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General Medicine

STUDY ON EVALUATION OF SERUM LACTATE LEVELS AS PREDICTOR OF MORTALITY IN SEPSIS

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ABSTRACT **Introduction:** Severe sepsis and septic shock represent leading causes of morbidity and death worldwide, with mortality rates approaching 20% to 30% in the most recent clinical trials. Incidence of severe sepsis and septic shock has been increasing over the years, despite efforts to improve early recognition and treatment

Aim and Objective of the study:

1. To evaluate the causes of sepsis.
2. To estimate the levels of lactate clearance in patients with sepsis admitted at our tertiary care center.
3. To evaluate the cutoffs and find out the association if any to predict the outcome at the 28th day after admission. **Materials and Methods:** Samples for the following laboratory investigations were taken before initiation of antimicrobial and resuscitative therapy: serum lactate, complete hemogram, kidney function test, liver function test, serum electrolytes, blood culture, urine routine microscopy, urine culture, sputum Gram stain and culture, sputum acid-fast bacilli, and arterial blood gas analysis. Radiological investigations, like chest X-ray and ultrasound (if required), were carried out to localize the site of infection. **Discussion and conclusion:** We found that the most common cause for sepsis in both survivors and non-survivors was pneumonia. Serum lactate levels were measured at 0 hour and 24 hour, the levels were increased in non-survivors as compared to survivors which were statistically highly significant. Similarly, absolute lactate clearance and lactate clearance rate were higher in survivors as compared to non-survivors. The increase was statistically highly significant. Low absolute lactate and lactate clearance rate are significantly associated with mortality at the 28th day. Old age and poor GCS are significantly associated with adverse outcomes in septic patients. High SOFA, qSOFA scores, as well as serum lactate levels (0 and 24 hours) are associated with poor outcomes.

KEYWORDS : lactate, lactate clearance rate, SOFA scores, mortality, pneumonia, survivors and non-survivors

INTRODUCTION

Severe sepsis and septic shock represent leading causes of morbidity and death worldwide, with mortality rates approaching 20% to 30% in the most recent clinical trials [1-3]. Incidence of severe sepsis and septic shock has been increasing over the years, despite efforts to improve early recognition and treatment [4].

Raised blood lactate levels in severe sepsis and septic shock usually indicate impaired oxidative phosphorylation secondary to reduced oxygen availability to the cells (hypoxic hypoxia) and/or tissue hypoperfusion (stagnant hypoxia). Because blood lactate levels can be measured easily and quickly, these have been used as a predictor of tissue hypoperfusion in critically ill patients admitted to the emergency department (ED) or intensive care unit (ICU) [5].

Because blood lactate levels can be easily and quickly determined, these have been used as a surrogate of tissue hypoperfusion in critically ill patients admitted to the emergency department (ED) or to intensive care unit (ICU). Indeed, increased blood lactate levels have been used to identify critically ill patients at high risk of death even before the development of hemodynamic instability, i.e. cryptic shock, as well as to trigger resuscitation [6-8].

Serum lactate level has been used for diagnosis of septic shock as well as for targeting fluid resuscitation in patients with sepsis. Usefulness of serum lactate level after the initial 6 hours of resuscitation (so-called golden hours) is still under investigation because many septic patients die even after resuscitation during these golden hours. Systematic studies on serum lactate and lactate clearance are lacking in the Indian subpopulation with sepsis [9].

Current guidelines for severe sepsis and septic shock resuscitation recommend that patients with severe sepsis or septic shock with an initial blood lactate level twice above the normal limit (≥4 mmol/L) should be promptly resuscitated. Nevertheless, an increasing number of studies have been suggesting that lower elevations of blood lactate levels are also associated with increased risk of death. Therefore, the optimal lactate cut-off that should trigger resuscitation in this population of critically ill patients remains unclear [10].

Aim And Objectives of The Study:

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2. To estimate the levels of lactate clearance in patients with sepsis admitted at our tertiary care center.
3. To evaluate the cutoffs and find out the association if any to predict the outcome at the 28th day after admission.

MATERIALS AND METHODS

Study Setting:

This was a prospective cross-sectional study carried out in the Dept. of General Medicine, Narayana Multispeciality Hospital, Barasat for a period of one year in the patients with sepsis and suspected cases of infections admitted in wards, emergency and ICU.

