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ASSESSING SERUM ESTROGEN LEVELS AS A POTENTIAL MARKER OF CHRONIC LIVER DISEASE SEVERITY IN MALE PATIENTS: A HOSPITAL-BASED OBSERVATIONAL STUDY IN PAKISTAN

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Abstract

Introduction

Chronic liver disease (CLD) is a significant public health issue in Pakistan, leading to high morbidity and mortality. Hormonal dysregulation, including alterations in estrogen metabolism due to impaired hepatic clearance, is a well-documented consequence of CLD. Estrogen, primarily known for its reproductive functions, has been implicated in liver disease progression, but its role as a biomarker of liver disease severity remains underexplored. This study aimed to evaluate the relationship between serum estrogen levels and the severity of CLD, as assessed by the Child-Turcotte-Pugh (CTP) score, and to investigate its association with various complications of the Chronic liver disease.

Methods

This prospective observational study was conducted in the Department of Medicine at a tertiary care hospital in Pakistan from January 2020 to March 2021. Patients diagnosed with CLD were evaluated for demographic characteristics, clinical history, and examination findings. Disease severity was classified using the CTP scoring system. Serum estrogen levels were measured using an electrochemiluminescence assay. Statistical analyses, including the Chi-square test, Kruskal-Wallis test, and independent sample t-tests, were used to assess associations between estrogen levels, disease severity, and complications. A p-value of <0.05 was considered statistically significant.

Results

The study included 135 patients with a mean age of 49.1 ± 11.2 years. Males comprised 82.2% of the cohort (male-to-female ratio: 4.6:1). The leading causes of CLD were hepatitis C virus infection (n=67, 49.6%), alcohol-related liver disease (n=32, 23.7%), and metabolic dysfunction-associated steatohepatitis (n=15, 11.1%). The mean serum estrogen level was 62.8 ± 14.6 pg/mL (range: 35 to

89 pg/mL), and the mean CTP score was 9.42 ± 2.05. Most patients were classified as CTP Class B (n=59, 43.7%), followed by Class C (n=51, 37.8%) and Class A (n=25, 18.5%).Serum estrogen levels showed a significant positive correlation with CTP scores (R = 0.412, p < 0.001), serum bilirubin (R = 0.361, p < 0.001), and international normalized ratio (R = 0.295, p = 0.002), along with a significant negative correlation with serum albumin (R = -0.419, p < 0.001). The Kruskal-Wallis test demonstrated a strong association between elevated estrogen levels and the severity of ascites (p < 0.001) as well as hepatic encephalopathy (p < 0.001). Using receiver operating characteristic analysis, an estrogen level cut-off > 65 pg/mL predicted severe CLD (CTP Class C) with 79.4% sensitivity and 81.2% specificity. Elevated estrogen levels were found in 74.8% of patients (n=101) with esophageal varices, 85.6% (n=36) with upper gastrointestinal bleeding, 89.7% (n=44) with hepatic encephalopathy, and 77.9% (n=74) with moderate-to-severe ascites. The overall mortality rate was 4.4% (n=6), and deceased patients had significantly higher estrogen levels compared to survivors (p < 0.001).

Conclusion

Serum estrogen levels demonstrate a strong correlation with CLD severity as determined by the CTP scoring system. The findings suggest that estrogen could serve as a valuable biomarker for assessing disease progression and predicting complications in CLD patients. Given its non-invasive nature and significant prognostic value, serum estrogen measurement may aid in risk stratification and clinical decision-making for patients with CLD.

Key words: Serum estrogen levels, Chronic liver disease, CTP score, Complications of CLD, Biomarkers of severity of CLD.

Citations. Ayesha Laraib-Ijaz[1], Noor ul Huda[2], Jamal afzal[3],Shabeer Ahmad Dar[4], Kashif khan[5], Sadeed Ahmed Darain[6], Fatima Shams[7], Aqsa Siddique[8], Farman Iqbal[9], Waqas Gohar[10].Assessing Serum Estrogen Levels as a Potential Marker of Chronic Liver Disease Severity in Male Patients: A Hospital-Based

Introduction

Chronic liver disease (CLD) is a progressive and multifactorial disorder characterized by sustained hepatic inflammation, fibrosis, and architectural distortion, culminating in cirrhosis and, ultimately, liver failure[1]. Globally, CLD represents a significant public health burden, contributing to considerable morbidity and mortality. According to the Global Burden of Disease Study, liver diseases accounted for over two million deaths annually, with a disproportionate impact on low- and middle-income countries where diagnostic and therapeutic resources remain limited[2]. Pakistan, in particular, bears a heavy burden of CLD, where liver disease-related mortality accounts for approximately 3.76% of all deaths, with an age-standardized mortality rate of 38.05 per 100,000 population[3] . This places Pakistan among the top 30 countries worldwide with the highest liver disease-related mortality, highlighting a critical need for early diagnosis and effective management strategies. The etiology of CLD in Pakistan is predominantly driven by chronic viral hepatitis, primarily hepatitis B virus (HBV) and hepatitis C virus (HCV) infections[4] . National seroprevalence surveys conducted in 2007–2008 revealed HBV and HCV prevalences of 2.5% and 4.8%, respectively, contributing to a combined viral hepatitis prevalence exceeding 7% in the general population[5]. Furthermore, the epidemiology of liver disease is evolving, with metabolic liver disorders such as nonalcoholic fatty liver disease (NAFLD) emerging as major contributors to CLD. Recent meta-analyses estimate the prevalence of NAFLD in Pakistan at approximately 30%, reflecting global trends driven by rising obesity, diabetes, and metabolic syndrome [6,7]. This epidemiological shift underscores the complex, multifactorial nature of CLD in the region and calls for comprehensive approaches to disease assessment and management.

