ORIGINAL ARTICLE

Utility of Serum Prolactin Levels as a Marker for Disease Severity and Short-term Prognosis in Patients with Cirrhosis: A Prospective Observational Study

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Abstract

Background: Cirrhosis, a leading cause of global mortality, necessitates an accurate assessment of disease severity and prognosis. While traditional scoring systems like Child-Turcotte-Pugh (CTP) and model for end-stage liver disease (MELD) are used to assess the severity, specific biomarkers are lacking. This study explores serum prolactin levels as a potential biomarker for evaluating cirrhosis severity and predicting short-term mortality.

Methods: A prospective observational study was conducted from December 2021 to December 2023. After a thorough clinical examination, serum prolactin levels were measured. The correlation between prolactin levels and established severity scores [CTP, MELD, chronic liver failure consortium organ failure (CLIF-C OF), and MELD-sodium (MELD-Na)] was analyzed. The study also evaluated the prognostic value of prolactin levels in predicting 28-day and 90-day mortality.

Results: A total of 90 patients with liver cirrhosis were included. There were 82% men, with a mean age of 47.6 years. Alcohol was the most common cause of cirrhosis (73%). The median (interquartile range (IQR)) serum prolactin level was 29 (10–54) ng/mL, with higher levels correlating with increased disease severity: CTP ($r = 0.73$), MELD ($r = 0.64$), MELD-Na ($r = 0.67$), and CLIF-C OF ($r = 0.82$) scores. Elevated prolactin levels were significantly associated with increased mortality, with an area under the receiver operating characteristic curve of 0.83 for predicting 28-day mortality and 0.79 for 90-day mortality. A prolactin cut-off of 35.12 ng/mL demonstrated high sensitivity (93% and 77%, respectively) and specificity (63% and 72%, respectively) for 28-day and 90-day mortality prediction.

Conclusion: Serum prolactin levels significantly correlated with the severity of cirrhosis and also effectively predicted the short-term mortality. Prolactin may offer a noninvasive and cost-effective adjunct for severity assessment and short-term prognosis in cirrhosis.

Keywords: Child-Turcotte-Pugh score, Chronic liver failure consortium organ failure score, Cirrhosis, Model for end-stage liver disease, Model for end-stage liver disease-sodium, Prolactin, Short-term mortality.

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Highlights

- Elevated prolactin levels were observed in patients with cirrhosis.
- Elevated prolactin levels were correlated with the severity scores used in cirrhosis.
- Prolactin levels had a strong correlation with grades of hepatic encephalopathy (HE).
- Prolactin demonstrated strong prognostic accuracy in predicting 28-day and 90-day mortality in patients with cirrhosis.

Introduction

Cirrhosis is a chronic hepatic disease characterized by irreversible fibrosis and loss of normal hepatic architecture, leading to several complications, including portal hypertension, ascites, variceal bleeding, hepatorenal syndrome, HE, spontaneous bacterial peritonitis, and an increased risk of hepatocellular carcinoma. The global prevalence of cirrhosis is increasing, driven by factors such as alcohol consumption, viral hepatitis, and metabolic syndrome.[1] In India, the burden of cirrhosis is particularly high, with a significant proportion attributed to alcohol-related liver disease.[2] The Child-Turcotte-Pugh (CTP) score and the model for end-stage liver disease (MELD) score are commonly utilized to assess treatment options, predict patient outcomes, and prioritize patients for liver transplantation. These scores have limitations. The CTP score relies on subjective assessment for ascites and HE. Creatinine used for MELD may be affected by low muscle mass in cirrhotic patients. Consequently, there is growing interest in identifying noninvasive biomarkers that can

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provide reliable and objective information about liver disease severity.

