

Original Research Article

Serum lactate as a prognostic marker in patients with sepsis: a prospective study

Suhas T. Shetty¹, Ramakant Balookar², Dayanand S. Biradar^{2*}, M. B. Patil²

¹Department of General Surgery, JSS Medical College Hospital and Research Center, Mysuru, Karnataka, India

²Department of General Surgery, Shri B. M. Patil Medical College Hospital and Research Center, Deemed to be University, Vijayapura, Karnataka, India

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*Correspondence:

Dr. Dayanand S. Biradar,

E-mail: drdayanandbiradar@gmail.com

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ABSTRACT

Background: A prospective study to estimate the serum lactate levels and as a prognostic marker in patients with sepsis.

Methods: 170 patients admitted with sepsis in B.L.D.E. (Deemed to be University) Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapur from October 2014 to June 2016.

Results: In this study the mean serum lactate value of first sample in survivors (146 patients) is 3.8 ± 1.2 and non-survivors (24 patients) is 6.2 ± 1.9 with p value < 0.001 which is significant. The serum lactate value of the second sample in survivors (146) is 2.7 ± 1.0 and in non survivors (24) is 6.3 ± 1.8 with p value < 0.001 which is significant. The mean value of serum lactate 1st sample collected at the time of admission is 4.1 ± 1.6 and the mean value of serum lactate second sample collected at 24 - 48 hours after admission is 3.1 ± 1.6 .

Conclusions: Lactate level more than 4 mmol/l, patients are at highest risk of mortality and an aggressive resuscitation strategy shall be warranted. Hence serum lactate is considered as an independent and significant prognostic marker in patients with sepsis and evaluates the treatment outcome.

Keywords: Prognostic marker, Sepsis, Serum lactate

INTRODUCTION

Sepsis is a clinical condition characterized by systemic inflammation due to infection. There is a continuum of severity ranging from sepsis to septic shock. Sepsis is a complication of infectious process that is characterized by systemic inflammation with widespread tissue injury. Even with optimal treatment, mortality due to severe sepsis or septic shock is approximately 40 percent and can exceed 50 percent in the sickest patients.¹ Septic shock is an extreme clinical condition involving tissue hypo perfusion where tissue oxygen demand can exceed the ability of tissues to extract oxygen from the limited

oxygen supply. Sepsis additionally impairs the ability of tissues to extract oxygen so that ATP generation from glucose oxidation is supplemented by ATP generation from glycolysis leading to lactate production.²

Arginine vasopressin is released by the posterior pituitary. Arginine vasopressin also increases tone in splanchnic beds.³ Peripheral tissue inflammation can directly stimulate the hypothalamus.⁴ These stress hormones are implicated in the relative hyperglycemia observed in physiologic stress states.^{5,6} Release of acetylcholine has been demonstrated to inhibit activation of the macrophages.⁷

Lactate is a product of anaerobic glucose metabolism. It is generated from pyruvate with lactate dehydrogenase as a catalyst. Lactate is cleared from blood, primarily by the liver, with the kidneys and skeletal muscles to a lesser degree. Cardiopulmonary failure, sepsis, trauma, oncologic pathology etc. can lead to lactic acidosis.

Hepatic and muscle clearance of lactate may also be impaired thus blood lactate concentration are often elevated in sepsis. Rather than thinking of lactate solely as a byproduct of inadequate blood perfusion it may be useful to consider lactate as a marker of strained cellular metabolism.²

The primary goal in management of sepsis is to restore adequate oxygen and substrate delivery to the tissues as quickly as possible and to improve the tissue oxygen utilization and cellular metabolism. Serum lactate was chosen because it is used as a prognostic marker of global hypoxia and the clearance of circulating lactate is prolonged in patients with sepsis. Samples of venous blood for lactate can be used as these samples are easily obtained and the results are roughly equivalent to those of assays of arterial samples.⁸ Hence as a measure of tissue hypoxia and risk stratification lactate measurement have now been incorporated in to treatment protocols of sepsis.⁹

Henceforth this study was being done to assess the role of serum lactate as a predictor of outcome in patients with sepsis.

METHODS

All patients with sepsis admitted to B.L.D.E. (Deemed to be University) Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka, India from October 2014 to June 2016 were included in study. Institutional ethical committee clearance was taken, informed consent was taken, history of patients was noted. Required basic investigations were done. Serum lactate investigation was done at the time of admission and after 24 - 48 hours after admission.

