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CORRELATION OF SERUM PROLACTIN LEVELS WITH CHRONIC LIVER DISEASE SEVERITY IN A TERTIARY CARE HOSPITAL

General Medicine

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ABSTRACT

Background -Cirrhosis represents the advanced stage of chronic liver injury and is associated with architectural distortion, portal hypertension, and many systemic complications. Endocrine abnormalities, including altered prolactin regulation, are increasingly recognised in chronic liver disease. Prolactin secretion is influenced by impaired hepatic metabolism of estrogens and disturbances in dopaminergic inhibition, both of which may be altered in cirrhosis. This study evaluates whether serum prolactin levels reflect the severity of liver dysfunction and correlate with major complications of cirrhosis.**Aim -**To evaluate the association between serum prolactin levels and the clinical, biochemical, ultrasonographic, and endoscopic markers of disease severity in chronic liver disease.**Methods -**A prospective observational study was conducted over 18 months at a tertiary-care centre in Mumbai, enrolling 100 adult patients with chronic liver disease. Individuals with endocrine disorders, renal failure, pregnancy, lactation, or medications known to affect prolactin were excluded. All participants underwent detailed clinical assessment, laboratory evaluation, abdominal ultrasonography, endoscopy, and serum prolactin measurement. Disease severity was graded using the modified Child Pugh (CTP) classification. Statistical analyses included t-tests, ANOVA, Pearson's correlation.**Results -** Serum prolactin concentrations demonstrated a progressive rise with worsening liver dysfunction. Higher prolactin levels were significantly associated with pallor, pedal oedema, icterus, increasing grades of ascites, presence of oesophageal varices with PHG/GAVE, and advancing hepatic encephalopathy ($p < 0.001$ for most comparisons). Strong correlations were observed between prolactin and albumin, bilirubin, prothrombin time, creatinine, and CTP score, with the highest prolactin levels recorded in CTP class C.**Conclusion -** Serum prolactin shows a strong, graded association with clinical, biochemical, and imaging markers of hepatic decompensation. These findings suggest, prolactin may serve as a convenient and inexpensive adjunct biomarker for assessing disease severity in chronic liver disease. Larger multicentre studies with standardized methodologies are warranted to validate its prognostic role.

KEYWORDS

Chronic Liver Disease, Prolactin, Modified Child Pugh Score.

INTRODUCTION –

Cirrhosis of the liver represents the endpoint of chronic parenchymal hepatic injury, during which regenerative nodules and fibrosis disrupt normal hepatic architecture, leading to portal hypertension and multisystem complications including ascites, variceal bleeding, encephalopathy and increased mortality.[1] Among the many disturbances seen in chronic liver disease (CLD) are endocrine derangements. Hormonal dysregulation may emerge via impaired hepatic clearance, altered secretion and feedback mechanisms, as the diseased liver fails to maintain homeostasis.[2]

One hormone of particular interest is prolactin (PRL), a lactotrophic pituitary hormone regulated chiefly by inhibitory dopaminergic input via the tuberoinfundibular tract, and also modulated by circulating estrogens. In cirrhosis, elevated peripheral aromatization of androgens (e.g., testosterone to estradiol) and reduced hepatic clearance lead to hyper-estrogenemia. These elevated estrogens may down-regulate hypothalamic dopamine release, attenuating the tonic inhibitory control of lactotrophs, and thereby promoting elevated prolactin levels. In addition, increased concentrations of aromatic amino acids in CLD drive production of "false" neurotransmitters, which may further inhibit central dopaminergic output, compounding the hyperprolactinemic state.[3]

Furthermore, though the exact pathogenic mechanisms remain to be fully elucidated, the role of prolactin in hepatic fibrogenesis has been suggested by increased expression of prolactin receptors in fibrotic and cirrhotic human liver tissue.[2]

Given the increasing incidence of CLD and cirrhosis in India, and the limitations of existing severity scores—such as CTP, which includes subjective measures (ascites, encephalopathy) and omits renal function—there is a compelling need to evaluate additional biomarkers.[4] The aim of this study is to assess the relationship between serum prolactin levels and the severity of chronic liver disease, as defined by CTP score, and to explore the association of prolactin with complications of cirrhosis.

MATERIALS & METHODS -

This was a prospective, observational, comparative study conducted in the Department of Internal Medicine, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai, a tertiary care teaching hospital in India. The study was carried out over an 18-month period. Approval was obtained from the Institutional Ethics Committee.

