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### RESEARCH ARTICLE

#### CLINICAL PROFILE AND EVALUATION OF SERUM PROLACTIN LEVEL IN CIRRHOSIS OF LIVER WITH SPECIAL REFERENCE TO CHILD PUGH SCORE

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#### Abstract

Clinical profile and evaluation of serum prolactin level in cirrhosis of liver with special reference to Child Pugh Score. Abstract Background: With the increasing incidence of liver cirrhosis the use of a biomarker such as prolactin, indicates the severity of the disease, its complications and serves as a tool for early intervention. Aim: To study the clinical profile and evaluation of serum Prolactin level in Cirrhosis of Liver with special reference to Child Pugh Score. Materials and Methods: A observational cross sectional study on 70 patients admitted under Department of Medicine, JMCH from July 2020 to June 2021. All the patients are subjected to the routine work up for chronic liver disease including serum prolactin level. Results: A total of 70 Patients analyzed in the study. The mean age is found to be 47 years with SD  $\pm$ 13 years, the male and female ratio is 4:1 with mean prolactin levels among the males, it is 36.9 ng/dl with SD  $\pm$ 15.3 ng/dl and in females it is 42.8 ng/dl with SD  $\pm$ 14.2 ng/dl . Of the 70 patients in this study, 59 (84.3%) of them had serum prolactin levels elevated above 19 ng/ml with various clinical profiles . The various clinical presentations noted in our study included ascites in 69 (98.5%) patients, portal hypertension in 63( 90 %) of the patients , oesophageal varices in 44 (62.85%) with upper GI bleed in 31 (44.3%) patients, hepatic encephalopathy (grades 1-4) in 50 (71.42%) patients. Out of 70 patients 55(78.5%) were of class C in child pugh score and the mean prolactin level is found to be 43.638 ng/ml while normal serum prolactin levels is seen in all patients with Class A of Child Pugh Class with p value < 0.001 . The Spearman coefficient value i.e. the r-value was 0.830 which is a strong positive correlation between the child pugh scoring system and serum prolactin level. Conclusion: Serum prolactin level correlated with the Child Pugh score in predicting the severity of the disease. Patients with a higher serum prolactin have a greater incidence of complications of cirrhosis like PHTN, HE and Esophageal varices.

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## Introduction:-

According to WHO, about 46% of global diseases and 59% of the mortality is because of chronic diseases and almost 35 million people in the world die of chronic diseases. Liver disease rates are steadily increasing over the years. Global prevalence of cirrhosis studies ranges from 4.5% to 9.5% of the general population<sup>1</sup>. Epidemiology of Liver Cirrhosis suggests that although Hepatitis B and C are still common in developing countries, alcohol related cirrhosis is increasing. Rising trends in alcohol consumption in North East India, makes it essential to analyze the influence of these changes in the epidemiology of liver cirrhosis.<sup>2</sup> Cirrhosis is typically classified as compensated or decompensated, based on the absence or presence (or previous history) of variceal bleeding, ascites, jaundice or encephalopathy<sup>3</sup>. The significantly longer survival, usually symptomless, and better quality of life experienced by patients with compensated cirrhosis compared to those with decompensated cirrhosis, has brought about the concept that compensated and decompensated cirrhosis are distinct clinical states of the disease<sup>4,5</sup>.

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<sup>6</sup>. 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<sup>7</sup>. 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<sup>8</sup>. Prolactin secretion is mainly regulated by tonic hypothalamic inhibition through dopamine and the stimulatory influences of hypothalamic releasing factors and circulating oestrogens. Circulating oestrogens are elevated in liver cirrhosis due to an increased peripheral aromatization of testosterone via androstenedione and to a lesser extent through a decreased elimination by the liver<sup>9-12</sup>. These oestrogens stimulate prolactin release by interfering with the dopamine secretion from the hypothalamus, and through a direct effect on the anterior pituitary<sup>9</sup>.

