

# The Role of Salivary Lactate Levels in assessing the Severity of Septic Shock

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## Abstract

**Background:** Sepsis is a major worldwide cause of morbidity and mortality. Hence, rapid and reliable diagnosis is essential. Emergency departments use a standard measure of sepsis, based upon an elevated Lactate level in blood. Saliva is more readily available and easier to obtain than blood samples, and is increasingly being studied as a new source of diagnostic information.

**Aim:** This study aimed to evaluate whether analysis of Lactate levels in saliva can substitute for that of Lactate levels in blood.

**Methods/Materials:** We processed saliva samples and serum samples from septic shock and non-septic shock patients. We found out Lactate levels in both the group. We plotted the concentration of Lactate in non-septic and septic patients and compared lactate levels in saliva to its levels in blood.

**Statistical analysis:** Results were statistically analyzed by independent sample t test and A Spearman rho correlation

**Results:** We found increased serum and salivary Lactate levels in all cases of sepsis compared to the control group. Notably, the increase in Lactate levels was higher in serum as compared to saliva in septic patients, suggesting saliva may not serve as a better indicator of sepsis compared to blood. Salivary lactate was more in septic shock patients compared to non-septic shock patients.

**Conclusions:** To our knowledge, this is the first study to compare lactic acid levels in serum and saliva in cases of sepsis. The increase in serum lactate in patients with sepsis is evident when compared to increase in salivary lactate, so serum lactate level would be easier for physicians to differentiate septic patients from non-septic patients. Salivary lactate may not serve as better indicator in septic shock patients.

**Keywords:** Saliva lactate, septic shock, serum lactate

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## INTRODUCTION

Shock is a life-threatening condition that occurs when the body is not getting enough blood flow. Lack of blood flow means the cells and organs do not get enough oxygen

and nutrients to function properly. Many organs can be damaged as a result. Shock requires immediate treatment and can get worse very rapidly.<sup>[1]</sup>

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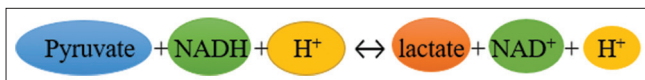
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Septic shock is an extreme clinical condition involving tissue hypoperfusion where tissue oxygen demand can exceed the ability of tissues to extract oxygen from the limited oxygen supply. Sepsis additionally impairs the ability of tissues to extract oxygen, so that ATP generation from glucose oxidation is supplemented by ATP generation from glycolysis, leading to lactate production. Hepatic and muscle clearance of lactate may also be impaired. Thus, blood lactate concentrations are often elevated. The recent guidelines for severe sepsis or septic shock management indicate that a blood lactate concentration of >4 mmol/L mandates prompt resuscitation of severe sepsis or septic shock.<sup>[2]</sup> The primary infection is most commonly caused by bacteria, but also may be by fungi, viruses, or parasites. It may be located in any part of the body, but most commonly in the lungs, brain, urinary tract, skin, or abdominal organs. It can cause multiple organ dysfunction syndrome (formerly known as multiple organ failure) and death. Frequently, people with septic shock are cared for in intensive care units (ICUs). It most commonly affects children, immune compromised individuals and the elderly, as their immune systems cannot deal with infection as effectively as those of healthy adults. The mortality rate from septic shock is approximately 25%–50%.<sup>[3]</sup>

Traditionally, hyperlactatemia in critically ill patients and particularly those in shock was normally interpreted as a marker of secondary anaerobic metabolism due to inadequate oxygen supply inducing cellular distress. Arterial lactate concentration is dependent on the balance between its production and consumption.<sup>[3]</sup> In general, this concentration is <2 mmol/l, although daily production of lactate is actually 1500 mmol/l. In physiological conditions, lactate is produced by muscles (25%), skin (25%), brain (20%), intestine (10%) and red blood cells (20%), which are devoid of mitochondria. Lactate is essentially metabolized by liver and kidney.

Lactate is produced in the cytoplasm according to the following reaction:



A normal blood lactate level is 0.5–1 mmol/L. Hyperlactatemia is defined as a persistent, mild to moderately elevated (2–4 mmol/L) lactate level without metabolic acidosis.<sup>[4]</sup> Lactic acidosis is the most common cause of metabolic acidosis in hospitalized patients. Impaired tissue oxygenation, leading to increased anaerobic metabolism, is usually responsible for the rise in lactate production.<sup>[5]</sup> Hyperlactatemia in shock

state is considered secondary to tissue hypoxia induced by a decrease in tissue perfusion. Measurement of serum lactate remains a primordial component for a sound diagnostic and therapeutic line of conduct in critical care. The concept of lactate merely as a metabolic waste product (bad lactate) has now evolved toward lactate being viewed as an energy shuttle (good lactate). In most clinical critical-care situations, hyperlactatemia must be perceived as an adaptive response to an aggressive state and not as a marker of tissue hypoxia. Nevertheless, irrespective of its mechanism of formation, hyperlactatemia remains an excellent prognostic marker.<sup>[6]</sup>

Saliva has an old history of study; it is of physiological importance. Saliva has hundreds of components which help detect systemic diseases and also provide biomarkers of health and disease status. Saliva has three major functions: digestion, protection and lubrication. Saliva also functions in maintenance of tooth integrity. Saliva is an accessible fluid that can easily be collected by the patient.

