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# Correlation of serum prolactin level to child pugh scoring system and meld score in liver cirrhosis

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**Abstract**

**Aim:** To assess the relation between serum prolactin levels and the severity of the disease (assessed by the Child Pugh system and MELD Score) in patients with cirrhosis of the liver.

**Materials and Methods:** The cross sectional study was carried out in Chattrapati Shivaji Subharti Hospital, Meerut in the Department of Medicine. 100 cases with cirrhosis of the liver and/or its complications, with their full informed consent were included in the study. The patients underwent a detailed history including past, treatment and personal history to identify possible etiologies and a thorough clinical examination to identify the evidence of cirrhosis of the liver and the presence of its complications including portal hypertension and ascites. The patients were scored based on the modified Child Pugh and MELD scoring system

**Results:** It was 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. It was found that significant positive correlation was found between prolactin level and Child Pugh as well as MELD scores i.e. with increase in Child Pugh and MELD scores, serum prolactin level also increases. 12.5% and 75% of the subjects having serum prolactin levels between 20-35 and 35-60 ng/ml respectively, suffered from mortality.

**Conclusion:** We concluded that serum prolactin levels can be used as a useful prognostic marker in patients with cirrhosis of the liver as well as an early indicator of its complications. Also prolactin level not only helps in assessing the severity of the disease, it also helps in predicting the mortality.

**Keywords:** correlation, serum prolactin, scoring system

## Introduction

Liver cirrhosis has a high morbidity and mortality, which is the 14th most common cause of death all over the world. It leads to 1.03 million deaths per year in the world [1]. The prevalence of liver cirrhosis may be underestimated, because patients at the early phase of liver cirrhosis are often asymptomatic, and most of patients with liver cirrhosis are admitted due to its related complications. The 1-year mortality of liver cirrhosis varies greatly from 1% to 57% according to the complications [2]. It is necessary to use the prognostic models to identify high-risk patients.

Cirrhosis of the liver is associated with various disturbances of the endocrine system, thought to be caused mainly by ineffective elimination of hormones by the diseased liver. It is now known that the pathogenesis of disturbed hormonal function in liver cirrhosis is rather more complex involving altered secretion and feedback mechanisms as well [3].

One such hormone in this respect is prolactin. Human prolactin is currently viewed as a hormone of pituitary origin, whose production (i.e., serum levels) is controlled by dopamine and its biological actions relate exclusively to lactation and reproductive functions [4]. Prolactin levels in patients with hepatic dysfunction have been debated in detail.

Elevation of prolactin occurs mainly due to the drop in dopamine levels in the tuberoinfundibular tract. Oestrogens stimulate prolactin release by interfering with the dopamine secretion from the hypothalamus, and through a direct effect on the anterior pituitary [5]. Hence, the use of a biomarker such as prolactin, whose levels give us an idea about the severity of the disease and the possibility of complications, is a very vital tool in early intervention in such cases.

Child–Pugh score [6] was firstly proposed by Child and Turcotte to predict the operative risk in patients undergoing portosystemic shunt surgery for variceal bleeding. The primary version of Child–Pugh score included ascites, hepatic encephalopathy (HE), nutritional status, total bilirubin, and albumin. Child–Pugh score has been widely used to assess the severity of liver dysfunction in clinical work.

Model for end-stage liver disease (MELD) score was initially created to predict the survival of patients undergoing transjugular intrahepatic portosystemic shunts (TIPS) [7]. The primary version of MELD score included the etiology of liver cirrhosis, but this variable was unnecessary. The present version of MELD score incorporated 3 objective variables, including total bilirubin, creatinine, and INR [8].

Child–Pugh and MELD scores have been widely used to predict the outcomes of cirrhotic patients. However, they have some drawbacks. First, 2 variables (i.e., ascites and HE) included in Child–Pugh score are subjective and may be variable according to the physicians' judgment and the use of diuretics and lactulose. Second, INR, which is one component of both Child-Pugh and MELD scores, does not sufficiently reflect coagulopathy and consequently liver function in liver cirrhosis. Third, there is an interlaboratory variation in INR value [9].

The aim of this study was to assess the relation between serum prolactin levels and the severity of the disease (assessed by the Child Pugh system and MELD Score) in patients with cirrhosis of the liver as well as to establish that serum prolactin is an early marker for complications in a patient with cirrhosis of the liver.

## Materials and Methods

The cross sectional study was carried out in Chattrapati Shivaji Subharti Hospital, Meerut in the Department of Medicine. 100 cases with cirrhosis of the liver and/or its complications, with their full informed consent were included in the study.

