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To Estimate The Level Of Serum Prolactin In Liver Cirrhosis And Its Correlation With Child Pugh Score

Dr. Abhiman Shetty B[1], Dr. Parvathi M[2], Dr. Hemanth Srivatsava Reddy Sanjamala[3]
Dr. Medha N Rao[4], Dr. Nirmala A C[5], Dr. Sanjana Lakshmisai Thimmannagari[6]
Department of General Medicine, Bangalore Medical College and Research Institute, Bangalore, karnataka, India

***Corresponding Author:**
Dr. Hemanth Srivatsava Reddy

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Abstract

Objective: Liver cirrhosis is the result of chronic liver injury and alcohol accounts for the majority of cases. In liver cirrhosis, hyperestrogenemia and increased prolactin levels are observed. The application of markers such as serum prolactin indicates the severity of liver dysfunction and helps in the early intervention of cases.

Methods: This is a Cross-Sectional study on 150 patients, confirmed with cirrhosis of the liver. Cirrhosis was confirmed clinically and was substantiated by radiological imaging. Serum Prolactin levels were estimated among all individuals and were compared with the Child-Pugh Score and complications of cirrhosis.

Results: The average Child-Pugh(C-P) score was 9.75±2.541. The average prolactin levels were 43.05 ±20.745 ng/ml. In statistical analysis, Prolactin levels showed a good correlation with the Child-Pugh score.

Conclusion: Serum prolactin can be used as an alternative marker as it's affordable, non-invasive, and correlates with the severity of cirrhosis.

Keywords: Child-Pugh Score, liver cirrhosis, Prolactin, Ascites

Introduction

Millions of people across the world are affected with liver dysfunction[1]. The Global Burden of Disease (GBD) said that about one million people lost their lives due to Liver failure in 2010[2].In this modern era, availability of liver transplant has stressed the need for accurate diagnosis and grading of the severity of liver dysfunction[3]. Cirrhosis is the end result of the fibrogenesis that occurs with chronic liver injury[4]. The etiology of cirrhosis ranges from congenital, toxic, infectious and metabolic causes[5]. Among these the most common etiological agent is alcohol followed by chronic hepatitis C and B infection, biliary disease and hemochromatosis[6]. Liver function tests (LFTs) are useful in the evaluation and treatment of patients with hepatic dysfunction. These include ALT, AST, alkaline phosphatase, bilirubin, albumin and prothrombin time[7].

Cirrhosis of the liver is associated with disturbances of the endocrine system, and it is caused mainly by ineffective elimination of hormones by the diseased liver. Prolactin is a polypeptide hormone, released from the cells of the anterior pituitary gland, the lactotrophs[8].Marked increase in serum prolactin levels in blood suggest that its activity may be specific indicator of liver dysfunction than other routine liver function tests[9].

Serum Prolactin levels demonstrate a strong correlation with serum albumin, Child Pugh score and the MELD score. The conventional tests used to assess the severity of cirrhosis are neither 100% sensitive nor specific .These serological markers are also raised in non-hepatic disease [10].

Methodology

Study Source: This Study was conducted on 150 Cirrhosis patients coming to Hospitals attached to

Bangalore Medical College and Research Institute, Bangalore. Written informed consent was taken from the patient after explaining the purpose and method of the study.

Method Of Collection Of Data:

1. Study Design: Cross sectional study
2. Period of study: November 2018 to May 2020
3. Place of study: Hospitals attached to BMCRI.
4. Sample size: 150

Inclusion Criteria:

1. Patients who have given consent for the study.
2. Patients of either sex aged 18 years and above.
3. Patients with Liver cirrhosis either radiologically or clinically in hospitals attached to BMCRI.

Exclusion Criteria:

1. Pregnancy and lactating women.
2. Patients with thyroid disorders
3. History of cranial surgery/irradiation.
4. Chronic renal failure
5. History of pituitary or hypothalamic disease.
6. Patient who are on medications/drugs which increase prolactin levels like antipsychotics,antiemetics, antihypertensives (Methyl dopa, Reserpine), aldosterone blockers and hormonal supplements.

Statistical Methods: Descriptive and inferential analysis of statistics was done on this present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are represented in Number (%). 5% level of significance is assessed.

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients.

