

Study of Serum Lactate in Patients of Cirrhotic Liver Disease as a Marker of Severity and its Prognosis**Ashok Kumar¹, Anuj Aggarwal²**¹Associate Professor, Department of General Medicine, ESIC Medical College & Hospital, Basaidarapur, New Delhi²Post Graduate Student, Department of General Medicine, ESIC Medical College & Hospital, Basaidarapur, New Delhi

Received: 01-06-2025 / Revised: 16-07-2025 / Accepted: 18-08-2025

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Conflict of interest: Nil

Abstract

Background and Objective: Cirrhotic liver disease represents a major global health burden, with rising incidence and mortality over the past decades. Disease progression from compensated to decompensated cirrhosis significantly worsens prognosis. Lactate, a byproduct of anaerobic metabolism, has recently emerged as a potential biomarker of disease severity and prognosis due to impaired hepatic clearance in cirrhosis. This study aimed to assess the role of serum lactate as a marker of severity and short-term prognosis in patients with cirrhotic liver disease.

Methods: This prospective, single-centre observational study was conducted from April 2023 to August 2024 at the Department of Medicine, ESI-PGIMS. A total of 70 adult patients (≥ 18 years) diagnosed with cirrhosis were enrolled after applying exclusion criteria. Serum lactate levels were measured at admission, and patients were followed for 30-day mortality outcomes. Data were analyzed using SPSS version 28. ROC analysis determined the sensitivity and specificity of serum lactate for predicting mortality, with $p < 0.05$ considered statistically significant.

Results: Among 70 patients, 38 (54.5%) were male, and 41 (58.5%) were aged ≥ 51 years. The overall 30-day mortality rate was 20%. Mean serum lactate levels were significantly higher among non-survivors (7.52 mmol/L) compared to survivors (mean 5.81 mmol/L). ROC analysis indicated that elevated serum lactate was a sensitive predictor of mortality in cirrhotic patients.

Conclusion: Serum lactate is a valuable prognostic biomarker in cirrhotic liver disease, correlating strongly with disease severity and short-term mortality. Routine lactate monitoring may aid in early risk stratification and management of cirrhotic patients.

Keywords: Cirrhotic Liver Disease; Serum Lactate; Prognostic Biomarker; Disease Severity; Mortality Prediction; Liver Function Impairment.

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Introduction

Chronic liver inflammation and damage result in cirrhosis, which is characterized by diffuse hepatic fibrosis and the replacement of normal liver structures with regenerating liver nodules. [1, 2] According to recent epidemiological studies, 5.2 million cases of chronic liver disease and cirrhosis occurred in 2017, representing a rise in the incidence of the condition in both men and women compared to 1990. In 2019, 1.48 million fatalities were attributed to cirrhosis, an 8.1% rise from 2017. In 2019, cirrhosis-related disability-adjusted life-years ranked 16th overall and 7th in individuals between the ages of 50 and 74. 3The most current GBD 2019 report on cirrhosis-related worldwide mortality is accessible. According to the GBD 2017

(1323000 cases), there were 1.43 million fatalities globally from cirrhosis in 2019, an 8.1% rise over 2017. This information was uncovered by a recent comprehensive examination of the GBD 2019. [4,5]

For decades, it has been understood that the natural history of cirrhosis is marked by a prognostic watershed, represented by the development of complications related to portal hypertension and impaired liver function, such as gastrointestinal bleeding, hepatic encephalopathy, jaundice, and ascites formation. This led to the concept that the course of the disease can be divided into two distinct clinical states: the usually asymptomatic compensated stage, characterized by preserved

quality of life and a median survival exceeding 12 years, and the decompensated stage, marked by the occurrence of complications, with median survival dropping to 2–4 year. [6]

