Section: Medicine

Original Research Article

SERUM PROLACTIN: A POSSIBLE NEW MARKER FOR SEVERITY OF HEPATIC ENCEPHALOPATHY IN CHRONIC LIVER DISEASE PATIENTS

Madhavi Sarkari[1] Varun Singh[2], Ajeet Pratap Singh[3]

[1]Professor and Head, Department of Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India
[2]Junior Resident, Department of Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India
[3]Associate Professor, Department of Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India

Received : 08/09/2024
Received in revised form : 28/10/2024
Accepted : 13/11/2024

Keywords:
Prolactin; Hepatic encephalopathy; Child Pugh Turcotte score; Chronic liver disease; Mortality.

Corresponding Author:
Dr. Varun Singh,
Email: harshit95varun@gmail.com

DOI: 10.47009/jamp.2024.6.6.14

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 65-71

Abstract

Background: Hepatic encephalopathy is a syndrome commonly found in patients with chronic liver disease, complicating the disease course and attributing to significant mortality. It is a neurocognitive disorder characterised by impaired brain function resulting in alteration in consciousness, personality changes and variable neurological signs. Given its public health burden, investigations into novel approaches for assessing disease severity and prognosis are warranted. The present study aimed to assess serum prolactin levels in hepatic encephalopathy patients with chronic liver disease and find out its prognostic implications. **Materials and Methods:** This observational study was conducted over three months(July to September 2024) in the Department of Medicine of BRD Medical College, Gorakhpur. 200 patients with confirmed &/or suspected diagnosis of chronic liver disease were selected and serum prolactin levels at time of admission were estimated and modified Child Pugh Turcotte(CPT) score calculated for each study participant. Hepatic encephalopathy was diagnosed and graded as per the West Haven criteria. Chi-square test was used for significance and Pearson's correlation coefficient to assess the correlation between variables. **Result:** The mean age of the study participants was 47.71±13.81 years. Serum prolactin levels were comparable between males and females presenting in same grade of HE. Ethanol induced CLD accounted for the maximum number of cases(69%) of HE and highest mean prolactin levels (90.14±62.20 ng/ml) among all other etiologies. Statistically significant association($p<0.001$) was found between prolactin levels and ascites status. Serum prolactin levels showed statistically significant positive correlation with CPT class($r=0.67$, $p<0.001$) and HE grading($r=0.21$. $p<0.002$). 93% patients improved and were discharged while 11% expired during course of hospital treatment. Statistically significant association was found between prolactin levels and in hospital mortality. **Conclusion:** Serum prolactin levels increase as severity of disease worsens in chronic liver disease patients with hepatic encephalopathy. Hence, we conclude that serum prolactin levels can be a useful surrogate prognostic marker.

INTRODUCTION

Hepatic encephalopathy (HE) is a syndrome commonly observed in patients with chronic liver disease (CLD). It is characterized by a spectrum of neuropsychiatric abnormalities resulting from liver dysfunction, once other brain diseases have been ruled out.[1] HE typically involves disturbances in consciousness and behaviour, fluctuating neurological signs, personality changes, asterixis (flapping tremors), and distinctive EEG abnormalities.[2]

While the exact pathophysiological mechanisms behind hepatic encephalopathy (HE) remain unclear, it is believed to involve neurotransmission defects rather than a primary deficiency in cerebral energy metabolism.[3] The diagnosis of overt HE is based on clinical examination. Symptoms of overt HE are reported in approximately 30-45% of patients with CLD and 10-50% of those with trans jugular intrahepatic portosystemic shunts.[4] According to previous studies, hyperammonaemia is a primary factor contributing to brain-related abnormalities in hepatic encephalopathy.[5] Various mechanisms have been proposed to explain how ammonia affects the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

central nervous system (CNS), including interactions between brain endothelium and astrocytes, alterations in transport across the blood-brain barrier, changes in energy metabolism, direct neurotoxic effects on astrocytes and neuronal membranes, and disruptions in glutamatergic neurotransmission due to reduced free glutamate production.[6] Among neurotransmitters, dopamine has been particularly noted, but its use is restricted by the fact that it cannot be determined in body fluids or brain tissue. Since dopamine negatively regulates prolactin, some studies suggest that prolactin may serve as a surrogate predictive marker for HE.[7]

With the increasing incidence of CLD, particularly in the Indian subcontinent, relying on diagnostic or prognostic scores and indices which need multiple variables and investigations may not be feasible in resource limited settings. Considering the void in this subject from an Indian context, this study was undertaken to evaluate serum prolactin levels in chronic liver disease patients with hepatic encephalopathy.