The anterior pituitary synthesizes and secretes prolactin, primarily regulated by dopamine from the hypothalamus. Dopamine inhibits prolactin production by acting on D2 receptors in lactotrophic cells.[3] Prolactin levels rise when dopamine decreases, particularly in the tuberoinfundibular tract. While prolactin release typically follows a periodic pattern, patients with liver cirrhosis show a constant 24-hour elevation, likely due to impaired dopamine regulation.[4]

The rise in serum prolactin levels in cirrhotic patients is thought to be due to increased estrogen levels, which result from both peripheral aromatization of testosterone and reduced elimination of steroid hormones in liver disease. This excess estrogen likely stimulates prolactin release by interfering with hypothalamic dopamine and directly affecting the anterior pituitary. However, the exact mechanism remains unclear.[5] Another pathway involves the increased synthesis of false neurotransmitters such as octopamine and phenyl ethanolamine in cirrhosis. This leads to a reduction in the true neurotransmitters like dopamine, which subsequently triggers an increase in prolactin secretion.[6] It was also proposed that alcohol might directly affect hypothalamic-pituitary function, impacting prolactin production.[7]

Previous studies have suggested a potential link between prolactin levels and liver disease severity, but comprehensive analyses and validation studies are limited.[8,9] Limited research has explored the accuracy of prolactin in predicting mortality in patients with cirrhosis. This study investigated the correlation between serum prolactin and severity scoring systems and its efficacy in predicting short-term mortality in cirrhosis.

Methodology

This prospective observational study was conducted at a tertiary care institute in South India, including patients with cirrhosis based on clinical examinations, biochemical tests, and radiological imaging. The study setting was inpatient and outpatient services of the Departments of Medicine and Medical Gastroenterology. Patients with conditions known to alter prolactin levels, such as prolactinoma, chronic kidney disease, hypothyroidism, pregnancy, history of cranial surgery or irradiation, and the use of medications like antiemetics (domperidone), antipsychotics, and antidepressants, were excluded. Figure 1 presents a flowchart illustrating the recruitment process of participants for the study.

Study Procedure

Data Collection

Patients' demographic details were collected. Clinical history encompassed a range of questions regarding the presentation and complications of cirrhosis. Additionally, inquiries were made regarding the duration, severity, progression, and prior episodes of decompensation. All the patients underwent a complete general examination and abdominal examination. Hepatic encephalopathy was diagnosed and graded using West Haven's classification system.

Laboratory investigations included a complete hemogram, renal and liver function tests, prothrombin time, and serum electrolytes. Upon admission, the CTP score, MELD, MELD-sodium (MELD-Na), and Chronic Liver Failure Consortium Organ Failure (CLIF-C OF) scores were calculated for all patients.[10–12] An abdominal ultrasonography was performed to look for cirrhotic changes.

Serum Prolactin Level Estimation

From each patient, two blood samples (each 3 mL) were taken within 24 hours of recruitment, and the serum collected after centrifugation was stored in a deep freezer at −80°C. Samples were processed in two batches. An average of two prolactin levels for each patient was used for interpretation of results. Prolactin was measured quantitatively using a paramagnetic particle chemiluminescent immunoassay using the Access Immunoassay Systems kits provided by Beckman Coulter India, Pvt. Ltd., with assay range for men of 2.1–17.7 ng/mL and women of 2.8–29.2 ng/mL, and lower detection limit 0.25 ng/mL.

Follow-up

We followed up with the patients for survival on day 28 and day 90.

Cirrhosis Definition

"The diagnosis of cirrhosis of liver was based on previous liver biopsy if available or based on clinical, imaging (heterogeneous echotexture of liver with irregular outline, altered liver size, or portosystemic collaterals), laboratory (low serum albumin, aspartate aminotransferase/alanine aminotransferase ratio > 1), and endoscopic findings (≥ grade II esophageal varices)."[13]

