# Serum lactate as a predictor of outcome of sepsis – study

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**Abstract**
**Introduction:** Serum Lactate is known to be elevated in subjects with sepsis. Increased blood lactate levels are common in critically ill patients. Some studies revealed its association with prediction of morbidity and mortality. Hence this study was taken up to assess the levels of serum lactate in sepsis and its outcome.
**Materials and Method:** This study comprised of age and sex matched groups consisting of 100 healthy individuals and 100 patients with septicemia who were admitted in MICU. Blood samples were collected and serum lactate levels were analyzed.
**Results:** It was observed that serum lactate altered significantly (P< 0.0001) in subjects with sepsis when compared with healthy control group. The serum lactate levels were raised significantly high in cases with sepsis with outcome as death (P< 0.0001) in comparison to the subjects who had recovery.
**Conclusion:** Hence serial lactate measurements would be useful as a very good predictor of morbidity and mortality during the course of sepsis in elderly individuals.

**Keywords:** Serum lactate, Sepsis, Medical Intensive Care Unit (MICU).

## Introduction

Sepsis is a potentially serious medical condition that is characterized by a whole-body inflammatory state (systemic inflammatory response syndrome or SIRS) and the presence of known or suspected infection.[1] Serum Lactate is recognized as an indicator for the presence of sepsis and literature have revealed, elevated serum lactate levels are found to be strongly associated with morbidity and mortality in various populations with sepsis.[2] Increased lactate levels may be considered an early indicator of a potentially reversible state, e.g., early septic shock, possibly indicating that "there is still room" to boost fast intervention for recovery.[3,4] Studies in past revealed adults with sepsis, the lactate level are important and well-studied prognostic marker of mortality.[3] In sepsis, an increased lactate level represents the increased glycolytic flux due to hypoxia.[4] A study revealed usefulness in identifying critically ill patients at higher risk of death and has led to the adoption of lactate measurement in most blood gas analyzers and the frequent measurement of lactate in the critically ill.[5]

It has been estimated that by 2050, globally, 21.4% of people will be aged 60 years or older. Thus, the burden of elderly population with sepsis is expected to be on the rise. Infections, sepsis syndrome, septic shock are a major threat to the geriatric population.[6] There are not many studies on lactate levels in the elderly age group with sepsis. The study was conducted with an objective to measure serial serum lactate levels in elderly patients with sepsis, and correlate with outcome of sepsis.

## Materials and Method

In age and sex matched prospective study, a total number of 100 subjects of age group 40-80 comprising of 56 males and 44 females admitted in Medical Intensive Care Unit (MICU) at NRI Institute of medical sciences and General hospital, Chinakakani with sepsis during the period of January 2009 to June 2010 were considered as cases. 100 apparently healthy subjects comprising 52 males and 48 females were considered as controls. Approval for study was taken from institutional ethical clearance committee. Prior informed consent was taken from the subjects/ blood relatives of the subjects for the study.
**Inclusion criteria:** 100 confirmed subjects with sepsis in age group of 40-80 admitted in MICU
**Criteria for selection of cases:**[1] Sepsis was confirmed by evaluating Systemic Inflammatory Response Syndrome (SIRS) Score. SIRS was defined as being the presence of at least two of the four clinical criteria:
1. Alternation of body temperature: either < 36˚c or >38˚c,
2. Increased heart rate > 90/min,
3. Increased respiratory rate > 24/min,
4. Changes in WBC count < 4000/cumm or >12000/cumm
**Exclusion criteria:** Patients suffering from diabetic ketoacidosis chronic kidney disease and chronic liver diseases and patients on benzodiazepines, etomidate, nitroglycerin and barbiturates were excluded from the study.
**Sample collection:** Venous Blood samples were collected in vacutainers on day 1, 2, 3, and 4 of admission to the MICU among cases and once among

controls. Blood was allowed to clot and centrifuged to separate the serum for estimation of lactate by Lactate Oxidase Method.[7]

Following Parameters were evaluated at the time of admission among cases to confirm sepsis
1. Body temperature- Manual Mercury Thermometer
2. Respiratory rate- Clinical Examination
3. Heart rate- Clinical Examination
4. WBC Count- Cell Counter

**Statistical Methods:** Data was calculated as mean and standard deviation (mean ± SD). Results were compared between case and control groups by unpaired student 't' test using SPSS Package version 16.