MATERIALS AND METHODS

This hospital based prospective observational study was conducted in the Department of Medicine, BRD Medical College, Gorakhpur from July 2024 to September 2024 on 200 patients. Ethical approval was sought from the IEC of BRD Medical College before study commencement. Patients of age > 18 yrs of either gender with confirmed/suspected diagnosis of chronic liver disease were included in this study. Pregnant and/or lactating women, patients with chronic renal failure, endocrinal disorders(involving pituitary, hypothalamus or thyroid), seizure disorder, Herpes zoster, chest wall trauma, patients on drugs influencing serum prolactin levels-e.g., phenothiazines, thioxanthene, haloperidol, SSRI, estrogen, anti-androgen, opiates and metoclopramide, methyl dopa, reserpine, patients with history of cranial irradiation/ surgery were excluded from the study.

Data was collected from the participants after informed, voluntary written consent. All patients underwent a detailed evaluation including thorough history taking and clinical examination to identify possible etiologies and evidence of hepatic encephalopathy. Patients' detailed demographic and disease-specific data was recorded in predesigned case record form. Patients were subjected to routine lab work up for hepatic encephalopathy which included Complete hemogram, Liver function test(LFT), Renal function test(RFT), Prothrombin time, international normalised ratio(INR), Hepatitis B surface antigen(HbsAg), Hepatitis C virus(HCV) antibodies, HIV screening, Ascitic fluid analysis for SAAG (Serum Ascitic Albumin Gradient) ratio, cytology and microbiological cultures, Ultrasound whole abdomen and Transient elastography. Serum prolactin at presentation was measured quantitatively by chemiluminescent microparticle immunoassay (CMIA) technology with flexible assay protocol referred to as Chemiflex using Architect 7K76 prolactin assay by Abbott Laboratories. Modified Child Pugh Turcotte(CPT) scoring system8 was calculated and patients were divided into classes A, B or C based on the score obtained. The West Haven criteria (WHC)4 was used for grading the severity of hepatic encephalopathy(grade 1 to grade 4). . Patients were followed up during duration of hospital stay to measure the outcome(HE improved and discharged/expired/HE not improved and not discharged).

Statistical Analysis

Microsoft Excel was used for tabulation of data. IBM Statistical Package for Social Sciences (SPSS) for Windows program (15.0 version) was used for statistical analysis. The continuous variables were summarised in form of mean +/- Standard Deviation (SD) or range value when required. The dichotomous variables were presented in number/frequency (n). Chi square test was applied for significance. Correlation between variables was assessed using Karl Pearson's correlation coefficient. A p value of < 0.05 was regarded as statistically significant.

RESULTS

The demographic profile of the study participants showed that the mean age of the study population was 47.71±13.81 years, with the majority (38.5%) of patients falling in 46-60 year age interval. Maximum number of patients with grade 4 hepatic encephalopathy (44 out of 50) belonged to 31-60 year age group. The study had 51(25.5%) female and 149(74.5%) male patients. The mean serum prolactin levels in males and females presenting with same grade of HE were comparable.

Hepatic encephalopathy due to ethanol induced chronic liver disease was identified as the primary etiological factor in our study, contributing to the condition in 138(69%) patients. Alcoholic chronic liver disease causing HE showed the highest mean prolactin level of 90.64 ng/ml among all etiologies and accounted for maximum number of patients presenting in each grade of HE(62.06% in grade 1 HE, 63.63 % in grade 2 HE, 79.24 % in grade 3 HE and 69.23 % in grade 4 HE).