The liver's pivotal role extends beyond metabolism and detoxification to include endocrine homeostasis, particularly the metabolism and clearance of sex hormones. In healthy individuals, the liver efficiently metabolizes estrogens through conjugation and biliary excretion[8]. However, CLD disrupts this homeostasis by impairing hepatic clearance, coupled with increased peripheral conversion of androgens to estrogens via aromatase activity in adipose tissue and other sites[9]. This hormonal imbalance results in elevated circulating estrogen levels, which are particularly evident in male patients. Clinically, this manifests as feminizing features such as gynecomastia, testicular atrophy, loss of body hair, and vascular abnormalities including spider angiomas and palmar erythema[10]. These signs are not only clinically significant but also reflect underlying pathophysiological derangements associated with advancing liver dysfunction. Despite these well-recognized clinical correlations, the utility of serum estrogen levels as an objective biomarker for assessing CLD severity remains inadequately investigated. Current severity scoring systems, notably the Child-Turcotte-Pugh (CTP) score, incorporate clinical parameters—encephalopathy and ascites—that are inherently subjective and prone to inter-observer variability[11]. Although widely used for prognostication and treatment stratification, the CTP score's limitations necessitate exploration of additional objective biochemical markers that could enhance disease severity classification and prognostic accuracy. Serum estrogen, given its mechanistic link to liver dysfunction and relative ease of measurement, presents as a promising candidate for such biomarker development[12]. This study aims to address this gap by evaluating the correlation between serum estrogen levels and CLD severity, categorized by the CTP score, in a cohort of male patients. Additionally, the study investigates the association of estrogen levels with common CLD complications, including ascites, hepatic encephalopathy, esophageal varices, and gastrointestinal bleeding, which significantly impact morbidity and mortality. By elucidating the relationship between serum estrogen and liver disease severity, this research seeks to establish estrogen as a potential non-invasive biomarker, thereby facilitating improved clinical risk stratification, earlier intervention, and optimized management strategies for male CLD patients in Pakistan and similar resource-limited settings.

Materials and Methods

This prospective observational study was conducted at the outpatient and inpatient departments of Medicine and Gastroenterology at Ayub Teaching Hospital, Abbottabad**,** from June 10, 2023, to June 10, 2024**.** Ethical approval was obtained from the Institutional Review Board (Approval No. ATH/IRB/0724/041)**,** and all participants provided written informed consent prior to enrollment.

Study Population

Chronic liver disease (CLD) was defined as hepatic dysfunction persisting for six months or longer, characterized by clinical, biochemical, and radiological evidence of liver impairment. Patients with CLD presented with features such as splenomegaly, coagulopathy (elevated INR), hypoalbuminemia, jaundice, ascites, esophageal varices, or ultrasound evidence of cirrhosis and portal hypertension.The study included:

- Adults aged ≥18 years with a confirmed diagnosis of CLD and its complications.
- Patients willing to provide informed consent and undergo required investigations.

Exclusion Criteria, Patients were excluded if they had:

- History of pituitary or hypothalamic disorders
- Hormonal disorders or malignancies affecting estrogen metabolism.
- Pregnancy or lactation (due to natural estrogen fluctuations).
- Current or recent use of medications affecting estrogen levels, including oral contraceptives, hormone replacement therapy, tamoxifen, spironolactone, or aromatase inhibitors.

Sample Size Calculation

A total of 150 patients were included in the study, accounting for an estimated 7% dropout rate**.**Data collection included demographic information (age, gender), clinical symptoms, and physical examination findings. Detailed medical history was recorded, including comorbidities (diabetes, hypertension, metabolic syndrome), history of alcohol use, viral hepatitis status, and prior treatments. The presence of CLD complications, such as ascites, hepatic encephalopathy (HE), esophageal varices, portal hypertension, hepatorenal syndrome, and spontaneous bacterial peritonitis (SBP), was documented.

Laboratory and Imaging Investigations

All participants underwent comprehensive diagnostic evaluations for CLD and its complications, including:

- *Liver function tests:* Serum bilirubin, ALT, AST, alkaline phosphatase, total protein, albumin, globulin, prothrombin time (PT), and INR.
- *Renal function tests:* Serum creatinine, blood urea nitrogen (BUN), and electrolytes.
- *Complete blood count (CBC***)** and *coagulation profile.*
- *Ascitic fluid analysis* (where applicable): Glucose, protein, lactate dehydrogenase (LDH), cell count, and microbiological cultures.
- *Hepatitis B and C serology* using enzyme-linked immunosorbent assay (ELISA).
- *Autoimmune and metabolic liver disease markers* (where indicated): Anti-nuclear antibody, anti-smooth muscle antibody, anti-liver kidney muscle antibody, anti-mitochondrial antibody, and serum ceruloplasmin.

Estrogen Measurement

Serum estradiol (E2) levels were measured at admission using a chemiluminescent immunoassay (provided by Roche Diagnostics, Indianapolis, USA). Blood samples were collected in the morning (8 AM–10 AM) after overnight fasting to minimize diurnal variations.

Radiological and Endoscopic Assessment

- *Abdominal ultrasound*: Assessed liver echotexture, size, splenic enlargement, portal vein diameter, and Doppler evaluation for hepatic and portal vein thrombosis**.**
- *Esophagogastroduodenoscopy (EGD):* Evaluated esophageal varices, portal hypertensive gastropathy, or duodenopathy**.**

Assessment of CLD Severity

The severity of CLD was classified using the *modified Child-Turcotte-Pugh (CTP) scoring system*, categorizing patients as:

- *Class A (5–6 points):* Compensated disease.
- *Class B (7–9 points):* Decompensated disease.
- *Class C (10–15 points):* Severe decompensated disease.

