

## ORIGINAL ARTICLE

## SERUM LACTATE AS PROGNOSTIC MARKER IN INDIAN ELDERLY WITH SEPTICEMIA

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## ABSTRACT

**Introduction:** Serum Lactate is recognized as a potentially useful prognostic marker to risk stratify patients with severe sepsis and elevated serum lactate is found to be strongly associated with morbidity and mortality in various populations with sepsis. The aim of our study was to determine correlation between serum lactate level in Indian elderly presenting with sepsis with the stage of sepsis and ultimate outcome.

**Method:** In a single centre prospective, observational study done in geriatric ward of tertiary care centre, 200 elderly patients (age > 60 yrs) with sepsis were included. The primary outcome was 14 days in hospital mortality. Risk factor variable was venous serum lactate (mg/dl) at presentation.

**Result:** Mortality at 14 days in elderly patients with sepsis was 20%. Mean serum lactate (mg/dl) in survivor group was  $30.16 \pm 19.48$  while  $61.52 \pm 31.52$  in non survivor group (p value < 0.001). The mean serum lactate level (mg/dl) in survivor and non survivors was  $24.83 \pm 13.71$  and  $33.58 \pm 15.11$  in sepsis,  $50.56 \pm 22.47$  and  $75.22 \pm 11.41$  in severe sepsis,  $70.75 \pm 19.32$  and  $86.82 \pm 11.6$  in Multiple organ dysfunction syndrome while  $83.50 \pm 31.68$  and  $104.88 \pm 14.14$  in septic shock group.

**Conclusion:** We conclude that initial high serum lactate level was associated with increased mortality independent of etiology of sepsis, it also correlate well with severity of sepsis and serum lactate level were high in those with septic shock and diabetic group.

**Keywords:** diabetes, Indian, elderly, lactate, sepsis.

## INTRODUCTION

Sepsis is a major cause of mortality and morbidity in the elderly. It is defined as the clinical syndrome with the presence of both infection and systemic inflammatory response<sup>(1)</sup>.

Serum Lactate is recognized as a potentially useful prognostic marker to risk stratify patients with severe sepsis and elevated serum lactate is found to be strongly associated with morbidity and mortality in various populations with sepsis<sup>(2,3,4,5,6)</sup>. The aim of our study was to determine correlation between serum lactate level in Indian elderly with sepsis at presentation with the stage of sepsis and ultimate outcome.

## MATERIAL AND METHODS

The study took place at the Geriatric Division in the Department of General Medicine, Sir Sunder Lal Hospital, BHU, Varanasi, with the collaboration of Microbiology Department, IMS-BHU, Varanasi, between July 2011 and June 2012. The study included 200 consecutive elderly patients ( $\geq 60$  years of age) with clinically suspected sepsis. Sepsis definition was based

on the presence of infection and 2 or more of the SIRS criteria<sup>(1)</sup>.

The primary outcome was the hospital mortality at 14 days. Risk factor variable was venous serum lactate (mg/dl) at presentation which was measured by Enzymatic UV test method as per standard protocol. In addition, routine biochemical and hematological tests, blood and other site cultures were done as per standard protocol, while several diagnostic procedures (chest x-rays, ultrasound etc) were performed to identify the source of infection. All patients were treated with an empirical antibiotic regimen based on protocols supervised by the treating consultants. The study protocol was approved by the Hospital Ethics Committee and written consent was obtained either from the patients or from care givers if patients were not in a state to give consent.

**Statistical Analysis:** Chi-Square test was used to test the significant association between the variables. Z test was applied to test the significant difference between the proportions. R value was used to see for the correlation between the two variables. P value was calculated to test the level of significance. P value < 0.05 was taken as significant.

## RESULTS

The mean age of the study population was  $67.62 \pm 6.69$  years with maximum number of patients (66%) were in 60-69 age group. There were more males (57.5%) than females (42.5%) and the M:F ratio was 1.35. The in-hospital mortality of the study population at 14 days was 20%. The Outcome of sepsis in relation to stage of sepsis was statistically significant ( $p=0.032$ ). The highest mortality was found in Multiple organ dysfunction syndrome and Septic shock group, as more than half of

patients expired in both groups. The level of mean serum Lactate (mg/dl) in non survivor group was  $61.52 \pm 31.52$  and  $30.16 \pm 19.48$  in the survivor group. Significant correlation was found between the outcome of sepsis and Serum Lactate with a  $p$  value  $< .001$ . (detailed results are given in table 1,2,3)

Table 1 shows the level of mean serum Lactate (mg/dl) in non survivor and survivor groups in different stages of sepsis. Significant correlation was found between the outcome of sepsis and serum Lactate level in all stages of sepsis, with a  $p$  value  $< .05$  in each of them.

