



To Study the Correlation of Serum Cholinesterase Level With Different Scoring Systems in Cirrhosis of the Liver

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Abstract

Background: Chronic liver disease in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis. The serum cholinesterase is mainly synthesized in the liver and it is released into the blood, which is reduced in liver dysfunction due to reduced synthesis, marked reduction of cholinesterase in liver dysfunction and restoration of synthesis with hepatocyte recovery suggest serum cholinesterase activity might be a more specific marker of liver dysfunction than traditional liver function tests. **Objectives:** To estimate the level of serum cholinesterase in patients with cirrhosis of the liver.

To correlate the level of serum cholinesterase with different scoring systems of cirrhosis of the liver and assess the utility of serum cholinesterase levels in prognostification. **Materials and Methods:** A cross-sectional, hospital-based, time-bound study conducted on 200 patients with cirrhosis of liver attending medicine OPD and getting admitted in hospitals attached to BMCRI from November 1st 2016 to August 30th 2018. All cirrhosis of liver patients were included and patients with Pregnancy, Acute infection, Chronic infection like tuberculosis and Oral contraceptive use were excluded. Serum cholinesterase, ultrasound abdomen, prothrombin Time, International Normalized Ratio, liver function test, Child-Pugh score, MELD score were measured. **Results:** In the study, the majority of the study subjects belonged to the age group 41 – 50 years (38.5%), followed by 31-40 years (21.5%), 51 – 60 years (18.5%). Sex distribution male 70% and female 30%. Serum Cholinesterase was positively correlated with Albumin and Prothrombin time and negatively correlated with MELD, Creatinine and Child-Pugh Score. The mean S. cholinesterase values found in study subjects belonged to Child-Pugh Score A, B and C were 4235.17 + 341.260, 3226.26 + 707.206 and 1764.09 + 808.797. The ANOVA results showed that there was a significant association found between child-pugh scores and S. cholinesterase ($p = 0.001$). **Conclusion:** The Study has demonstrated that the level of cholinesterase is correlated with the severity of the liver disease. Serum cholinesterase shows a good correlation with serum albumin, PT INR, Child-pugh score, MELD score. Compared to the above parameters serum cholinesterase is less complex and not easily affected by treatments for decompensated cirrhosis.

Keywords: Cirrhosis of liver; Serum cholinesterase; Child-pugh score; MELD

Introduction

Cirrhosis is defined as a diffuse process with fibrosis and nodule formation. It is the result of the fibrogenesis that occurs with chronic liver injury^[1]. The causes of cirrhosis are multiple and include metabolic, inflammatory, congenital, and toxic liver diseases^[2]. The most common causes of cirrhosis are chronic alcoholism and chronic hepatitis C and B, followed by biliary diseases and hemochromatosis^[3]. Regardless of the cause of cirrhosis, the pathologic features consist of the development of fibrosis to the point that there is architectural distortion with the formation of regenerative nodules^[4].

Liver function tests (LFTs) are useful in the evaluation and treatment of patients with hepatic dysfunction, comprising ALT, AST, alkaline phosphatase, bilirubin, albumin and prothrombin time. These tests reveal abnormal results in patients with clinical problems other than liver dysfunction^[5].

Serum Cholinesterase is synthesized in the liver and its levels are reduced in cirrhosis of the liver and its levels are not affected by treatment compared to other markers^[6].

Cholinesterase is the enzymes classified by Mendel and Rudney into true cholinesterase (acetylcholinesterase) present in erythrocytes and glial tissue and pseudocholinesterase (serum cholinesterase) present in the serum and synthesized in the liver^[7]. Marked decrease in serum cholinesterase synthesis in liver disease

suggest that its activity might be a specific indicator of liver dysfunction than other liver function tests [8].

Serum cholinesterase shows a good correlation with serum albumin, PT INR, Child-pugh score and the MELD score. Since it discriminates well between De-compensated Cirrhosis and Compensated Cirrhosis, low levels in cirrhosis may be considered as a prognostic marker of advanced liver disease [9].

To diagnose liver disease a large number of conventional liver function tests are being performed for many years but they don't have 100% sensitivity, specificity. Many times conventional parameters of liver function tests are raised in nonliver diseases [10].

