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ORIGINAL RESEARCH

Serum Cholinesterase Level in Patients with Cirrhosis of Liver and its Correlation with Child Pugh Turcotte Score

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ABSTRACT

Background: Liver cirrhosis is major global cause of morbidity and mortality. Serum cholinesterase is synthesized by liver and compared to other enzymes serum cholinesterase is decreased in liver dysfunction. Liver cirrhosis severity is calculated by Child Pugh score in which Class A (5-6) show mild disease Class B (7-9) show moderate disease and Class C (10-15) show severe disease. **Material and methods:** Present hospital based cross sectional study was single centric, conducted in 80 liver cirrhosis patients. Serum cholinesterase was measured within 72 hours of admission using colorimetric methods. Child Turcotte Pugh scores (CTP) were used to assess the severity of liver disease in patients with cirrhosis. Statistical analysis was done using SPSS, Version 2.0. **Results:** In the present study majority of participants are between the ages of 40 and 49 years with males outnumber the females (91.3%). Alcohol is the common cause of about 75% of patients. There were two patients in child class A, twenty-six in class B, and fifty-two in class C. Mean serum cholinesterase is 1728 with standard deviation of 979 IU/L. Serum cholinesterase had significant correlation among Child pugh score ($p < 0.001$) and was positively correlated with albumin and negatively correlated with serum plasma prothrombin time. **Conclusion:** Serum cholinesterase had significant correlation with Child pugh score in liver cirrhosis and can be used in routine clinical practice.

Key Words: Cirrhosis, serum cholinesterase, Child-Pugh class.

INTRODUCTION

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injuries (1). Cirrhosis involves extensive liver scarring and the development of abnormal nodules, leading to about 2 million deaths annually (2). In India, liver cirrhosis is a significant issue, causing 259,749 deaths in 2017, which accounted for 2.95% of all deaths and 18.3% of cirrhosis deaths worldwide (3).

The primary causes of cirrhosis are heavy alcohol use and viral hepatitis, though other factors like autoimmune diseases, fatty liver and genetic disorders also contribute(4). Liver cirrhosis is the end result of various chronic liver conditions, with fibrosis being the stage that comes before it. Many different cells, cytokines and the onset and progression of liver cirrhosis and fibrosis are influenced by microRNAs (miRNAs). A key event in fibrosis is the activation of hepatic stellate cells (HSCs) (5). Child pugh score is used for prognosis of liver cirrhosis. It includes parameters like serum albumin, bilirubin, international normalized ratio (INR), ascites and hepatic encephalopathy. Each parameter had score 1 to 3 depend on their blood level and examination finding. Then patients are classified in Child pugh Turcotte (CTP) class either A/B/C after summation of all score(6,7). Serum cholinesterase, is a form of serine hydrolase that can hydrolyze esters like acetylcholine, succinylcholine, and mivacurium as well as ester-type local anesthetics including procaine etc.

The liver produces Pseudocholinesterase (PChE) also known as serum cholinesterase or plasma cholinesterase or Butyrycholinesterase, which is present in the brain, pancreas, heart, and plasma. It is an alpha 2 globulin, a tetramer with a molecular weight of 342000, and it has an 8–12 day serum half-life(8). The hepatic origin of the enzyme has been confirmed by the discovery that serum cholinesterase level is increased in second week of successful liver

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transplant in comparison to pre liver transplant level(9). It was also used to differentiate between liver and non liver disorder(10). There is limited literature available assessing the relation of serum cholinesterase with child Pugh Turcotte score among the liver cirrhosis patients. Hence the present study designed to assess the serum cholinesterase levels in cirrhosis of liver and its relationship with Child Pugh Turcotte score.

MATERIALS AND METHODS

Research Design: Cross sectional study

Study Sample: This study included 80 patients from inpatient wards.

Inclusion criteria: The study includes male and female, aged >18 years with a confirmed diagnosis of cirrhosis based on clinical, radiological (abdominal ultrasound) and biochemical studies. Every patient underwent a medical examination in accordance with the predetermined pro forma. Patients were included in the study only after providing written, informed consent.

