Journal of Cardiovascular Disease Research

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

Comparison of Serum Prolactin Levels with Child Turcotte- Pugh Score for Prognosis in Chronic Liver Disease

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Abstract
Background: Liver cirrhosis and its complications are a leading cause of mortality and morbidity in most of the population. Individuals with Cirrhosis demonstrate 90% greater risk of hospitalization, prognostic criteria like the Child Pugh scoring system do not give us an idea of the probability of complications in a patient presenting with cirrhosis of the liver. So use of biomarker such as prolactin, indicate the severity of disease and its complication and serves as a tool for early intervention. The aim is to Compare Serum Prolactin Level with Child Turcotte-pugh Score for Prognosis in Chronic Liver Disease and establish that serum prolactin is an early marker for complication of cirrhosis if liver. **Material and Methods:** This was a Descriptive Observational study from July 2021 to August 2022 on 100 patients were admitted in TMMC&RC. **Results:** In the present study Mean age were 44±12.8 years. The ratio of male CLD patients were higher compared to females. Majority of respondents gives history of alcohol abuse, due to which high level of prolactin is found in them. Almost everyone shows clinical examination like clubbing, edema, pallor and cyanosis. Variables were in a normal range and significance association was found between patients of liver cirrhosis and the different parameters. When CPS test was done taking Age as variant the result came out to be not significant. Majority of patients lies in class B. While when done using occupation as variable, the value came out to be significant. Using ANOVA test, we found that in the Comparison Mean among CPS Class-A, B and C, Total Bilirubin, SGOT, Albumin were found to have significant ($P<0.05$) at 95% CI. Patients with cirrhosis and elevated prolactin levels have a poor prognosis. Class-A (Pugh-scores) have lower prolactin levels than patients with class-C (Pugh scores). **Conclusion:** Increased level of prolactin is seen in patients of liver cirrhosis and CPS is a prognostic factor in determining and classifying the patients into groups. Thus, prolactin levels not only aid in assessing disease severity, but also in predicting complications at an earlier stage of the disease process. Strong relationship have been discovered between the Child-Pugh score and serum PRL So High PRL level could therefore prove useful as a negative prognostic marker of liver cirrhosis.
Keywords: Cirrhosis, Prolactin, Chronic liver disease

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Introduction

Cirrhosis is a significant health concern that can lead to death and illness, which can be prevented.[1] "Cirrhosis" originated from the two greek words "Kirrhos" which means "tawny or orange," and "Osis" which means "condition".[2] It is highly prevalent all over the globe and can occur from a wide range of factors, including obesity, non-alcoholic fatty liver disease (NAFLD), alcohol, cholestasis, Hepatitis B, Hepatitis C, auto-immune diseases.[3] Splenomegaly, Cholestasis and Jaundice are some of side effects of liver cirrhosis, along with Portal hypertension (P-HTN), Spontaneous Bacterial Peritonitis, Porto-systemic Shunt, Ascites, bleeding from varices, haemorrhagic syndrome, hepatic encephalopathy and hepatocellular carcinoma (HCC).[4]

Early indications of cirrhosis include a loss of appetite, fatigue, and weakness, nausea, fever, or sudden weight loss. Other well-known cirrhosis symptoms, such as simple bleeding and bruising, begin to appear as liver function declines, and also results in Jaundice, rough skin, Edema (swelling) in ankles, feet, and legs, Ascites, change in urine and stools, confusion, brain fog, memory loss, and personality shifts, Blood vessels that resemble spiders that encircle tiny, red skin lesion, Loss of sex desire, gynecomastia, and shrinking testicles are all symptoms in men, and premature menopause in women.[5]

Cirrhosis patients frequently have severe, perhaps fatal side effects. Additionally, the illness is linked to decreased life quality, diminished ability to work, easy fatigability, incidence of minor hepatic encephalopathy, sexual dysfunction, and sleep difficulties.[6] It is now understood that altered secretion and feedback mechanisms are also part of the pathophysiology of disrupted hormonal function in liver cirrhosis. Prolactin is one such hormone in