## Results

This study included 100 patients admitted to the MICU with sepsis and 100 controls. The mean age among the cases and controls were 57.10±10.11 and 59.64±10.99 respectively with no statistical significant difference. Among the cases and controls there were 56 males, 44 females and 52 males, 48 females respectively. This was an age and sex matched study (Table 1).

Serial serum lactate measurements were taken on day 1, 2, 3, 4 of admission in MICU among cases. Controls were evaluated for Serum lactate once. Mean serum lactate level in cases at the time of admission was 51.41±20.79 and for controls was 12.48 ± 2.95with p-value <0.0001 indicating highly significant statistical difference (Table 2).

Of the 100 cases admitted in the MICU on day 1, 49 had mean serum lactate 68.84 ± 13.67 and continued to be in MICU. The other 51 had 34.77± 43.52 who recovered and were shifted to the wards on the same day, with p-value <0.0001 indicating significant statistical difference between the cases shifted to ward and who continued to be present in MICU on day 1 (Table 3).

Out of 49 cases who continued to stay in MICU after day 1, 28 had mean serum lactate 74.51± 12.62 and continued to stay in MICU and 14 cases had Serum lactate 30.00±18.47 who recovered and were shifted to

ward on 2nd day of admission with p-value <0.0001 indicating significant statistical difference between cases shifted to ward and who continued to be in MICU (Table 3).

Death was observed in 7 cases who continued to stay in MICU on day 2.The mean serum lactate level was 87.507± 5.82. The mean serum lactate level of cases who were shifted to ward at the end of day 2 was 30.00± 18.47. A significant statistical difference (<0.001) was observed between these groups for serum lactate levels (Table 4).

Out of 28 cases who continued to stay in MICU after day 2, 20 had mean serum lactate 65.64± 14.94 and continued to stay in MICU and 6 cases had Serum lactate 26.94±3.12 who recovered and were shifted to the ward at the end of 3rd day of admission with p-value <0.0001 indicating significant statistical difference between cases shifted to ward and those who continued to be present in MICU (Table 3).

Death was observed in 2 cases who continued to stay in MICU on day 3. The mean serum lactate level was 90.40± 6.82. Mean serum lactate level of cases who were shifted to the ward at the end of day 3 was 26.94± 3.12. A significant statistical difference (<0.001) was observed between these groups for serum lactate levels (Table 4).

Out of 20 cases who continued to stay in MICU after day 4, 12 had mean serum lactate 50.95± 20.12 and continued to stay in MICU and 6 cases had Serum lactate 20.55±10.51 who recovered and were shifted to the ward on the 4th day of admission with p-value <0.0001 indicating significant statistical difference between cases shifted to ward and those who continued to be present in MICU (Table 3).

Death was observed in 2 cases who continued to stay in MICU on day 4.The mean serum lactate level was 91.40± 7.82. Mean serum lactate level of cases who were shifted to the ward at the end of day 4 was 20.55± 10.51. A significant statistical difference (<0.001) was observed between these groups for serum lactate levels (Table 4).

**Table 1: Comparison of Age, Sex among Controls and Cases**

| Parameters | Cases (n = 100) | Controls(n=100) | p-Value |
|---|---|---|---|
| Age (Years) | 58.70 ± 11.54 | 57.39± 9.45 | 0.08* |
| Sex (M/F) | 56/44 | 52/48 | |

*not significant

**Table 2: Comparison of Mean ±SD serum lactate among Controls and Cases**

| Parameter | Normal Range | Cases | Controls | p-Value |
|---|---|---|---|---|
| Serumlactate | 4.5-20 mg/dl | 51.41±20.79 | 12.48±2.95 | < 0.0001** |