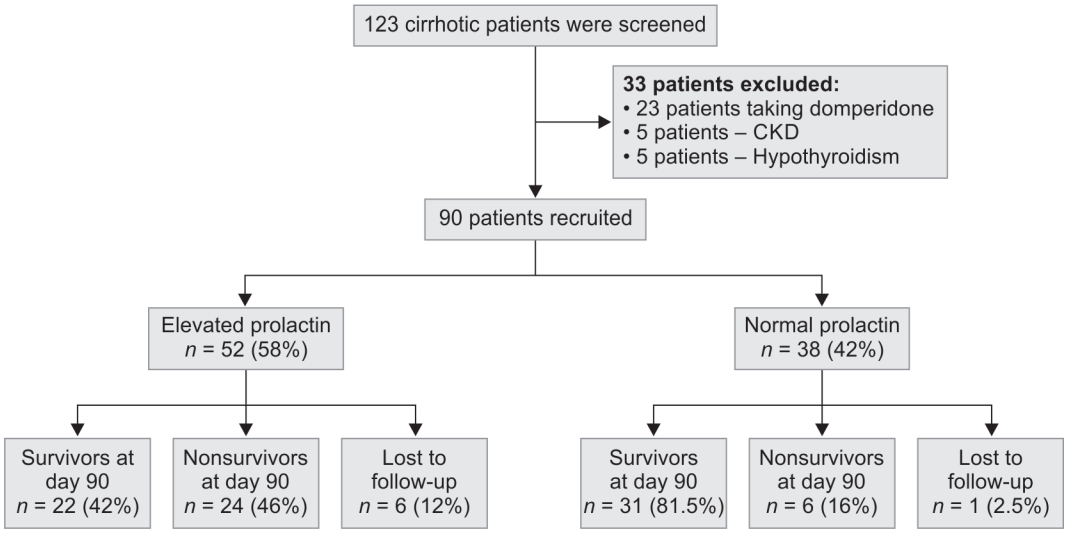


Fig. 1: Study flow diagram

Table 1: Comparison of baseline characteristics, biochemical parameters, and disease severity based on survival status at day 90

Variables	*Total patients (n = 90)**	*Survivors at day 90 (n = 53)*	*Nonsurvivors at day 90 (n = 30)*	*p-value*
Age (years), mean ± SD	47.6 ± 11.6	46.8 ± 12.4	49.2 ± 11	0.37
Gender – male, *n* (%)	74 (82)	41 (77)	26 (87)	0.3
Duration of cirrhosis (months), median (IQR)	12 (2–24)	12 (4–23)	6 (2–22)	0.6
Newly diagnosed cirrhosis, *n* (%)	11 (12)	7 (13)	4 (13)	0.9
Alcohol consumption, *n* (%)	68 (76)	36 (68)	26 (87)	0.06
Duration of alcohol intake (months), mean ± SD	17 ± 6	16 ± 7	17 ± 5.5	0.85
Previous decompensation, *n* (%)	44 (49)	20 (38)	17 (57)	0.09
Hepatic encephalopathy, *n* (%)	56 (62)	26 (49)	24 (80)	<0.001
Bilirubin (mg/dL), median (IQR)	3 (2–6.9)	2 (1–4)	5 (3–13.6)	0.004
AST (IU/L), median (IQR)	66 (42–120)	55 (40–109)	82 (48–157)	0.1
ALT (IU/L), median (IQR)	30 (23–50)	29 (23–51)	32 (24–48)	0.6
Albumin (g/dL), mean ± SD	2.7 ± 0.8	3 ± 0.9	2.4 ± 0.7	0.008
Creatinine (mg/dL), median (IQR)	1 (0.8–1.3)	1 (0.8–1.2)	1.05 (0.8–2)	0.19
INR, Median (IQR)	1.6 (1.1–2.1)	1.3 (1–2)	1.9 (1.5–2.2)	0.002
Sodium (mEq/L), mean ± SD	133 ± 5.5	134 ± 6	130 ± 4	0.03
Prolactin levels (ng/mL), median (IQR)	29 (10–54)	17 (8–40)	54 (35–75)	<0.001
Elevated prolactin levels, *n* (%)	46 (55.4)	22 (41)	24 (80)	<0.001
CTP score, mean ± SD	10 ± 3.1	8.9 ± 3	11.7 ± 2.8	<0.001
MELD, mean ± SD	18.5 ± 8.4	15.9 ± 8	22.4 ± 8	<0.001
MELD-Na, mean ± SD	21.4 ± 8.7	18 ± 8	26.5 ± 7.4	<0.001
CLIF-C OF score, mean ± SD	8.2 ± 2.1	7.5 ± 1.8	9.5 ± 2.1	<0.001

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CLIF-C OF, chronic liver failure consortium organ failure; CTP, Child-Turcott-Pugh score; INR, international normalized ratio; IQR, interquartile range; MELD, model for end-stage liver disease; Na, sodium; SD, standard deviation. *Seven patients were lost to follow-up on day 90