Inclusion criteria

Must be an adult (>18 years) Meet 2 or more criteria for systemic inflammatory response syndrome, temperature >38°C or <36°C (100.4°F/96.8°F), pulse rate >90/min, respiratory rate >20/min or PaCO₂ 12,000 cumm³ or 10% immature (bands), must have sepsis with any of these signs of hypoperfusion, systolic blood pressure (SBP) 40 mmHg drop in standard BP even after adequate fluid resuscitation, serum creatinine >2.0 mg/dl or urine output 4 mg/dl, lactate >2.5 mMol/l were included.

Exclusion criteria

Chronic liver disease, end stage cardiopulmonary disease, neoplasms, HIV positive cases with known end stage processes were excluded.

Study methods

The present study was a prospective study. The study period was from October 2014 to June 2016.

A total of 170 sepsis patients were taken for the study. All these patients were evaluated thoroughly by clinical, radiological and laboratory methods. Serum lactate 1st and 2nd samples were collected. Serum lactate levels were categorized into low positive (0-2.0 Mol/l), moderate positive (2.1-3.9 mMol/l) and highly positive (>4 mMol/l)

Statistical methods

Statistical analysis was performed using Chi-square test, student 't' test and Odd's ratio. Sample size was calculating using the formula,

$$n = \frac{Z\alpha^2 p(1-p)}{d^2}$$

Where, n=sample size, Z α =1.96 at 5% level of significance, p=prevalence, rate=20%, d=allowable error = \pm 6%.

Following statistical tests were used to compare the results Student t test, Chi-square test, Mean \pm standard deviation.

Investigations or interventions

Investigations or interventions required in this study were routine standardized procedures. There were no animal experiments involved in this study.

Serum lactate levels at 0 and 24 hrs, Hb%, TC, DC, ESR, platelet count, urea, creatinine and electrolytes, urine routine, RBS following investigations (as and when required), ABG, chest X-ray, blood culture or urine culture or pus culture, USG abdomen and pelvis and LFT were needed for the study

RESULTS

In present study it was observed that highest number of patients were observed in age group 56-70 years, with mean age group of 31.2 years with 62.9% being males (Table 1).

Serum lactate 1st value in between 2.5 - 3.9 is more i.e 51.8% and serum lactate value>4.0 in 42.9% and serum lactate value 0 - 2.4 in 5.3%. It is observed that in 42.2% of the patients the serum lactate second sample value was found to be in between 0 - 2.4 mmol/l (Table 2). 103 patients showed lactate clearance from 1 to 50% (decrease in serum lactate values compared to 1st and 2nd) and 17 patients showed lactate clearance >50%. (Table 3).

Table 1: Distribution of cases according to age (years) and sex.

Age (years)	Male		Female	
	N	%	N	%
18-25	7	6.5	11	17.5
26-40	27	25.2	16	25.4
41-55	28	26.2	17	27.0
56-70	37	34.6	16	25.4
>70	8	7.5	3	4.8
Total	107	100.0	63	100.0

Table 2: Distribution of cases according to serum lactate (mmol/L) 1st sample and 2nd sample.

Serum lactate (mmol/L) 1st sample	N		Serum lactate (mmol/L) 2nd sample		N		%	
	N	%	N	%	N	%	N	%
0-2.4	9	5.3	0-2.4	68	42.2			
2.5-3.9	88	51.8	2.5-3.9	60	37.3			
>4.0	73	42.9	>4.0	33	20.5			
Total	170	100	Total	161	100			

Table 3: Distribution of cases according to lactate clearance from 1st to 2nd sample.

Lactate clearance from 1st to 2nd sample	N	%
No clearance	41	25.4
1% to 50%	103	64.0
>50%	17	10.6
Total	161	100.0

It was observed that more number of patients who presented with sepsis were in the age group 56 - 70 years with 2nd sample of serum lactate value >4.0 mmol/L.

Table 4: Distribution of patient's condition.

Patient condition	N	%
Death	24	14.1
Improved (lower value of serum lactate in second sample)	120	70.6
Improved (higher value of serum lactate in second sample)	26	15.3
Total	170	100.0

Table 5: Distribution of cases by source of infection.