**highly significant

**Table 3: Levels of serum Lactate (mg/dl) (Mean±SD) in patients who continued to be in MICU and patients who were shifted to the ward post recovery at the end of day 1, 2, 3 and 4**

|       | Serum lactate in Cases who continued to be in MICU | Serum lactate in cases who recovered and were shifted to the ward | p- Value |
|-------|------------------|------------------|------------|
| Day 1 | 68.84 ± 13.67    | 34.77± 43.52     | <0.0001** |
| Day 2 | 74.51± 12.62     | 30.00±18.47      | <0.0001** |
| Day 3 | 65.64± 14.94     | 26.94±3.12       | <0.0001** |
| Day 4 | 50.95± 20.12     | 20.55±10.51      | <0.0001** |

**\*\* highly significant**

**Table 4: Comparison of mean serum lactate in subjects with outcome as death and recovery on respective days**

|       | Serum lactate in death Cases | Serum lactate in cases recovered | p- Value |
|-------|------------------|------------------|------------|
| Day 2 | 87.50 ± 5.82     | 30.00±18.47      | <0.0001** |
| Day 3 | 90.40± 6.82      | 26.94±3.12       | <0.0001** |
| Day 4 | 91.40± 7.82      | 20.55±10.51      | <0.0001** |

**\*\*highly significant**

## Discussion

Lactate is generated by skeletal muscle, erythrocytes, brain and gut. Lactate is constantly produced during normal metabolic and athletic events. Lactate levels do not rise until production begins to exceed clearance. Lactate may be used by many organ systems (heart, liver, kidneys) as fuel. Additionally, erythrocytes, devoid of mitochondria, are able to generate small amounts of energy by converting glucose to pyruvate. Endotoxemia may also lead to rise in lactate because of blunting of gluconeogenesis, increase in oxygen consumption and marked elevations of pyruvate production. Through these actions, additional pyruvate is diverted to lactate resulting in hyperlactemia.[8] Studies revealed the lungs can create lactate during acute lung injury without tissue hypoxia,[9] and leukocytes also generate lactate during phagocytosis or when activated in sepsis.[10]

The present study was designed to judge the use of serum lactate as a prognostic marker in septicemia. A statistically significant increase in the levels of serum lactate was observed among cases on day1 of admission in MICU and controls (P < 0.001). Our study was in accordance with the study done by Krishna et al;[11] who found significant increase in the serum lactate levels in patients with sepsis and stated that it was a good predictor of mortality in those patients.

In our study, the serum lactate levels on day 1, 2, 3, and 4 of admission among subjects who continued to be in MICU and among those subjects who recovered on the same day and got shifted to the ward were 68.84±13.67, 74.51±12.62, 65.64±14.94, 50.95±20.12 and 34.77±43.52, 30.00±18.47, 26.94±3.12, 20.55±10.51 respectively. A highly significant difference was observed between both the groups.

Mean serum lactate levels in subjects who had death on day 2, 3, 4 were 87.50 ± 5.82, 90.40± 6.82, 91.40± 7.82 and showed statistically significant difference of p value (>0.0001) in comparison to subjects who recovered on day 2, 3, 4 with mean serum lactate 30.00±18.47, 26.94±3.12, 20.55±10.51 respectively. From these observations, it was clear that serum Lactate had a positive association with outcome of sepsis.

In a similar study, Shapiro et al;[12] reported that increasing lactate levels were strongly associated with increased mortality in patients with sepsis. Londono et al;[13] proposed that mortality increased with a linear way with serum lactate from detectable values in patients admitted to the Emergency Department with clinical diagnosis of sepsis. The association of elevated lactate levels with higher mortality was also reported by Weil et al.[14]

In a similar study done by Arvind anand et. al;[2] there was a significant relation found between outcome of sepsis and mean lactate level in elderly individuals. Henrique Palombal et al; demonstrated that age was associated with a significantly increased risk of death in elderly patients with sepsis.[15]

## Conclusion

Hyperlactatemia is common in patients with sepsis, a marker of severity of illness and a strong predictor of mortality. Our study revealed serum lactate levels were highly elevated in subjects with sepsis and correlated well with the outcome in subjects with death and recovery. Hence serial lactate measurements would be useful as a very good predictor of morbidity and mortality during the course of sepsis in elderly individuals.

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