Chi-square/ Fisher Exact test studies the significance between 2 or more groups. Fisher Exact test used as non-parametric test when cell samples are very small.

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of date in this study.

Sample Size Estimation

Based on the previous study conducted by Ramy A. Metwally et al. mean prolactin level were 18.76±9.14ng/ml.

The sample size calculation is as follows, using the formula. $\mathbf{N = Z^2\alpha\sigma^2/ d^2}$,Where Zα is the standard table value at 95% CI, $\mathbf{Z\alpha = 1.96}$, $\mathbf{\sigma = 9.14}$, **d = absolute precision = 1.5**

N = 143 ~ 150 = 150 patients of cirrhosis

Results

Comparison Of Serum Prolactin And Child Pugh Score

Table 1: Comparison of Serum Prolactin and Child Pugh Score

	Mean	Standard Deviation	Pearson correlation	p value
CP SCORE	9.75	2.541	0.790	0.0001
S. PROLACTIN	43.16	20.72		

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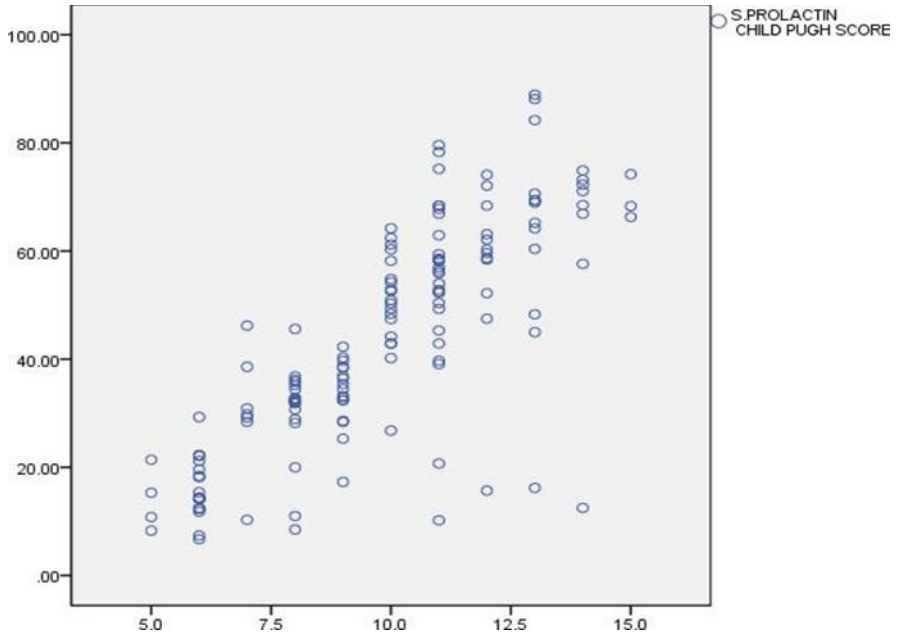
Figure 1: Scatter Diagram showing relationship between Serum Prolactin and Child pugh Score



Comparison Of Prolactin With Child Pugh Class

Table 2: Comparison of Prolactin with Child Pugh Class

C P score	N	S. Prolactin		Least value	Highest value	F score	p score
		Mean	Standard. Deviation				
A	24	15.25	5.28	7	29	124.43	0.0001
B	43	31.63	8.27	8	46		
C	83	57.00	15.73	10	89		