Aims and objectives

1. To estimate the level of serum cholinesterase in patients with cirrhosis of the liver.
2. To correlate the level of serum cholinesterase with different scoring systems of cirrhosis of the liver and assess the utility of serum cholinesterase levels in prognostification.

Materials and Methods

The study was conducted on 200 patients with cirrhosis of liver attending medicine OPD and getting admitted in hospitals attached to BMCRI from November 1st 2016 to August 30th, 2018.

Inclusion criteria:

1. Patients willing to give written informed consent
2. Patients of either sex aged 18 years and above.
3. All patients diagnosed to have cirrhosis of the liver clinically and radiologically in hospitals attached to BMCRI.

Exclusion criteria:

1. Age less than 18 years
2. Pregnancy
3. Acute infection
4. A Chronic infection like tuberculosis
5. Oral contraceptive use
6. Drugs-anticholinesterase-inhibitor, glucocorticoids, esmolol, metoclopramide, cyclophosphamide.
7. Extensive burn injuries.
8. Organophosphate poisoning.

Methodology

After obtaining clearance and approval from the institutional ethics committee and written informed consent, the patients with cirrhosis of liver fulfilling inclusion and exclusion criteria will be enrolled in the study.

For each patient the following data will be collected: History, clinical examination, Serum cholinesterase, ultrasound abdomen, prothrombin Time, International Normalized Ratio, liver function test, Child-Pugh score, MELD score.

Sample size: 200 cases. Calculated using the following

Formula $N = Z^2pq/d^2$ Where, N=Sample size

Z2 at 95% confidence interval = 1.96

$p=0.615$ $1-p=q=0.38$ $d^2=0.10$

With 10% absolute precision (α) at 95% confidence interval, sample size (N) is 180.

Expecting the 10% non-response, the final sample size of 200 will be taken for the study.

Statistical Analysis

Categorical variables will be analyzed using descriptive statistics. ANOVA test was used to compare 3 or more groups. Pearson correlation test used to correlate quantitative variable. The P values < 0.05 were considered statistically significant.

Results and Analysis

In the study, the majority of the study subjects belonged to the age group 41 – 50 years (38.5%), followed by 31-40 years (21.5%), 51 – 60 years (18.5%). Sex distribution male 70% and female 30%

Table1: Etiology of cirrhosis of the liver

Etiology	Frequency	Percent
Alcohol	176	88
HBsAg	14	7
HCV	3	1.5
NASH	7	3.5

Alcohol is the most common etiology present in 88% of cases followed by HBsAg in 7%, NASH in 3.5% and HCV in 1.5% of cases.

Alcohol consumption was given to 88% of the study subjects. Nonalcoholics were 12%.

Child-Pugh Class(CPS)

The Majority of the study subjects belonged to Child-Pugh class 'C' (76%), followed by 'B' (21%) and 'A' (3%).