Clinical severity of ascites was graded as mild, moderate, or severe**,** based on the International Club of Ascites criteria**.**

Hepatic encephalopathy (HE) was classified using the West Haven criteria, and hepatorenal syndrome (HRS) was diagnosed according to the revised International Club of Ascites guidelines**.**

Statistical Analysis

Data were analyzed using SPSS version 26.0**.** Continuous variables (e.g., serum estrogen levels, liver function tests) were presented as mean ± standard deviation (SD)**,** while categorical variables (e.g., CTP class, presence of complications) were expressed as frequencies and percentages**.**

- Comparison of estrogen levels across CTP classes was performed using ANOVA or Kruskal-Wallis test**.**

• Correlation between estrogen levels and CLD severity was assessed using Pearson's or Spearman's correlation coefficient**.**
• Multivariate regression analysis was conducted to identify independent predictors of estrogen elevation in CLD patients**.**

Parameter	**Score 1 (Mild)**	**Score 2 (Moderate)**	**Score 3 (Severe)**
Bilirubin (mg/dL)	<2.0	2.0–3.0	>3.0
Albumin (g/dL)	>3.5	2.8–3.5	<2.8
INR	<1.7	1.7–2.3	>2.3
Ascites	None	Mild (controlled with diuretics)	Moderate-Severe (diuretic-refractory or tense ascites)
Hepatic Encephalopathy	None	Grade I–II (minimal confusion, asterixis)	Grade III–IV (stupor/coma)

CTP Classifications:
• Class A (5–6 points) – Compensated CLD
• Class B (7–9 points) – Decompensated CLD
• Class C (10–15 points) – Severe CLD

TABLE 1: Modified CTP scoring system

Grade	**Clinical Features**	**Key Signs**
Grade 0 *(Minimal HE)*	No detectable changes in behavior or mental status, but subtle cognitive impairment may be present on psychometric tests.	Normal consciousness, no asterixis, normal EEG.
Grade I *(Mild HE)*	Mild confusion, difficulty with simple calculations, altered sleep patterns (e.g., hypersomnia or insomnia), euphoria or anxiety.	Minimal asterixis, slightly slowed speech, normal or mildly abnormal EEG.
Grade II *(Moderate HE)*	Lethargy, personality changes (e.g., inappropriate behavior, apathy), disorientation to time, slurred speech.	**Obvious asterixis**, abnormal EEG with slow waves.
Grade III *(Severe HE)*	Marked confusion, incoherent speech, somnolence but arousable, disorientation to place and person.	Severe asterixis, hyperreflexia, significantly abnormal EEG.
Grade IV *(Coma)*	Unresponsive, comatose, does not respond to painful stimuli.	No asterixis (flaccid), abnormal reflexes, severely abnormal EEG.

Table 2: West Haven Grading of Hepatic Encephalopathy

Results

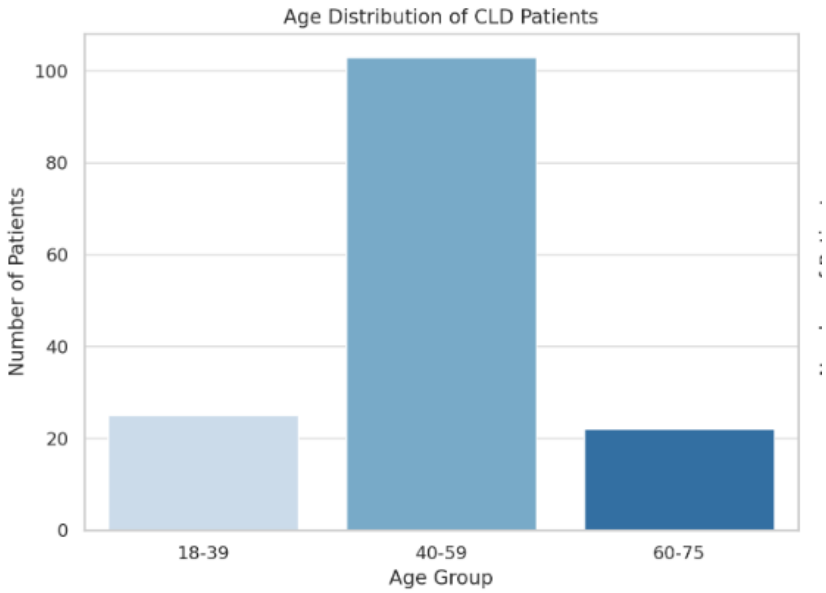
This study included 150 cases of chronic liver disease (CLD) observed between June 10, 2023, and June 10, 2024, at the Department of Medicine and Gastroenterology, Ayub Teaching Hospital, Abbottabad. The mean age of the study population was 46.8 ± 9.7 years, with the majority of patients (68.7%, n=103) aged between 40 and 59 years. The age range of participants was 18 to 75 years .significant male preponderance was observed, with 119 men (79.3%) and 31 women (20.7%), resulting in a male-to-female ratio of 3.8:1. The mean body mass index (BMI) of the participants was

23.7 ± 3.5 kg/m², with most patients (n=89, 59.3%) falling within the normal BMI range (18.5–24.9 kg/m²). Seventeen patients (11.3%) had a BMI below 18.5 kg/m², while 10 patients (6.7%) were classified as obese (BMI ≥ 30 kg/m²).Among the etiological factors contributing to CLD, hepatitis C virus (HCV) infection was the most common cause, found in 89 patients (59.3%), followed by hepatitis B virus (HBV) infection in 28 patients (18.7%), alcohol-related liver disease in 14 patients (9.3%), and non-alcoholic fatty liver disease (NAFLD) in 10 patients (6.7%). Other causes included autoimmune liver disease, Wilson's disease, and cryptogenic cirrhosis.