Decompensated liver function leads to a change in the type of amino acids entering the central nervous system. Circulating concentrations of aromatic amino acids have been found to increase leading to an increase in the synthesis of false neurotransmitters such as octopamine and phenylethanolamine<sup>13</sup>. These false neurotransmitters inhibit the dopamine release contributing to hyperprolactinemia<sup>14</sup>. This study was undertaken with the aim to study the prolactin level as a biomarker in cirrhosis patients and determine its association with the severity of disease based on Child Pugh Scores.

## Materials And Methods:-

It was a Observational Cross Sectional Study conducted in the Department of Medicine, Jorhat Medical College and Hospital (JMCH), Jorhat for a period of one year i.e. 1<sup>st</sup> July 2020 – 30<sup>th</sup> June 2021. About 70 patients were studied during this period of study. Consecutive sampling was done, cases were selected taking into account both inclusion and exclusion criteria.

### Inclusion criteria:

Patients with Cirrhosis of liver admitted in medicine department, JMCH. Patients who gave informed consent for the Study. Both the sexes were included

### Exclusion Criteria

History of cranial surgery, chest wall trauma, Endocrine diseases or hormonal disorders, medications that causes Hyperprolactinemia, viral hepatitis and pregnancy are excluded. **Ethical Permission** obtained from Institutional Ethics Committee(H), Jorhat Medical College And Hospital. **Written informed consent** which is validated in the local language obtained from the participants prior to collection of data. Data have been collected in a pre-designed, pre tested structured Proforma - 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, ascites, and hepatic encephalopathy. Patients were subjected to the routine work up for chronic liver disease in the Central Clinical Laboratory, JMCH

The collected data were summarized in terms of mean  $\pm$  Standard Deviation (SD) and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the different clinical features and serum prolactin level along with Child Pugh Score were carried out using the Chi-square test ( $\chi^2$ ), Fisher's Exact Test

(FET) and Spearman correlation coefficient to compare proportions as appropriate and scatter diagram has been established. Statistical significance was taken as  $P < 0.05$ . The data was analyzed using SPSS version 21 and or Microsoft Excel 2021.

**Results And Observations:-**

During the study period in one year (2020 -2021), those who met the inclusion and exclusion criteria were included in the study. A total of 70 Patients analyzed in the study. The mean age is found to be  $47 \pm 13$  years SD, the male and female ratio is 4:1 with mean prolactin levels among the males , it is 36.9 ng/dl with SD  $\pm 15.3$  ng/dl and in females it is 42.8 ng/dl with SD  $\pm 14.2$  ng/dl .

Of the 70 patients in this study, 59 (84.3%) of them had serum prolactin levels elevated above 19 ng/ml with various clinical profiles. The various clinical presentations noted in our study included ascites in 69 (98.5%) patients, portal hypertension in 63 (90 %) of the patients, oesophageal varices in 44 (62.85%) with upper GI bleed in 31 (44.3%) patients, hepatic encephalopathy (grades 1-4) in 50 (71.42%) patients. The mean prolactin level is found to be raised more than the normal value among all the clinical profile as shown in table 1.