Statistical Analysis

Continuous data were described as mean with standard deviation or median with interquartile range (IQR), depending on whether the data followed a parametric or nonparametric distribution. Continuous variables were analyzed using either the Student's *t*-test or the Mann–Whitney *U*-test, depending on the distribution of the data. Categorical variables were expressed as percentages and compared using the Chi-square test. Correlation analysis was performed to evaluate the relationship between severity scores and prolactin levels. The area under the receiver operating characteristic curves (AUROC) was calculated to assess the predictive accuracy of prolactin, Child-Pugh, MELD, MELD-Na, and CLIF-C OF scores. Additionally, sensitivity and specificity for the optimal cut-off values of these scoring systems and prolactin levels were determined. All statistical analyses were conducted at a 5% significance level, with a p-value < 0.05 was considered statistically significant. Data analysis was performed using Stata Statistical Software: Release 12 (StataCorp LP, College Station, Texas, USA).

Results

Demographic and Clinical Profile

Table 1 summarizes the baseline characteristics, biochemical parameters, and disease severity scores of the study participants. Among the 90 liver cirrhotic patients recruited, 74 (82%) were men. The mean age was 47.6 ± 11.6 years. Around 12% of participants were newly diagnosed with cirrhosis. The median duration of cirrhosis was 12 months. A significant proportion of participants (76%) reported alcohol consumption. Alcohol was the most common etiological factor, observed in 66 patients (73%), followed by nonalcoholic fatty liver disease (12.2%) and chronic viral hepatitis (10%) — with three cases of hepatitis B and six cases of hepatitis C. Jaundice was the most common presenting complaint seen in 80% of cases followed by abdominal distention (65%). Altered sensorium was found in 43% of cases. The most common clinical sign was icterus in 77 (85%) cases, followed by pallor (65%). Around 62% of patients had HE.

Among nonsurvivors, both total bilirubin and international normalized ratio (INR) (prothrombin time) were significantly elevated compared with survivors. In contrast, serum creatinine levels showed no significant difference between the two groups. Furthermore, nonsurvivors had notably lower serum albumin and sodium levels.

Mortality

Among the 90 patients, 14 expired by day 28 and 30 expired by day 90. Four patients were lost to follow-up on day 28 and seven patients on day 90. Table 1 compares various parameters among alive and deceased patients on day 90. No significant differences were noted in age or gender. Markers of severe liver dysfunction are significantly higher in nonsurvivors: Median bilirubin, INR, CTP, MELD, MELD-Na, and CLIF-C OF scores were all elevated in nonsurvivors. The proportion of patients having elevated prolactin levels was significantly higher in nonsurvivors [80 vs 41%, $p < 0.001$, odds ratio: 5.6 (2–16)].

Severity Assessment Using Various Scores

The mean CTP score was 10 ± 3.1. Among the 90 patients in the study, 49 patients (54.4%) belonged to CTP class C, 22 (24.4%) patients belonged to CTP class B, and the remaining 19 (21.1%) patients were in class A. The mean MELD and MELD-Na scores were 18.5 ± 8.4 and 21.4 ± 8.7, respectively. The mean CLIF-C OF score was 8.2 ± 2.

Severity Scores and Prolactin

The mean serum prolactin level of all patients was 34.6 ± 26.2 ng/mL. The mean prolactin levels for CTP classes A, B, and C were 10.9 ± 6.7, 20.2 ± 17.7, and 48.5 ± 24.4 ng/mL, respectively. Figure 2 is a scatter plot showing the relationship between prolactin levels and CTP score. The Spearman correlation coefficient was 0.73 (0.64–0.82), which shows a significant positive correlation. Similarly, to see the relationship of serum prolactin level with other severity scores, a correlation coefficient was calculated, which is shown in Tables 2 and 3. The correlation coefficient was 0.64 (0.52–0.77) for MELD, 0.67 (0.59–0.79) for MELD Na, and 0.82 (0.75–0.89) for CLIF-C OF score. The CLIF-C OF score had a higher correlation than the other scores.