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

this regard.[7] This hormone is produced by the pituitary which encourages breast development and production of milk in females. In Males, it was believed that prolactin has no known physiological role. PRL (short for Prolactin) is a polypeptide hormone that is composed of 199 amino acids. Its production and release are regulated by various factors within the hypothalamus, a region of the brain that plays a key role in the regulation of many bodily functions.[8]

With a clear nocturnal surge, prolactin production displays a pulsatile pattern. Cirrhosis has been observed to be associated with an increased 24-hour prolactin level as well as disruption of the normal circadian rhythm. Disruption of the normal circadian rhythm can have a range of negative impacts on overall health and well-being. High levels of PRL have been linked to an increased risk of hepatic encephalopathy and a worsening of liver disease. Several endocrine dysfunctions found in end-stage liver disease including changes in the hypothalamic pituitary-gonadal axis function and sex hormone levels in the blood. When examining the causes of gynecomastia, it was found that cirrhosis elevated production of Sex Hormone Binding Globulin (SHBG) and prolactin in liver, and that a higher levels of liver oestrogen receptors added to the direct suppression of oestrogen on Leydig cell functions. Prolactin levels were observed to be high in patients with hepatic encephalopathy complicating liver cirrhosis, low blood total T3, and high serum cortisol levels. These are warning signs of developing liver disease and hepatic encephalopathy. According Jha S. K. et al, 39 to 75% of cirrhotic patients had increased serum prolactin levels.[9,10]

Menstrual dysfunction, amenorrhea, galactorrhoea, infertility, hirsutism, and reduction in libido are all caused by an abnormally high level of serum PRL hormone in women, whereas erectile dysfunction and decreased libido are caused by an abnormally high level of secondary hypogonadism in men. Pregnancy, puerperium, and breast stimulation are all physiological causes of high PRL hormone levels. Tumours in pituatory, head trauma, hypothyroidism, brain surgery, chronic kidney diseases (CKD), Cushing's syndrome, Celiac, chronic liver disease (CLD) especially cirrhosis, and PCODs are all pathological causes.[11]

AIM

- To Compare Serum Prolactin Level with Child Turcotte-pugh Score for Prognosis in Chronic Liver Disease.

OBJECTIVES

- To identify patient of CLD
- To identify etiology of liver cirrhosis
- To measure the level of serum prolactin
- To compare serum prolactin level with disease severity using child pugh scoring
- To correlate serum prolactin with complications of CLD

Methodology

This was a Descriptive Observational study from July 2021 to August 2022 on 100 patients were admitted in Teerthanker Mahaveer Medical College & Research Centre, Moradabad as per inclusion and exclusion criteria.

Inclusion criteria

All the patient (age >18 years) with clinical/ biochemical/ radiological evidence of Chronic Liver Disease were included in the study.

Exclusion criteria

- History of any intracranial surgery/ irradiation
- Patients diagnosed with endocrinal disorders, pregnant and lactating women,
- Pituitary or hypothalamic disease history
- Herpes-zoster virus
- Chronic renal failure
- Prolactin levels in the patient are elevated by drugs such neuroleptics, metoclopramide, methyl dopa, reserpine, cyproterone acetate, morphine, cimetidine, and metiamide

Statistical Analysis: SPSS version 20.0 was used for all analyses. Mean and standard deviation were computed for quantitative data, and frequency and percentages were computed for qualitative data. The Independent T-test is used to compare Means, while the Chi-square test or Fixer Exact Test is used to establish the association between categorical variables. The significance level was set at 0.05, or 5%.

RESULTS

Table 1: Frequency distribution of case based on Age interval wise.

Age Interval	No of Cases	Percentage
21-30 Year	20	20.0

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

31-40 Year	21	21.0
41-50 Year	23	23.0
51-60 Year	22	22.0
>60 Year	14	14.0
Total	100	100.0