Maximum patients in our study, i.e. 103(51.5%) had mild to moderate ascites, 61(30.5%) had gross ascites, and 36(18%) had no ascites. The group with severe to gross ascites exhibited the highest mean prolactin level at 113.36 ng/ml, followed by those with mild to moderate ascites having a mean of 84.17 ng/ml, whereas patients without ascites showed a mean of 47.66 ng/ml.

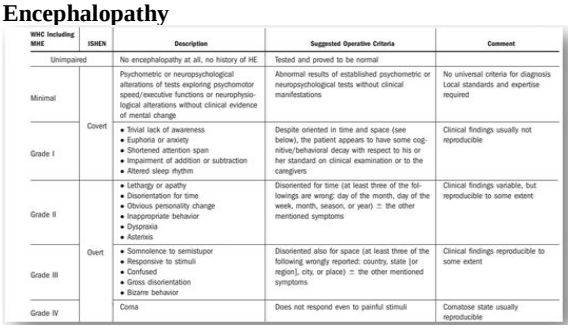
43(21.50%) patients were categorised as CTP Class B and 157(78.5%) patients as CTP Class C based on their respective modified Child-Turcotte-Pugh (CTP) scores, indicating different stages of liver cirrhosis severity. None of the patients fell in the category of Child Class A. The patients classified as Child-Pugh

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Class B exhibited a mean prolactin level of 43.45 ±27.11 ng/ml, while those classified as Child-Pugh Class C showed a higher mean prolactin level of 98.25± 63.58 ng/ml.

Majority of patients in our study, i.e 66 out of 200(33%) presented in grade 2 HE, followed by 53(26.5%) patients in grade 3 HE, 52(26%) patients in grade 4 HE, and 29(14.5%) patients in grade 1 HE. In terms of outcome status, 186(93%) patients improved from HE and were discharged from the hospital. 65 of them were admitted with grade 2 HE, 47 with grade 3 HE, 44 with grade 4 HE and 30 with grade 1 HE. The mean serum prolactin in improved and discharged patients was 86.13±62.96 ng/ml. 11(5.5%) patients expired during course of hospital treatment. 6 of them were admitted with grade 4 HE and 5 patients with grade 3 HE. None of the expired patients belonged to grade 1 or 2 HE. The mean serum prolactin of expired patients was 91.36±52.83 ng/ml. 3 out of 200 patients neither improved nor expired during course of hospital stay, their mean serum prolactin levels being 78.92±27.9 ng/ml. The Receiver Operating Characteristic (ROC) analysis of prolactin levels for prediction of outcome yielded an area under the curve (AUC) of 0.845, with a p-value of less than 0.0001.The identified optimal cutoff value for prediction of mortality was 108.25 ng/ml with a sensitivity of 90.9% and a specificity of 76.2%.

Table 1: West Haven Scoring for Hepatic Encephalopathy



WHC including MHE	ISHEN	Description	Suggested Operative Criteria	Comment
Unimpaired		No encephalopathy at all, no history of HE	Tested and proved to be normal	
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	Abnormal results of established psychometric or neuropsychological tests without clinical manifestations	No universal criteria for diagnosis Local standards and expertise required
Grade I		• Trivial lack of awareness • Euphoria or anxiety • Shortened attention span • Impairment of addition or subtraction • Altered sleep rhythm	Despite oriented in time and space (see below), the patient appears to have some cognitive/behavioral decay with respect to his or her standard on clinical examination or to the caregivers	Clinical findings usually not reproducible
Grade II	Overt	• Lethargy or apathy • Disorientation for time • Obvious personality change • Inappropriate behavior • Dyspraxia • Asterixis	Disoriented for time (at least three of the followings are wrong: day of the month, day of the week, month, season, or year) ± the other mentioned symptoms	Clinical findings variable, but reproducible to some extent
Grade III		• Somnolence to semistupor • Responsive to stimuli • Confused • Gross disorientation • Bizarre behavior	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) ± the other mentioned symptoms	Clinical findings reproducible to some extent
Grade IV		Coma	Does not respond even to painful stimuli	Comatose state usually reproducible