Advantages of saliva testing sample are easy and noninvasive collection procedure that is neither painful nor traumatic. Saliva is reliable for early detection of certain diseases and monitoring the disease course in conjunction with treatment and detection of addictive drugs.

These characteristics make it possible to monitor several biomarkers in infants, children and elderly subjects and in many circumstances in which blood and urine sampling is not available. The most commonly used laboratory diagnostic procedures involve the analyses of cellular and chemical constituents of blood. No special equipment is needed for collection of saliva. Diagnosis of disease via the analysis of saliva is potentially valuable for children and older adults. Further, analysis of saliva may provide a cost-effective approach for the screening of large populations.<sup>[7]</sup>

In our study, we find out whether salivary lactate levels can be used as a prognostic marker in assessing the severity of septic shock.

### Objectives

1. Estimation of salivary lactate levels in septic shock patients
2. Estimation of salivary lactate levels in nonseptic shock patients
3. To find out the correlation between salivary lactate and blood lactate levels in septic shock patients.

### METHODS

The study was carried out after taking the approval from the Bioethics Committee of Subbaiah Medical College,

Shivamogga, in the respiratory ICU of Maax Super speciality hospital, Super speciality wing of Subbaiah Institute of medical sciences, which provides a 24-h care to the critically ill patients of respiratory diseases transferred from the wards/operation theater or admitted through emergency. A cohort of minimum 30 subjects with sepsis was taken as cases and 30 subjects without sepsis served as controls. All of them were consecutively enrolled in the study irrespective of age, sex, nature of complaints or presence of comorbidity on the same day of their admission in ICU.

- Inclusion criteria: Patients with septic shock and patients with nonseptic shock.
- Exclusion criteria: Critically ill patients and unconscious patients.
- Study duration: 3 months
- Study type: Laboratory investigations

**Sample collection:**

1. The subject was made to sit comfortably in a calm and isolated room
2. He/she was made to rinse the mouth thoroughly using distilled water or deionized water to remove any food debris
3. The subjects were then asked to spit out the saliva that has been collected in the initial 30 s. They were also trained to collect the saliva in the floor of the mouth for whole Saliva collection
4. High-quality polypropylene was used for collection. Initial 2 min of unstimulated saliva was discarded, to avoid salivary diluting effect
5. Collection was made at a standard time, preferably between 8 and 11 am. The subject was in the fasting state or 2 h after breakfast
6. The participants were asked not to brush their teeth for a duration of 45 min prior to the sample collection
7. 5 ml of saliva is collected.<sup>[8]</sup>

The collected saliva was then sent for analysis of lactate levels, and serum of the same patients was also sent for analysis of lactate levels.

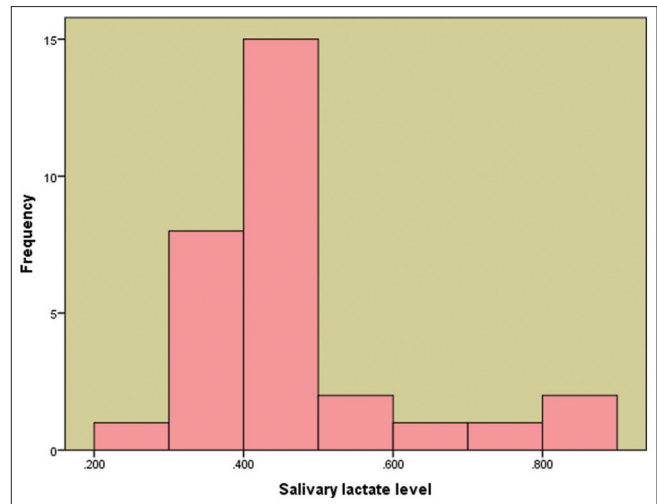
**Statistical analysis**

A Spearman’s rho correlation was performed to determine the relationship between blood lactate levels and salivary lactate

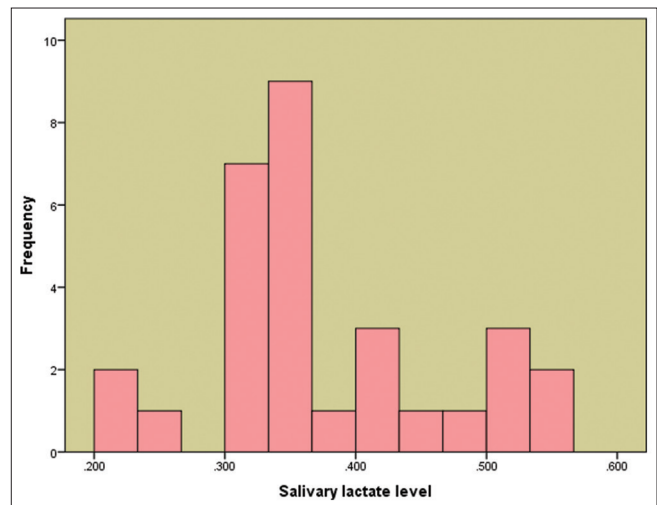
**Table 1: Salivary lactate levels across in septic shock patients and nonseptic shock patients**