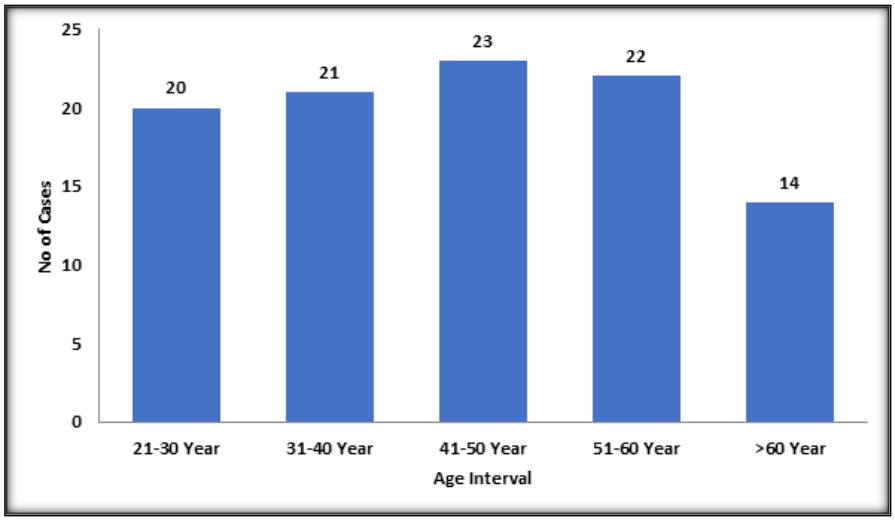

Figure 1: Frequency distribution of case based on Age interval wise.

[Table 1 and Figure 1] shows the frequency distribution of Age interval, where 20 subjects were found in 21-30 Year i.e. 20.0%, 21 subjects were found in 31-40 Year i.e. 21.0%, 23 subjects were found in 41-50 Year i.e. 23.0%, 22 subjects were found in 51-60 Year i.e. 22.0% and 14 subjects were found in >60 Year i.e. 14.0%

Table 2: frequency distribution of based on etiology.

	No of Cases N=100	**Percentage**
Alcohol	51	51.0
HBSAG+	12	12.0
HCV+	19	19.0
Other	18	18.0

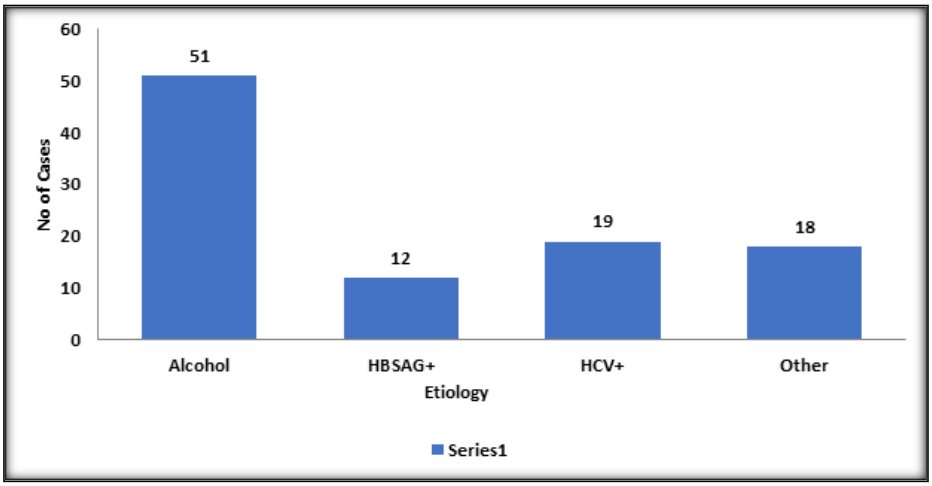

Figure 2: frequency distribution of based on etiology.

[Table 2 and Figure 2] shows the frequency distribution of Risk Factor, where no subjects were found in Diabetes i.e. 0.0%, 49 subjects were found in Alcohol i.e. 49.0%, 1 subjects were found in Tobacco i.e. 1.0%, 7 subjects were found in Student i.e. 7.0%.

Table 3: Comparison of prevalence among CPS Classes with variables.

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

Test Variable	CPS CLASS			P-Value
	A (Mean± SD)	B (Mean± SD)	C (Mean± SD)	
Pallor	5(9.3)	36(66.7)	13(24.1)	0.53
Icterus	0(0)	9(39.1)	14(60.9)	0.001
Edema	2(3.8)	34(64.2)	17(32.1)	0.24
Clubbing	Nil	Nil	Nil	--
Lymphadenopathy	Nil	Nil	Nil	--
Cyanosis	Nil	Nil	Nil	--
Hepatic flap	Nil	Nil	Nil	--
Gynecomastia	Nil	Nil	Nil	--
Spider naevi	Nil	Nil	Nil	--
Temperature	Nil	Nil	Nil	--

[Table 3] represent Comparison of prevalence among CPS Class-A, B and C. We ware found Pallor, Edema ware not found significant because p-value (>0.05). And Icterus ware found significant because (P < 0.05) at 95% CI.