All patients aged 18 years and above with a diagnosis of chronic liver disease (CLD) who provided informed consent were included in the study.

Patients were excluded if they were pregnant or lactating, had a history of cranial surgery or cranial irradiation, known endocrine disorders, coexisting renal failure, or were taking medications known to alter serum prolactin levels such as antipsychotics, antidepressants, dopamine-2 receptor blockers, oral contraceptive pills, or H_2 receptor antagonists.

A total of 100 consecutive patients who met the inclusion and exclusion criteria were recruited during the study period.

Each participant was evaluated using a structured clinical proforma that included detailed demographic information, medical history, comorbidities, ongoing medications, and relevant clinical findings.

All enrolled patients underwent routine laboratory investigations, including:

Complete blood count
- Renal function tests
- Liver function tests
- Random blood glucose and serum electrolytes
- Serum lipid profile, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)

In addition, specific investigations relevant to liver disease were performed:
- Viral serology for HIV, HBV, and HCV
- Ultrasonography (USG) of the abdomen and pelvis, portal venous Doppler studies
- Esophagogastroduodenoscopy (EGD) for evaluation of varices
- Serum prolactin levels, measured using a standardized immunoassay technique

Each participant underwent a thorough clinical assessment, with attention to signs and complications of chronic liver disease such as portal hypertension, ascites, and hepatic encephalopathy. Disease severity was assessed using the modified Child-Turcotte-Pugh (CTP) score, and patients were classified into Class A, B, or C based on the calculated total.

Hepatic encephalopathy was diagnosed and graded according to the West Haven criteria, where grades I–II were considered mild and grades III–IV as advanced for the purpose of CTP scoring. The serum prolactin concentrations were then statistically correlated with the Child-Pugh severity class and the presence of major complications of cirrhosis.

All data were entered and organized using Microsoft Excel and subsequently analysed with the Statistical Package for the Social Sciences (SPSS), version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the data. Quantitative variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages.

A p-value < 0.05 was considered statistically significant for all analyses.

RESULTS -

Demographic Profile -

A total of 100 patients were included in the study. Of these, 19% were between 29 and 40 years of age, half of the participants fell within the 41–50-year age group, and the remaining 31% were above 50 years. The average age of the study population was 46.89 ± 7.09 years. The cohort was predominantly male, comprising 90% of the subjects, while females accounted for 10%.

Clinical Characteristics and Serum Prolactin -

Pallor was noted in 54% of patients, icterus in 68%, and pedal oedema in 42%. When serum prolactin levels were compared across these clinical findings using an independent sample t-test, patients with pallor and those with icterus had similar prolactin concentrations (22.18 ± 6.39 ng/ml and 22.05 ± 6.57 ng/ml, respectively), while individuals with pedal oedema exhibited a higher mean level of 25.39 ± 4.81 ng/ml. These differences were statistically significant, indicating that the presence of these clinical signs was associated with elevated prolactin levels (p = 0.001).

Correlation With Laboratory and Clinical Parameters -

Table 1 - CORRELATION OF SERUM PROLACTIN LEVELS WITH VARIOUS CLINICAL AND BIOCHEMICAL PARAMETERS

PARAMETERS	MEAN ± SD	PEARSON'S CORRELATION BETWEEN THE PARAMETERS AND SERUM PROLACTIN LEVELS	
		r value	p value
Pulse	82.86 ± 10.33 bpm	-0.172	0.086
Systolic blood pressure	114.64 ± 8.81 mmHg	0.054	0.594
Diastolic blood pressure	76.48 ± 5.93 mmHg	0.134	0.183
Haemoglobin	7.85 ± 1.57 g/dl	-0.610	0.001*
Total leucocyte count	5896 ± 1404.75 cells/cumm	-0.062	0.542
Platelets	101340 ± 21283.66/UL	-0.304	0.002*
Total bilirubin	6.30 ± 7.12 mg/dl	0.758	0.001*
Direct bilirubin	3.32 ± 3.94 mg/dl	0.760	0.001*
SGOT	69.60 ± 30.33 U/L	-0.044	0.661
SGPT	27.90 ± 13.09 U/L	-0.112	0.268
Total protein	5.89 ± 0.92 g/dl	-0.443	0.001*
Albumin	2.75 ± 0.62 g/dl	-0.796	0.001*
Prothrombin time	15.71 ± 4.11 seconds	0.737	0.001*
INR	1.53 ± 0.69	0.670	0.001*
BUN	12.54 ± 4.13 mg/dl	-0.149	0.139
Creatinine	0.87 ± 0.17 mg/dl	-0.201	0.045*
Modified Child Pugh class	9.14 ± 2.98	0.966	0.001*