Source of infection	N	%
Abdominal surgeries	46	27.2
Abscess	36	21.0
Necrotising fasciitis	36	21.0
Cellulitis	35	20.0
Burns	14	8.2
Urinary infection	3	1.8
Total	170	100.0

Table 6: Mean parameters of patients (N=170).

Parameters	Mean	SD	Range
Age (years)	48.1	16.9	18-87
Serum lactate (mmol/l) 1st sample	4.1	1.6	1.8-10.8
Serum lactate (mmol/l) 2nd sample	3.1	1.6	0.8-11.1
PR	100.4	7.3	82-130
RR	23.9	2.4	16-36
SBP	95.5	16.0	70-160
DBP	62.0	11.0	0-90
Temp	38.5	0.8	34.4-39.9
Total count	17359.3	7472.5	2000-77100
Neutrophils	84.4	7.2	46-98
RBS	137.5	67.0	50-504
B. urea	55.4	38.3	14-370
S. creatinine	1.7	1.0	0.4-5.4

Number of patients who recovered with decrease in the serum lactate value (compared to 1st and 2nd sample) 120 (70.6%). Number of patients who recovered with increase in serum lactate values (compared to 1st and 2nd sample) 26 (15.3%). Number of patients who died because of septic shock and associated comorbidities with significant increase in serum lactate values (serum lactate values > 4 in both 1st and 2nd sample 16 (9.41%) Number of patients who died within 2 days of admission with significant 1st sample serum lactate value (serum lactate value >4) 8 (4.7%) (Table 4).

Table 7: Comparison of mean parameters by survival.

Parameters	Survivors (n=146)		Non-survivors (n=24)		P value
	Mean	SD	Mean	SD	
Age (years)	47.6	16.9	51.5	17.2	0.292
PR	99.6	6.6	105.2	9.6	<0.001*
RR	23.8	2.4	24.5	1.9	0.180
SBP	95.6	16.0	94.7	16.4	0.782
DBP	62.4	11.3	60.0	9.0	0.328
Temp	38.4	0.8	38.6	0.6	0.234
Total count	16978.0	5327.3	19678.0	14994.0	0.101
Neutrophils	84.3	6.7	85.0	9.7	0.675
RBS	137.1	66.8	140.4	69.6	0.824
B. urea	54.7	39.5	60.2	30.8	0.516
S.creatinine	1.6	1.0	2.1	1.0	0.019*
Serum lactate (mmol/l) 1st sample	3.8	1.2	6.2	1.9	<0.001*
Serum lactate (mmol/l) 2nd sample	2.7	1.0	6.3	1.8	<0.001*

*P value significant

Serum lactate mean value of 1st sample in survivors was 3.8 mmol/l and in non survivors was 6.2 mmol/l. Serum lactate mean value of 2nd sample in survivors was 2.7 mmol/l and in non survivors was 6.3 mmol/l (Table 6).

Table 8: Serum creatinine other studies.

Studies	Survivors (mg/dl)	Non-survivors (mg/dl)	P value
Michael et al	1.0	1.3	<0.001
Bryant et al	2.3	2.9	0.13
Present study	1.6	2.1	0.019*

*P value significant

Mean pulse rate was 99.6 in survivors and 105.2 in non survivors. Mean respiratory rate was 23.8 in survivors and 24.5 in non survivors. Mean systolic blood pressure was 95.6 in survivors and 94.7 in non survivors. Mean diastolic blood pressure was 62.4 in survivors and 60 in

non survivors. Mean of total count was 16978 in survivors and 19678 in non survivors. Mean of neutrophils was 84.3 in survivors and 85.0 in non survivors. Mean random blood sugar value was 137.1 in survivors and 140.4 in non survivors. Mean serum creatinine value was 1.6 in survivors and 2.1 in non survivors (Table 7).

Table 9: Serum lactate other studies.

Studies	Survivors (mmol/l)	Non-survivors (mmol/l)	P value	
Michael et al	1.8	2.9	<0.001	
Bryant et al	6.1	8.0	0.01	
Vorwer et al	3.6	5.0	0.0054	
Present study	1st Sample	3.8	6.2	<0.001*
	2nd Sample	2.7	6.3	<0.001*

*P value significant

Table 10: Source of infection.