Table 4: Comparison of prevalence among CPS Classes with variables.

		CPS CLASS			P-value
		CLASS-A	CLASS-B	CLASS-C	
Ascites		0(0)	34(66.7)	17(33.3)	0.012
Hepatic Encephalopathy		0(0)	1(14.3)	6(85.7)	0.01
Viral Marker	HBSAG+	0(0)	9(69.2)	4(30.8)	0.77
	HCV+	0(2)	69.2(13)	30.8(4)	
	Non-Reactive	2(10.5)	13(68.4)	4(21.1)	

[Table 4] represent Comparison of prevalence among CPS Class-A, B and C. We ware found Viral Marker ware not found significant because p-value (>0.05). And Ascites and Hepatic Encephalopathy ware found significant because p-value (<0.05) at 95% CI.

Table 5: Comparison of mean among CPS Classes with variables.

Test Variable	CPS CLASS			P-Value
	A (Mean± SD)	B (Mean± SD)	C (Mean± SD)	
S Prolactin	20.3±6.8	33.4±27.6	40.9±23.3	0.143

[Table 5] represent Comparison mean among CPS Class-A, B and C. We ware found S prolactin ware not found significant because p-value (>0.05). at 95% CI.

Table 6: Comparison of S Prolactin among CPS Classes with variables in male.

Male (S Prolactin)	CPS CLASS			P-value
	CLASS-A	CLASS-B	CLASS-C	
Normal	3(42.9)	13(19.7)	2(7.4)	0.780
Abnormal	4(57.1)	53(80.3)	25(92.6)	
Total	7(100)	66(100)	27(100)	

[Table 6] represent Comparison of S Prolactin among CPS Classes with variables in male. We ware found S Prolactin ware not found significant because p-value (>0.05).

Table 7: Comparison of S Prolactin among CPS Classes with variables in female.

Female (S Prolactin)	CPS CLASS			P-Value
	CLASS-A	CLASS-B	CLASS-C	
Normal	3(42.9)	18(27.3)	3(11.1)	0.120
Abnormal	4(57.1)	48(72.7)	24(88.9)	
Total	7(100)	66(100)	27(100)	

[Table 7] represent Comparison of S Prolactin among CPS Classes with variables in female. We ware found S Prolactin ware not found significant because p-value (>0.05).

Table 8: Comparison of mean among CPS Classes with variables.

Test Variable	CPS CLASS			P-Value
	A (Mean± SD)	B (Mean± SD)	C (Mean± SD)	

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

SGOT	39.9±12.2	52.2±20.5	91.2±58.2	0.001
SGPT	44±20.6	47.1±21.3	60.3±63.1	0.277
Albumin	2.7±0.7	2.5±0.4	2.3±0.4	0.023
S Prolactin	20.3±6.8	33.4±27.6	40.9±23.3	0.143
CPS Score	0.8±0.1	0.8±0.2	0.8±0.1	0.474
Na+ mmol/l	134.3±3.4	134.5±3.8	134.8±2.9	0.934
K+mmol/l	3.8±0.3	3.8±0.4	3.8±0.4	0.856

[Table 8] represent Comparison mean among CPS Class-A, B and C. We ware found SGPT, Sprolactin, SPS Score, Na+ mmol/l and K+mmol/l ware not found significant because p-value (>0.05). And SGOT and albumin ware found significant because p-value (<0.05) at 95% CI.

Table 9: Comparison of mean among CPS Classes with variables.