Table 2: Modified Child Pugh Turcotte classification for chronic liver disease

Clinical and laboratory criteria	POINTS		
	1	2	3
Hepatic Encephalopathy	None	Mild-moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild-moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin(mg/dl)	<2	2-3	>3
Albumin(gm/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time Seconds prolonged -International Normalized ratio(INR)	<4 <1.7	4-6 1.7-2.3	>6 >2.3

- Child-Pugh class A: 5 to 6 points(least severe)
- Child-Pugh class B: 7 to 9 points(moderately severe liver disease)
- Child-Pugh class C: 10 to 15 points(most severe liver disease)

Table 3: Distribution of patients' age among HE grades

Age intervals (yrs)	Total no. of Patients (n)	Percentage (%)	Grade I HE	Grade II HE	Grade III HE	Grade IV HE
18-30	26	13	5	10	8	3
31-45	66	33	9	18	17	22
46-60	77	38.5	11	25	19	22
61-75	25	12.5	2	12	7	4
76-80	5	2.5	2	1	1	1
>80	1	0.5	0	0	1	0
Total	200	100	29 (14.5%)	66 (33%)	53 (26.5%)	52 (26%)
Mean±SD	47.71 ± 13.81 YRS					

Table 4: Distribution of patients' gender among HE grades

Gender Distribution	No. of Patients (n)	%	Grade I HE	Grade II HE	Grade III HE	Grade IV HE	Prolactin Mean± SD(ng/ml)
Female	51	25.5	10	20	8	13	85.08± 62.39
Male	149	74.5	19	46	45	39	86.09 ±62.24
Total	200	100					

Table 5: Distribution of etiology among HE Grades and its comparison to serum prolactin levels

Etiology	Total patients (n)	%	No of patients				Prolactin Mean± SD (ng/ml)
			Grade 1 HE	Grade 2 HE	Grade 3 HE	Grade 4 HE	
Ethanol Induced	138	69	18	42	42	36	90.64± 62.20
Cryptogenic	38	19	5	17	7	9	78.83± 60.51
HBV Associated	18	9	5	5	3	5	78.08± 68.08
HCV Associated	3	1.5	0	1	1	1	60.60± 47.24
Auto Immune	3	1.5	1	1	0	1	60.49± 66.07

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Total	200	100					

Table 6: Distribution of Ascites status in HE grades and its comparison to serum Prolactin levels

Ascites	Total no. of patients (n)	%	No. of patients				Prolactin Mean ±SD (ng/ml)	P value
			Grade I HE	Grade II HE	Grade III HE	Grade IV HE		
Absent	36	18	9	8	7	12	47.66 ± 35.89	<0.001
Mild-moderate	103	51.5	12	43	26	22	84.17 ± 58.43	
Gross	61	30.5	8	15	20	18	113.36 ± 67.17	
	200	100						

Table 7: Distribution of HE grades at admission among CTP class and comparison to Serum Prolactin levels

HE Grade at admission	Child Class B				Child Class C			
	No. of Patients(n)	%	Prolactin Mean(ng/ml)	Prolactin SD(ng/ml)	No. of Patients(n)	%	Prolactin Mean(ng/ml)	Prolactin SD(ng/ml)
Grade 1	11	25.58	28.26	16.04	19	12.10	57.78	53.5
Grade 2	20	46.51	48.74	29.75	46	29.30	87.55	59.87
Grade 3	7	16.28	45.66	23.82	46	29.30	106.75	57.22
Grade 4	5	11.63	52.57	33.59	46	29.30	117.32	68.96
Total	43	100.00			157	100.00		

Table 8: Distribution of patient outcome among HE grades and comparison to Serum Prolactin levels

Outcome	No. of Patients	%	No. of patients				Prolactin (ng/ml)	
			Grade 1 HE	Grade 2 HE	Grade 3 HE	Grade 4 HE	Mean	SD
Expired	11	5.5	0	0	5	6	91.36	52.83
Improved & Discharged	186	93	29	65	47	45	86.13	62.96
Not Improved and Not Expired	3	1.5	0	1	1	1	78.92	27.97