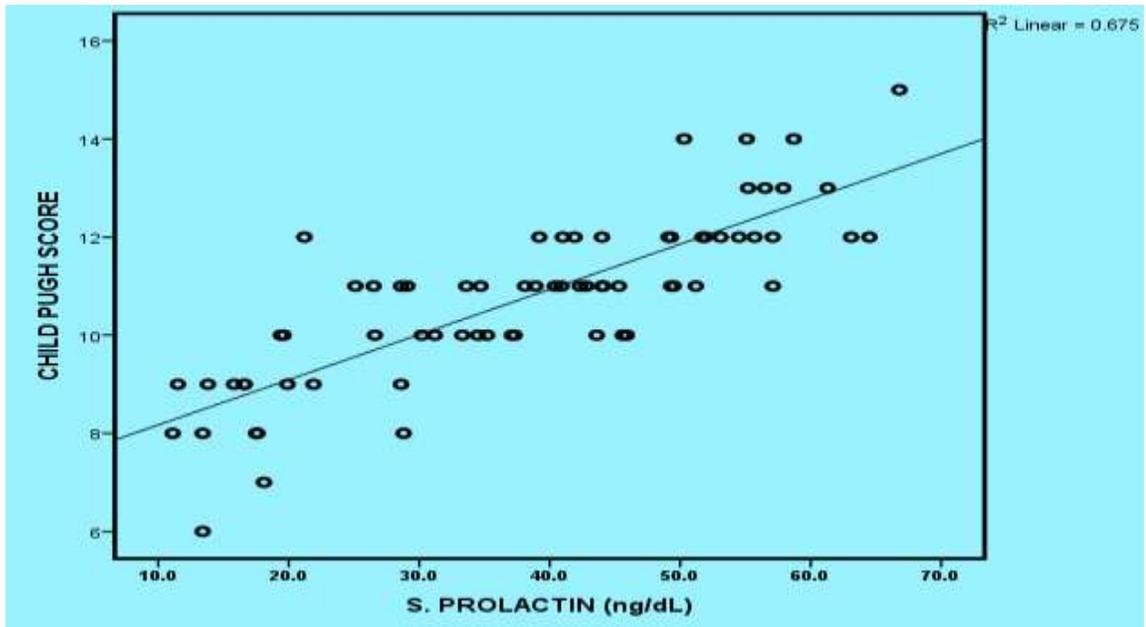
Cirrhosis with various complications	Frequency	Mean Prolactin level (ng/dl)	Standard Deviation
Ascites	69(98.7%)	32.61	$\pm 4.36$
Portal hypertension	63(90%)	38.51	$\pm 6.25$
Oesophagial Varices	44(62.85%)	38.836	$\pm 9.32$
Hepatic encephalopathy	50(71.42%)	41.6	$\pm 6.35$

**Table 1:-** Showing the prolactin level in cirrhosis patients with various complications or presentations.

Out of 70 patients 55(78.5%) were of class C in child pugh score and the mean prolactin level is found to be 43.638 ng/ml while normal serum prolactin levels is seen in all patients with Class A of Child Pugh Class with p value  $< 0.001$  as shown in table 2 .

CHILD PUGH SCORE	N	Mean S. PROLACTIN (ng/dL)	Standard Deviation	p value
A	1	13.4		$<0.001$
B	14	17.943	$\pm 5.4463$	
C	55	43.638	$\pm 11.8725$	

**Table 2:-** Showing the p value along with child pugh class and the prolactin level.



**Fig 1:-** Scatter diagram showing linear distribution of Child Pugh Score And S. Prolactin Level.

The **Spearman coefficient value** i.e. the **r-value** was 0.830 which is a strong positive correlation between the child pugh scoring system and serum prolactin level and the **p-value** was less than 0.001.

### Discussion:-

The present study is a cross sectional study based on clinical profile and evaluation of serum prolactin level in cirrhosis of liver with special reference to child pugh score of 70 patients. The study was undertaken to compare the efficacy of serum prolactin level with the child pugh scoring system. In this section an effort has been undertaken to discuss the present study and to find out its correlation with the studies of previous researchers who had undertaken similar types of study .

The present study the mean age of the patients is found to be 47 years with standard deviation 13 years. A similar trend was seen in the studies conducted by Paul SB et al in 2007<sup>15</sup> and Chaitanya H et al in 2017<sup>16</sup>, the finding of these studies shows that most of the patients were above 45 years of age. Another study done among multiracial Asian population by Qua CS et al among 460 patients showed a mean age of 58.8 yrs range (15-87 yrs)<sup>17</sup>. When cirrhosis occurs at a young age, it causes prolonged morbidity. Earlier reports from the West, reported that younger age group (<35yrs) consisted <5% of the cirrhotics<sup>18</sup>.

In the present study out of 70 studies the male and female ratio is 4:1 with mean prolactin levels among the males, it is 36.9 ng/dl with SD 15.3 ng/dl and in females it is 42.8 ng/dl with SD 14.2 ng/dl. This difference is due to high incidence of ethanol intake among men compared to women, which is the major etiology of chronic liver disease and also due to differences in the medical care seeking practice among both sexes. Similar to findings noted in a study by Pathak O.K et al 2009, where 80.7% among 181 patients were males<sup>19</sup>. Higher incidence was also reported by Paul SB et al 2007 with a M: F ratio of 6.1:1, among cirrhotics<sup>20</sup>.