This severe, irreversible condition characterized by the scarring (fibrosis) of liver tissue due to long-term damage. One of the major complications is portal hypertension, which occurs when scar tissue obstructs blood flow through the liver, increasing pressure in the portal vein. This leads to additional problems such as variceal bleeding, ascites (fluid build-up in the abdomen), and splenomegaly (enlarged spleen). Another serious complication is hepatic encephalopathy, a condition where toxins that are normally filtered by the liver accumulate in the bloodstream, affecting brain function. As cirrhosis progresses, patients are also at a higher risk of liver cancer, particularly hepatocellular carcinoma. Other potential complications include jaundice, kidney dysfunction, and coagulopathy (impaired blood clotting). Managing cirrhosis involves addressing the underlying cause, slowing the progression of liver damage, and treating complications as they arise. [7,8]

Lactate has become a more reliable indicator of prognosis in recent years. Numerous clinical research and animal trials have demonstrated that the lactate level is a useful tool for forecasting a patient's prognosis and evaluating how they are developing.

An essential metabolic route that aids in controlling the body's levels of lactate and glucose is the Cori cycle. Recycling lactate that is created by muscles during vigorous physical activity is its main purpose. Because there is not enough oxygen in the muscles, anaerobic glycolysis occurs, which breaks down glucose into pyruvate and lactate. Although this mechanism keeps the body producing energy, it also causes lactate to build up in the blood. By moving the extra lactate to the liver, where gluconeogenesis transforms it back into glucose, the Cori cycle helps eliminate it. The bloodstream then receives this freshly created glucose, giving the muscles and other tissues a new source of energy. The Cori cycle maintains sustained energy supply, overall metabolic balance, and helps avoid lactate accumulation by turning lactate into glucose. [14] Increased lactate synthesis or poor clearance are frequently indicated by elevated serum lactate levels. The liver's capacity for gluconeogenesis and lactate processing is severely impaired in the setting of liver cirrhosis as a result of increasing damage and fibrosis. Because the liver cannot efficiently convert lactate into glucose, people with cirrhosis frequently have increased serum lactate levels. The crucial connection between liver health and lactate metabolism is highlighted by the possibility that this compromised function may lead to further

problems and metabolic disruptions. Patients with cirrhotic liver disease may have high lactate because of faster glycolysis in the splanchnic area, decreased hepatic gluconeogenesis, and impaired lactate clearance as a result of hepatocyte failure. [13,14]

The aim of the present study was to assess the role of serum lactate in patients of cirrhotic liver disease as a marker of severity and prognosis. The elevated serum lactate is associated with higher mortality in sepsis, whereas liver dysfunction is associated with higher serum lactate levels. The prognostic value of lactate is not well established in liver cirrhosis and acute-on-chronic liver failure (ACLF). Also, the available literature gives conflicting and variable results in the study of the role of serum lactate in patients with cirrhotic liver disease. Hence, we aim to provide evidences for conducting larger trials.

Materials and Method

Study design: This was a single-centre, observational and prospective study conducted between April 2023 and August 2024 in Department of Medicine, ESI-PGIMSIR. The study protocol was approved by the Ethics The study protocol was approved by the Ethics Committee (ESIPGIMSIR- IEC/2023013). Owing to the prospective nature of the study, the requirement for written informed patient consent was waived

Study setting and population: During the study period, we enrolled 70 adult patients (≥ 18 years old) who visited the department with liver cirrhosis were enrolled. However, the patients with the pre-existing conditions (haemoglobinopathies, haematological malignancies) or taking certain drugs or toxins (nucleoside reverse transcriptase inhibitors, biguanides) were excluded.

Statistical Analysis: Data was analyzed using Statistical Package for Social Sciences (SPSS) version 28, IBM Inc. Descriptive data was reported for each variable. The data was normally distributed as tested using the Shapiro-Wilk W test (p-value was less than 0.05). An independent t-test was used to compare the results across the grading. Sensitivity and specificity were calculated along with the ROC curve for serum lactate to predict the outcome. A level of $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics: The age distribution of the 70 individuals in the sample shows a notable concentration in the middle-aged and older age groups. The sub group analysis of the age shows that cirrhosis is more prevalent in the patients aged 51-81 years and above (58.5%). This shows that among 70 patients, 32 are female (45.7%), and 38 are male (54.5%). The distribution indicates a

slightly higher prevalence of males in the patient population.