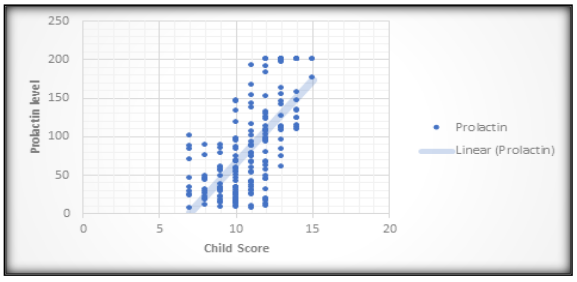


Figure 1: Scatter plot between Child Score and Prolactin Levels

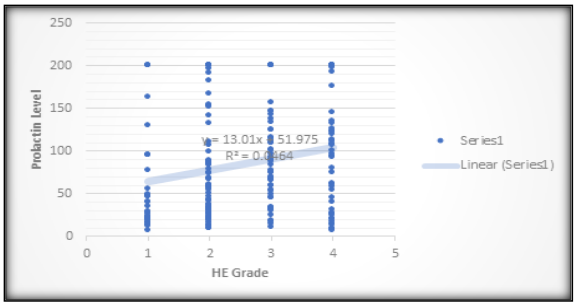


Figure 2: Scatter plot between HE Grade at admission and Prolactin Levels

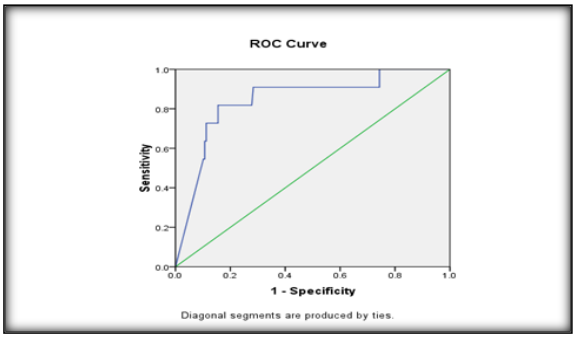


Figure 3: ROC Analysis of Prolactin level for the prediction of outcome

DISCUSSION

In the present study, we observed that majority of the patients, i.e. 77 out of 200 were aged 46-60 years, followed by 66 patients that were aged 31-45 years, 26 patients that were aged between 18-30 years, 25 patients aged 61-75 years, 5 patients aged 76-80 years, and 1 patient over 80 years old. The mean age of the study population was 47.71±13.81 years. Maximum number of patients with grade 4 hepatic encephalopathy (44 out of 50) belonged to 31-60 year age group. In the study by Rao BM et al9, 61.3%(46 out 0f 75) patients fell within the 51-60 years category, followed by those aged 41-50 years constituting 25.3% (19 out of 75), and individuals under 40 years old comprising 13.3% (10 out of 75). Hence, our study findings concurred with previously conducted studies in that majority of the patients with HE belonged to 40-60 year age group.

Our study had 51 female patients (25.5%) and 149 male patients(74.5%). 20 out of 51 females(39.21%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

and 46 out of 149 males(30.87%) presented in grade 2 HE. The mean serum prolactin levels in males and females presenting with same grade of HE were comparable. Our study found no significant association between serum prolactin levels and gender of the patients. Giri R et al10 reported that out of 70 cases, 61.4% (43) were male and 38.6% (27) were female. As was the case in our study, Babu A et al,[11] also did not find statistically significant association between serum prolactin levels and gender distribution in their study.

Hepatic encephalopathy due to ethanol induced chronic liver disease was identified as the primary etiological factor in our study, contributing to the condition in 138 (69%) patients. Alcoholic chronic liver disease causing HE showed the highest mean prolactin level of 90.64 ng/ml, and accounted for maximum number of patients presenting in each grade of HE (62.06% in grade 1 HE, 63.63 % in grade 2 HE, 79.24 % in grade 3 HE and 69.23 % in grade 4 HE). Our findings correlated with the study by Giri R et al,[10] who reported that alcoholic liver disease was the most common cause of HE (45.71%), followed by hepatitis B induced CLD(22.85%) then hepatitis C induced CLD(14.29%). 14.3% patients had no identifiable cause of HE. Similarly Ramani S et al,[12] identified alcohol consumption as the primary etiological factor in 68% of cases, followed by hepatitis B virus (HBV) infection (12%), non-alcoholic steatohepatitis (NASH) (8%), and hepatitis C virus (HCV) (6%). Hence, our findings corroborated with the prior studies that ethanol induced CLD is found to be the most common etiological factor for HE.