Study Population:

Patients with sepsis and suspected cases of infections admitted in wards, emergency and ICU.

Inclusion criteria:

Patients willing to give voluntary consent.Patients aged >18 years. Diagnosed cases of sepsis based on qSOF A score (score >2 points) and SOFA score (rise of >2 points from baseline).

Exclusion criteria:

we excluded following patients with polytrauma, HIV, malignancy, history of major surgery, known c/o CLD, CKD, ESRD, MI, hospital acquired infections, pregnancy, and Diabetic patients on biguanides or salicylates.

Design of the Study: Cross-sectional study,

Study Period: The study was carried out for a period of one year from December 2021 to November 2022.

Control – Not required

Methods of Data Collection:

After taking informed consent, 100 patients with sepsis admitted to ED and ICU were included in this study based on inclusion and exclusion criteria.

A detailed history had been taken from the patient or patient's family. Data is collected for general physical examination and systemic examination of the patients. Data were collected from patient's case sheets and transferred to data entry format for evaluation. Sepsis was diagnosed based on qSOFA score.

Study Procedure:

Samples for the following laboratory investigations were taken before initiation of antimicrobial and resuscitative therapy: serum lactate,

complete hemogram, kidney function test, liver function test, serum electrolytes, blood culture, urine routine microscopy, urine culture, sputum Gram stain and culture, sputum acid-fast bacilli, and arterial blood gas analysis. Radiological investigations, like chest X-ray and ultrasound (if required), were carried out to localize the site of infection.

Calculation of SOFA score: to calculate SOFA score, data like mean arterial pressure, PaO_2/FiO_2, platelet count, creatinine, urine output, total bilirubin, and GCS were obtained. SOFA score was calculated to confirm the diagnosis of sepsis. Two samples for serum lactate levels were drawn, the first sample at the time of diagnosis of sepsis (0 hour) and the second sample after 24 hours. At least 2 mL of whole venous blood was collected in a heparinized green-topped vial for measuring serum lactate levels. All samples were transported to the Department of Biochemistry immediately on an ice slurry and processed without any delay.

In all samples, serum lactate levels were measured in fully automated biochemistry analyser. Patients were managed according to Surviving Sepsis Campaign international guidelines for the management of sepsis and septic shock. Patients were followed up for 28 days to document the outcomes in terms of mortality. Then data were collected and statistical analysis was carried out. Lactate clearance (absolute lactate clearance, relative lactate clearance and lactate clearance rate) was calculated as per formula as mentioned in the study by Filho et al. [5].

RESULTS:

We included a total of 100 subjects with sepsis as per SOFA score based on inclusion and exclusion criteria in the age group more than 18 years and less than 85 years admitted in ED and ICU.

Table 1: Shows age-wise/gender-wise distribution of study subjects (total patients =100)

VARIABLES	Survivors (n=68)	Non-survivors (n = 32)
Age (in years)	49.8 ± 14.2	52.8 ± 11.6
Gender (M/F)	38/30	28/14
Quick SOFA	2.08 ± 0.19	2.59 ± 0.62*
SOFA score		
At 0 hours	4.42 ± 1.8	6.38 ± 2.43*
At 24 hours	2.1 ± 1.5	6.42 ± 2.67*

Table 2: Distribution of study population based on the cause of sepsis (total patients = 100)

	Survivors (n=68)	Percentage	Non-survivors (n = 32)	Percentage
Pneumonia	24	35.3	12	50
UTI	12	17.6	7	21.8
Liver abscesses	11	16.17	5	15.6
Skin and soft tissue infections	09	13.2	4	12.5
Others	12	17.6	4	12.5

Table 3: Association of serum lactate (mmol/L) levels with outcomes

	Non-survivors	Survivors
Lactate at 0 hour	9.26 ± 2.43	5.98 ± 1.98*
Lactate at 24 hour	7.26 ± 2.51	2.42 ± 1.51*
Absolute lactate clearance	1.21 ± 1.67	2.91 ± 1.43*
Lactate clearance rate	0.56 ± 1.56	2.43 ± 0.56*

