much things remains to be done to decreasing the mortality rate.[11] One way to accomplish this is the early identification of severe sepsis and septic shock patients likely to die. There are lots of studies about sepsis done in developed countries but data are lacking in developing countries.[12] There are currently inadequate data outlining the incidence, prevalence, predicting factors and mortality from severe sepsis and septic shock alone with bacteriological profiles, antibiotic sensitivity patterns of isolates from blood cultures in Nepal. The most important factor in decreasing mortality among severe sepsis and septic shock patients is the implementation of care bundle approaches of the Surviving Sepsis Campaign.[13] If we can predict the mortality of patients with severe sepsis and septic shock in the emergency room and aggressively resuscitate them, the survival rate can be expected to increase. Authentic risk stratification tool could be used which recognizes the seriousness of the condition and assist in the best choice of early management. When there is low oxygen saturation and oxygen supply is inadequate to tissue demand anaerobic metabolism will occur, and subsequently increase in lactate production. It is established that the increased lactate is prognostic marker of generalized tissue hypoxia in distributive shock.[14] There is significant increase in mortality rate in normotensive patients in the presence of systemic inflammatory response syndrome when lactate concentration is greater than 4 mmol/l.[15] Serum albumin comprises 75-80% of normal plasma colloid oncotic pressure and the degree of low serum albumin in critically ill patients directly related with the severity of infection.[16] It is a negative acute phase protein and marker of outcome of severe sepsis and septic shock which decrease during the response of active phase of infections.[17] Therefore, serum lactate and albumin levels which diverge during severe sepsis and septic shock merges together and provide an prognostic index that correlate positively with infection, that are inexpensive and readily available in most emergency room, with and without scoring systems.

METHODOLOGY

This was a hospital based prospective, cross sectional study approved by the institutional review board of institute of medicine tribhuvan university. The study was conducted at Department of Emergency and General Practice, Tribhuvan University Teaching Hospital (TUTH), Maharajgunj, Kathmandu Nepal, from November 2015 to October 2016. Written consent was obtained from participants. Patients with an age less than 16 years, do-not-resuscitate order, acute coronary syndrome, referred to other center, left against the medical advice, were excluded. For each patient, at emergency room conscious level, temperature, heart rate, respiratory rate, systemic blood pressure, capillary refill time, hematocrit, blood glucose level, total leukocyte counts, serum sodium, serum potassium, serum creatinine, platelets count, serum bicarbonate, Fio2, arterial PH, serum lactate level, serum albumin alone with comorbidity like chirrosis of liver, chronic kidney disease, chronic obstructive pulmonary diseases, immune-compromised status were recorded. All patients were resuscitated according to surviving sepsis campaign 2012 guideline. 0.9% normal saline at the rate of 30 ml per kg was used for fluid resuscitation for the first three hours, if mean arterial pressure (MAP) is not increased by 65 mm of Hg then inj. Noradrenalin was started within first 6 hours with target MAP of >65 mm of Hg. Acute physiological and chronic health evaluation (APACHE) II score was calculated by using APACHE II scoring system calculator –MD Calc. Serum Lactate, serum albumin and serum lactate albumin ratio was calculated within first 6 hours period. The patient were admitted in intensive care unit (ICU), medical intensive care unit (MICU), surgical intensive care unit (SICU) of TUTH after fully resuscitation in emergency room. The patient were follow up at 28th day in terms of mortality outcome by using hospital land line phone. The associations of 28-day outcome with APACHE II score, serum lactate value, serum albumin value and serum lactate albumin ratio value is examined.

RESULTS

From Nov 2015 to Oct 2016, two hundred forty criteria fulfilled patients were included in the study. There were fifty-seven patients with severe sepsis and one hundred eighty three patients with septic shock. Out of 240 patients 53.8 percent in male group and 46.2 percent in female were expired with p value of 0.128 (Table 1).

**Table 1: Distribution of gender among expired and improved patients (n=240)**

Sex	Outcome				P- value
	Improved		Expired		
	(n)	%	(n)	%	
F	55	56.7%	66	46.2%	
M	42	43.3%	77	53.8%	0.128
Total	97	100.0%	143	100.0%	

In table 2, it was found that as there is gradually increase in serum lactate albumin ratio there is corresponding increase in mortality, when the serum lactate albumin ratio is in range of 0.01-0.20 mortality in severe sepsis and septic shock were 43.1 and 58.1% respectively.