Comparison Of Serum Prolactin With Complications Of Cirrhosis

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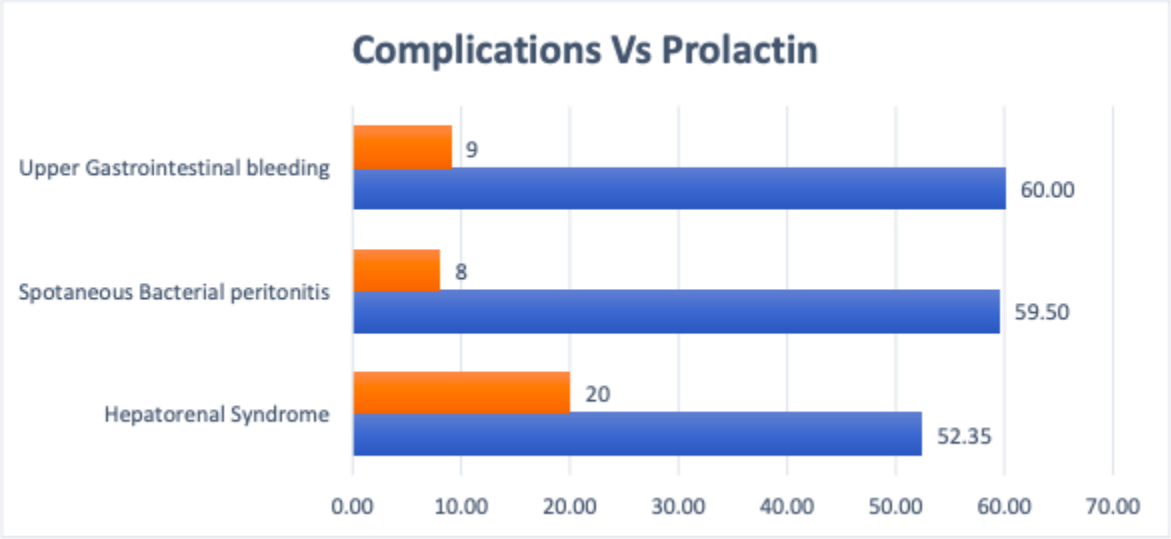
Table 3: Comparison of Serum Prolactin with Complications of Cirrhosis

Complications	Mean Prolactin level	Number of patients	Std. Deviation	F value	P value
Hepatorenal Syndrome	52.35	20	17.694	7.37	0.0001
Spontaneous Bacterial peritonitis	59.50	8	22.084		
Upper Gastrointestinal bleeding	60.00	9	11.790		

Figure 2: Prolactin levels with complication of Cirrhosis



Diagnostic Accuracy Of Serum Prolactin In Predicting Liver Cirrhosis Severity

Table 4: Table showing diagnostic accuracy of serum prolactin with severity of cirrhosis

Best cut -off point	**23.8ng/ml**
Sensitivity	**92.06**

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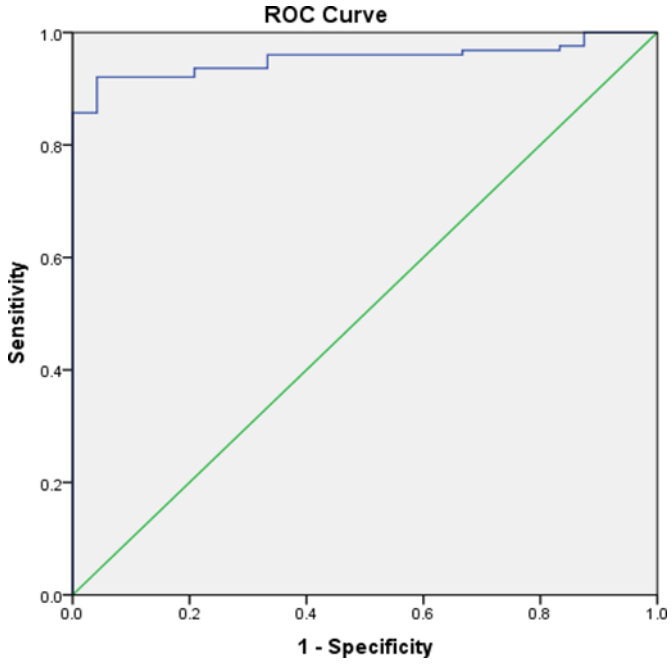
Specificity	**95.83**
Area Under curve	**0.953**

Figure 3: Receiver operating characteristics analysis of prolactin level as an indicator of severity of liver cirrhosis



Discussion

There is a pulsatile pattern of prolactin release in humans, but a continuous and constant increase in prolactin is found in the blood in patients with liver cirrhosis. The priniciple neurotransmitter altered was dopamine. Since dopamine has a negative effect on serum prolactin, many research projects showed prolactin to be a prognostic marker in liver cirrhosis.[17,18]. Serum Prolactin is increased in liver dysfunction due to ineffective elimination of hormones by the diseased liver. Circulating estrogens are elevated in cirrhosis which affects dopamine release and false neurotransmitter which is normally detoxified in the liver reach the central nervous system which affects dopamine release, both of which will increase the prolactin level in cirrhosis of liver [11,12]

Of the 150 patients enrolled, 125 were male, which accounts for 83.3% of cases and 25 were female, which accounted for 16.7% of cases. The bulk of patients fell into the age group of 41-50 years.