**Table 1. Mean serum lactate (mg/dl) in different stages of sepsis in survivor and non survivor groups in study population (n=200).**

Group	Survivor (n=160)		Non survivor (n=40)		p-value
	Number	Serum lactate	Numbers	Serum lactate	
Sepsis (n=151)	132	$24.83 \pm 13.71$	19	$33.58 \pm 15.11$	0.011
Severe sepsis (n=24)	18	$50.56 \pm 22.47$	6	$75.22 \pm 11.41$	0.018
MODS (n=19)	8	$70.75 \pm 19.32$	11	$86.82 \pm 11.6$	0.036
Septic shock (n=6)	2	$83.50 \pm 31.68$	4	$104.88 \pm 14.14$	0.046

**Table 2: Mean serum Lactate level (mg/dl) in diabetic and non diabetic patients in non survivor and survivor groups**

Outcome of sepsis	Survivor (n=52)		Non survivor (n=148)		P value
	Number	Serum lactate	Number	Serum lactate	
Improved (n=16)	37	$44.03 \pm 20.13$	123	$27.12 \pm 17.23$	.001
Expired (n=40)	15	$83.93 \pm 20.22$	25	$56.23 \pm 28.34$	.002

**Table 3: Mean serum Lactate level (mg/dl) in different stages of sepsis in both survivor and non survivor groups in diabetic subgroup (n=52).**

Group	Survivor (n=37)		Non survivor (n=15)		p-value
	Number	Serum lactate	Number	Serum lactate	
Sepsis (n=35)	30	$37.57 \pm 14.63$	5	$60.40 \pm 10.28$	.002
Severe sepsis (n=9)	5	$66.60 \pm 17.82$	4	$92.75 \pm 7.63$	.030
MODS (n=6)	2	$84.50 \pm 4.950$	4	$93.50 \pm 15.000$	.476
Septic shock (n=2)	0	$0.00 \pm 0.00$	2	$106.00 \pm 5.65$	-

Table 2 shows that mean serum Lactate level (mg/dl) was higher in diabetic patients in both survivor and non survivor groups as compared to non diabetic patients, showing a significant correlation with a  $P$  value  $< .05$  in each of them.

Table 3 shows the level of mean serum lactate in non survivor and survivor groups in different stages of sepsis in diabetic patients. Significant correlation was found between the outcome of sepsis and mean Lactate level in the stage of sepsis and severe sepsis, with a  $p$  value  $< .05$ . No significant correlation was found in Multiple organ dysfunction syndrome group. This may be due to sample size being low in this group.

## DISCUSSION

The present study was conducted to evaluate the role of serum lactate as a prognostic marker in Indian elderly

presenting with sepsis. The elderly patients with suspected septicemia were the study subjects in this study.

In our study, the mean serum lactate level was  $30.16 \pm 21.56$  mg/dl in survivor and  $61.52 \pm 31.52$  mg/dl in non survivor group. There was a significant correlation found between the outcome of sepsis and mean lactate level in Indian elderly with a  $R$  value = .469 and  $p$  value  $< .001$ . Similar to our study, Shapiro et al;2005<sup>(7)</sup> with 1278 patients demonstrated that increasing lactate levels were associated with increased mortality in the patients presenting with sepsis. Similarly, Nguyen et al;2004<sup>(8)</sup> examined a cohort of 111 Emergency department and Intensive Care Unit patients with severe sepsis and septic shock and they concluded that lactate clearance had an inverse relationship with mortality - the higher the lactate clearance, the lower the mortality. In fact, mortality was reduced approximately 11% for each 10%

increase in lactate clearance. These findings suggest an important role for serial sampling and lactate clearance as a prognostic indicator of sepsis<sup>(9,10)</sup>. Mikkelsen et al;2009<sup>(11)</sup> concluded that Initial serum lactate level was associated with mortality independent of clinically apparent organ dysfunction and shock in patients admitted to the Emergency department with severe sepsis. They concluded that elevated serum lactate level was independently associated with mortality.

