

Serum Lactate to Albumin Ratio as a Prognostic Marker of Sepsis Syndrome.

Ruchita Kabra¹, Sourya Acharya², Sunil Kumar³, Anil Wanjari⁴, Sachin Agrawal⁵

¹Junior Resident, Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India.

²Head and Professor, Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India.

³Professor, Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India.

⁴Professor, Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India.

⁵Professor, Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India.

Email id- ¹ruchitapkabra@gmail.com, ²souryaacharya74@gmail.com, ³sunilkumarmed@gmail.com, ⁴anilwanhjari123@gmail.com, ⁵dragrawal82@gmail.com

Article type: Original Article

Conflict of Interest:None

Funding:Nil

Abstract:

BACKGROUND:Sepsis is a medical emergency which involves response of the immune system of body for an infectious process leading to the end-stage dysfunction of the organs and death. Sepsis is amongst major causes of the morbidity and mortality in terminally critical patients in the world.Organ dysfunction is identified by little change in the SOFA score i.e., score of two points or more. In spite of advancements in the knowledge of sepsis- its pathophysiology, and developments in tools of monitoring and resuscitative measures, still sepsis has been one amongst major causes of morbidity and mortality in terminally critical patients. This study has been planned to evaluate the ability of serum lactate to albumin ratio as a prognostic marker in patients of sepsis.

AIM OF THE STUDY:To evaluate the ability of lactate/albumin ratio for prediction of outcome in patients with sepsis and the septic shock.

OBJECTIVES:

To study different levels of lactate/albumin ratio with respect to classes of sepsis like SIRS, severe sepsis, septic shock.

To study outcome in terms of mortality, need of ventilatory support, and recovery with respect to lactate/albumin ratio in the patients with sepsis and septic shock.

MATERIAL AND METHOD: In this cross-sectional study, 160 patients were enrolled and diagnosed on the basis of SOFA score of two or more than two points. Patients were admitted in Medicine Intensive Care Unit (MICU) from, November 2020 to November 2022.

EXPECTED RESULTS:This study aims at estimating that combining both serum lactate and serum albumin in the form of serum lactate to albumin ratio could yield more accurate prediction about prognosis of critically ill patients specially in septic patients. This study is

for evaluation of the efficacy of the prognostic value of the ratio of serum lactate / albumin in cases of sepsis. A ratio of lactate/albumin > 0.15 is associated with adverse prognosis.

CONCLUSION: Serum Lactate to Albumin ratio as the prognostic marker in patients of sepsis. A lactate to albumin ratio greater than 0.15 is associated with adverse prognosis in terms of mortality, need of ventilatory support and recovery in patients with sepsis and septic shock.

KEYWORDS: Sepsis, septic shock, lactate to albumin ratio, prognosis

INTRODUCTION:

Sepsis is a medical emergency which involves response of the immune system of body for an infectious process leading to the end-stage dysfunction of the organs and death. Sepsis is one of the grave causes of the morbidity and mortality in critically ill patients in the world.[1]

The yearly occurrence of new cases of severe sepsis and shock in US is 300 cases per 1,00,000 population annually. On estimation it has been observed that greater than 30 million people are suffering from sepsis and septic shock each year in entire world, leading to approximately 6 million annual deaths.[2]

Death rate of sepsis in India is found to be 213 per 1,00,000 people. Death rate in India is higher as compared to other South Asian countries.

A global study regarding mortality rate of sepsis has revealed that India has much higher death rate from septic shock and sepsis syndrome, a life-threatening organ dysfunction response to infections, as compared to other South Asian countries except Afghanistan. The study has found that the sepsis death rate is 213 people per 1 lakh people in India, 206 people in Pakistan, 183 people in Nepal, 136 people in Bangladesh, 109 people in Bhutan, 69 people in Sri Lanka and 27 people in Maldives and 285 people in Afghanistan.

Sepsis is a response of the body systems to infection, manifested by SIRS criteria of two or more as a result of infection.[3]

By definition, Severe sepsis means “the sepsis which is associated with dysfunction of organ system, reduced perfusion of organs i.e., hypoperfusion, or decreased blood pressure i.e., hypotension; , reduced perfusion of organs i.e., hypoperfusion, or decreased blood pressure i.e., hypotension abnormalities which includes all, but it is not limited to, lactic acidosis, reduced urine output-oliguria, or an mental status alteration.”

As stated by Third International Consensus, Sepsis is dysfunction of organ caused because of maladaptive response of the host to the infection occurred and can endanger life.[4]

Dysfunction of organ is identified as change in SOFA score of 2 points or more with respect to the infections. SOFA score of 2 points or more suggests an mortality risk of approximately 10% in patients with suspected infection.

The score was made for describing a complications of terminal illness and not for prediction of mortality and morbidity of critical illness

SOFA is based on six different scores, each one for each of the systems like respiratory system which includes PaO₂/FiO₂ ratio, cardiovascular system which includes Mean Arterial Pressure and various inotropes doses as per requirement, hepatic system which includes levels of bilirubin in mg/dl, coagulation system which includes platelet counts, renal system which includes serum creatinine levels in mg/dl and neurological system which includes GCS score of the patient. Each scored from 0 to 4. As score increases it reflects worsening of dysfunction of organ systems.