Exclusion criteria: The study excludes patients who do not meet the inclusion criteria, liver transplant patients, liver cancer patients, pregnant women, patients with sepsis.

Study site: The current study is a hospital-based investigation conducted from September 2022 to February 2024 in the Gastroenterology Department at Shri B. M. Patil Medical College Hospital and Research Centre, BLDE (Deemed to be University), Vijayapura. Approval from the institutional ethical committee was obtained before the study began (IEC/743/2022-2023).

An analysis of complete blood count, renal function tests, liver function tests, viral markers (HIV, HBSAG, HCV), serum cholinesterase, ultrasonography were done in the included patients and Child Pugh Scoring was calculated. Patients with CTP score divided into class A (5-6), class B (7-9), class C (10-15) respectively. Accordingly, serum cholinesterase was calculated using the ORTHO CLINICAL DIAGNOSTICS VITROS 5.1 FS, a fully automated clinical chemistry analyzer utilizing colorimetric methods. Measurements is conducted following the manufacturer's instructions, with a reference range of 5900 -12220 U/L applicable to both male and female subjects and correlated with child Pugh scoring system to assess the severity of liver cirrhosis.

STATISTISTICAL ANALYSIS

A Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS, Version 20). All statistical tests were performed in two-tailed; data was summarized with Mean ± Standard Deviation and the results were considered statistically significant if the *p*-value was <0.005.

RESULTS

Table 1 shows the age and gender of the individuals included for the present study The study included a total of 80 participants, with a minimum age of 24 years and maximum age was 84 years. The majority of participants fell within the age group of 40-49 years comprising 35.0% of the total sample. This was followed by participants aged 30-39 years (21.3%) and 50-59 years (25.0%). The smallest proportion of participants were in the age group of above 70 years constituting only 1.3% of the total sample. Male outnumber the females with 91.3%.

The majority of study participants (75.0%) received a diagnosis of cirrhosis linked to alcohol consumption. This is followed by cases where alcohol consumption was combined with infection of hepatitis B virus (HBV) (3.8%) or hepatitis C virus (HCV) (5.0%). HBV and HCV infection alone each accounted for 2.5% of cases. Non-alcoholic steatohepatitis (NASH) and unspecified causes represented a proportion of 2.5% and 8.8% respectively (Table 2).

Table 3 depicts that, majority of the participants considered for this study were in Class C (65%) followed by Class B (32.5%) and least proportion in Class A (2.5%). Serum cholinesterase levels decreased as Child-Pugh Class worsened, reflecting decline in liver function. Participants in Child-Pugh Class A had the highest mean serum cholinesterase level with a range from 1883.5 to 4491.2 U/L. Participants in Class B showed a moderate decrease in mean serum cholinesterase whereas participants in Child-Pugh Class C had the lowest mean serum cholinesterase level of 1329.944 U/L.

The Kruskal-Walli's test was conducted to assess the differences in serum cholinesterase levels across different Child-Pugh classes, indicative of varying degrees of liver cirrhosis severity and the results showed a significant difference in serum cholinesterase levels between the various Child-Pugh classes ($H = 23.627$, $p < 0.0001$). This suggests that serum cholinesterase is a sensitive marker for detecting differences in liver function and disease severity among patients with cirrhosis (Fig 1). In this study, pairwise comparisons between classes C and B ($p < 0.0001$) and C and A ($p < 0.038$) were significant, whereas those between classes B and A were not ($p = 0.596$).

Serum Cholinesterase was positively correlated with serum albumin ($r=0.86$, $p < 0.001$) whereas there is a negative correlation with Child Pugh score ($r= -0.625$, $p < 0.001$) and with PT-INR ($r =-0.459$, $p <0.001$) showing that those substances were produced in the liver and that their synthesis was decreased in liver dysfunction (Fig 2,3)

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Table 1 Total study population distribution based on gender and age

Parameter	Frequency	Percentage
Gender		
Male	73	91.3%
Female	07	8.7%
Total	80	100%
Age Group (Years)		
<30	03	3.8
30-39	17	21.3
40-49	28	35.0
50-59	20	25.0
60-69	11	13.8
70+	01	1.3
Total	80	100%