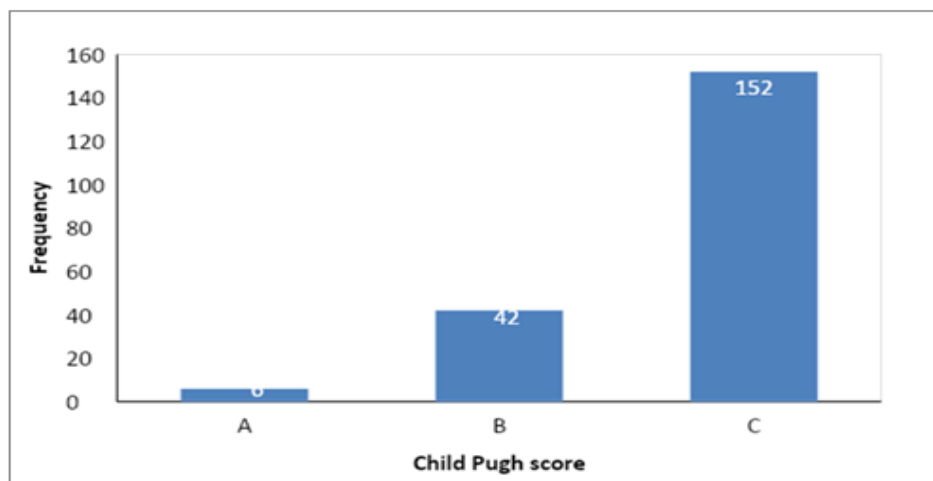


Figure 1: CPS

Table 2: Distribution of Parameters in the study

	Mean	SD	Minimum	Maximum
Hb (gm/dl)	9.70	2.30	2.40	16.40
TLC(/cumm)	10834.14	6613.41	21.0	39834.14
PLT(lakh/cumm)	1.34	0.82	0.17	5.72
Creatinine	1.46	1.41	0.20	8.50
T.Bilirubin	7.64	8.32	0.20	36.90
S.Albumin	2.42	0.18	1.30	4.90
PT	20.91	9.64	9.20	90.84
INR	1.93	1.29	0.35	13

Table 3.correlation of different variables with serum cholinesterase

S. Cholinesterase	MELD	ALBUMIN	CREATININE	CP Score	Prothrombin time
Pearson Correlation	-.517**	.596**	-.203**	-0.740	0.424
Sig. (2-tailed)	.000	.000	.004	0.000	0.000

S. Cholinesterase was positively correlated with Albumin (r – 0.596) and Prothrombin time (r - 0.424) and negatively correlated with MELD (r - -0.517), Creatinine (r - -0.203) and CP Score (r - -0.740). All the variables were significantly correlated with S. cholinesterase (p < 0.05)

Table no 4: Serum cholinesterase in alcoholic and non alcoholic liver cirrhosis

Alcoholic history	N	S. Cholinesterase		t-test	p-value
		Mean	Std. Deviation		
Alcoholic	176	2157.18	1071.549	0.435	0.664
Nonalcoholic	24	2058.00	836.398		

The mean S. Cholinesterase in alcoholic and nonalcoholic was 2157.18 + 1071.549 and 2058 + 836.398. The t-test value shows that there was no significant difference between alcoholic history and S. Cholinesterase (p – 0.664).

Table 5: Correlation of serum cholinesterase and child-pugh score

	Mean	Std. Deviation	t-test	p-value
CP SCORE	11.52	2.429	28.885	0.001
CHE	2145.28	1044.814		

The mean CP score was 11.52 + 2.429 and the mean S. Cholinesterase was 2145.28 + 1044.814.The t-test value shows that there was a significant difference between CP Score and S. Cholinesterase (p – 0.001).

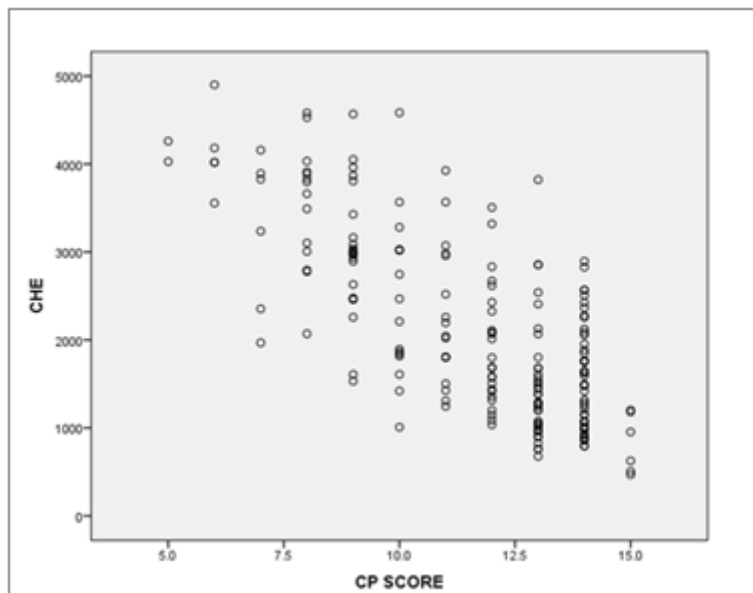


Figure 2: correlation of serum cholinesterase and child-pugh score

Table 6: Correlation of serum cholinesterase and child-pugh class

Child-Pugh score	N	S. Cholinesterase		Minimum	Maximum	F-value	p-value
		Mean	Std. Deviation				
A	6	4235.17	341.260	4019	4901	80.015	0.001
B	42	3226.26	707.206	1532	4582		
C	152	1764.09	808.797	468	4584		
Total	200	2145.28	1044.814	468	4901		