Test Variable	CPS CLASS			P-Value
	A (Mean± SD)	B (Mean± SD)	C (Mean± SD)	
Pulse	76.71±9.19	79.45±7.1	75.26±7.06	0.041
SBP	118.3±8	115.3±6.9	113.9±5.7	0.291
DBP	74.3±9.8	72.1±6.4	72.2±7.5	0.737
Spo2(%)	1±0	1±0	1±0	0.520
HB	8.9±1.3	9.2±1.4	9.2±1.6	0.865
TLC	8636.1±1699.8	7775.6±2421.2	8511.1±3424.8	0.409
MCV	84.8±8.8	90±7.4	90.9±11.9	0.268
Platelet Count	1.3±0.3	1±0.3	0.9±0.4	0.064
Total Bilirubin	1.4±0.6	1.7±1.1	5.3±3.6	0.001

Used ANOVA Test**

[Table 9] represent Comparison mean among CPS Class-A, B and C. We ware found SBP, DBP, HB, TLC, MCV, Platelet Count, Spo2 ware not found significant because p-value (>0.05). And pulse and Total Bilirubin ware found significant because p-value (<0.05) at 95% CI.

Table 10: Representation of Correlation between variables with CPR Score.

Correlations With CPS SCORE		Correlation Coefficient (r=)
Age	Pearson Correlation	0.005
	P-Value	0.960
SBP		-0.124
		0.219
DBP		-0.071
		0.481
Pulse		-0.130
		0.196
Spo2		0.053
		0.602
HB		0.033
		0.745
TLC		0.068
		0.500
MCV		0.075
		0.459
Platelet Count		-0.189
		0.060
Total Bilirubin		0.678**
		0.000
SGOT		0.496**
		0.000
SGPT		0.242*
		0.015
Albumin		-0.248*
		0.013
S Prolactin		0.195

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

		0.052
Na+ mmol/l		0.106
		0.295
K+mmol/l		-0.066
		0.516
Cr.mg/dl		-0.111
		0.270

[Table 10] Representation of Correlation between variables with CPR Score. We ware found weak positive correlation of age, HB, TLC, MCV, Spo2, Cr.mg/dl, SGPT, S Prolactin, Bilirubin, SGOT and Na+ mmol/l ware not found significant because p-value (>0.05) at 95% 95% CI. We ware found weak negative correlation of SBP DBP, Pulse, Platelet Count, K+mmol/l, Albumin ware not found significant because p-value (>0.05) at 95% confidence Interval.

DISCUSSION

Cirrhosis is a major cause of morbidity and mortality caused by excessive alcohol intake hepatitis, or NAFLD. It is frequently a dormant disease, with majority of patients remaining asymptomatic until decompensation occurs. Biochemical data and clinical symptoms were used to determine the presence of cirrhosis (Ascites or encephalopathy). The Child-Pugh prognostic index and PRL levels are also assessed. A higher chance of developing hepatic encephalopathy and a worsening of the severity of the condition are both associated with higher serum PRL levels. Hepatic encephalopathy and ascites are the most frequent side effects of liver cirrhosis and are associated with lower quality of life (QOL), an increased risk of infection, renal failure, and endocrine hormone disruption.[11,12]

Most of the attendees give past or present history of Alcohol consumption, therefore alcohol can be found as the major cause for liver cirrhosis, and people who consumes more alcohol, high prolactin levels are found in those respondents.[13] No significant association was found between diabetes and liver cirrhosis patients while smoking and tobacco play an acute role in this. Many clinical signs and symptoms like clubbing in 99% of patients, followed by Pallor and Oedema with 54% and 53% respectively, is seen among the cases. On other hand, interestingly no significant sign of Lymphadenopathy, cyanosis, Hepatic flap, Gynecomastia, spider naevi, or temperature is to be found in the present study.[14-18] The mean serum PRL in cases of alcoholic cirrhosis, however, is not significantly different from cases of non-alcoholic cirrhosis (46.629.4 ng/ml, $p > 0.05$), according to a study by Sakhnani D. R. et al 2021.[14]