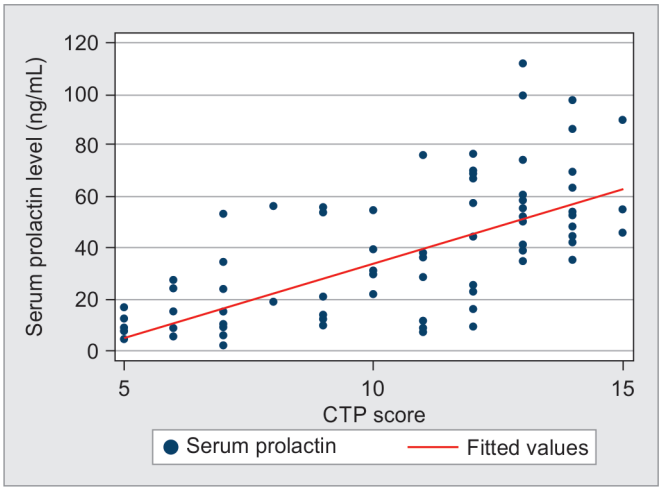


Fig. 2: Scatter plot between serum prolactin and CTP score

HE and Prolactin

Figure 3 is a box plot showing the comparison of prolactin levels in cirrhotic patients with different grades of HE. The mean prolactin level of cirrhotic patients without HE was 9.2 ± 3.4 ng/mL, whereas cirrhotic patients with HE grades I, II, III, and IV had 24.4 ± 4.7, 44.7 ± 12, 60 ± 21.3, and 73.3 ± 12.1 ng/mL, respectively. We observed a few outliers in HE grades III and IV, represented as dots. These dots indicate values that lie beyond 1.5 times the IQR above the third quartile.

Patients with Elevated vs Normal Prolactin Levels

Table 2 compares baseline characteristics, biochemical parameters, and disease severity of cirrhotic patients with elevated and normal prolactin levels. The criteria for elevated prolactin for

Table 3: Correlation coefficients of severity scores with prolactin levels

Variables	*Correlation coefficients (r)*	*r-square values*
CTP score	0.73 (0.64–0.82)	0.53
MELD score	0.64 (0.52–0.77)	0.41
MELD–Na score	0.67 (0.59–0.79)	0.45
CLIF–C OF score	0.82 (0.75–0.89)	0.67

CLIF-C OF, chronic liver failure consortium organ failure; CTP, Child-Turcott-Pugh score; MELD, model for end-stage liver disease; Na, sodium

Table 2: Comparison of baseline characteristics, biochemical parameters, and disease severity between patients with elevated prolactin and normal prolactin levels

Variables	*Total patients (n = 90)*	*Elevated prolactin (n = 52)*	*Normal prolactin (n = 38)*	*p-value*
Age (yrs), mean ± SD	47.6 ± 11.6	47.3 ± 10.8	48 ± 12.8	0.76
Gender – male, *n* (%)	74 (82)	49 (94)	25 (66)	0.002
Duration of cirrhosis (months), median (IQR)	12 (2–24)	12 (5–24)	10.5 (1–22)	0.88
Previous decompensation, *n* (%)	44 (49)	34 (66.6)	10 (26.3)	<0.001
Hepatic encephalopathy, *n* (%)	56 (62)	52 (100)	4 (11)	<0.001
Bilirubin (mg/dL), median (IQR)	3 (2–6.9)	6.2 (3–12.1)	1.6 (1–2.8)	<0.001
Creatinine (mg/dL), median (IQR)	1 (0.8–1.3)	1 (0.8–1.9)	1 (0.8–1.1)	0.03
INR, mean ± SD	1.7 ± 0.7	1.9 ± 0.75	1.3 ± 0.44	<0.001
Sodium (mEq/L), mean ± SD	133 ± 5.5	131 ± 5.7	135 ± 4.7	0.93
CTP score, mean ± SD	10 ± 3.1	11.9 ± 2.2	7.6 ± 2.3	<0.001
MELD, mean ± SD	18.5 ± 8.4	22.7 ± 8.3	12.6 ± 3.7	<0.001
MELD-Na, mean ± SD	21.4 ± 8.7	25.9 ± 8.0	15.2 ± 5.2	<0.001
CLIF-C OF score, mean ± SD	8.2 ± 2.1	9.4 ± 1.9	6.5 ± 0.83	<0.001
28-day mortality, *n* (%)	14 (15.5)	13 (27)	1 (2.6)	0.01
90-day mortality, *n* (%)	30 (33.3)	24 (52.1)	6 (16.2)	0.001