Table 2: Prevalence of cirrhosis in patients based on etiology

Etiology	Frequency (n)	Percentage (%)
Alcohol	60	75.0%
HBV	02	2.5%
HCV	02	2.5%
Alcohol+HBV	03	3.8%
Alcohol+HCV	04	5.0%
NASH	02	2.5%
Unspecified	07	8.7%

Table 3: Mean level of Serum Cholinesterase in Child Pugh Class

Child-Pugh Class	N	Mean	Std. Deviation	Minimum	Maximum
Class A (5-6)	2	3187.350	1843.9224	1883.5	4491.2
Class B (7-9)	26	2413.558	974.8251	822.0	3980.7
Class C (10-15)	52	1329.944	685.1670	266.0	3672.0
Total	**80**	**1728.554**	**979.6519**	**266.0**	**4491.2**

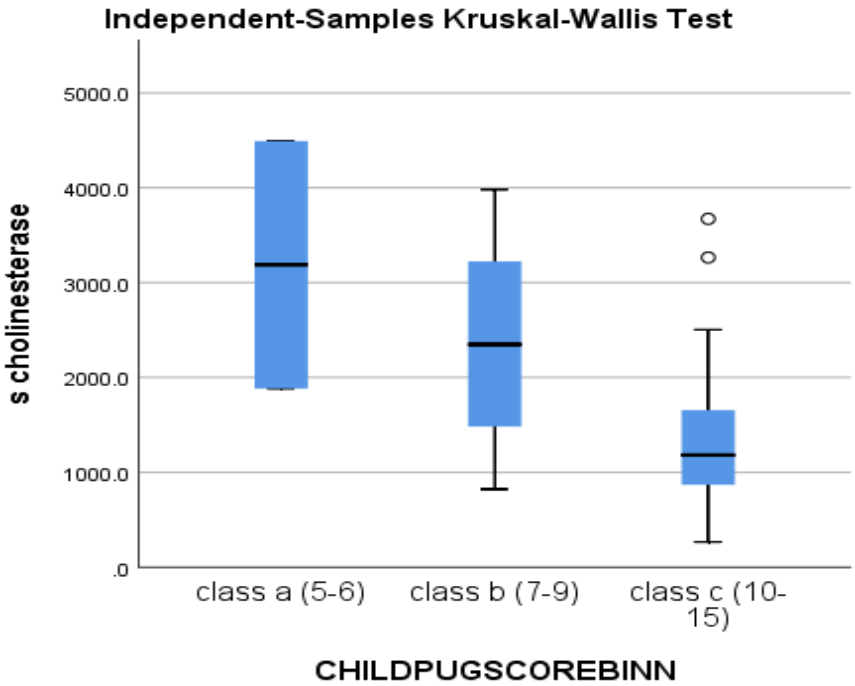

Figure 1: Kruskal-Wallis test of Child Pugh Score with Serum Cholinesterases

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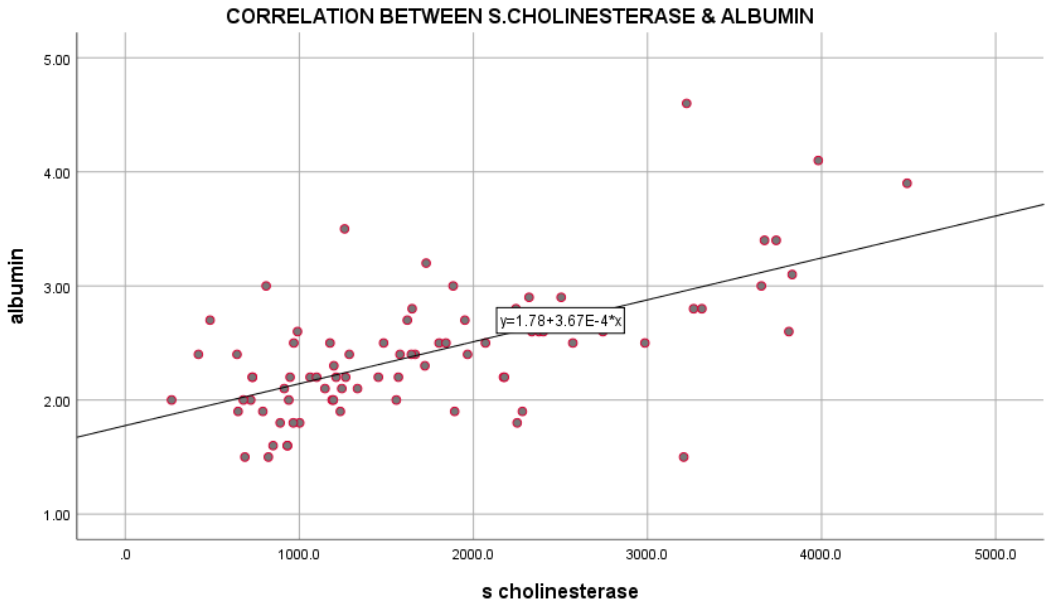