Prolactin concentration in cirrhotic patients with HE was found to be greater than in patients without HE by Arafa M. et al. (2012). They also found that a cut-off value of >18.8 ng/dl could accurately predict cirrhotic patients' development of HE with an 88% sensitivity and a 90.3% specificity.[18] Serum prolactin levels PRL were higher in most cirrhotic patients with probable portal-systemic encephalopathy than in those without encephalopathy (P=0.05).[19,20] The clinico-biochemical severity of hepatic dysfunction was closely co-related to serum PRL. The study's authors, Nearly 17% of patients exhibited raised serum PRL, significantly higher Child-Pugh and MELD scores, ascites, and encephalopathy stage, according to Koller T. et al 2009 research.[19] In the study, we represent mean with standard deviation of variables, and found - Age (44.89), SBP (115.16) DBP (72.30), Pulse (9.181), HB (9.181), TLC (8034.41), MCV (89.887), Platelet Count (1.05), Spo2 (97.12%), Cr.mg/dl (2.63), Total Bilirubin (2.63), SGOT (61.87), SGPT (50.46), Albumin (2.475), S Prolactin (34.50), CPS Score (8.65), Na+ mmol/l (134.59) and K+mmol/l (3.830). Through these findings, we can indicate that the variables were in a normal range and significance association was found between patients of liver cirrhosis and the different parameters. A connection between serum PRL and serum bilirubin was shown to be statistically significant in a study by Jha S. K. & Kannan S. from 2016 (P=0.67, P = 0.04).

When represented occupation CPS wise as Class A, B and C the result came out to be significant at P-Value (<0.05) at 95% CI. Majority of the cases were employees who fall into class B, followed by housewife's and then farmers. This analysis was done using Fisher exact test. No employee fall into class A and only 2 students were found among all the cases who lies in class B. hence, from here it can be interpretated that occupation plays a vital role in cases of liver cirrhosis patients.[16]

Using ANOVA test, we found that Comparison Mean among CPS Class-A, B and C. We ware found age, SBP DBP, Pulse, HB, TLC, MCV, Platelet Count, Spo2, Cr.mg/dl, SGPT, S Prolactin, CPS Score, Na+ mmol/l and K+ mmol/l are found significant because (P<0.05) at 95% CI and Bilirubin, SGOT, Albumin ware found significant (P<0.05) at 95% CI. Child-Pugh score and prolactin level were discovered to have a statistically significant linked in a study by Punekar P. et al 2022 ($x2=12.2$, P=0.003). Age, albumin, creatinine, ascites, oesophageal varices, cirrhosis aetiology, or hepatic encephalopathy were not associated with prolactin levels. In a study published by authors Singh V. et al 2022 found that serum prolactin>19 was reported among 97.78% of the subjects having Child Pugh Score of 10-15. Similarly MELD score of 20-29 and ≥30 was found among 95.24% and 100% of the subjects having serum prolactin>19 respectively.[17] The study revealed that significant +ve

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

correlation was observed between prolactin level and Child Pugh as well as MELD scores i.e., with elevation in Child Pugh and MELD scores, serum prolactin level also increases. 12.5% and 75% of the subjects having PRL between 20-35 and 35-60 ng/ml respectively, suffered from deaths. We came to the conclusion that in cirrhosis patients, serum PRL can be employed as a prognostic diagnostic and an early indication of liver cirrhosis problems. Furthermore, prolactin levels not only aid in determining the severity of the disease, but also in predicting mortality.[15] Modified Child Pugh Class-C cases had statistically substantially higher mean serum PRLs than Class B (33.26, 7.41 ng/ml) and Class A (10.03, 4.01 ng/ml) cases.

CONCLUSION

Prolactin levels significantly associated with the severity of liver disease, showing the risk of complications, and aiding in their prevention. The Child Pugh Scoring system was used to assign the prolactin level increase, establishing its usage as a prognostic marker in cirrhosis. This study aimed to find that Serum Prolactin level with Child Turcotte-Pugh Score for Prognosis in CLD and with a well-structured questionnaire and in-depth research the conclusions obtained from the study was that Serum PRL are higher in male cirrhotic patients than in female cirrhotic patients.

Therefore, from the following findings one can easily conclude that an increased level of prolactin is seen in patients of liver cirrhosis and CPS is a prognostic factor in determining and classifying the patients into groups. Thus, prolactin levels not only aid in assessing disease severity, but also in predicting complications at an earlier stage of the disease process. Strong relationship have been discovered between the Child-Pugh score and serum PRL. However, CPS is a predictor of morbidity in people with liver cirrhosis, serum PRL can also be used as an indicator for high-risk patients whether they will develop complications or die from cirrhosis.

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