CLIF-C OF, chronic liver failure consortium organ failure; CTP, Child-Turcott-Pugh score; INR, international normalized ratio; IQR, interquartile range; MELD, model for end-stage liver disease; Na, sodium; SD, standard deviation

men and women were standard laboratory references provided by the manufacturer. The elevated prolactin group had a higher proportion of males (94.2 vs 65.7%). The history of the previous decompensation was significantly more prevalent in the elevated prolactin group. Bilirubin, INR, and creatinine levels were significantly elevated in the group with high prolactin. Additionally, CTP, MELD, MELD-Na, and CLIF-C OF scores were markedly higher in this group. A clear correlation was observed, with prolactin levels increasing in line with disease severity. Mortality rates were higher among the patients having elevated prolactin, for both 28-day and 90-day periods. The overall trend of worse outcomes with elevated prolactin was evident.

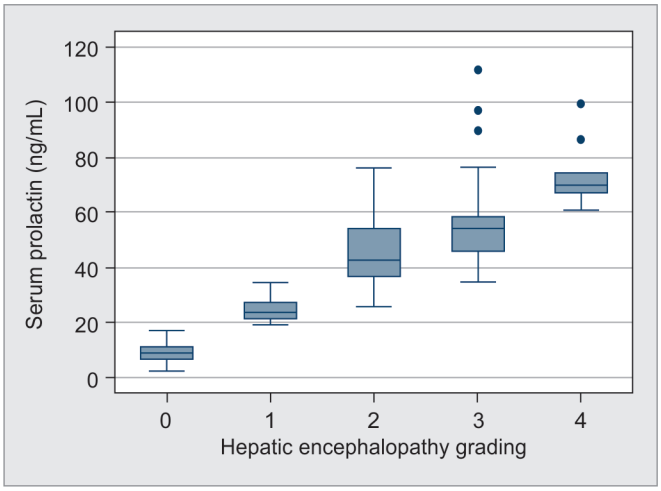


Fig. 3: Box–Whisker plot between serum prolactin and HE grades

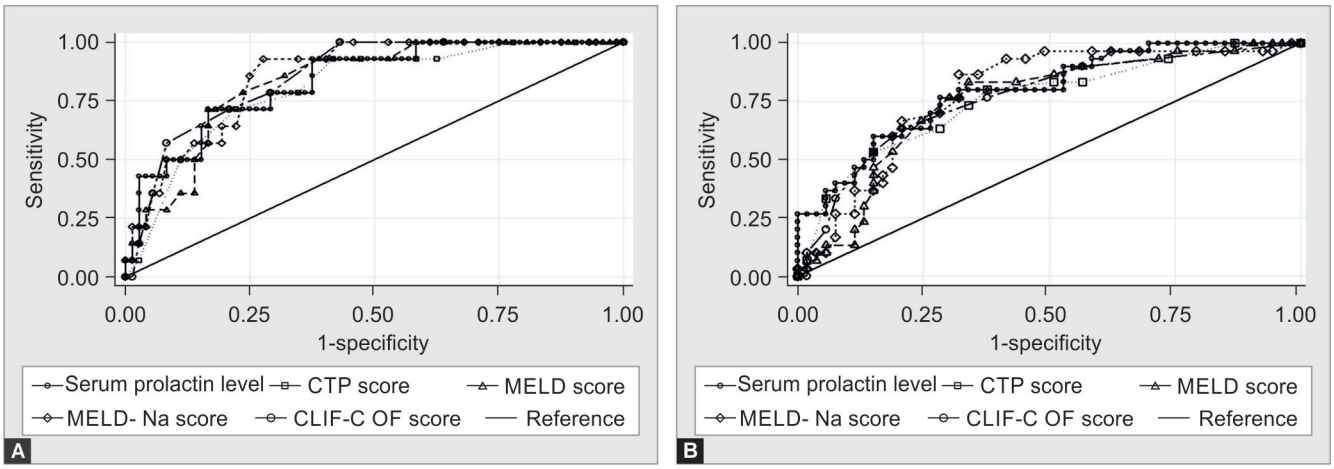
Prognostic Accuracy of Severity Scores and Prolactin

For calculating the prognostic accuracy of prolactin levels for 28-day and 90-day mortality, the AUROC was employed. Figure 4 shows that AUROC was 0.83 and 0.79 for mortality on days 28 and 90, respectively. AUROC of serum prolactin level was compared with that of all four severity scores for predicting mortality on days 28 and 90. Table 4 shows AUROC for serum prolactin and severity scores showing that all the scores are almost equal in predicting the mortality on days 28 and 90.