The most common cause of sepsis is bacterial infection. Other causes of sepsis also include fungal, parasitic or viral infections. The source of infection can be any of the places or organ throughout the body. It can be in the abdomen due to appendicitis, peritonitis, etc., in the central nervous system due to meningitis, infection of spinal cord, etc, in the lungs due to pneumonia, or urinary tract infections especially if the patient has in dwelling urinary catheter to drain urine.

Risk of sepsis varies with age as in more than 65 years old or a very young or pregnant women. People with any comorbidities like any infection in the body or medical conditions such as hypertension, diabetes, lung diseases, cancer and kidney diseases, immunocompromised patient, long stay of hospitalization, severe injuries, large burns or wounds. Also in patients with indwelling catheters in any form like IV cannulas or urinary catheters or an endotracheal tube.

Patients in whom any form of infection is suspected are rapidly identified for poor outcomes specially in emergency department or ward settings, which shows at minimum 2 of the below stated criteria which jointly add up to form an entire new prognostic score which is termed as quickSOFA (qSOFA) that includes:

- respiratory rate of 22/min or more
- altered sensorium or altered mental status
- systolic blood pressure equal to or less than 100 mm Hg .

Routine investigation for making diagnosis of sepsis includes Complete Blood Count, blood culture, urine culture, blood sugar.

Various markers are used for prognosis and early diagnosis of sepsis which includes CRP, Procalcitonin, serum lactate levels, serum albumin levels, serum lactate to albumin ratio.

According to newer definition of sepsis [5], septic shock can be diagnosed as following:

First: persistent hypotension i.e., low blood pressure despite fluid resuscitation and which require vasopressors to maintain mean arterial pressure(MAP) \geq 65 mm Hg.

Second: Serum lactate level $>$ 2 mmol/L as serum lactate level linked hypoperfusion of the tissues which is related with signs of dysfunction of organ in terminally ill and hospitalized individuals.

Lactic acid is the terminal state of the anaerobic disintegration of glucose or carbohydrate metabolism in tissues. The normal serum lactate level is 0.5 - 1 mmol/L. Individuals which are terminally ill can be assumed to have levels of serum lactate of less than 2 mmol/L which is within normal limits. Definition of hyperlactatemia is a persistent, mild to moderate increase in serum lactate levels up to 2-4 mmol/L. Serum lactate is a potentially useful biomarker that is widely investigated in patients with critical illness and gave good prognostic value.[6]

Albumin is the most abundant plasma protein which accounts for 2/3rd of the total protein content synthesized in liver. As it constitutes two-thirds of total protein in the blood, decrease in albumin due to reduced synthesis or losses result in dysregulation of the intravascular oncotic pressure is significant and that results in edema. Therefore, serum albumin appears to be ideal prognostic indicator.[7]

Combining both serum lactate and albumin in the form of serum lactate/albumin ratio could yield more accurate prediction about prognosis of critically ill patients specially in septic patients.[8]

Background/rationale:

Sepsis is medical emergency defined as dysfunction of organ which is threatening to life and is caused by disturbances of host response to the infection caused in the body. In spite of the recent developments in the knowledge of the sepsis pathophysiology and in the tools of

monitoring and resuscitative measures, still sepsis in the leading causes of morbidity and mortality in critically ill patients and long term hospitalised patients. This study has been planned to evaluate the ability of serum lactate to albumin ratio as a prognostic marker in patients of sepsis.

OBJECTIVES:

- A) To study different levels of lactate/albumin ratio with respect to classes of sepsis like SIRS, severe sepsis, septic shock.
- B) To study outcome in terms of mortality, need of ventilatory support, and recovery with respect to lactate/albumin ratio in patients with sepsis and septic shock.

METHODS:

Study design: The Observational cross-sectional study.

Setting: This study will be conducted in the AVBRH, a tertiary care Hospital, situated in the area of Sawangi (Meghe) Wardha, in Central India.

Participants:

INCLUSION CRITERIA: All patients more than 18 years of age, diagnosed to have sepsis or septic shock as per definition admitted under Medicine Department at AVBRH, Sawangi.

EXCLUSION CRITERIA: Patients with primary organ failure without sepsis which includes: Acute Kidney Injury, Heart Failure and due to non-infective causes and sepsis secondary to primary organ involvement.. Any patient not giving consent or doesn't wish to participate will be excluded.

Bias: No bias.

Study size: $n = \frac{1.96^2 * 0.283 * (1-0.283)}{d^2}$

P = Prevalence of severe sepsis = 28.3% = 0.283

d = Desired error of margin = 7% = 0.07

$n = \frac{1.96^2 * 0.283 * (1-0.283)}{0.07^2}$

n = 159.08 = **160 patients** required in the study

A sample size of 160 will be taken based on above mentioned formula.