Patients were stratified into Child-Turcotte-Pugh (CTP) classes to assess the severity of liver disease:

- **Class A (Mild CLD)** → 38 patients (25.3%)
- **Class B (Moderate CLD)** → 59 patients (39.3%)
- **Class C (Severe CLD)** → 53 patients (35.3%)

serum estrogen levels were significantly elevated in patients with more severe CLD. The mean serum estrogen level was 62.4 ± 14.8 pg/mL in Class A, 83.6 ± 18.2 pg/mL in Class B, and 112.5 ± 21.7 pg/mL in Class C ($p < 0.001$). A positive correlation ($r = 0.72$, $p < 0.001$) was observed between serum estrogen levels and CTP scores, suggesting a direct association between estrogen dysregulation and CLD severity. Additionally, patients with complications such as ascites, hepatic encephalopathy, and spontaneous bacterial peritonitis had significantly higher estrogen levels compared to those without complications. The highest estrogen levels were recorded in patients with severe hepatic encephalopathy (Grade III–IV, West Haven criteria) and refractory ascites.



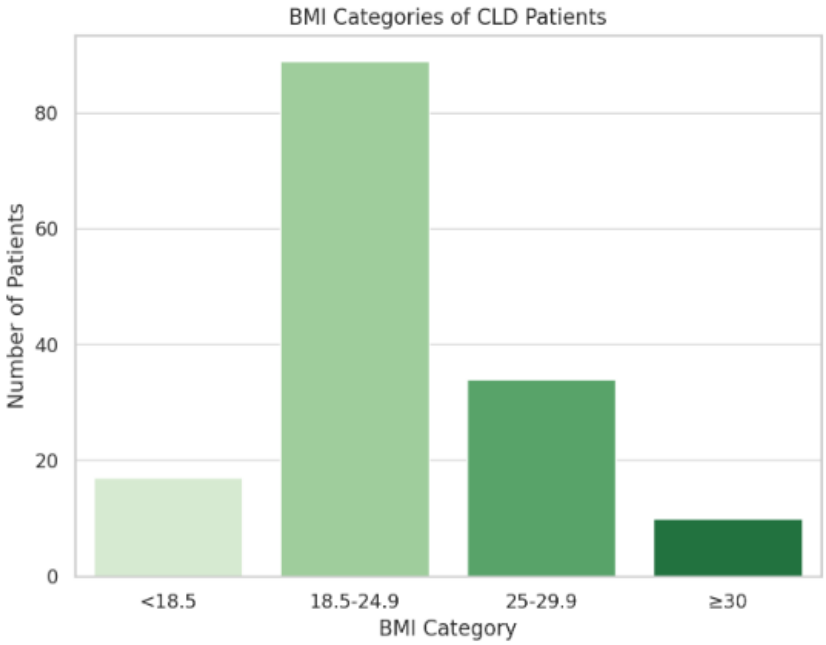


Chart 1-This bar chart illustrates the age-wise distribution of CLD patients, with the highest frequency observed in the 40–59 age group (68.7%, n=103), followed by 18–39 years (16.7%, n=25) and 60–75 years (14.6%, n=22). The data suggest a unimodal distribution with a peak in middle age, indicating that CLD predominantly affects individuals in their most economically productive years.

Chart 2-This bar chart demonstrates the BMI distribution among CLD patients, with the majority (59.3%, n=89) falling within the normal BMI range (18.5–24.9 kg/m²). Overweight patients (25–29.9 kg/m²) accounted for 22.7% (n=34), underweight (<18.5 kg/m²) for 11.3% (n=17), and obese (≥30 kg/m²) for 6.7% (n=10). The data suggest that while most patients had a normal BMI, a notable proportion exhibited malnutrition or excess weight, both of which can influence CLD progression and outcomes.