Table 1: Baseline characteristics

Characteristics	N=70
Sex n (%)	
Male	38 (54.5)
Female	32 (45.7)
Age Range n (%)	
19-50 years	29 (41.4)
51-81 years and above	41 (58.5)

Out of 70 patients, 80%, survived, while 14 individuals, or 20%, did not survive (mortality). This shows that most of the group had a positive outcome, with a survival rate of just over 80%. However, nearly one-fifth of the group experienced mortality, reflecting a significant impact on the group as shown in table 2.

Table 2: Distribution of patients according to outcome (30-day mortality)

	N (%)
Survived	56 (80%)
Mortality	14 (20%)

The mean serum lactate level is 5.81 mmol/L.

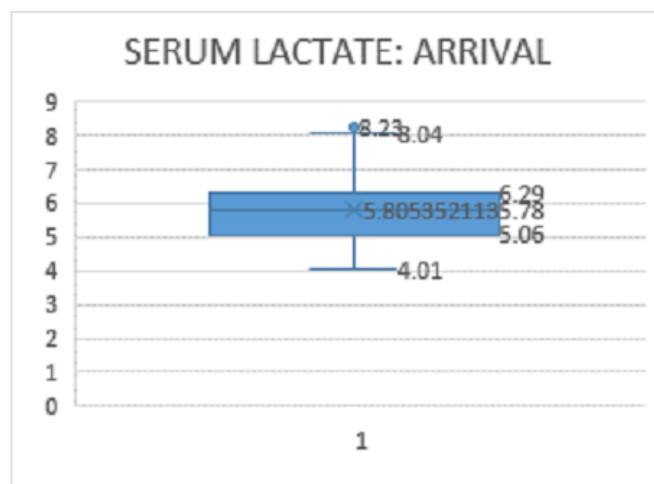


Figure 1: Descriptive of variables of the study

The mortality group had a significantly higher average serum lactate level of 7.52 mmol/L as shown in figure 2.