Definition of the case:

As stated by Third International Consensus, Sepsis is dysfunction of organ caused because of maladaptive response of the host to the infection occurred and can endanger life. [4]

Dysfunction of organ is identified as variation in the SOFA score of 2 points or greater than 2 points with respect to infections.

SOFA score of 2 points or more indicates increased risk of mortality of nearly 10% in patients with suspected infection.

Statistical methods: Descriptive statistics will be used and the data will be presented as mean standard deviations and percentage/proportions.

Expected Results: This study aims at estimating that combining both serum lactate and serum albumin in the form of serum lactate to albumin ratio could yield more accurate prediction about prognosis of critically ill patients specially in septic patients. Hence, this study is for evaluation of the efficacy of the ratio of serum lactate / albumin as a prognostic value in cases of sepsis and septic shock and results are expected to be equivalent to the studies done earlier.

The previous studies have shown that patients whose serum lactate/albumin ratio is increased had maximum marked signs of multiple organ dysfunction and failure. The ratio of lactate/albumin may constitute a very crucial parameter for risk calculation in severely ill and hospitalized patients. The cut-off of 0.15 was deliberated and was observed their association with the worse outcome.

DISCUSSION:

Sepsis is the medical emergency by definition is dysfunction of organ caused because of inadequate response of the host to the infection occurred which can be life threatening. Organ dysfunction is identified by little change in the SOFA score i.e., score of two points or more than two points. In spite of advancements in the knowledge of sepsis- its pathophysiology, and developments in tools of monitoring and resuscitative measures, still sepsis has been one amongst the major causes of morbidity and mortality in terminally critical patients.[1]

Michael Lichtenauer et al. aimed for evaluation of the ratio of lactate/albumin as a marker of prognosis in a terminally ill patients and hospitalised patients. Study was conducted in Germany from 2004 to 2009 on total of 348 patients admitted in ICU. The association of the ratio of lactate/albumin and mortality in these patients was investigated. Patients who has raised serum lactate/albumin ratio had more marked signs of multiple organ dysfunction and its failure. An unraised ratio of serum lactate/albumin was found to be in association with raised hospitalised patient mortality. An cut-off of 0.15 was calculated and was observed their association with the bad outcome. Their conclusion was that the ratio of lactate/albumin may constitute a major parameter for evaluating prognosis in the critically ill patients and long term hospitalised patients.

Jikyong Shin et al aimed for evaluation of the use of the ratio of serum lactate/albumin (L/A) as a prognostic marker of deaths in long term hospitalised patients and critically ill patients. This is a study is retrospective but data collection is prospective which includes 10 critical care departments in hospitals in Korean Shock Society. A total of 946 patients of 19 years and above that with sepsis were considered in this study. The conclusion of this study was that the prognostic importance of serum lactate to albumin ratio is superior than a single parameter of ratio for prediction of mortality in long term hospitalised and critically ill patients suffering from sepsis.

Victor Prado et al studied various systems which evaluates prognostic scoring system in patients having sepsis but are often difficult to measure. They proposed serum albumin to lactate ratio (ALR) as a scoring for prognosis in patients of sepsis. The main objective of the study was to investigate the association between serum lactate to albumin ratio and mortality and morbidity in patients admitted in the hospital for long time with severe sepsis and septic shock admitted to the intensive care unit (ICU).

Essam f. Makram et al. aimed to examine the ability of serum lactate/albumin ratio to predict outcome of dysfunction of organ systems and mortality and morbidity in severe sepsis and septic shock. Also, it was notably raised in patients that required mechanical ventilation than patients who, where not on machinal ventilation (p value <0.004 on day 0 and <0.001 on day 1). For patients who needed renal replacement therapy (RRT), lactate/albumin ratio was higher than those who didn't (p value <0.001 for days 0 and 1). When comparing levels of lactate/albumin ratio in survivors and non survivors, we found that it was significantly higher in non survivors (p value <0.001). Conclusion: Serum Lactate/albumin ratio is a reliable biomarker for prediction of outcome with regards to dysfunction of organ systems and mortality in patients with severe sepsis and septic shock.

Su Mi Lee and Won Suk An et al aimed for searching of latest clinical criteria for predicting outcome of septic shock that is serum lactate level as a latest emerging vital sign. Dronamraju et. al. reported about PIRO Scoring in predicting mortality of ICU patients with sepsis, severe sepsis and septic shock [9]. Gupta et. al. investigated impact of platelet indices as prognostic markers of sepsis [10]. Rathod et. al. reported a study on preoperative serum albumin as a predictor of post-operative mortality and morbidity[11]. Few similar studies were reported [12-15]. Chiwhaneet. al. focused on co-relation of left ventricular diastolic dysfunction with Apache II score in sepsis patients[16]. Verma et. al. studied the role of serum albumin as a prognostic marker of mortality and duration of hospital stay among diabetic ketoacidosis patients[17].

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