In diabetic subgroup (n=52), the mean serum Lactate level (mg/dl) in survivor group was  $44.03 \pm 20.12$  and  $83.93 \pm 20.22$  in non survivor group, which was found to be higher as compared to non diabetic group(n=148). There was a significant rise of 62.9% and 48.2% in mean serum Lactate level in diabetic patients as compared to non diabetic in both survivor and non survivor groups respectively, which was statistically significant with P value < .05. From these observations, it was clear that serum Lactate had a positive correlation with outcome of sepsis and it was also evident in diabetic patients. There are many studies and proposed mechanisms<sup>(12,13,14,15)</sup> for the increased serum lactate level in diabetic patients as compared to non diabetics, but there is no study or literature regarding the significance of serum lactate as a prognostic markers of sepsis in diabetic elderly presenting with sepsis. Though serum lactate was higher in diabetic group as compared to non diabetic group in all stages of sepsis, it retains its value as a prognostic marker of sepsis; correlated significantly with outcome of sepsis in both sepsis and severe sepsis stage in our study. The trend was positive in multiple organ dysfunction syndrome stage but statistically insignificant, this may be due to very small number of patients in this group. We conclude that initial high serum lactate level was associated with increased mortality independent of etiology of sepsis, it also correlate significantly with the severity of sepsis. In diabetic elderly with sepsis, though serum lactate was higher than nondiabetic group but its significance as prognostic marker was maintained in both sepsis and severe sepsis stage.

## REFERENCES

- American College of Chest physicians / Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failures and guidelines for the use of innovative therapies in sepsis. *Crit. Care Med.* 1992;20:864-874.
- Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med.* 2004;32(3):858-873.
- Dellinger RP, Levy MM, Carlet JM et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med.* 2008; [published correction appears in *Crit Care Med.* 2008; 36:1394-1396] 36:296-327.
- Varpula M, Tallgren M, Saukkonen K, Voipio-Pulkki LM, Pettila V. Hemodynamic variables related to outcome in septic shock. *Intensive Care Med.* 2005;31(8):1066-1071.
- Bakker J, Coffernils M, Leon M, et al. Blood lactate levels are superior to oxygen derived variables in predicting outcome in human septic shock. *Chest.* 1991;99:956-962.
- Bakker J, Gris P, Coffernils M, Kahn RJ, Vincent JL. Serial blood lactate levels can predict the development of multiple organ failure following septic shock. *Am J Surg.* 1996;171(2):221-226.
- Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. *Ann Emerg Med.* 2005;45(5):524-528.
- Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med.* 2004;32(8):1637-1642.
- levraut j, ichai c, petit i, ciebierra jp, perus o, grimaud d. low exogenous lactate clearance as an early predictor of mortality in normolactatemic critically ill septic patients. *crit care med.* 2003;31(3):705-710.
- J.L. Falk, E.C. Rackow, J. Leavy et al. Delayed lactate clearance in patients surviving circulatory shock. *Acute Care*, 11 (1985), pp. 212-215.
- Mikkelsen, M, Miltiades, A, Gaieski, D, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Crit Care Med.* 2009;37:1-8.
- Stacpoole PW, Wright EC, Baumgartner TG, Bersin RM, Buchalter S, Curry SH, et al. Natural history and course of acquired lactic acidosis in adults. DCA-Lactic Acidosis Study Group. *Am J Med.* Jul 1994;97(1):47-54.
- Uribarri J, Oh MS, Carroll HJ. D-lactic acidosis. A review of clinical presentation, biochemical features, and pathophysiologic mechanisms. *Medicine (Baltimore).* Mar 1998;77(2):73-82.
- Cohen R, Woods H. *Clinical and Biochemical Aspects of Lactic Acidosis.* Blackwell Scientific Publications; 1976.
- Salpeter SR, Greyber E, Pasternak GA, Salpeter Posthumous EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. *Cochrane Database Syst Rev.* Jan 20 2010;CD002967.