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BLOOD LACATE LEVELS AS PROGNOSTIC MARKER IN SEPSIS

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ABSTRACT

Objectives: 1. To study the role of blood lactate levels in sepsis., 2. To study blood lactate levels in sepsis in relation to survival outcome. **Materials and methods:** This is an observational cohort study done in 67 patients admitted to R.L. Jalappa Hospital. Subject's history and clinical examination suggestive of sepsis satisfying the inclusion and exclusion criteria were taken into the study. Arterial Blood lactate levels were measured at the time of admission, 12 hours, 24 hours and 36 hours by using epoc blood gas analyzer. Relevant investigations including haemogram, blood gas analysis, blood urea, serum creatinine, electrocardiogram and x-ray were done. The patients were followed till the time of discharge or death. **Results**: The mean arterial blood lactate levels at the time of admission, 12 hours, 24 hours, 36 hours in sepsis patients who survived are 3.47 ± 3.21, 2.86 ± 2.89, 2.19 ± 1.49, 1.84 ± 0.81mmol/lit respectively and mean blood lactate levels in non survivors are 5.61 ± 3.75, 4.75 ± 3.28, 3.60 ± 1.94, 2.42 ± 1.84 mmol/lit at the time of admission, 12 hours, 24 hours, 36 hours respectively. There was a significant association between blood lactate levels and outcome. In the non-survivors lactate levels was found to be greater than 4 mmol/lit in 64% patients. At admission sensitivity and specificity for lactate in predicting mortality is 76.5% and 30% respectively. Lactate levels at 24 hours has got much higher sensitivity of 77.8% and specificity of 32% in predicting mortality. **Conclusion:** Arterial blood lactate is elevated in sepsis patients and there is an increased risk of mortality if the elevation is above 4 mmol/lit.

KEY WORDS: sepsis, arterial blood lactate, prognostic marker.

INTRODUCTION

Sepsis is a systemic response to infection.[1,2] It is heterogeneous syndrome characterized by wide spread inflammation and continuum ranging from sepsis to severe sepsis and septic shock. It is a lethal incapacitating syndrome, with a high mortality rate that is an important burden to the health care system. Severe sepsis is the most common cause of death in non-coronary intensive care units.[3] Even with advanced medical care in developed countries mortality is around 20% for severe sepsis and increases to 50% for those group with septic shock.[4,5] Lactate is a product of anaerobic metabolism secondary to tissue hypoperfusion and is also seen in aerobic metabolism due to extensive inflammation.[6] Blood lactate levels rise early because of increased glycolysis as well as impaired clearance of the resulting lactate and pyruvate by liver and kidney. Before the vasodilatory phase of septic shock, a hypodynamic period exists during which the blood lactate concentration is elevated.[7] Lactate levels can be elevated in hemodynamically stable patients who have normal vital signs.[8] Hyperlactatemia is a marker of stress response, its severity and duration are related to mortality in critical ill.[9] Timely identification of ongoing events before they take an ominous turn is essential in the management of the patient in shock.[10,11] A normalization of serum lactate with aggressive treatment within 24 hours of the insult has been shown to have a favorable outcome.[11] Many studies have shown the relation between lactate values and sepsis since the identification of lactate in human blood. Its relation with survival outcome has been documented in very fewer studies. This study helps in providing further information regarding blood lactate levels in sepsis and its role in prognosis of patients with sepsis.

MATERIALS AND METHODS

Source of data

The study was conducted in 67 patients admitted to R.L. Jalappa hospital and research centre, Kolar, who satisfied

the criteria of SIRS, sepsis, severe sepsis or septic shock. It is a prospective observational cohort study. The "Ethics committee" of the institution approved the study.

Inclusion criteria: Age > 18 years and Patients meeting criteria for sepsis.

