

Correlation of Serum Lactate in Patients of Cirrhotic Liver Disease with Child Turcott Pugh Score (CTP) and Model for End Stage Liver Disease Score (MELD)

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Abstract:

Background and Objective: Lactate levels are widely used as a marker of tissue hypoxia and disease severity in critically ill patients. The liver is the principal site of lactate clearance; hence, impaired hepatic function in cirrhosis may lead to hyperlactatemia and poor outcomes. Although elevated serum lactate has been associated with higher mortality in sepsis, its prognostic role in liver cirrhosis remains uncertain. This study aimed to assess the correlation of serum lactate levels with the Child-Turcotte-Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores in patients with cirrhotic liver disease.

Methods: A single-centre, prospective, observational study was conducted at the Department of Medicine, ESI-PGIMSIR, between April 2023 and August 2024. Seventy adult patients (≥ 18 years) with liver cirrhosis were enrolled. Patients with haematological malignancies, haemoglobinopathies, or drug-induced lactate alterations were excluded. Serum lactate levels were measured at admission and correlated with CTP and MELD scores. Statistical analysis was performed using SPSS v28, with $p < 0.05$ considered significant.

Results: Among 70 patients, 54.5% were male and 45.7% female. Mortality was observed in 20% ($n=14$). Serum lactate levels showed strong positive correlations with MELD ($r=0.611$, $p=0.001$) and 30-day mortality ($r=0.652$, $p=0.001$), and moderate correlation with CTP score ($r=0.456$, $p=0.001$). Patients who died had significantly higher MELD (34.19 ± 2.56) and CTP (12.43 ± 1.09) scores than survivors ($p=0.001$).

Conclusion: Serum lactate levels significantly correlate with MELD and CTP scores and predict short-term mortality in cirrhotic patients. Elevated lactate serves as a simple, reliable biomarker for assessing disease severity and prognosis in liver cirrhosis.

Keywords: Serum lactate; Liver cirrhosis; Child-Turcotte-Pugh score; MELD score; Prognostic marker; Hyperlactatemia.

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Introduction

Lactate can be measured in critically ill patients to evaluate the severity of disease.[1] Patients are considered to have higher lactate levels (hyperlactatemia) at concentrations of more than 2 mmol/L. Hyperlactatemia occurs when lactate production exceeds clearance.[2] Tissue hypoxia and subsequent anaerobic metabolism are considered to be the main mechanisms of hyperlactatemia.[3]

Liver cirrhosis is considered an irreversible end result of chronic liver diseases. Hospital mortality of cirrhotic patients admitted to the ICU ranges from 34 to 86%. [4] The combination of decompensated cirrhosis, organ failure(s) and high mortality rate marks the diagnosis of acute-on-

chronic liver failure (ACLF). Hyperlactatemia upon admission to the ICU was strongly associated with adverse outcomes in cirrhotic patients. [5] The liver exhibits a higher net lactate clearance than any other organ, accounting for up to 70% of lactate clearance.[6] Lactate kinetics in cirrhotic patients are significantly different from those in patients without hepatic impairment.[7] Fulminant liver dysfunction has been shown to impair lactate clearance.[8]

One important factor contributing to the morbidity and death of people with chronic liver disease is cirrhosis. Prognostic models must therefore be used to identify people who are at high risk. In individuals with cirrhosis, new prognostic factors

have surfaced in recent years. Three primary categories can be used to categorize prognostic ratings obtained from critically ill cirrhotic patients in the intensive care unit (ICU): liver-specific (CTP and MELD), general (SAPS II and APACHE), and organ failure (OSF and SOFA). [9,10] The prognosis of cirrhotic patients is non-invasively evaluated using the Child-Pugh and the Model for End-Stage Liver Disease (MELD) Scores. [9,11] Due of the subjectivity of the criteria used to calculate the score—such as ascites and hepatic encephalopathy—the Child-Pugh score has an inherent disadvantage. However, end-stage patients are better suited for the MELD score. The usefulness of both scores as prognostic indicators for cirrhosis patients has been compared in a number of studies, but the inclusion of all included patients is limited due to the populations' heterogeneity. Therefore, it is essential that new ratings be developed in order to evaluate the prognosis of liver cirrhosis patients. [12,13]