Cut-offs for predicting 28- and 90-day Mortality

Table 4 presents the cut-off values for various scores in predicting mortality on days 28 and 90. The cut–off of prolactin is 35.12 ng/mL for predicting mortality at 28 days, with a sensitivity of 93% and specificity of 63%. Except for the MELD score, all other scores and prolactin had a sensitivity of 93% or more for predicting mortality on day 28.

Whereas, for the same cut-off of serum prolactin level, the sensitivity and specificity were 77% and 72%, respectively, for mortality on day 90. The sensitivity values generally range from 77 to 87%, indicating a good ability to identify patients at risk of dying within 90 days. The CLIF-C OF score shows the opposite trend, with lower sensitivity (63%) but higher specificity (79%) compared with the 28-day analysis.



Figs 4A and B: The AUROCs of serum prolactin and different severity scores to predict: (A) 28-day mortality and (B) 90-day mortality

Table 4: Cut-off values for predicting 28-day and 90-day mortality

	28-day mortality				*90-day mortality*			
Variables	*AUROC (95% CI)*	*Cut-off*	*Sensitivity (%)*	*Specificity (%)*	*AUROC (95% CI)*	*Cut-off*	*Sensitivity (%)*	*Specificity (%)*
Prolactin	0.83 (0.72–0.94)	35.12	93	63	0.79 (0.69–0.89)	35.12	77	72
CTP	0.80 (0.69–0.92)	10.5	93	58	0.75 (0.65–0.87)	9.5	80	62
MELD	0.83 (0.73–0.93)	19.5	79	76	0.75 (0.64–0.86)	15.5	83	66
MELD-Na	0.85 (0.77–0.94)	23.5	93	72	0.78 (0.68–0.88)	20.5	87	68
CLIF-C OF	0.85 (0.76–0.94)	7.5	100	57	0.76 (0.65–0.87)	8.5	63	79

CI, confidence interval; CLIF-C OF, chronic liver failure consortium organ failure; CTP, Child-Turcott-Pugh score; MELD, model for end-stage liver disease; Na, sodium

Discussion

This study substantiates the role of serum prolactin as a biomarker for assessing the severity of liver cirrhosis and predicting short-term mortality. The findings demonstrate a clear relationship between elevated prolactin levels and the severity of liver dysfunction, as quantified by established clinical scoring systems (CTP, MELD, MELD-Na, and CLIF-C OF). These results are similar to the previous studies that have suggested hormonal dysregulation in cirrhosis, potentially due to impaired hepatic clearance of prolactin and systemic inflammatory responses.[8,9]

Several scoring methods are commonly utilized to assess the severity of cirrhosis. Child-Pugh score accurately forecasts short-term mortality in cirrhotic liver patients.[10] According to the CTP scoring system, the mortality risk at 1 year varies by class: it is 0% for class A, 20% for class B, and 55% for patients classified as class C.[14] The limitations of the CTP score include the reliance on subjective evaluations for grading ascites and encephalopathy, the exclusion of renal function in its assessment, and the limited range of scores (only 10 variations), which restricts the ability to distinguish between patients' wide range of disease severity effectively.[15]

The MELD score had a higher accuracy compared with the CTP score in predicting mortality at 90 days.[16] Despite its widespread use in liver transplantation prognosis, the MELD score has certain inherent limitations. Its dynamic nature leads to changes over time. The use of serum creatinine as a measure of renal function is not entirely accurate, as it is influenced by factors like muscle mass, gender, and ethnicity.[10] This score was revised by incorporating sodium, creating the MELD-Na score, and enhancing its mortality prediction capabilities.[11] The MELD-Na provided a more accurate prediction of mortality, particularly in those cirrhotic patients with hyponatremia. While it improves MELD's accuracy by incorporating serum sodium, it adds complexity to calculations and interpretation, and rapid changes in serum sodium levels might impact the score's predictive value.[17] Another study found that simpler scores like CTP and MELD were sufficient for assessing prognosis.[18]

The CLIF-C OF score was developed by modifying the Sequential Organ Failure score (SOFA score) and has been used for patients with cirrhosis.[12] It predominantly evaluates acute decompensation of cirrhosis and might not be as effective in chronic or stable cirrhosis situations. It is used in acute-on chronic liver failure to predict short-term mortality.[19]

These scores do not encompass the dynamic nature of liver cirrhosis. They might not adequately account for acute exacerbations or improvements in liver function over time, thereby limiting their predictive accuracy in certain clinical scenarios. In light of these limitations, the advent of serum prolactin as a serum marker to estimate the severity and prognosis of liver cirrhosis holds significant promise. It could offer objective and reproducible quantification of disease severity.