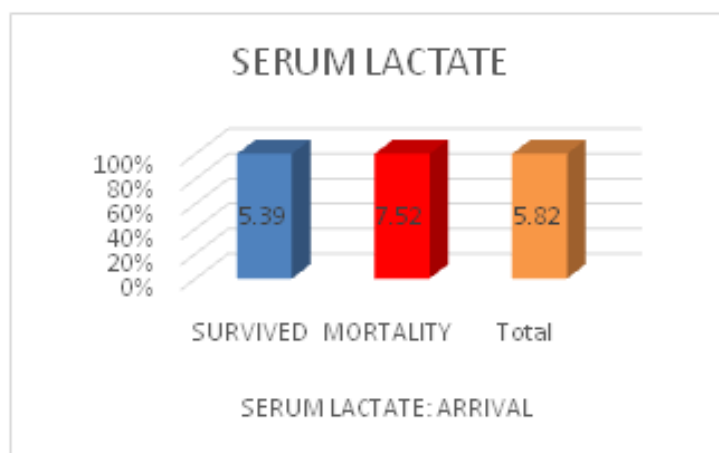


Figure 2: Comparison of serum lactate levels according to the outcome

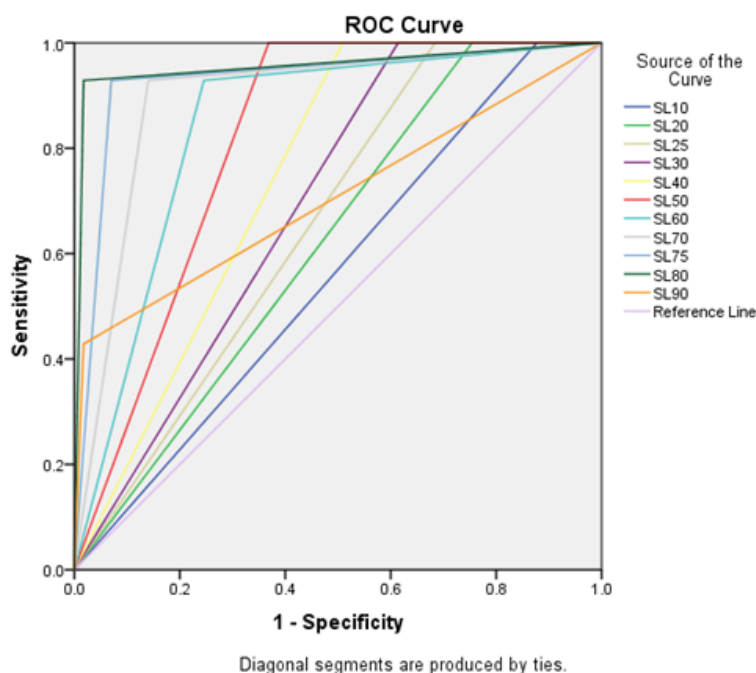


Figure 3: The sensitivity and specificity of serum lactate levels

Discussion

Evaluating the prognosis for patients with cirrhosis, particularly those being treated at the hospital, is extremely important for determining the necessary treatment strategies. Levels of serum lactate, which are closely connected to tissue hypoxia and anaerobic metabolism, are also strongly linked to mortality. [15]

Several studies offer substantial evidence supporting the predictive value of lactate in critically ill patients. Elevated lactate levels upon hospital admission have been suggested as a potential indicator of postoperative complications and death, with high sensitivity and specificity for adverse outcomes. Presently, serum lactate levels are utilized to assess the risk for patients with sepsis, trauma, and pulmonary embolism. Multiple studies have shown that lactate levels are associated with mortality in cirrhotic patients admitted to the ICU. [15,16]

In the present study, Survival outcomes reveal that 80% of the individuals survived, while 20% did not. This indicates a generally positive outcome for the majority of the sample, although nearly one-fifth experienced mortality. This mortality rate is likely attributed to the fact that a majority of patients included were in advance stage of disease.

The study demonstrates a predominance of middle-aged and older individuals in the sample, with a skew towards severe liver cirrhosis. The survival rate is relatively high, but significant mortality is observed. The serum lactate level is crucial in assessing disease severity and predicting outcomes.

The analysis confirms serum lactate emerging as a significant predictor of mortality. The ROC curve analysis underscores the utility of serum lactate levels in outcome prediction, with varying levels of sensitivity and specificity across different cut-off percentiles. This comprehensive evaluation highlights the importance of serum lactate levels as a key indicator in the management and prognosis of liver disease.

Limitations

The study's relatively small sample size of 70 individuals may limit its application to a broader population. An increased sample size could yield more robust and dependable results. Since the study was carried out at a single institution, the results may not be broadly applicable to other populations or settings.

It primarily focuses on 30-day mortality, offering a short-term perspective on outcomes. Including long-term follow-up could provide a further understanding of the durability of the findings and the long-term prognosis. The variations in clinical management or treatment protocols among patients could impact outcomes.

Conclusion

The study demonstrates a predominance of middle-aged and older individuals in the sample, with a skew towards severe liver cirrhosis. The survival rate is relatively high, but significant mortality is observed. The serum lactate level is crucial in assessing disease severity and predicting outcomes. The ROC curve analysis underscores the utility of serum lactate levels in outcome prediction, with

varying levels of sensitivity and specificity across different cut-off percentiles. This comprehensive evaluation highlights the importance of serum lactate levels as a key indicator in the management and prognosis of liver disease.

Acknowledgment

Authors are thankful to Dr. Jaykumar Sharma (Intas Pharmaceutical Ltd, Gujarat, India) for critical review of the manuscript. Authors also acknowledge Ms. Sakshi Srivastava and Dr. Mehul R. Chorawala, Intas Pharmaceutical Ltd, Gujarat, India for medical writing assistance and additional editorial communication.

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