Maximum patients in our study, i.e. 103(51.5%) had mild to moderate ascites, 61(30.5%) had gross ascites, and 36(18%) had no ascites. The group with severe to gross ascites exhibited the highest mean prolactin level at 113.36 ng/ml, followed by those with mild to moderate ascites having a mean of 84.17 ng/ml, whereas patients without ascites showed a mean of 47.66 ng/ml. The patients with gross ascites predominantly presented in grade 3 HE (32.78%), while those with mild to moderate ascites were mainly admitted with grade 2 HE(41.74%). We found statistically significant rise in serum prolactin levels with increasing levels of ascites(p value <0.001). Sakhnani DR et al,[13] also found that the mean serum prolactin level was 81.36 ±19.85 ng/ml in severe ascites, 60.09 ±18.05 mg/ml in moderate ascites, 36.15± 15.06 ng/ml in mild ascites and 19.79± 12.29 ng/ml in cirrhosis cases without ascites. The difference in mean serum prolactin level was statistically significant among different severity of ascites(p<0.00001). Qadir A et al,[14] also concurred that in their study out of the 68 patients with ascites, 59 had elevated (>19.40 ng/ml) serum prolactin level, with statistically significant association between serum prolactin and ascites status(p<0.001).

43(21.50%) patients were categorised as CTP Class B and 157(78.5%) patients as CTP Class C based on their respective modified Child-Turcotte-Pugh (CTP) scores, indicating different stages of liver cirrhosis severity. None of the patients fell in the category of Child Class A. The patients classified as Child-Pugh Class B exhibited a mean prolactin level of 43.45 ±27.11 ng/ml, while those classified as Child-Pugh Class C showed a higher mean prolactin level of 98.25± 63.58 ng/ml. Furthermore, we found a Pearson correlation coefficient (r) of 0.676 between serum prolactin levels and Child-Pugh scores, thereby indicating a moderately strong positive correlation between these two variables. The associated p-value of less than 0.001 suggests that this correlation is statistically significant, implying that higher serum prolactin levels tend to be associated with higher Child-Pugh scores in our dataset. Rao BM et al9 observed serum prolactin levels of 10.6 ng/mL, 18.8 ng/mL, and 22.9 ng/mL in CTP Classes A, B, and C, respectively. Their study highlighted a significant association between prolactin levels and CTP class ($p < 0.0001$), suggesting that prolactin levels rise with increasing severity of liver dysfunction as assessed by CTP scores. Balakrishnan CH et al,[15] in their study observed that 73.33%(44 out of 60) patients had elevated serum prolactin levels (cutoff being >35ng/ml), with all of them belonging to CTP Class C. Normal serum prolactin levels were seen in all but one patient with CPT Class A. The study showed moderate positive correlation(r=0.787) between serum prolactin levels and CTP scores. Ramani S et al,[12] reported mean serum prolactin levels of 14.75 ng/mL in Class A, 22.26 ng/mL in Class B, and 29.96 ng/mL in Class C, showing statistically significant increase in prolactin levels with increasing CTP scores. Kumar D et al16 reported that among patients with normal serum prolactin levels (3-19 ng/ml), 7 cases were in CTP Class A, 7 in Class B, and 4 in Class C. In contrast, among those with elevated serum prolactin levels (20-35 ng/ml), 8 cases were in CTP Class A, 16 in Class B, and 22 in Class C. All cases with very high serum prolactin levels (36-60 ng/ml) were exclusively in CTP Class C, with none in Class A or B. These findings underscored a significant association (p value<0.0001) and positive correlation (spearmann's correlation coefficient of 0.713) between high serum prolactin levels and the severity of liver disease as assessed by CTP score.