Source of infection	Emanuel et al ¹¹ (%)	Bryant et al ¹⁰ (%)	Trzeciak et al ¹² (%)	Present study (%)
Abdominal pathology	10.11	20.5	19	27.1
Abscess	1.7	5.1	7	20.0
Cellulitis, necrotizing fasciitis	23.11	1.32	9	39.4
Urinary complication	27.2	19.3	24	1.8

DISCUSSION

Lactate is a product of anaerobic glucose metabolism. It is generated from pyruvate with lactate dehydrogenase as a catalyst. Lactate is cleared from blood, primarily by the liver with the kidneys and skeletal muscles to a lesser degree. Serum lactate was chosen because the clearance of circulating lactate is prolonged in patients with sepsis. This study was conducted to evaluate the role of serum lactate as a prognostic marker in patients with sepsis. The serum lactate value was measured at the time of admission and the second sample within 24 to 48 hours. In present study the mean serum lactate value of first sample in survivors (146 patients) was 3.8±1.2 and non survivors (24 patients) was 6.2±1.9 with p value<0.001 which is significant. The serum lactate value of the second sample in survivors was 2.7±1.0 and in non survivors was 6.3±1.8 with p value<0.001 which is significant. Number of patients who recovered with decrease in the serum lactate value (compared to 1st and 2nd sample) 120 (70.6%). Number of patients who recovered with increase in serum lactate values (compared to 1st and 2nd sample) 26 (15.3%). Number of patients who died because of septic shock and associated comorbidities with significant increase in serum lactate values (serum lactate values>4 in both 1st and 2nd

sample 16 (9.41%). Number of patients who died within 2 days of admission with significant 1st sample serum lactate value (serum lactate value>4) - 8 (4.7%). The present study can be compared to Michael et al and Bryant et al with similar results.^{13,14} The mean value of serum lactate 1st sample collected at the time of admission was 4.1±1.6 and the mean value of serum lactate second sample collected at 24 - 48 hours after admission was 3.1±1.6. Highly significant difference is there between 1st and 2nd sample with p value<0.001 which is significant. Hence serum lactate is considered as a prognostic marker in patients with sepsis and evaluates the treatment outcome. Using lactate as an indicator of impaired metabolism in trauma and sepsis patients may help emergency care givers further diagnosis, risk stratify and treat patients. Serial lactate measurements over the early diagnostic and treatment period can assist in monitoring treatment progress.

In comparison with other studies present study shows Mean of 64.5 year age in survivors group and 68.7 years in non survivors group with p value of <0.292. In comparison with other studies present study shows mean value of pulse rate 99.6 in survivors and 105.2 in non survivors with p value<0.001 which is significant. In comparison with other studies present study shows mean

value of respiratory rate 23.8 cpm in survivors and 24.5 cpm in non survivors with p value<0.001 which is significant. In comparison with other studies present study showed a mean temperature value of 38.4°C in survivors and 38.6°C in non survivors with p value 0.234. In comparison with other studies present study showed a mean total count of 16978 cells in survivors and 19678 cells in non survivors with p value 0.101. In comparison with other studies present study showed a mean value of serum creatinine 1.6 in survivors and 2.1 in non survivors with p value 0.019 which is significant. (Table 8).

The mean value of serum lactate 1st sample collected in survivors at the time of admission was 2.7 and the mean value of serum lactate second sample collected at 24-48 hours after admission was 6.3. Highly significant difference is there between 1st and 2nd sample with p value <0.001 which is significant (Table 9).

In present study 27.1% of the patients presented with abdominal pathology and 39.4% of the patients presented with cellulitis, necrotizing fasciitis and 20% of the patients presented with abscess (Table 10).

CONCLUSION

The fall in lactate concentration following the initiation of treatment for sepsis is due to an attenuation of the stress response. Lactate levels are one of the most used biomarkers in sepsis. When their level is more than 4 mmol/L patients are at highest risk of mortality and an aggressive resuscitation strategy shall be warranted in these patients. The findings in our study suggest an important role for serial sampling of the subsequent two lactate values and lactate clearance as a prognostic indicator of sepsis. The patients with initial serum lactate value >4.0 mmol/L were independently associated with high mortality. It was clear that serum lactate had a positive correlation with outcome of sepsis. Hence serum lactate is considered as a independent and significant prognostic marker in patients with sepsis and evaluates the treatment outcome.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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