Exclusion criteria: Patients with known Ischemic heart disease, Congestive heart failure, Renal failure, Malignancy, Acute alcohol ingestion, Toxic compounds consumption, Chronic medication for diabetes with Metformin, AIDS, Inborn errors of lactate metabolism

Study methodology

After taking an informed consent, a detailed clinical history including demographic data, chief complaints, past medical history, personal and family history was taken. A general physical examination was done and axillary temperature, heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. Systemic examination of cardiovascular, respiratory, abdomen and nervous system was done. Arterial Blood was drawn for measuring lactate levels. Blood was drawn from radial artery in a 2ml-heparinized syringe. Heparinized syringe was prepared by first filling the barrel of syringe until 1ml marking and then flushing out all the heparin solution and air 4 times so that no visible heparin solution was left in syringe. Modified Allen's test was performed before drawing blood from radial artery. The femoral artery sampling was done in patients who presented with shock and in whom there was difficulty in obtaining radial arterial blood sample. Once the sample was obtained it was analyzed within 5 minutes in epoc blood gas analyzer, with CT-1004-00-00 epoc BGEM Test Card. Lactate was measured by amperometry. The sensor comprises an immobilized enzyme first layer coated onto a gold electrode of the electrode module, with adiffusion [41] Haemogram, arterial blood gas analysis, serum creatinine, blood urea, ECG, chest X-ray.Above investigations were done and recorded. Diagnosis was made clinically and based up on relevant other investigations. Treatment was given as required and no intervention was done. Patients were followed till the time of discharge or death.

RESULTS

67 subjects who met the inclusion criteria for sepsis were included in the study and their data was analyzed using SPSS 22 version software. The mean age of subjects was 45.34 ± 18.39 years. Minimum age of the subjects included was 18 years and the maximum age of the subjects in the present study was 85 years. The age in 50^{th} percentiles was 45years. Number of females were 32 [47.8%] and males were 35 [52.2%], with a slight male preponderance. Out of 67 patients with sepsis 50 patients (74.6%) had survived during the course of treatment and 17 patients (25.4%) had mortality.

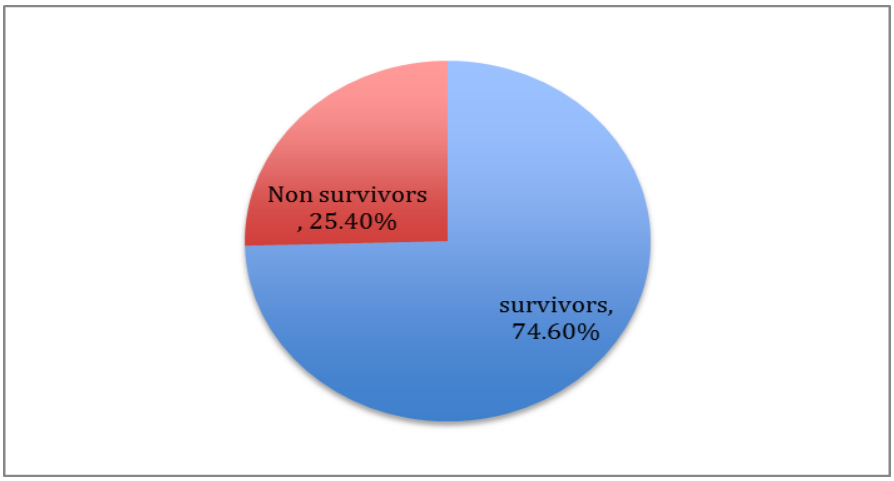

Fig-1 Pie Diagram Showing Outcome In Subjects

Table-1comparison of Arterial Blood Lactate Levels Between The Outcome Groups

Arterial blood lactate levels in mmol/lit	Outcome				P value
	Survived		Non survivor		
	Mean	SD	Mean	SD	
At admission	3.47	3.21	5.61	3.75	0.026*
At 12 hours	2.86	2.89	4.75	3.28	0.034*
at 24 hours	2.19	1.49	3.60	1.94	0.016*
at 36 hours	1.84	0.81	2.42	1.84	0.02*