Majority of patients in our study, i.e 66 out of 200(33%) presented in grade 2 HE, followed by 53(26.5%) patients in grade 3 HE, 52(26%) patients in grade 4 HE, and 29(14.5%) patients in grade 1 HE. The Pearson correlation coefficient between serum prolactin level and HE grading was 0.21, indicating weak positive correlation. The p value of 0.002 suggests that this correlation is statistically significant. Ramani S et al,[12] found that mean serum prolactin levels were 17.05 ng/ml, 24.76 ng/ml, 30.57 ng/ml and 32.73 ng/ml in grade 1, 2, 3 and 4 of HE respectively. There was statistically significant increase in serum prolactin levels with increase in severity of HE from grade1 to grade 4(p <0.001), with serum prolactin levels being in normal range in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

minimal HE. Similarly, Arafa M et al,[17] in their study of 75 cirrhotic patients with HE and 50 cirrhotic patients without HE noticed that prolactin levels in cirrhotic patients with HE was significantly increased vs patients without HE(p=0.007), and that prolactin levels in HE increase with progression of HE from grade 1 to 4(p=0.000). Metwally R et al,[18] also concurred in their study that there exists a statistically high significant correlation (spearman coefficient 0.71, p value <0.002) between serum prolactin levels and encephalopathy severity.

In terms of outcome status, 186(93%) patients improved from HE and were discharged from the hospital. 65 of them were admitted with grade 2 HE, 47 with grade 3 HE, 44 with grade 4 HE and 30 with grade 1 HE. The mean serum prolactin in improved and discharged patients was 86.13±62.96 ng/ml. 11(5.5%) patients expired during course of hospital treatment. 6 of them were admitted with grade 4 HE and 5 patients with grade 3 HE. None of the expired patients belonged to grade 1 or 2 HE. The mean serum prolactin of expired patients was 91.36±52.83 ng/ml, which was higher compared to those of improved patients. Kumar D et al,[16] reported 12 deaths out of 76 patients(15.7%) in their study. All 12 cases had serum prolactin level in range of 36-60 ng/ml. Prolactin levels showed statistically significant association with mortality (p value <0.0001). Similarly, Rao BM et al,[9] reported 11 deaths out of 75 participants in their study. A positive significant correlation was found between serum prolactin levels on admission and mortality among study participants(p<0.0001). Hence, our study was in agreement with previous research that higher serum prolactin levels in individuals with HE was associated with higher mortality and thus, worse prognosis.

The Receiver Operating Characteristic (ROC) analysis for prolactin levels for prediction of outcome yielded an area under the curve (AUC) of 0.845, indicating good discriminatory ability. The p-value of less than 0.0001 suggests that this AUC is statistically significant, meaning that prolactin levels effectively distinguish between different outcomes in our study population. The identified optimal cutoff value for prediction of mortality was 108.25 ng/ml with a sensitivity of 90.9% and a specificity of 76.2%. Jha SK et al,[19] evaluated serum prolactin's diagnostic accuracy using a cutoff value of 50 ng/ml to predict mortality in cirrhosis and viral hepatitis. In cirrhotic patients, they reported a sensitivity of 40% and specificity of 73.3%. The positive predictive value (PPV) for cirrhosis was 66.7% and the negative predictive value (NPV) was 47.8%. Kumar D et al,[16] conducted ROC analysis and identified a serum prolactin cutoff of >33.3 ng/ml as a predictor of mortality in cirrhosis, with a sensitivity and specificity of 100% each. Similarly, Arafa M et al,[17] investigated prolactin levels in cirrhotic patients with hepatic encephalopathy (HE) and found that a prolactin level cutoff of >18.85 ng/dl had a sensitivity of 88% and specificity of 90.3% for predicting HE in cirrhotic patients.

Limitations and Future Scope: The study had certain constraints. It lacked randomization and blinding, which may have contributed to a degree of bias in case selection. The sample size was small (n=200) and the study was single-centric. A larger sample size and multi-centric analysis with randomization and blinding may be advised for better extrapolation of results of the study. Further studies inculcating more clinical parameters and follow up are needed to enhance the robustness of the research.