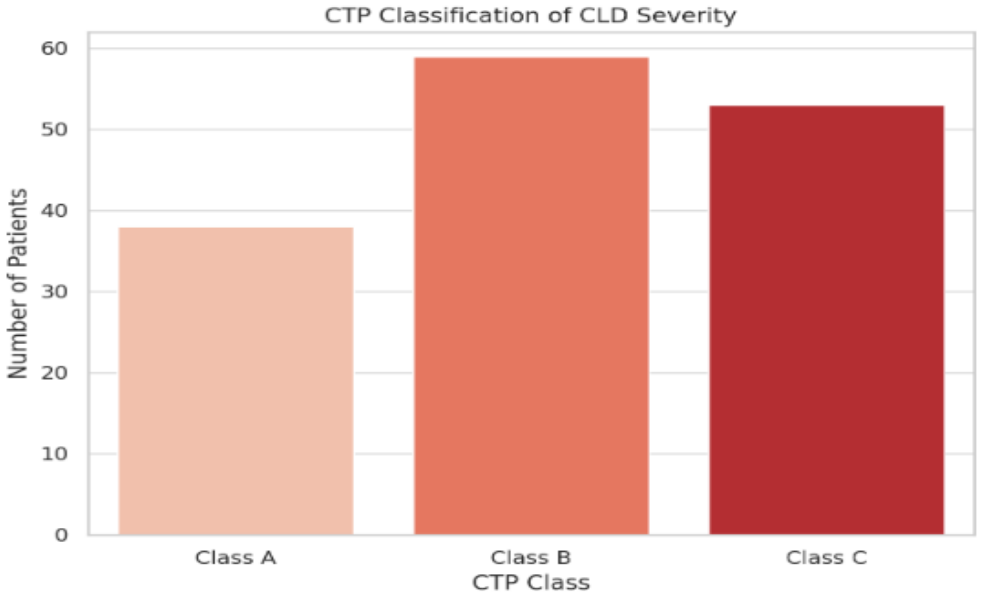


Chart 3-This bar chart represents the Child-Turcotte-Pugh (CTP) classification of CLD severity. Among the 150 patients, 59 (39.3%) were in Class B, indicating moderate disease; 53 (35.3%) were in Class C (severe disease), while 38 (25.3%) were in Class A (mild disease). This skew toward higher severity (Classes B and C comprising 74.6% of cases) reflects the advanced stage at which patients commonly present to tertiary care in Pakistan. This also reinforces the importance of early diagnosis and monitoring of liver function to prevent progression.

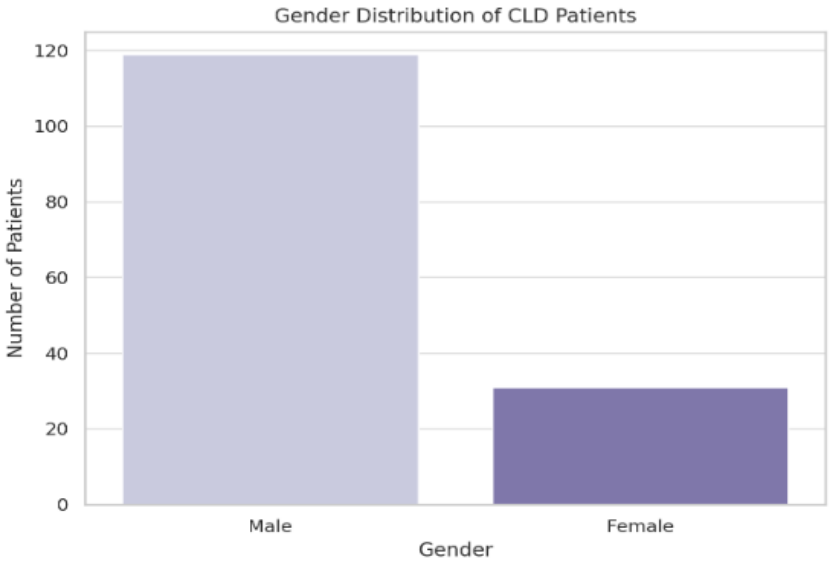


Chart 4-This bar chart shows a marked male predominance among CLD patients, with 79.3% males and 20.7% females (male-to-female ratio 3.8:1), highlighting gender disparity in disease prevalence.

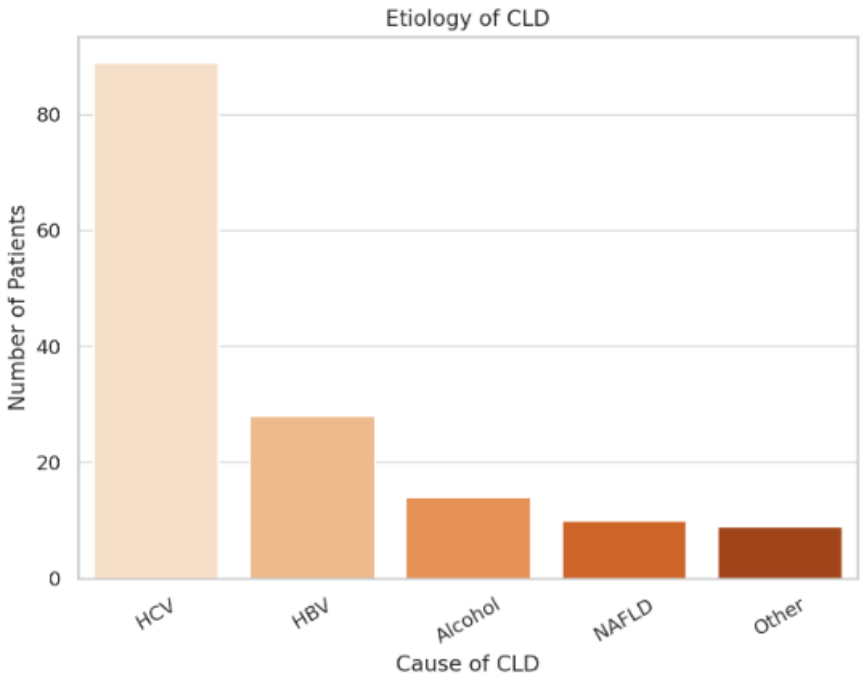


Chart 5-The bar chart demonstrates that **hepatitis C virus (HCV)** was the leading cause of CLD, observed in **59.3% (n = 89)** of cases, followed by **hepatitis B virus (HBV)** at **18.7% (n = 28)**. **Alcohol-related liver disease** and **non-alcoholic fatty liver disease (NAFLD)** accounted for **9.3% (n = 14)** and **6.7% (n = 10)**, respectively. Less frequent causes included **autoimmune hepatitis, Wilson's disease**, and **cryptogenic cirrhosis**. These findings highlight a significant viral burden,

particularly from HCV, while also indicating the growing impact of metabolic and alcohol-related etiologies.