The mean S. cholinesterase values found in study subjects belonged to Child-Pugh Score A, B and C were 4235.17 + 341.260, 3226.26 + 707.206 and 1764.09 + 808.797. The ANOVA results showed that there was significant association found between child-pugh scores and S. cholinesterase ($p = 0.001$)

Table 7: Correlation of serum cholinesterase and meld score

	Mean	Std. Deviation	t-test	p-value
MELD	21.83	9.62	28.7409	0.001
CHE	2145.28	1044.814		

Table 8: Correlation of serum cholinesterase and meld score

MELD	N	S. Cholinesterase		Minimum	Maximum	F-value	P-value
		Mean	Std. Deviation				
< 10	12	3610.67	809.470	1968	4901	36.516	0.000
10 – 20	90	2477.79	954.047	871	4584		
> 20	98	1660.47	851.117	468	4568		
Total	200	2145.28	1044.814	468	4901		

The mean MELD was 21.83 + 9.62 and the mean S. Cholinesterase was 2145.28 + 1044.814. The t test value shows that there was a significant difference between MELD and S. Cholinesterase ($p = 0.001$).

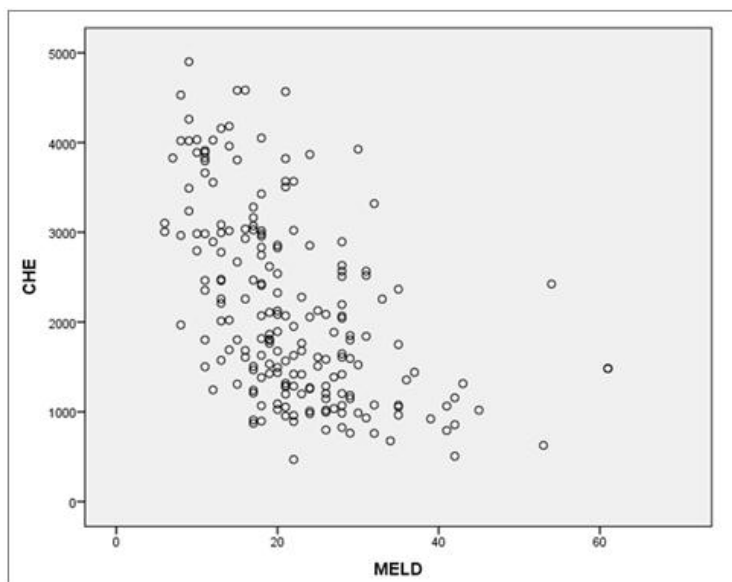


Figure 3: Correlation of serum cholinesterase and meld score

The mean S. cholinesterase value was found in study subjects with a MELD score of less than 10 was 3610.67 + 809.47, followed by a MELD score of 10 – 20 (2477.79 + 954.047) and > 20 (1660.47 + 851.117). The ANOVA results showed that there was a significant association found between MELD scores and S. cholinesterase ($p < 0.001$)