CONCLUSION

This study concluded that increased levels of serum prolactin had a significant correlation with the severity of chronic liver disease, its complications such as hepatic encephalopathy and mortality. Serum prolactin can serve as a valuable prognostic marker in patients with hepatic encephalopathy, aiding in severity stratification. Understanding the relation between prolactin abnormalities and hepatic encephalopathy may also result in future therapeutic interventions, potentially offering avenues for more targeted treatment strategies.

REFERENCES

1. GBD 2017 Cirrhosis Collaborators. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020;5(3):245-266.
2. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med. 2014;12:145.
3. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. Lancet. 2021;398(10308):1359–76.
4. American Association for the Study of Liver Diseases, European Association for the Study of the Liver. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. 2014;61:642 59
5. Poordad FF. Review article: the burden of hepatic encephalopathy. Alimentary Pharmacol Therap. 2007;25(1):3-9.
6. Häussinger D. Hepatic encephalopathy. Acta Gastro Enterologica Belgica. 2010;73(4):457-64.
7. Tapper EB, Henderson JB, Parikh ND, Ioannou GN, Lok AS. Incidence of and Risk Factors for Hepatic Encephalopathy in a Population-Based Cohort of Americans With Cirrhosis. Hepatol Commun. 2019;3(11):1510-1519
8. Pugh RN, Murray- Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. British journal of surgery. 1973 Aug;60(8):646-9.
9. Rao BM, Mahadevaiah M, Vanama LS. A correlative study of serum prolactin with the severity of liver disease. J Datta Meghe Inst Med Sci Univ 2023;18:656-62.
10. Giri R, Pandey S, Kushwaha JS. Assessment of serum prolactin level in hepatic encephalopathy patient. Int J Adv Med 2021;8:793-9.
11. Babu A, Sumitha PS, Thomas P E, Krishnan S. Assessment of Serum Prolactin Levels in Patients with Liver Disease: A Cross Sectional Study. National Journal of Laboratory Medicine. 2024 Apr, Vol-13(2): BO10-BO13

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Ramani S, Yangala S R, Pilli P R. Serum prolactin as a marker of severity of hepatic encephalopathy in cirrhosis. Int J Acad Med Pharm 2022; 4 (4); 390-396.
13. Sakhnani D R,Sharma C K,Mathur A. Serum Prolactin: A Possible New Marker for Severity of Liver Cirrhosis European Journal of Molecular& Clinical Medicine 2021; 08(4):53-60.
14. Qadir A ,Waseem A, Jamal A, Amitabh V. Serum Prolactin as a Marker of the Severity of Liver Cirrhosis in a Tertiary Hospital in India: A Cross-Sectional Study. Niger J Clin Pract. 2024 Jul 1;27(7):844-849.
15. Balakrishnan C H, Rajeev H. Correlation of Serum Prolactin Level to Child Pugh Scoring System in Cirrhosis of Liver. Journal of Clinical and Diagnostic Research. 2017;11(7): OC30-OC33.
16. Kumar D, Kampani G. Correlation of serum prolactin levels with severity of liver disease and its association with hepatic encephalopathy in patients of cirrhosis liver. Global journal for research analysis (2021):10(2);47-49.
17. Arafa M, Besheer T, Elkannishy G, El-hussiny MA, Rakha EB. Features of Hormonal Disturbances in Cirrhotic Patients with Hepatic Encephalopathy. Euroasian J Hepato-Gastroenterol 2012;2(2):84-89.
18. Metwally R, Rizk M, Awadein A. Serum prolactin level as a biological marker of severity in liver cirrhosis. International Journal of Development Research 2017;7(8):14787-91.
19. Singh V, Jha S K, Singhal S, Singh A. Correlation of serum prolactin level to child pugh scoring system and meld score in liver cirrhosis. International Journal of Medical and Health Research(2022);8(1):70-75..

ISSN (O): 2687-5365; ISSN (P): 2753-6556