*statistically significant

Analysis of correlations as seen in table 1 revealed that serum prolactin demonstrated significant associations with several key clinical and biochemical variables. Notable correlations were observed with haemoglobin, platelet count, serum bilirubin (total and direct), serum albumin, prothrombin time, INR, creatinine, and the modified Child–Pugh score. Among these, the strongest correlations were seen with albumin, direct bilirubin, and the Child–Pugh classification, each showing a high degree of statistical significance, suggesting a meaningful relationship between prolactin levels and the severity of hepatic dysfunction.

As per table 2, serum prolactin levels increased progressively with the degree of ascites. ANOVA confirmed that these differences across ultrasonographic categories were statistically significant (p = 0.001).

Table 2 - COMPARISON OF THE MEAN PROLACTIN LEVELS BASED ON USG ABDOMEN USING ANOVA

USG ABDOMEN	N	Minimum	Maximum	Mean	S.D	p value
Only Coarse echotexture of liver	32	5.00	16.00	8.228	2.359	0.001*
coarse echotexture of liver with gross Ascites	12	24.00	31.00	28.2817	2.35079	
coarse echotexture of liver with mild Ascites	36	13.00	28.00	18.349	3.841	
coarse echotexture of liver with moderate Ascites	20	23.00	31.00	26.815	2.449	

*statistically significant

Table 3 shows, patients with varices and PHG had a mean level of 17.57 ± 7.34 ng/ml, those with varices, PHG, and GAVE had substantially higher levels at 27.24 ± 3.24 ng/ml, and individuals with only PHG had a mean value of 10.55 ± 6.88 ng/ml. These differences were statistically significant according to ANOVA (p = 0.001), indicating a relationship between endoscopic severity and prolactin elevation.

Table 3 - COMPARISON OF THE MEAN PROLACTIN LEVELS BASED ON UPPER GI ENDOSCOPY USING ANOVA

UPPER GIENDOSCOPY	N	Minimum	Maximum	Mean	S.D	p value
Oesophageal Varix with PHG	68	5.00	29.70	17.570	7.340	0.001*
Oesophageal Varix with PHG with GAVE	16	23.00	31.00	27.249	3.245	
Portal Hypertensive Gastropathy	16	6.00	28.00	10.550	6.881	

*statistically significant

Hepatic Encephalopathy -

Hepatic encephalopathy was present in 18% of the cohort, with 12% exhibiting mild (grades 1–2) and 6% showing advanced (grades 3–4) encephalopathy. Mean serum prolactin levels were higher in patients with more severe neurological impairment. Individuals with grades 1 and 2 encephalopathy had a mean prolactin concentration of 25.39 ± 4.72 ng/ml, while those with advanced grades 3 and 4 had markedly

elevated levels of 30.56 ± 0.67 ng/ml. ANOVA demonstrated that prolactin levels differed significantly with the severity of encephalopathy (p = 0.001).

Table 4 - COMPARISON OF THE MEAN PROLACTIN LEVELS BASED ON ENCEPHALOPATHY USING ANOVA

ENCEPHALOPATHY	N	Minimum	Maximum	Mean	S.D	p value
Mild (Grade 1 and 2)	12	15.50	28.99	25.397	4.725	0.001 *
Advanced (Grade 3 and 4)	6	29.70	31.00	30.567	0.671	
No	82	5.00	29.50	15.992	7.507	

*statistically significant

Modified Child–Pugh Classification -

Based on the modified Child–Pugh scoring system, 30% of the patients were categorized as class A, another 30% as class B, and 40% as class C. Serum prolactin levels rose consistently across these categories, reflecting increasing hepatic decompensation. The mean prolactin concentration was 7.70 ± 1.22 ng/ml in class A, increased to 16.58 ± 1.94 ng/ml in class B, and was highest in class C at 26.76 ± 2.69 ng/ml. These differences were statistically significant on ANOVA (p = 0.001).