Mean arterial blood lactate levels were higher in non-survivors than in survivors. The mean blood lactate levels were 5.61 ± 3.75, 4.75 ± 3.28, 3.60 ± 1.94, 2.42 ± 1.84 mmol/lit at the time of admission, 12 hours, 24 hour and 36 hours respectively in the non-survivors. The mean blood lactate levels of survivors are 3.47 ± 3.21, 2.86 ±

2.89, 2.19 ± 1.49, 1.84 ± 0.81 at the time of admission, 12 hours, 24 hours and 36 hours respectively. This difference between the groups was statistically significant with p values of 0.026, 0.034, 0.016, and 0.02 at the time of admission, 12 hours, 24 hours and 36 hours respectively.

Table-2 Comparison of Arterial Blood Lactate Levels Within The Outcome Groups

Arterial blood lactate levels in mmol/litre	Outcome					
	Survived			Non survivors		
	Mean	SD	P value	Mean	SD	P value
At admission	3.47	3.21		5.61	3.75	
At 12 hours	2.86	2.89	<0.001*	4.75	3.28	0.334
At 24 hours	2.19	1.49	<0.001*	3.60	1.94	0.210
At 36 hours	1.84	0.81	<0.001*	2.42	1.84	0.02*

There was a significant continuous decrease in lactate levels in survivors and non-survivors from admission to 12, 24 and 36 hours. But the fall in lactate levels at 12 hours & 24 hours after admission was not statistically significant in non-survivors. It was statistically significant only for fall in lactate levels for 24 to 36 hours.

From the ROC curves of lactate levels with outcome in our study, it was observed that the area under curve was 0.711, 0.749, 0.764, 0.264 at admission, 12 hours, 24 hours and 36 hours post admission respectively. The maximum are under curve was at 24 hours after admission. So the highest sensitivity [77%] and specificity [32%]of lactate levels for predicting mortality was 1.83 mmol/lit was at 24 hours after admission

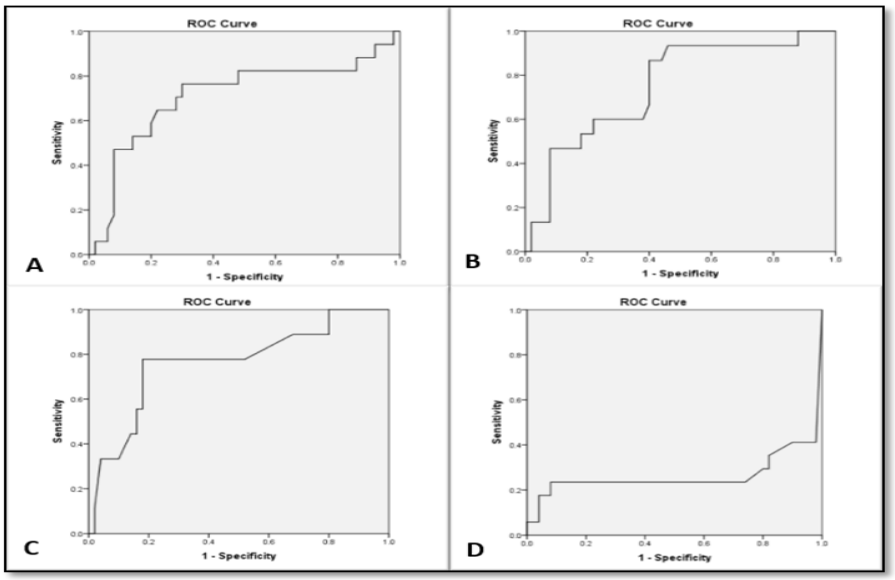

FIG-2 ROC curve for lactate levels and outcome A: At admission, B: At 12 hours, C: At 24 hours, D: At 36 hours

Table-3 Comparison Of Various Characters Observed In Sepsis In Both Survivors And Non Survivors