Of the 70 patients in this study, 59 (84.3%) of them had serum prolactin levels elevated above 19 ng/ml. Similar study by Als-Nielsen et al., 2003 shows increase in prolactin level in decompensated cirrhosis<sup>21</sup>. Most patients present late with advanced disease with various clinical presentation. The complications of cirrhosis noted in our study included ascites in 69 (98.5%) patients, portal hypertension in 63( 90 %) of the patients, oesophageal varices in 44 (62.85%) with upper GI bleed in 31 (44.3%) patients, hepatic encephalopathy (grades 1-4) in 50 (71.42%) patients. Ascites, UGI bleeding, jaundice and encephalopathy were the commonest presentation in our study. Ascites and upper GI bleeding was the commonest complications in other studies too; Maskey R et al 2011 (ascites 84.4% and Upper GI bleeding in 35.5%)<sup>22</sup> and Md Shahid Aziz et al 2009; (Ascites 53.8% and upper GI bleed 25.1%) too had similar findings<sup>23</sup>. Complications noted in our study population were similar to those observed in many other studies like Hamzullah Khan et al 2006<sup>24</sup> that also showed ascites in 27.86 %, variceal bleeding in 18.03% .In another small study by Hajiani et al, ascites was present in 32%, acute variceal haemorrhage was seen in 8%, HE in 1% and HCC in 6% of patients<sup>25</sup>.

In the present study all the 69 patients who were presented with ascites had raised serum prolactin levels. The mean serum prolactin level in mild ascites patients were found to 22. 1 ng/dl followed by 39.398 ng/dl and 36.34ng/dl among the patients with moderate and severe ascites respectively. The 63 (90%) patients who suffered from portal hypertension also had an elevated level of mean serum prolactin which is 38.51ng/dl. Again, elevated mean serum prolactin level (38.836%) was observed among 44 out of 70 patients with esophageal varices and 31 patients of which developed upper GI bleeding. Highest mean serum prolactin level (41.6ng/dl) was observed among the 50(71.42%) patients with hepatic encephalopathy with proportionately raising trend along with various grade of hepatic encephalopathy.

Based on the Child Pugh classification, 70 patients were divided into three Classes – A (score of 5-7), B (score of 7-9) and C (score 10-15). In this study, 1 (1.4%) patients were Class A, 14(20%) patients were Class B and 55 (78.6%) belonged to Class C. When compared to the study by Velissaris D et al., where 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<sup>26</sup>. Highest levels of serum prolactin (value >35 ng/ml) were seen in patients of Class C of Child Pugh class where the mean S. prolactin level is 43.638 ng/dl, while normal serum prolactin levels were seen in all patients with Class A of Child Pugh Class. The 65 patients with elevated serum prolactin in the present study; it was also noted that patients with a serum prolactin level above 35 ng/ml all belonged to Child Pugh Class C. The Spearman coefficient value i.e. the **r-value** was 0.830 which is a moderate positive correlation and the **p-value** was less than 0.001. This was similar to

the findings in a study done by Arafa M et al. who found that prolactin levels increased as the Child Pugh class increased from A to C<sup>26</sup>.

### Limitations

This was a study done in a single centre with a small Sample size and has been affected by Covid Pandemic and crisis, within short duration. There were few confounding factors, which may lead to rise in the S. prolactin levels, however we have attempted to exclude as many as of these factors possible.

### Conclusion:-

Patients with a higher serum prolactin at admission had a greater incidence of complications of cirrhosis. Thus, serum prolactin is an inexpensive, non invasive blood marker which probably can be used for estimating the severity and the complications of cirrhosis. However the sample size of this study was relatively small, therefore further studies with a large sample size will be helpful to draw more specific results or conclusions.

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