Figure 2: Correlation Between Serum Cholinesterase and Albumin

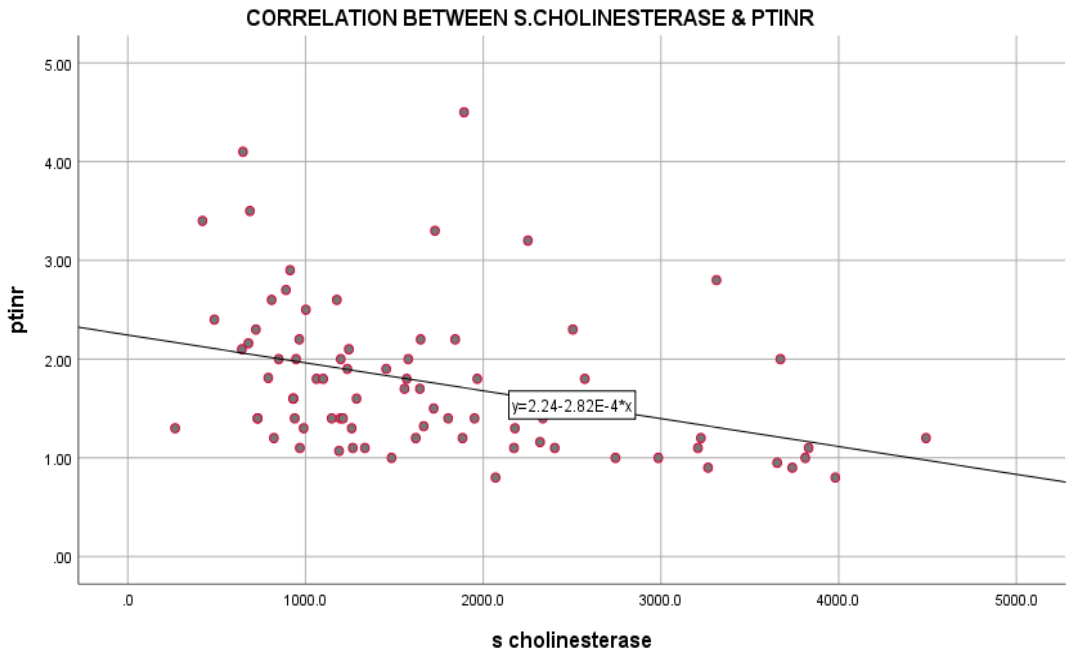

Figure 3: Correlation Between Serum Cholinesterase and PT-INR

DISCUSSION

Liver cirrhosis represents a significant global health burden characterized by progressive liver fibrosis and impaired liver function. Assessing the severity of liver cirrhosis is crucial for guiding clinical management and predicting patient outcomes. Biochemical tests used to assess liver function include measurements of ALT and AST, serum bilirubin, serum protein The Child-Pugh score and serum cholinesterase level are established markers used in clinical practice to evaluate the severity and prognosis of liver cirrhosis. The Child-Pugh score categorizes patients into classes A, B and C based on clinical parameters including bilirubin levels, albumin levels, prothrombin time, presence of ascites, and hepatic encephalopathy. Class A represents well-compensated cirrhosis, while Class C indicates decompensated cirrhosis with poorer prognosis and severe liver dysfunction. This study aimed to investigate the correlation between serum cholinesterase levels and Child-Pugh scores, providing insights into their utility as biomarkers for assessing disease severity.