The patients underwent a detailed history including past, treatment and personal history to identify possible etiologies and a thorough clinical examination to identify the evidence of cirrhosis of the liver and the presence of its complications including portal hypertension and ascites. All participants were told about the study and informed consent was taken. The subjects were recruited according to the following inclusion and exclusion criteria:

### Inclusion Criteria

1. Patients above the age of 18 years with diagnosis of liver cirrhosis and/or its complications who consented to participate in this study.

### Exclusion Criteria

1. History of cranial surgery/ irradiation
2. Patients with known bleeding disorders
3. History of pituitary or hypothalamic disease
4. Patients with established kidney disease with deranged renal function parameters (except hepatorenal syndrome)
5. All patients with ascites of etiology other than liver cirrhosis.
6. Patient on medications known to elevate prolactin levels such as neuroleptics, metoclopramide, methyldopa, reserpine, cyproterone acetate, aldosterone antagonists, morphine, cimetidine, metiamide.
7. Extreme of Age (>80yrs) and Moribund Patients.
8. Patients with Known Seizure Disorder.
9. Pregnant and Lactating Women.

### Investigations

Patients were subjected to the routine work up for chronic liver disease including:

- Complete blood counts, Urine Routine and Microscopy, Renal Function Test.
- Liver function tests including Coagulation profile
- Serum prolactin (Early morning)
- Ascitic fluid analysis for glucose, proteins, cytology, microbiological cultures
- Upper Gastrointestinal Endoscopy (if required)
- Ultrasound abdomen including echotexture and size of the liver, splenic enlargement and portal vein diameter.
- Hepatitis B Antigen (HBsAg) and anti Hepatitis C Virus (HCV) antibodies via ELISA method.

### The patients were scored based on the modified Child Pugh and MELD scoring system

### Methods

MELD incorporates 3 widely available laboratory variables including the international normalized ratio (INR), serum creatinine, and serum bilirubin. The original mathematical formula for MELD is: MELD=9.57*$\log_e$ (creatinine) + 3.78*$\text{Log}_e$ (total bilirubin) + 11.2*Loge (INR) + 6.43

MELD = MELD+1.32*(137-Na)-[0.033*MELD*(137-Na)

MELD score= 6to40

United Nation for Organ Sharing (UNOS) modification of original model.

1. Any value less than 1 is automatically given a lower limit value of 1 to prevent generating a negative score.
2. The lower limit of serum sodium (Na) is capped at 125, and the upper limit is at 137.
3. The upper limit of serum creatinine is capped at 4; in addition, if the patient had dialysis at least twice in the past week, the value for serum creatinine was automatically adjusted to 4.0.
4. The maximum MELD score is 40.

For the calculation of the Child-Pugh score, we applied the commonly used Pugh's modification. The sum of the scoring points from the five clinical parameters (ascites [none = one point, moderate = two points, severe = three points], serum bilirubin [<2 mg/dl = one point, 2–3 mg/dl = two points, >3 mg/dl =three points], albumin [>3.5 g/dl = one point, 2.8–3.5 g/dl = two points, <2.8 g/dl = three points], hepatic encephalopathy [absent = one point, grades 1 and 2 = two points, grades 3 and 4 = three points], and prothrombin index [>70%= one point, 40–70%= two points, <40%= three points]) corresponds to one of three groups of patients with different expected survival (Child-Pugh A = 5–6 points, Child-Pugh B = 7–9 points, Child-Pugh C = 10 or more points).

**Statistical analysis**

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 24.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using well as chi square test and the level of significance was set at $p < 0.05$.

**Results**

Out of 100 subjects, there were 77 males and 23 females. 6%, 17%, 64%, 9% and 4% of the subjects belonged to 21-30, 31-40, 41-50, 51-60 and >60 years of age group respectively. Hence maximum subjects were from the age group of 41-50 years (table 1).