The aim of the present study was to assess the role of serum lactate and its correlation with Child Turcott Pugh Score (CTP) and Model for End Stage Liver Disease Score (MELD). 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 evidence 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 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). The correlation coefficient was calculated for serum lactate with MELD and child Turcott Pugh scores. 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. 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)
CTP categoriesn (%)	
Child-Pugh A: 5 to 6	0 (0)
Child-Pugh B: 7 to 9	6 (8.6)
Child-Pugh A: 10 to 15	64 (91.4)

Child-Pugh A (Score 5 to 6): mildest form of liver cirrhosis (0%)

Child-Pugh B (Score 7 to 9): moderate liver cirrhosis

Child-Pugh C (Score 10 to 15): severe liver cirrhosis and a poorer prognosis

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 MELD score, which assesses the severity of liver disease, is 28.41 on average, with a standard deviation of 4.64, reflecting some variability in disease severity. The CTP score, used to evaluate the prognosis of liver disease, has an average of 11.32.

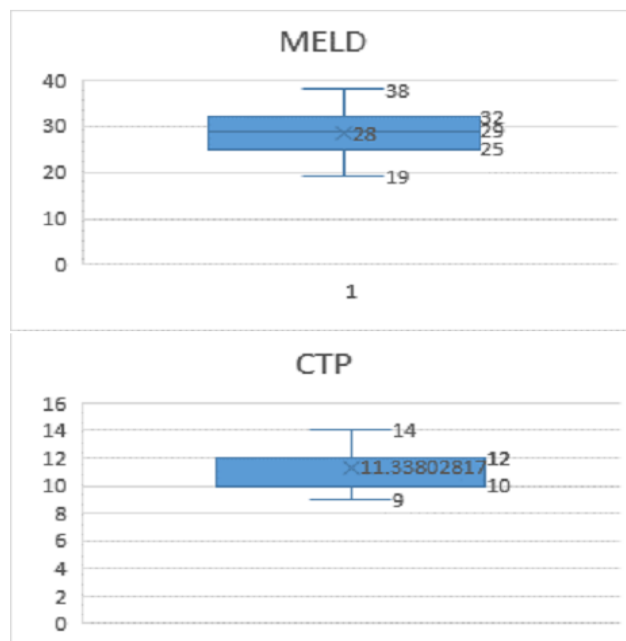


Figure 1: Descriptive of variables of the study

Table 3: The correlation of serum lactate, MELD, CTP and final outcome

--			MELD	CTP	30 Day Mortality
Spearman's rho	Serum Lactate at Arrival	Correlation Coefficient	0.611**	0.456	0.652**
		Sig. (2-tailed)	0.001*, sig	0.001*, sig	0.001*, sig

Interpretation changes

- 0.00-0.19 “very weak”
- 0.20-0.39 “weak”
- 0.40-0.59 “moderate”
- 0.60-0.79 “strong”
- 0.80-1.0 “very strong”

The correlation coefficient is 0.611, which is statistically significant ($p = 0.001$). This indicates a strong positive correlation, suggesting that higher serum lactate levels at arrival are associated with higher MELD scores. With CTP Score, the correlation coefficient is 0.456, which is also significant ($p = 0.001$). This indicates a moderate positive correlation, meaning higher serum lactate levels at arrival are moderately associated with

higher CTP scores. The correlation coefficient is 0.652, which is highly significant ($p = 0.001$). This shows a strong positive correlation, indicating that higher serum lactate levels at arrival are strongly associated with increased 30-day mortality. The mortality group had a significantly higher average MELD score of 34.19, with a standard deviation of 2.56 and scores ranging from 28.7 to 38 as shown in table 4.

Table 4: Comparison of MELD according to the outcome

		N	Mean	Std. Deviation	Minimum	Maximum	P value
MELD	Survived	56	26.98	3.87	19.4	36.0	0.001*, sig
	Mortality	14	34.19	2.56	28.7	38.0	
	Total	70	28.42	4.65	19.4	38.0	

Mann Whitney U test, level of significance set at $p < 0.05$

Ns: non-significant, sig: significant

In the mortality group, the average CTP score is higher at 12.43. The CTP score of 70 patients is 11.33. The p-value of 0.001 again indicates a significant difference between the two groups.