Table 5 - COMPARISON OF THE MEAN PROLACTIN LEVELS BASED ON MODIFIED CHILD PUGH CLASS USING ANOVA

MODIFIED CHILD PUGH CLASS	N	Minimum	Maximum	Mean	S.D	p value
A	30	5.00	9.40	7.709	1.226	0.001*
B	30	13.00	19.33	16.589	1.943	
C	40	23.00	31.00	26.765	2.699	

*statistically significant

DISCUSSION –

Principal findings -

In this study of 100 patients with chronic liver disease, serum prolactin concentrations rose in parallel with clinical and ultrasonographic markers of hepatic decompensation: higher prolactin was seen in patients with pallor, icterus and pedal oedema, with progressively larger means across ascending degrees of ascites, more severe endoscopic lesions (varices ± GAVE/PHG), higher grades of hepatic encephalopathy, and worse modified Child–Pugh class. These results support the concept that prolactin elevation parallels disease severity and the burden of complications in cirrhosis.

Comparison with previous work -

Our findings are consistent with multiple prior reports that describe higher prolactin levels in more advanced liver disease and their association with complications. Early work first documented altered prolactin homeostasis in liver disease, and subsequent clinical series have repeatedly noted correlations between prolactin and Child–Pugh stage, encephalopathy and indices of synthetic dysfunction. For example, Morgan and colleagues described abnormal prolactin activity in patients with liver disease decades ago, and more recent observational studies have shown progressively higher prolactin with worsening Child–Pugh class and with presence of encephalopathy and significant portal hypertension. [1,3,4,5,6]

Several contemporary Indian and regional series report closely similar patterns to those we observed: significant positive correlations of serum prolactin with bilirubin and prothrombin time and higher mean prolactin in patients with encephalopathy and advanced Child–Pugh class. Some larger cross-sectional analyses and single-centre cohorts have even suggested cut-off values that predict severe disease or complications with reasonable sensitivity and specificity.[7,8]

There are, however, divergent reports. A minority of studies that carefully excluded drug effects and confounders found hyperprolactinaemia to be uncommon, implying that comorbid conditions, medications, or selection differences may explain some variability between cohorts. Such heterogeneity highlights the need for standardized exclusion criteria and larger, multicentre validation before prolactin can be widely recommended as a standalone marker.[9]

Possible mechanisms -

Several biologically plausible mechanisms may explain prolactin elevations in cirrhosis. Hepatic failure increases peripheral aromatization of androgens to estrogens and decreases hepatic clearance of steroid hormones; hyperestrogenemia can suppress hypothalamic dopamine release and thereby disinhibit pituitary lactotrophs, raising prolactin secretion. In addition, disturbances in amino-acid metabolism in liver failure (notably elevated aromatic amino acids and formation of "false neurotransmitters") can impair central dopaminergic tone, further decreasing prolactin inhibition. These pathways—together with portosystemic shunting and altered pituitary blood flow—provide a mechanistic link between advancing hepatic dysfunction and higher circulating prolactin. [1,3,10]

Clinical implications -

Our results add to the growing literature that serum prolactin could function as a simple, inexpensive adjunct biomarker that reflects hepatic decompensation and complications such as ascites and encephalopathy. In resource-limited settings where comprehensive scoring or invasive testing may be difficult, a readily measurable hormone that rises with worsening disease could help triage patients, prompt early referral, or enrich risk stratification models. Several recent studies have suggested threshold values of prolactin that may predict severe disease or in-hospital complications; if prospectively validated, such thresholds could be clinically useful.[8]

CONCLUSION -

In summary, serum prolactin in our cohort correlated strongly with clinical, biochemical and imaging markers of hepatic decompensation and rose with increasing Child–Pugh class and encephalopathy grade. These data, concordant with several recent regional studies, support further evaluation of prolactin as a complementary, low-cost biomarker for disease severity in chronic liver disease. Prospective validation, assay standardization, and outcome-linked research are required before routine clinical adoption.

LIMITATIONS -

This study is observational and cross-sectional, so causal relationships cannot be proven. Single-centre sampling and a predominance of males may limit generalizability. Although we excluded obvious confounders where possible, unmeasured factors (e.g. acute intercurrent illness) can affect prolactin and may have influenced levels in some patients; this is an issue noted in other series that reported lower prevalence of hyperprolactinaemia after strict exclusions. Additionally, differences in assay methods and reference ranges between laboratories complicate direct numerical comparisons and the translation of cut-offs. Finally, longitudinal data linking baseline prolactin to outcomes (mortality, readmission, transplant need) are needed before recommending routine clinical use.

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CONFLICTS OF INTEREST -

There are no conflicts of interest.

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