Salivary lactate	n	Mean	SD	Independent sample t-test level
<b>Groups</b>				
SSP	30	0.47	0.15	t=2.9
Non SSP	30	0.37	0.1	P=0.006

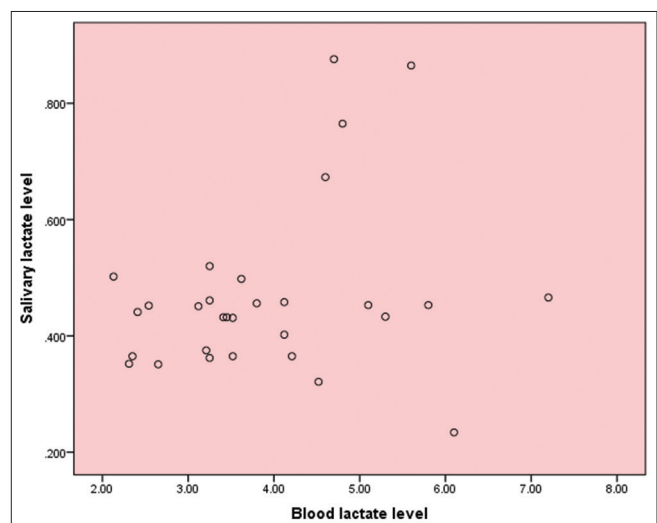
SD: Standard deviation



**Figure 1:** Histogram of salivary lactate levels in septic shock patients. Data are mean ± standard error of the mean



**Figure 2:** Histogram of salivary lactate levels in nonseptic shock patients. Data are mean ± standard error of the mean



**Figure 3:** A graph showing weak correlation between blood lactate levels and salivary lactate levels

levels in septic shock patients. We found that there is a weak correlation between blood lactate levels and salivary lactate levels, which is statistically not significant ( $\rho = 0.26, P = 0.169$ )

Independent samples *t*-test was done to compare salivary lactate levels across septic shock patients and nonseptic patients [Table 1].

## RESULTS

There is a statistically significant difference in mean salivary lactate levels across septic shock patients and nonseptic patients [Table 1 and Figures 1 and 2].

We found that there is a weak correlation between blood lactate levels and salivary lactate levels, which is statistically not significant [Figure 3].

## DISCUSSION

In our study, we have found differences in salivary lactate responses in septic shock and nonseptic patients, while the changes in blood lactate concentration were high in septic shock patient. Weak correlation was noted between salivary lactate and blood lactate in septic shock patients.

Saliva plays a very important role in the diagnosis of several oral diseases. This property of saliva is attributed to variation in its constituents and composition.<sup>[9,10]</sup> Salivary analysis as an alternative approach to serological investigations has proven to be an effective and a noninvasive investigation with emerging trends in various aspects of diagnosing several oral diseases.<sup>[11]</sup>

Lactate dehydrogenase, a metabolic enzyme in the anaerobic glycolysis, is present in the cytoplasm of all living normal cells, which becomes extracellular upon cell death. Therefore, its extracellular presence is always related to cell necrosis and tissue breakdown.<sup>[12]</sup>

Raised serum levels of the enzyme are observed in several other systemic conditions including malignancies, myocardial infarction, liver disease, megaloblastic anemia's, renal disease and periodontal disease; therefore, its raised levels in serum are not specific.<sup>[12]</sup> These conditions were listed as exclusion criteria in our study to avoid obtaining a false result. Saliva, an alternative to serum, can be used as a screening test for the diagnosis of oral malignancies. Biomarkers in saliva are proven to be raised in oral carcinomas. Thus, the presence of increased levels of these biomarkers is a nonspecific indicator of the disease process.<sup>[13]</sup>

Our study was aimed to obtain an easily performable test that can be carried out with minimal discomfort to the patients providing accurate results. Saliva, the oral fluid

with its enormous diagnostic properties, was considered an appropriate medium to aid the study.<sup>[14]</sup>

Even though high level of blood lactate level indicates severe septic shock and aids in adequate amount of fluid resuscitation in these patients.

## CONCLUSION

Our data suggest that measuring salivary lactate might be a suitable indicator in septic shock patients. Further studies in larger samples may help in getting the better correlation between salivary lactate and blood lactate in septic shock patients. If so, it would play a major role in quick diagnosis of septic shock in emergency department.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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