Table 5: Comparison of CTP according to the outcome

		N	Mean	Std. Deviation	Minimum	Maximum	P value
CTP	Survived	56	11.05	1.23	9.0	13.0	0.001*, sig
	Mortality	14	12.43	1.09	10.0	14.0	
	Total	70	11.33	1.32	9.0	14.0	

Mann Whitney U test, level of significance set at $p < 0.05$

Ns: non significant, sig: significant

The correlation of serum lactate, MELD, CTP and final outcome is presented in table 6.

Table 6: The correlation of serum lactate, MELD, CTP and final outcome

			Serum Lactate	MELD	CTP	30 Day Mortality
Spearman's rho	Serum Lactate At Arrival	Correlation Coefficient		0.611**	0.456	0.652**
		Sig. (2-tailed)		0.001*, sig	0.001*, sig	0.001*, sig
	MELD	Correlation Coefficient	0.611**		0.542**	0.601
		Sig. (2-tailed)	0.001*, sig		0.001*, sig	0.001*, sig
	CTP	Correlation Coefficient	0.456**	0.542**		0.409**
		Sig. (2-tailed)	0.001*, sig	0.001*, sig		0.001*, sig

Discussion

In the present study, The MELD score, which assesses liver disease severity, averaged 26.98 for survivors. Similarly, Tas A et al (2012) MELD scores were significantly higher in patients who died than in those who were discharged from the ICU (p values were 0.001). El Serafy M et al (2014) reported MELD were significantly higher in patients who died than in those who survived. Sy E, Ronco JJ, Searle R, Karvellas CJ (2016) evaluated severity of illness scores. On ICU admission, patients had the following median (interquartile range): MELD, 26 (19-35).

The CTP score, which evaluates the prognosis of liver disease, averaged 11.05 for survivors. Tas A et al (2012) CTP scores were significantly higher in patients who died than in those who were discharged from the ICU (p values were 0.001). El Serafy M et al (2014) reported CTP, MELD was significantly higher in patients who died than in those who survived. Sy E, Ronco JJ, Searle R, Karvellas CJ (2016) evaluated severity of illness scores. On ICU admission, patients had the following median (interquartile range): MELD, 26 (19-35); CTP, 12 (10-13).

The Serum lactate levels at arrival show a strong positive correlation with MELD scores (correlation coefficient = 0.611, $p = 0.001$) and a moderate positive correlation with CTP scores (correlation coefficient = 0.456, $p = 0.001$). MELD scores and CTP scores exhibit a moderate positive correlation (correlation coefficient = 0.542, $p = 0.001$), indicating that higher MELD scores are related to higher CTP scores. Both MELD and CTP scores show strong positive correlations with 30-day mortality, with MELD scores having a correlation

coefficient of 0.601 and CTP scores 0.409, underscoring their importance as predictors of mortality.

In agreement to these findings, Sarmast et al in 2020 studied the Model for End-Stage Liver Disease-Lactate and prediction of mortality in patients with Chronic Liver Disease and concluded that MELD-Lactate is an early and objective predictor of inpatient mortality and may serve as model for risk assessment and guide therapeutic options.

Bhakta D. et al in 2021 studied the Model for End-Stage Liver Disease Lactate Score and Prediction of Inpatient Mortality in Critically Ill Patients with Cirrhosis and concluded that MELD-Lactate had excellent performance for assessment of mortality in the ICU and 1 month as well as when limited to patients on ventilator. Li X, Gong M, Fu S, Zhang J, Wu S in 2022 studied MELD-lactate clearance scoring system in predicting death risk of critically ill cirrhotic patients and concluded that MELD- Δ LA score is a simple scoring system in predicting the risk of ICU death, 28-day, 90-day and 1-year mortality for critically ill cirrhotic patients, which may have a good predictive performance.

The study demonstrates that clinical parameters such as serum lactate levels, MELD scores, and CTP scores are crucial in assessing disease severity and predicting outcomes. The analysis confirms strong correlations between serum lactate levels, MELD scores, and mortality, with 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

Clinical parameters such as serum lactate levels, MELD scores, and CTP scores are crucial in assessing disease severity and predicting outcomes. The analysis confirms strong correlations between serum lactate levels, MELD scores, and mortality, with 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.

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