CHARACTER	SURVIVORS	NON-SURVIVORS
Duration of stay	6.86 ± 3.31 days	3.35 ± 2.37 days
Temperature in degree Fahrenheit	99.42 ± 1.61^{0}F	98.06 ± 1.71^{0}F
Pulse rate (beats per min)	92 ± 18	106 ± 24
Systolic blood pressure(SBP) in mm of Hg	114 ± 24	96 ± 24
Diastolic blood pressure(DBP) in mm of Hg	74 ± 12	70 ± 14
Respiratory rate per minute	30 ± 22	36 ± 10
O_2 saturation percentage	92 ±12	85 ± 7
pH	7.36 ± 0.11	7.25 ± 0.11
Bicarbonate in mmol/lit	20.65 ± 4.20	15.87 ± 7.36
PCO_2 in mm of Hg	35.63 ± 9.45	38.34 ± 16.32
PO_2 in mm of Hg	130.42 ± 72.32	82.07 ± 22.75

White blood cells (WBC) / mm^3	12800 ± 8570	15575 ± 5943
Platelets / mm^3	161176 ± 134699	152529 ± 108959
Random blood sugar (RBS) in mg/dl	144.46 ± 105.59	180.47 ± 98.62
Blood urea in mg/dl	38.80 ± 24.33	84.88 ± 42.77
Serum creatinine in mg/dl	1.03 ± 0.35	2.41 ± 2.04

Table 3 depicts the various characteristics taken in study and compared. There is a significant difference in values noted for temperature, pulse rate, systolic blood pressure, O_2 saturation, pH, bicarbonate, PCO_2 , PO_2 ,blood urea and creatinine .

DISCUSSION

Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection.[12] Hyperlactatemia is one of the diagnostic criteria of sepsis.[13] Current guidelines from the SSC advocate lactate measurement in patients with infection and possible severe sepsis to help identify patients at high risk of death who should be treated aggressively.[12]

Lactate is derived from glycolysis, an increased glucose turnover implies that increased lactate production, regardless of any "anaerobic" state. In sepsis patients there is increase in both glucose and insulin blood concentration. Insulin resistance favors glycolysis and glucose-lactate cycling, thus fostering lactate production and perpetuating hyperlactatemia.[9]

The incidence and prevalence of sepsis varies from region to region. In thepresent study, mortality was 25.4% [n=17] where as it was 46.3% in the study by Chatterjee et al[3] in India. Kauken et al[4] reported mortality of 18.4% in a study of sepsis conducted in Australia and Newzealand. The threshold of eligibility for treatment differs by time and country, with different cultural approaches to end-of-life care, different availability of acute hospital and ICU beds, varying levels of universal health insurance, and other cultural and economic factors.[4] Varied treatment modalities and other factors may affect mortality in sepsis.

The rise of lactate production after initial resuscitation effort could be due to activation of glycolytic pathway triggered by mechanism such as Na+/K+-ATPase rather than the impact of tissue hypoxia.[15] It was also suggested that a high initial lactate levels had caused irreversible organ damage.[16] A significant reduction in lactate levels in survivors indicates that an aggressive therapy for treating the cause of sepsis and thus lowering of lactate levels could reduce the mortality With progression of time there is lowering of lactate value with high sensitivity in predicting mortality. However the lactate levels at 24 hours with 1.83 mmol/lit has got highest sensitivity and specificity with maximum area under ROC curve which indicates that lactate levels >1.83 mmol/lit at 24 hours is a better prognostic marker than at the time of admission. This finding is in accordance with the study by Smith et al.,[17] where the ROC area under curve was more at 24hours than at admission. It was observed that in patients whose blood lactate levels remain high even after 24 hours of treatment had higher mortality, so probably lactate levels at 24 hours has got better prognostication than at admission.

CONCLUSION

1. Arterial blood lactate levels are elevated in sepsis.
2. The mean arterial blood lactate values were always more in non-survivors as compared with survivors.
3. Lactate levels at 24 hours are a better prognostic indicator than lactate levels at admission.

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