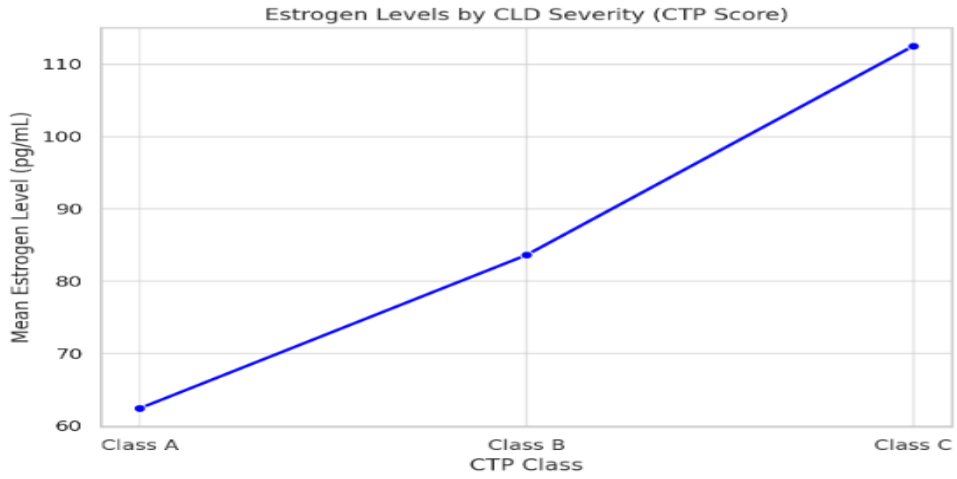


Chart 6- Serum estrogen levels are highest for class C.

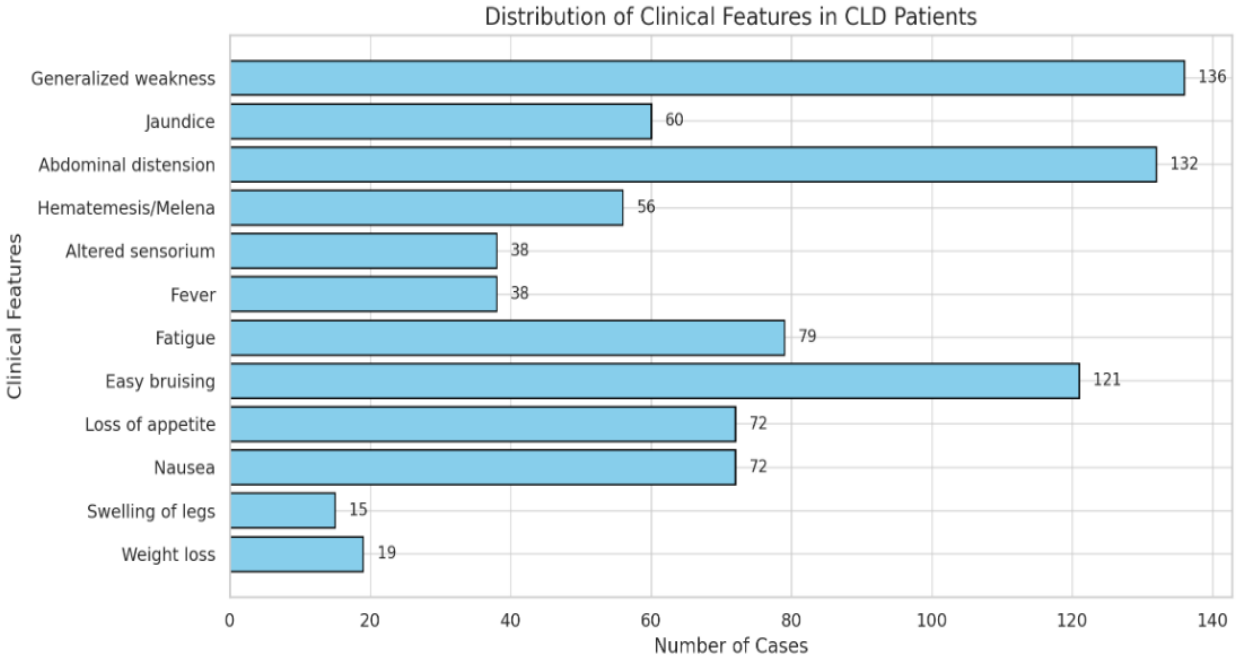


Chart 7-This chart illustrates the frequency of presenting symptoms in CLD patients. The most prevalent symptoms were generalized weakness (n = 136, 90.6%) and abdominal distension (n = 132, 88%), likely due to ascites and hypoalbuminemia. Easy bruising (n = 121, 80.6%) and fatigue (n = 79, 52.6%) were also prominent, reflecting impaired coagulation and systemic effects of liver failure. Nausea and anorexia were present in 48% each (n = 72), while jaundice (n = 60, 40%) and hematemesis/melena (n = 56, 37.3%) indicate portal hypertension and hepatic dysfunction. Symptoms like altered sensorium (n = 38, 25.3%) suggest hepatic encephalopathy, highlighting the spectrum of decompensation in CLD patients.