A study conducted by Sakhnani et al. investigated the association between serum prolactin levels and liver cirrhosis severity.[20] It was found that the more the CTP class the higher the serum prolactin levels. Compared with the mild HE (grades I and II) cases, the serum prolactin level was higher in severe HE (grades III and IV) cases. Cases of cirrhosis without encephalopathy exhibited a lower level than those with HE. In our study also, serum prolactin levels were positively correlated with both CTP class and HE grade.

Giri et al. assessed prolactin levels in patients with HE.[8] The prolactin level in cirrhosis cases with HE was higher than that in both cirrhotic patients without HE and normal healthy controls. In this cross-sectional study, an arbitrary cut-off of 50 ng/mL was kept for comparing statistical significance among cirrhotic patients with HE, cirrhotic patients without HE, and fulminant hepatic failure patients. The lack of laboratory-defined cut-offs separately for male and female patients might raise questions about the significance of the results. We followed the different cut-offs defined for men and women to determine the prolactin elevation.

Another study by Jha et al. explored prolactin levels in cirrhosis and viral hepatitis patients, with or without encephalopathy features, revealing elevated mortality rates among patients with cirrhosis and viral hepatitis exhibiting prolactin levels above a predefined threshold of 50 ng/mL. Lack of well-defined follow-up and putting acute liver failure patients in the same cohort as cirrhosis patients might limit the clinical applicability of the study findings. We estimated the predictive accuracy of serum prolactin levels for mortality on days 28 and 90 using AUROC. Furthermore, we identified the optimal cut-off value that has a balanced sensitivity and specificity, providing a clinically meaningful threshold for prognostic use.[21]

Balakrishnan and Rajeev found in their observational study on 60 cirrhotic patients that all the patients with HE ($n = 15$) had markedly elevated serum prolactin levels.[22] In our study, 93% (52/56) of HE patients had elevated prolactin levels. The correlation of prolactin levels with HE severity is particularly noteworthy. The progressive increase in prolactin levels across HE grades indicates a possible link between this hormone and the neuropsychiatric complications of liver disease.

Our study uniquely explored the correlation between serum prolactin levels and four different scoring systems used to evaluate liver cirrhosis severity. The study findings suggest that serum prolactin can serve as a valuable adjunct to traditional scoring systems in the clinical evaluation of cirrhosis. Its measurement is noninvasive, cost-effective, and provides objective data that can complement subjective clinical assessments. Given its high sensitivity in predicting short-term mortality, prolactin levels could be integrated into routine clinical practice for the stratification of patients, identifying those at higher risk of adverse outcomes and potentially guiding decisions regarding hospitalization and intensive monitoring. Moreover, the ability of prolactin to predict mortality on days 28 and 90 suggests its utility in short-term prognosis, which is crucial for timely intervention and resource allocation in clinical settings.

While the findings are promising, the study has certain limitations. It was a single-center study, which limits the generalizability of the results. Additionally, the sample size, although sufficient for preliminary analysis, could be expanded in future studies to enhance the robustness of the findings. The study also did not consider long-term outcomes beyond 90 days, which could provide a more comprehensive understanding of prolactin's prognostic value over extended periods.

Conclusion

This study shows that serum prolactin levels were markedly elevated in cirrhotic patients in the nonsurvivor group compared with survivors. Furthermore, elevated prolactin levels in cirrhotic patients

were associated with disease severity and short-term mortality. These findings support the potential role of prolactin as a noninvasive biomarker for assessing the severity of liver disease and predicting outcomes in cirrhotic patients. Incorporating prolactin measurement into clinical practice could enhance the precision of patient evaluation and facilitate more tailored therapeutic approaches.

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