Table 2: Association of Serum lactate albumin ratio with mortality in severe sepsis and septic shock (n=240)

Serum Lactate albumin ratio	No. of severe sepsis	Mortality number(%)	P-Value	No. of septic shock	Mortality number (%)	P-value
0.01-0.20	51	22(43.1%)		160	93(58.1%)	
0.21-0.40	4	3(75.0%)		17	17(100.0%)	
0.41-0.60	1	1 (100.0%)	<0.158	4	4(100.0%)	
0.61-0.80	0	0		2	2(100.0)	<0.001
>0.81	1	1 (100.0%)		0	0	
Total	57	27		183	116	

The age range of participants was 18 to 92 years and a mean age of 49.60 years. There is increase in mortality rate as age increases with highest mortality of 73.52% is found in age group of 58-77 years and low mortality of 46.3% in age group of 18-27 years (Figure 1).
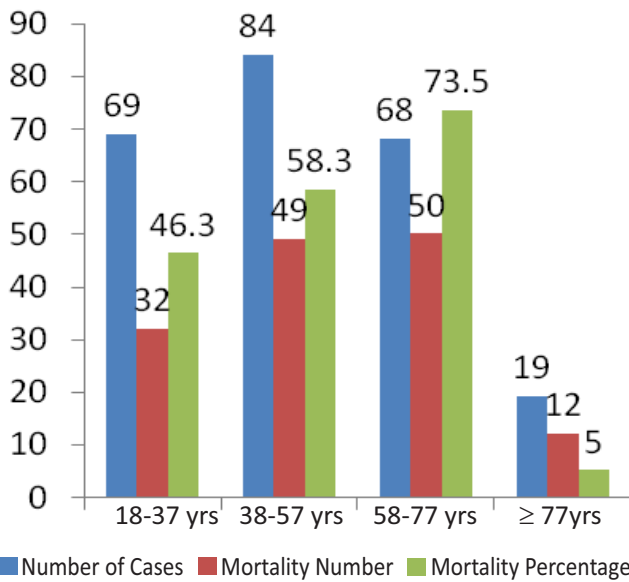

Figure 1: Overview of patient demographics (n=240)

Receiver operating characteristics (ROC) curve analysis comparing serum lactate, serum lactate albumin ratio and APACHE II score in predicting mortality shows in Table 3 (n=240, mortality=143). The area under the ROC curve as shown in figure 2 for lactate and lactate albumin ratio were

similar in predicting mortality (lactate, 0.91 [95% CI, 0.87–0.0.95; p<0.001]) (lactate albumin ratio, 0.90 [95% CI, 0.86–0.94; p<0.001]) where as value under the ROC curve for APACHE II score is slightly higher (APACHE II, 0.96 [95% CI, 0.94–0.0.98; p<0.001]).

Table3: Receiver operating characteristics curve (ROC) analysis between APACHE II score, serum lactate and serum lactate albumin ratio (n=240)

Test Variable(s)	Area	Std. Error	P value	95% Confidence Interval	
				Lower Bound	Upper Bound
Serum lactate	0.91	0.02	<0.001	0.87	0.95
Serum lactate albumin ratio	0.90	0.02	<0.001	0.86	0.94
APACHE 2 SCORE	0.96	0.01	<0.001	0.94	0.98
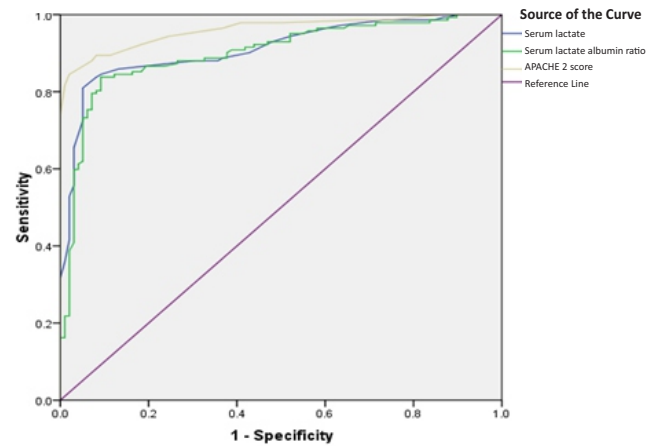
Figure 2: ROC analysis between serum lactate, serum lactate albumun ratio and APACHE II score

On correlating between APACHE II score and serum lactate albumin ratio it shows positive deflection with correlation coefficient of 0.637 and P value <0.01 indicating that serum lactate albumin ratio shows strong correlation with APACHE II score in predicting mortality in severe sepsis and septic shock (Figure 3).