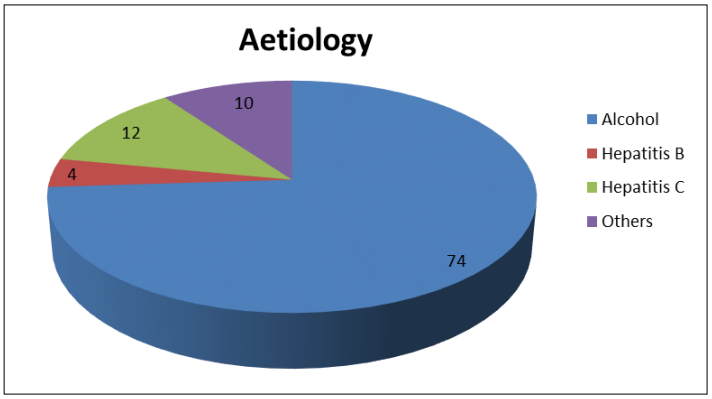
Most common etiology was alcohol (74%) followed by hepatitis C (12%). Hepatitis B was reported among 4% of the subjects (graph 1). In our study, Child Pugh scores were classified into Class A (5-7), Class B (7-9) and Class C (10-15) respectively. Class A (5-7), Class B (7-9) and Class C (10-15) was reported among 13%, 42% and 45% of the subjects respectively. MELD scores were classified into Group 1 (≤9), Group 2 (10-19), Group 3 (20-29) and Group 4 (≥30). Group 1 (≤9), Group 2 (10-19), Group 3 (20-29) and Group 4 (≥30) was revealed among 3%, 37%, 42% and 18% of the subjects respectively. Serum prolactin levels i.e. 3-19, 20-35 and 35-60 were reported among 31%, 48% and 21% of the subjects respectively (table 2).

It can be appreciated from the table 3 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. When Child Pugh and MELD scores was compared statistically according to serum prolactin level, it was found to be statistically significant as $p<0.05$ (table 3). It was found that significant positive correlation was found between prolactin level and Child Pugh as well as MELD scores i.e. with increase in Child Pugh and MELD scores, serum prolactin level also increases.

In our study, mortality was reported among 24% of the subjects. Mortality was not found in any of the subjects who were having 3-19 ng/ml. 12.5% and 75% of the subjects having serum prolactin levels between 20-35 and 35-60 ng/ml respectively, suffered from mortality. Hence chances of mortality increase with increase in serum prolactin level. When serum prolactin level was compared with the outcome, it was found to be statistically significant as $p<0.05$ (table 4).

**Table 1:** Gender and age distribution among the study subjects

| Gender | N | % |
|---|---|---|
| Male | 77 | 77 |
| Female | 23 | 23 |
| Age Group (in years) | | |
| 21-30 | 6 | 6 |
| 31-40 | 17 | 17 |
| 41-50 | 64 | 64 |
| 51-60 | 9 | 9 |
| >60 | 4 | 4 |
| Total | 100 | 100 |




**Graph 1:** Aetiology of cirrhosis among the study subjects

**Table 2:** Distribution of Child Pugh scores, MELD Scores and serum Prolactin levels among the study subjects

| Child Pugh Scores | N | % |
|---|---|---|
| Class A (5-7) | 13 | 13 |
| Class B (7-9) | 42 | 42 |
| Class C (10-15) | 45 | 45 |
| MELD Scores | | |
| Group 1 (≤9) | 3 | 3 |
| Group 2 (10-19) | 37 | 37 |
| Group 3 (20-29) | 42 | 42 |
| Group 4 (≥30) | 18 | 18 |
| Serum Prolactin Levels | | |
| 3-19 ng/ml | 31 | 31 |
| 20-35 ng/ml | 48 | 48 |
| 35-60 ng/ml | 21 | 21 |

**Table 3:** Distribution of prolactin level according to Child Pugh and MELD scores

| Variables | Serum Prolactin Levels (ng/ml) | | | | Chi Square | P value |
|---|---|---|---|---|---|---|
| | 3-19 (N=31) | | >19 (N=69) | | | |
| | N | % | N | % | | |
| Child Pugh Scores | | | | | | |
| Class A (5-7) | 12 | 92.31 | 1 | 7.69 | 19.26 | <0.01* |
| Class B (7-9) | 18 | 42.86 | 24 | 57.14 | | |
| Class C (10-15) | 1 | 2.22 | 44 | 97.78 | | |
| MELD Scores | | | | | | |
| Group 1 (≤9) | 3 | 100 | 0 | 0 | 23.71 | <0.01* |
| Group 2 (10-19) | 26 | 70.27 | 11 | 29.73 | | |
| Group 3 (20-29) | 2 | 4.76 | 40 | 95.24 | | |
| Group 4 (≥30) | 0 | 0 | 18 | 100 | | |

*: statistically significant

**Table 4:** Distribution of Serum prolactin levels among the study subjects according to mortality

| Serum Prolactin Levels | N | Mortality | |
|---|---|---|---|
| | | N=24 | % |
| 3-19 ng/ml | 31 | 0 | 0 |
| 20-35 ng/ml | 48 | 6 | 12.5 |
| 35-60 ng/ml | 21 | 18 | 75 |
| Chi Square | | 10.51 | |
| p value | | 0.002* | |

*: statistically significant

**Discussion**

Prolactin level in hepatic dysfunction is always controversial. Among the neurotransmitter alteration, the principal one to be documented was dopamine. Dopamine is limited by the fact that it cannot be measured in any of the body fluids or brain. Since dopamine exerts negative control over prolactin, few studies from the west have shown prolactin to be a prognostic marker [10].