Table 4: ROC of lactate levels for predicting mortality

	AUC	P value	Cut-off
Lactate at 0 hour	0.88	HS	>5.8
Lactate at 24 hour	0.96	HS	>3.8
Absolute lactate clearance	0.78	HS	<1.6
Lactate clearance rate	0.97	HS	<1.78

DISCUSSION

In the present study, we included a total of 100 subjects with sepsis as per SOFA score based on inclusion and exclusion criteria in the age group more than 18 years and less than 85 years admitted in ED and ICU. Out of 100 patients, 68 survived and 32 did not survive. Out of 68 survivors 38 were males and 30 were females. Similarly, out of 32 non-survivors 28 were males and 14 were females. The mean age in years in survivors was found to be 49.8 ± 14.2 an and in non-survivors 52.8 ± 11.6 years. Quick SOFA score in survivors was found to be 2.08 ± 0.19 and in non-survivors 2.59 ± 0.62*. There was increased qSOFA score in non-survivors compared to survivors which was statistically highly significant ($p < 0.001$). The SOFA scores at 0 hour and 24 hours in survivors and non-survivors were 4.42 ± 1.8, 2.1 ± 1.5, 6.38 ± 2.43*& 6.42 ± 2.67* respectively. We found elevated SOFA scores at 0 hour and 24 hour in non-survivors as compared to survivors which were statistically highly significant.

We evaluated the causes of sepsis, we found that the most common cause of sepsis in both survivors and non-survivors was pneumonia, followed by other causes which include liver abscess, UTI, Skin and soft tissue infections and other causes. Pneumonia accounted for 35% in survivors and 50% in non-survivors.

Serum lactate levels were measured at 0 hour and 24 hour, the levels were increased in non-survivors as compared to survivors which were statistically highly significant. Similarly, absolute lactate clearance and lactate clearance rate were higher in survivors as compared to non-survivors. The increase was statistically highly significant.

Cut-offs of Serum Lactate and Clearances for Predicting Mortality:

Using the ROC curve, cutoffs to predict mortality at the 28th day were predicted and they were Serum lactate level at 0 hour > 5.8 mmol/L, Serum lactate level at 24 hours > 3.8 mmol/L, Absolute lactate clearance ≤ 1.6 mmol/L and Lactate clearance rate ≤ 1.78 % per hour.

In a study done by Nguyen et al. in Detroit, a total of 111 patients were included where 59 were males (53.2%) and 52 were females (46.8%). This gender distribution was comparable to our study. Mean age of patients was 64.9 ± 16.7 years. However, advancing age was not associated with poor outcomes or low lactate clearance. Most common etiologies of sepsis in this study were pneumonia (47.7%) and urosepsis (12.6%), which was comparable to our study [11].

In another study conducted by Ryoo et al. in South Korea, mean age of the study population was 65 ± 12.2 years. Old age was not a significant risk factor for poor outcomes. This study included a total of 1,060 patients out of which 662 (62.5%) were males and 398 (37.5%) were females. The etiology of sepsis was not included in data collection in this study [12].

In a study done by Nguyen et al., serum lactate levels at the time of ED admission were significantly associated with 60th-day mortality. Mean serum lactate level in nonsurvivors was 8.0 ± 4.7 mmol/L, while lactate level in survivors was 6.1 ± 4.4 mmol/L. In this study, lactate clearance was calculated by the given formula: (lactate at presentation—lactate after 6 hours/ lactate at presentation) *100 (which was equivalent to relative lactate clearance in our study). It was 12.0 ± 51.6% in nonsurvivors, and this was comparable to our study. However, this study used Systemic Inflammatory Response Syndrome (SIRS) criteria as the entry point, 6-hour lactate clearance, and mainly ICU patients, while our study used qSOFA score, 24-hour lactate clearance, and both ICU and non-ICU patients. In both the studies, results showed that low lactate clearance was significantly associated with higher mortality. They have calculated ≤10% is the optimal cut-off of relative lactate clearance at 6 hours after admission to predict mortality at the 60th day with sensitivity of 44.7% and specificity of 84.4% [11].

CONCLUSION

Low absolute lactate and lactate clearance rate are significantly associated with mortality at the 28th day. Old age and poor GCS are significantly associated with adverse outcomes in septic patients. High SOFA, qSOFA scores, as well as serum lactate levels (0 and 24 hours) are associated with poor outcomes.

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