Studies conducted by Ramanathan Kalpana et al[,] had shown, 80% population were male and 68% of patient had alcohol as etiological cause for cirrhosis (11). Present study depicts that 91.3 % of population is male and 75% patient had alcohol as a cause of their liver disease. The reason could be due to high alcoholism in males.Varsha et al reported that 83% of patients had ascites and 31 % had hepatic

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encephalopathy. In our study we found that 91.2% patient have ascites and 35% had hepatic encephalopathy (12). Majority of our study patients were in Class B and class C with a least in Class A (2.5%) in comparison to 24% patient in class A of previous studies. Thus, percentage of patients with ascites and hepatic encephalopathy are more in our study.

In the current study 2.5% of patients were class A, 32.5 % of class B and 65% of class C. Previous findings of Thatiya et al., shows that, 24% population is of class A , 41% of class B and 35% of class C . The majority of patients who came to our tertiary care facility as their illnesses worsened may be the cause of the discrepancy.

Serum cholinesterase, an enzyme synthesized primarily in the liver, plays a crucial role in various physiological processes including hydrolyzing acetylcholine and detoxifying organophosphates. In the context of liver cirrhosis, reduced serum cholinesterase levels reflect compromised hepatocellular function and decreased liver synthetic capacity (Oogunkeye). This was evident in our study where participants classified under Child-Pugh Class C exhibited significantly lower serum cholinesterase levels compared to those in Class A and Class B. Our results demonstrated that as the Child-Pugh class worsened from A to C, there was a progressive decrease in serum cholinesterase levels.

The distribution of Child-Pugh scores among study participants provides insight into the severity and clinical status of liver disease within the study population. Serum cholinesterase levels decreased as Child-Pugh class worsened, reflecting declining liver function. In Meng et al.' study, the mean serum cholinesterase levels have significant differences among the groups (15). Our study's findings align closely with those and demonstrating a significant decline in serum cholinesterase levels across Child-Pugh classes. These consistent findings across different studies reinforce the reliability of serum cholinesterase as a biomarker for evaluating liver function and the severity of cirrhosis. In our study we found a negative correlation between serum cholinesterase and Child Pugh score. Amin et al. study depicted, a significant negative correlation between serum cholinesterase levels and child scores (16). In our study correlation of serum cholinesterase with albumin was positive, significant and with PTINR it was negative and significant. These studies align with those of Md. Mamun-ur Rashid et al., who demonstrated a positive correlation with albumin and a negative correlation with PTINR. This relationship likely results from the progressive loss of hepatocyte residual functional capacity as the disease advances (17). Ramachandra et al., estimated the sensitivity and specificity of serum cholinesterase to be approximately 98.7% and 80.3% respectively, when serum cholinesterase level is less than 3506IU/L. They also concluded that, to investigate liver dysfunction, serum cholinesterase should be a standard diagnostic test in addition to other liver function tests. These findings highlight the potential of serum cholinesterase as a sensitive biomarker for monitoring liver function deterioration and evaluating the severity of cirrhosis (18). Despite having these studies, this simple biochemical test serum cholinesterase is not routinely done with liver function test worldwide.

The statistical analysis, including the Kruskal-Wallis test, confirmed the significant differences in serum cholinesterase levels across Child-Pugh classes. This statistical significance strengthens the validity of serum cholinesterase as a discriminatory marker in stratifying patients based on liver cirrhosis severity. Moreover, significant correlation between serum cholinesterase levels and other parameters within the Child-Pugh scoring system further supports its clinical relevance and utility in prognostication (19).

One of our study's limitations is the small sample size. Larger prospective cohort studies are necessary in the future to confirm our findings and investigate other variables affecting serum cholinesterase levels in liver cirrhosis.

CONCLUSION

Monitoring serum cholinesterase levels alongside the Child-Pugh score can enhance the accuracy of liver cirrhosis assessment and aid in therapeutic decision-making. Early detection of declining serum cholinesterase levels may prompt timely interventions to prevent disease progression and improve patient outcomes.

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