Pearson Correlation	0.637
P-value	<0.001
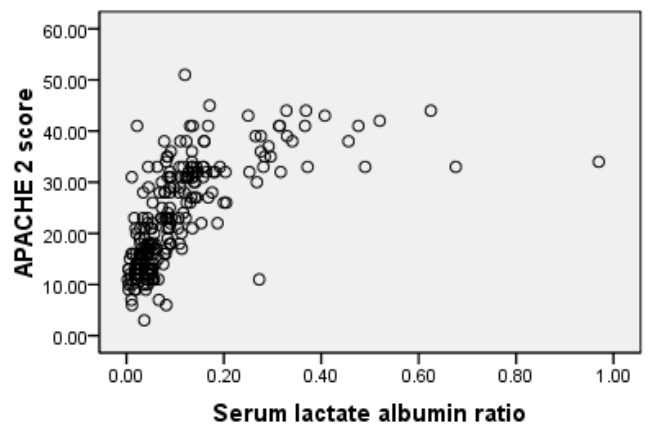
Figure 3: Pearson correlation between APACHE II score and serum lactate albumin ratio

DISCUSSION

With the gradual introducing initial resuscitation methods, which decreases mortality in severe sepsis and septic shock, the focus has now moved to predicting mortality. Our study shows that in the patients with severe sepsis and septic shock lactate/albumin ratio obtained at admission in the emergency room can be used as an independent predictor of 28-day mortality. Lots of studies have been done to investigate the procalcitonin, pro-BNP, CRP to predict mortality in critically ill patients.[18] But only few studies have evaluate the prognostic significance of serum lactate albumin ratio in a patient with severe sepsis and septic shock treated with end goal directed therapy.

Hypoalbuminaemia represent the inflammatory status and use in predicting outcomes in chronic and inflammatory disease.[19,20] As the albumin levels are affected by both the chronic inflammatory and nutritional status this marker alone can create bias. The measurement of single lactate value in emergency room has several limitation, patient with trauma, seizure, cardiac arrest, excessive muscle activity, regional ischemia, burn and smoke inhalation, diabetic ketoacidosis, thiamine deficiency, liver dysfunction and patient under metformin all have a higher lactate. Hyperlactemia may also occur despite of hypoxia like up-regulation in epinephrine-stimulated Na/K-adenosine triphosphatase activity in skeletal muscle and inhibition of pyruvate metabolism.[21,22] Thus, rather than an analysis serum lactate and serum albumin, we used serum lactate /albumin ratio as a prognostic index. The combination of these two markers merged inflammatory and nutritional factors, both of which predicts prognosis.[23]

In our study there are total 240 patients of severe sepsis and septic shock. Out of 240 patients 57 (23.75%) were diagnosed as severe sepsis and 183 (76.25%) were diagnosed as septic shock. The patients were followed up till 28 days and mortality outcome were calculated. 28th day mortality was 143 (59.6 %). It shows that in every two patient diagnosed as severe sepsis and septic shock one will die, similar results were found by study done by Christian brun et al.[24] The single lactate value as a prediction of mortality in severe sepsis and septic shock is controversial as it may increase in non pathological condition for instance as a result of a high adrenaline level or alcohol intake and several studies were not able to show lactate as predictive value of mortality.[25-28] APACHE II scoring system were used widely to assess out come in severe sepsis and septic shock but this is time consuming, expensive and lengthy process having multiple variables to calculate, so it is very impractical to use APACHE II scoring system in busy emergency room. So we use serum lactate albumin ratio as a marker of outcome in sepsis. It is found that as there is gradually increase in serum lactate albumin ratio there is corresponding increase in mortality. Our study findings were similar with study done by B wang et

al which found that mortality in patients with severe sepsis and septic shock correlates with increased lactate/albumin ratio.[23] Similar finding were also found in study done by Seung J et al.[29]

It is found that APACHE II score has slight higher area of 0.96 under the ROC curve in comparison with serum lactate albumin ratio, 0.90. The reason behind is APACHE II used sum of acute physiology score, age and chronic health score with maximum score of 71 where as in lactate albumin ratio we use only two variable. So there are differences between area under the curve between APACHE II score and serum lactate albumin ratio.

However serum lactate albumin ratio shows strong correlation with APACHE 2 score in predicting mortality in severe sepsis and septic shock.

CONCLUSION

It is known that taking measurement of single lactate has several limitations. Lactate is found to be increase in numerous physiological and pathological condition as well as increased by using different types of drugs. With a cutoff value of 0.07, this study has shows that patients with lactate/albumin ratio greater than 0.07 on day 1 had a more chance of mortality within 28 days. In the very busy emergency room where calculating APACHE 2 score is time consuming and expensive, serum lactate albumin ratio could be used as alternative marker to predict mortality in severe sepsis and septic shock.

RECOMMENDATION

Such studies could be done in multiple centre so that conclusion can be generalized. Number of the study subject could be increased to increase the power of the study.

LIMITATION OF THE STUDY

Here are several limitations to our study. First, Patients who were admitted to different unit of hospital might get different level of care which might have the effect on outcome. Second Patients with comorbid like chirrosis of liver, CKD, malnutrition were included in the study which might effect lactate albumin levels. Third all patients of severe sepsis and septic shock were generalized once they come to emergency room in spite of their level of treatment outside the hospital. In addition, this was a single-center and relatively small-sized study.

CONFLICT OF INTEREST

We declare no conflict of interest.

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