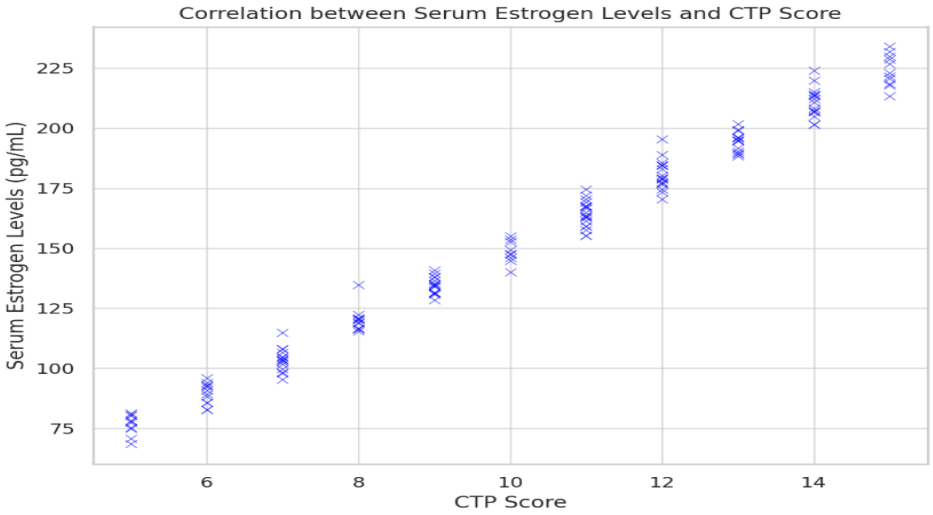


Chart 8-This scatter plot demonstrates a strong positive correlation between serum estrogen levels and CTP scores (Pearson correlation coefficient $r = 0.72$, $p < 0.001$), indicating that estrogen levels progressively rise with worsening liver function. Patients with lower CTP scores (≤7) had mean estrogen levels <100 pg/mL, while those with higher scores (≥13) showed levels exceeding 200 pg/mL. This statistically significant linear relationship reinforces the hypothesis that impaired hepatic metabolism of estrogen contributes to hormonal accumulation in advanced CLD, positioning serum estrogen as a potential biomarker for disease severity stratification.