Of the 150 patients, 96 were alcoholics, and this is the most common etiology which accounts for about 64% of the cases. Etiological agents in the order of their incidence are Ethanol (64%), hepatitis B (12.7%), NASH (9.3%), hepatitis C (7.3%), Autoimmune (2.7%), Cryptogenic (2.7%) and Wilsons (1.3%).

Out of 150 patients, 83 cases belonged to Child Pugh Class C (55.3%), Class B about 43 (28.7%) cases and 24 (16.0%) patients to class A.

Out of 150 patients, ascites was absent in 14%, controlled in 72% and refractory in 14%. Prolactin levels were higher in individuals with refractory ascites as compared to patients with controlled and absent ascites with a significant p-value ($p<0.0001$), this was the same according to the study done by Dr. T.K Rajasekarapandian et al[16]

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The study shows a significant increase in serum prolactin with the severity of cirrhosis with a p-value <0.0001. The mean ± Standard Deviation of prolactin in this study was 43.05 ±20.745, this is in accordance with the study by Ramy a. Metwally et al [15], where the mean prolactin levels were 20.26±12.33

In this study, alcoholic status didn't correlate with prolactin levels (p - 0.062). Hence proving that Serum prolactin correlates with the severity of liver cirrhosis irrespective of the etiology. This study was in accordance with the study done by Chaitanya H. Balakrishnan et al[14]

Serum prolactin positively correlated with prothrombin time (r=0.338 and p=0.0001), Total bilirubin (r=0.947 and p=0.0001) and negatively correlated with albumin. These data were similar with Fawzy M. Khalil et al[13], in which prolactin level indicated the severity of cirrhosis.

Serum prolactin level and serum albumin showed statistically significant negative correlation, and this was consistent with Arafa et al. (2012)[19] study

The mean Prolactin values of Child Pugh class A, B and C are 15.2±5.2 ,31.63±8.2 and 57.0±15.731 respectively. The statistical results showed that there was good significance found between Child Pugh scores and Serum Prolactin (p – 0.0001). These is in accordance with study by Ramy a. Metwally et al,[15] where the patients with Child Pugh class A had a prolactin value 12.9±7.9, class B- 23.33±9.68 and class C- 24.51±19.05, which showed serum prolactin tend to increase significantly with increase in child Pugh scoring in cirrhosis of liver

Serum Prolactin level and liver cirrhosis severity, where r=0.790 and P=0.0001, showed significant positive correlation and This was similar with the study reported by Arafa et al,[19] where the level of elevation of Prolactin was associated with severity of liver disease from Child Pugh A to Child Pugh C progressively.

There was a highly significant positive correlation between serum Prolactin level and encephalopathy grades, with r=0.68 and P less than 0.0001. This is consistent with the study done by Arafa et al[19], that showed significantly increased serum level of Prolactin in patients with Hepatic Encephalopathy than patients without Hepatic Encephalopathy and correlated with severity of liver dysfunction.

Out of 150 patients, 20 patients had hepatorenal syndrome, 8 patients had spontaneous bacterial peritonitis, 9 patients had upper gastrointestinal bleeding. There was significant correlation of serum prolactin with complications of cirrhosis like hepatorenal syndrome, spontaneous bacterial peritonitis and upper gastrointestinal bleeding with F value of 7.37 and p value of 0.0001 and this was consistent with study done by Chaitanya H. Balakrishnan et al[14], which also showed prolactin levels are more in patients who have developed complications of cirrhosis.

Conclusion

The results of this study have demonstrated and proved that Serum Prolactin levels have a significant correlation with the Child Pughs grading system and thus with the severity of liver cirrhosis. It demonstrated a strong correlation with other serological markers of liver dysfunction like serum albumin, total bilirubin, Prothrombin time, INR. It also demonstrates that the incidence of complications in cirrhotic patients is directly correlated to the serum prolactin levels.

Serum prolactin is not altered by treatment in cirrhosis of the liver. The use of prolactin with other liver function tests will help in the accurate detection, management and prevention of complications in cirrhotic patients.

So, we can infer that Serum Prolactin is an affordable, objective, and non-invasive marker which can be used for both diagnostic and prognostic purposes.

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