This cross sectional study was carried out in Chattrapati Shivaji Subharti Hospital, Meerut in the Department of Medicine among 100 cases with cirrhosis of the liver and/or its complications, with their full informed consent were included in the study.

Out of 100 subjects, there were 77 males and 23 females. 6%, 17%, 64%, 9% and 4% of the subjects belonged to 21-30, 31-40, 41-50, 51-60 and >60 years of age group respectively. Hence maximum subjects were from the age group of 41-50 years in our study. A similar study on 70 patients by Velissaris D et al [11], showed a median (range) age in years of 56 (34-68) and male: female ratio of 2:1. Chaitanya H. Balakrishnan et al [10] in their study reported that 60 patients had a male to female ratio of 5:1 with the 75% of the patients in the age group of 40-50 years of age.

Class A (5-7), Class B (7-9) and Class C (10-15) was reported among 13%, 42% and 45% of the subjects respectively in our study. In a study by Chaitanya H. Balakrishnan et al [10], the Child Pugh class distribution in our study showed 10% belonging to Class A, 40% to Class B and 50% to Class C. According to Velissaris D et al [11], 34.3% patients with liver cirrhosis belonged to category A of Child Pugh classification, 22.9% were B and the remaining 42.9% were C type.

Serum prolactin levels i.e. 3-19, 20-35 and 35-60 was reported among 31%, 48% and 21% of the subjects respectively. 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. When Child Pugh and MELD scores was compared statistically according to serum prolactin level, it was found to be statistically significant as $p<0.05$. It was found that significant positive correlation was found between prolactin level and Child Pugh as well as MELD scores i.e. with increase in Child Pugh and MELD scores, serum prolactin level also increases.

Prolactin release in human beings is normally associated with a pulsatile pattern, but a constant 24 h elevation has been found in patients with cirrhosis liver. This was similar to the findings in a study done by Arafa M et al [12], who found that prolactin levels increased as the Child Pugh class increased from A to C. Zeitz B et al [13] revealed prolactin to be highest in patients with Child Pugh Class C. Similarly Chaitanya H. Balakrishnan et al [10] in their study showed that serum prolactin levels were elevated in 73.33% of the patients and higher prolactin levels were noted in patients with higher Child Pugh classes (B and C). McClain et al[51] and Sharma et al[44] observed a higher risk of mortality with serum prolactin values of >50 ng/ml. Mukherjee et al analyzed the prolactin levels in patients with hepatic cirrhosis and found a higher levels in both patients with encephalopathy and mortality. Also, the authors found out a direct correlation between the clinico-biochemical severities of the condition and mortality.

Model for End-stage Liver Disease (MELD) score was developed as a simple, and more objective hepatic score compared to Child-Pugh score. The MELD score accurately predicts short-term mortality on the liver transplant waiting list. The three variables included by this score, which are two hepatic (serum bilirubin and one international normalized ratio) and one renal (serum creatinine), highlight the prognostic significance of the interactions between liver and renal functions in cirrhotic patients. It is worth mentioning that since MELD score was introduced, increased utilization of combined kidney and liver transplants without a significant change in post-transplant survival has been reported [14].

In our study, mortality was reported among 24% of the subjects. Mortality was not found in any of the subjects who were having 3-19 ng/ml. 12.5% and 75% of the subjects having serum prolactin levels between 20-35 and 35-60 ng/ml respectively, suffered from mortality. Hence chances of mortality increase with increase in serum prolactin level with statistically significant difference as $p<0.05$. Similarly in a study by Chaitanya H. Balakrishnan et al [10], deaths were recorded in 17 of the 60 patients (28.33%) and it was observed that all 17 patients had elevated serum prolactin level. Thus prolactin level not only helps in assessing the severity of the disease, it also helps in predicting the mortality.

**Limitations**

This was a study done with a small sample size. There was no correlation established with the aetiology of the liver cirrhosis. The extent of prolactin elevation was not compared to the incidence of complications.

**Conclusion**

The study shows that serum prolactin levels in patients with cirrhosis of the liver can serve as a marker for the severity of the disease as it closely correlates with the Child Pugh and MELD scoring system. Hence, we conclude that serum prolactin levels can be used as a useful prognostic marker in patients with cirrhosis of the liver as well as an early indicator of its omplications. Also prolactin level not only helps in assessing the severity of the disease, it also helps in predicting the mortality.

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