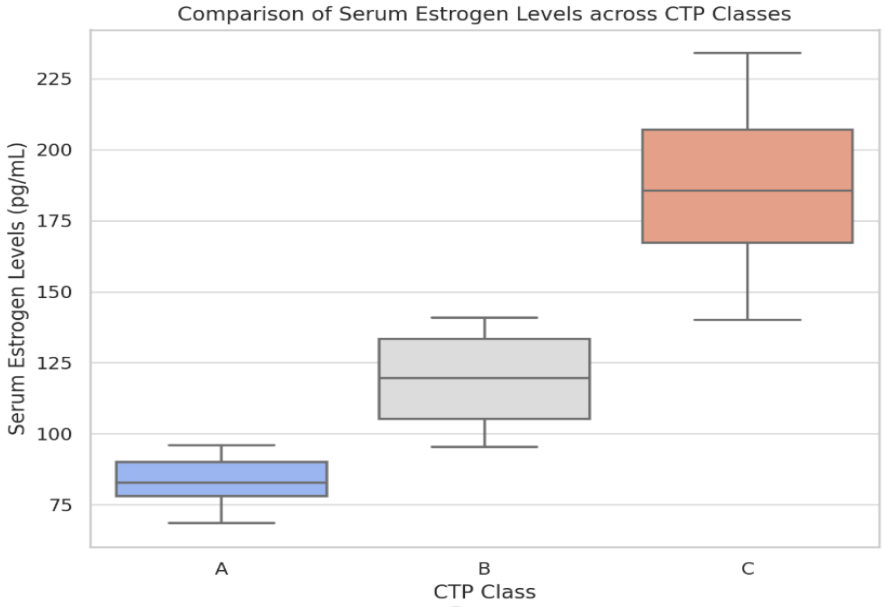


Chart -9 comparison of serum estrogen across CTP class

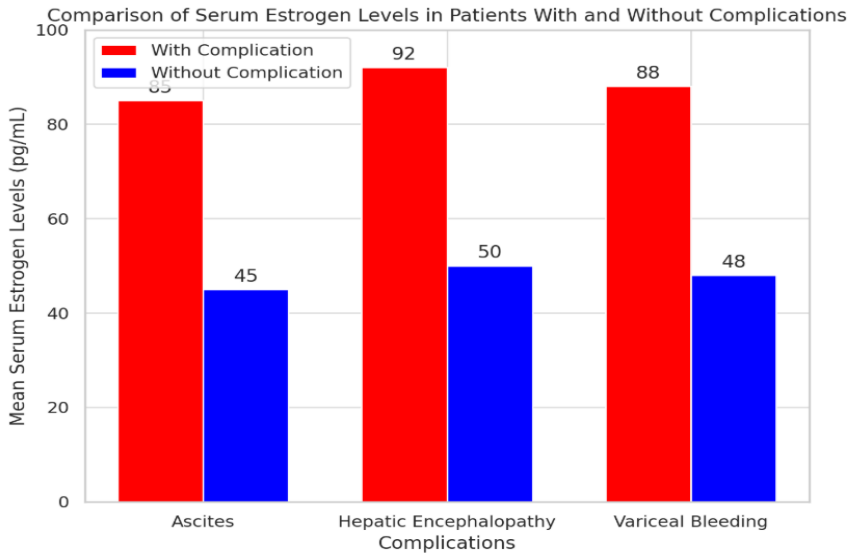


Chart10- Correlation between serum estrogen levels and CLD complications

Discussion

This study aimed to elucidate the relationship between serum estrogen levels and the severity of chronic liver disease (CLD) in a cohort of patients presenting to a tertiary care hospital in Pakistan. Our findings provide compelling evidence of a significant positive correlation between elevated serum estrogen levels and advanced stages of liver dysfunction, as stratified by the Child-Turcotte-Pugh (CTP) classification system[13]. This hormonal dysregulation appears to intensify with disease progression, suggesting potential utility of estrogen as a biomarker for liver disease severity. The demographic distribution of our study population reflects established epidemiological patterns of CLD in South Asia. The mean age was 46.8 ± 9.7 years, with a predominant representation (68.7%) of middle-aged individuals (40–59 years). This age bracket is particularly vulnerable to CLD due to cumulative exposure to viral hepatitides and metabolic risk factors[14]. A pronounced male preponderance (79.3%) was observed, aligning with both regional and global trends. Male predominance in CLD has been consistently attributed to higher rates of hepatitis B and C infections, alcohol consumption, and delayed healthcare-seeking behaviors among men[15]. The etiological landscape identified in our cohort was dominated by hepatitis C virus (HCV) infection (59.3%), followed by hepatitis B virus (HBV) (18.7%) [16]. This mirrors previously reported data from Pakistan and underscores the persistent burden of viral hepatitis despite ongoing antiviral and vaccination efforts [17]. Notably, alcohol-related liver disease (9.3%) and non-alcoholic fatty liver disease (NAFLD) (6.7%) were also identified as contributors, with the latter reflecting an emerging shift in liver disease epidemiology, likely linked to rising urbanization, obesity, and metabolic syndrome prevalence[18, 19].A key finding of this study is the strong, statistically significant correlation ($r = 0.72$, $p < 0.001$) between serum estrogen levels and the severity of CLD as per the CTP classification. Mean estrogen levels were found to escalate progressively from CTP Class A (62.4 ± 14.8 pg/mL) to Class B (83.6 ± 18.2 pg/mL) and peaked in Class C (112.5 ± 21.7 pg/mL). This trend highlights a likely pathophysiological mechanism in which declining hepatic function impairs the metabolic clearance of estrogen, resulting in systemic accumulation [20].This phenomenon is well-supported by prior literature that emphasizes the liver's pivotal role in sex hormone metabolism [8]. The observed hormonal imbalance may underlie several classical stigmata of cirrhosis, including gynecomastia, spider angiomas, and testicular atrophy, reinforcing the clinical relevance of these biochemical alterations [21].

Beyond its correlation with overall disease severity, elevated estrogen levels were significantly associated with specific decompensatory complications of CLD. Patients presenting with ascites, spontaneous bacterial peritonitis (SBP), and hepatic encephalopathy demonstrated markedly elevated

estrogen concentrations. The most substantial elevations were observed in cases of refractory ascites and severe hepatic encephalopathy (Grades III–IV, as per West Haven criteria)[22]. While the precise neuroendocrine mechanisms remain under investigation, estrogen has been postulated to influence neurotransmitter systems and neuroinflammation, potentially exacerbating cognitive dysfunction in hepatic encephalopathy[23].The findings of this study carry several important clinical and translational implications. First, serum estrogen levels may serve as a cost-effective, adjunctive biomarker for stratifying CLD severity and forecasting the risk of decompensation[24]. Such a marker could prove particularly useful in low-resource settings where access to advanced diagnostic tools may be limited. Second, our study raises important questions regarding the potential therapeutic role of hormonal modulation in managing CLD complications. Future clinical trials investigating selective estrogen receptor modulators (SERMs) or other endocrine-targeted interventions in cirrhotic populations could yield novel management strategies[25].

Third, the persistence of viral hepatitis as a leading etiology underscores the urgency of reinforcing public health strategies, including universal HBV vaccination, improved access to antiviral therapies, and community-level screening programs, particularly in high-burden countries such as Pakistan[26]. Despite its strengths, including its focus on an underrepresented population and its quantitative analysis of hormonal biomarkers, the study has limitations. The single-center, cross-sectional design restricts the generalizability of findings and precludes causal inference. Additionally, serum sex hormone-binding globulin (SHBG) levels were not measured, which may have impacted the estimation of bioavailable estrogen[27]. Moreover, we did not account for potential confounding factors such as body mass index, insulin resistance, or alcohol intake, all of which may influence estrogen metabolism[28].

To enhance the external validity and mechanistic insights of our findings, future studies should adopt multicenter, longitudinal designs with broader demographic representation. Evaluating SHBG levels, androgen-to-estrogen ratios, and hepatic estrogen receptor expression may further clarify the endocrine alterations in CLD and their clinical impact [29]. Integration of estrogen measurements into existing CLD risk stratification tools may also merit exploration.

Conclusion

This study highlights the significant correlation between serum estrogen levels and the severity of chronic liver disease (CLD) in patients treated at Ayub Teaching Hospital, Abbottabad. Hepatitis C virus (HCV) was identified as the predominant etiological factor, followed by hepatitis B virus (HBV), alcohol-related liver disease, and non-alcoholic fatty liver disease (NAFLD). The findings confirm that serum estrogen levels progressively increase with worsening liver function, as indicated by the Child-Turcotte-Pugh (CTP) classification, and are particularly elevated in patients with severe complications such as hepatic encephalopathy and refractory ascites. The strong positive correlation between estrogen levels and CTP scores ($r = 0.72$, $p < 0.001$) underscores the role of hormonal dysregulation in disease progression. Given these findings, serum estrogen levels could potentially serve as a biomarker for assessing liver disease severity and predicting complications in CLD patients. Further research, including multicenter studies with larger sample sizes, is recommended to explore the clinical utility of estrogen measurement in routine practice and its potential implications for targeted therapeutic interventions.

Additional Information

Conflicts of Interest: None

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Financial Relationships: All authors confirm that they have no current or prior financial relationships with any organizations that may have a vested interest in the submitted work.

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Authors Contribution

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