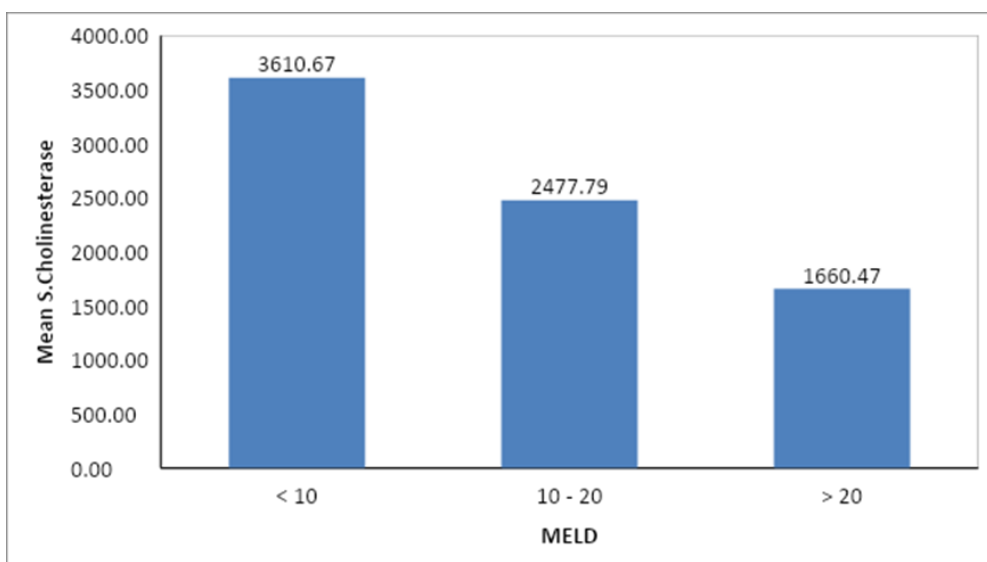


Figure 4: Correlation of serum cholinesterase and meld score

Discussion

Chronic liver disease in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis [1]. The serum cholinesterase is mainly synthesized in the liver and is released into the blood, which is reduced in liver dysfunction due to reduced synthesis, marked reduction of cholinesterase in liver dysfunction and restoration of synthesis with hepatocyte recovery suggest serum cholinesterase activity might be a more specific marker of liver dysfunction than traditional liver function tests.

In our study 200 patients of clinically or radiologically diagnosed cases of cirrhosis were taken and serum cholinesterase was estimated for all patients, which is correlated with child-pugh score and meld score. Among 200 cases 181 patients were male accounting for 91% of cases and the remaining 19 patients were females accounting for 9.5% of cases. The Majority of patients belonged to the age group between 41- 50 years.

Out of 200 patients 176 were alcoholics with significant alcohol consumption, which is being the most common cause of cirrhosis accounting for 88%, followed by hepatitis B(7%) and hepatitis c (1.5%). The Majority of patients belonged to child-pugh class C, accounting for 76%(152) followed by class B accounting for 21% of cases and 3% (6) of cases belonged to class A. The mean MELD score in our study was 21.

In this study, the serum cholinesterase levels were decreased in all patients compared to standard value, with a significant p-value of <0.001. The mean \pm SD of serum cholinesterase in cases was 2145.28 ± 1044.814 , this is by the study by Jeyamani Ramachandran et al., where serum cholinesterase levels in cirrhotic ranged between 110 to 8143IU/l with a median of 1590IU/L.

In our study there was no statistically significant difference in serum cholinesterase between alcoholic and non-alcoholic patients ($p = 0.664$). Serum cholinesterase was positively correlated with prothrombin time, Total bilirubin and negatively correlated with serum albumin. These results were matched with Jeyamani Ramachandran et al., where ChE levels reflect the functional integrity of liver.

The mean S. cholinesterase values found in study subjects belonged to Child-Pugh Score A, B and C were $4235.17 + 341.260$, $3226.26 + 707.206$ and $1764.09 + 808.797$. The ANOVA results showed that there was a significant association found between child-pugh scores and S. cholinesterase ($p = 0.001$). This by a Fanping Ming et al., where the patients with child-pugh class a had a cholinesterase value $5368+1657$, class B had $2943 +1212$ and class C had $1832 + 710$, which showed serum cholinesterase tend to decrease significantly in three grades of cirrhosis.

The mean S. cholinesterase value was found in study subjects with aa MELD score of less than 10 was $3610.67 + 809.47$, followed by a MELD score of 10 – 20 ($2477.79 + 954.047$) and > 20 ($1660.47 + 851.117$). The ANOVA results showed that there was a significant association found between MELD scores and S. cholinesterase ($p < 0.001$). In our study we found a

significant correlation between serum cholinesterase and MELD score in cirrhotic patients, where patients with higher MELD scores have a lower level of cholinesterase($p < 0.001$). This by study done by Jayamani Ramachandran et al., where the patients with MELD score <15 had a mean serum cholinesterase of 1940IU/L and patients with MELD score >15 had a mean serum cholinesterase of 1084 IU/L with a significant correlation coefficient($p < 0.001$)

Conclusion

In conclusion, the findings of this study have demonstrated that the level of cholinesterase is correlated with the severity of liver disease. It shows a good correlation with serum albumin, PT INR, Child-pugh score, MELD score. Compared to the above parameters serum cholinesterase is less complex and not easily affected by treatments for decompensated cirrhosis. The combination of cholinesterase with above parameters may be more subjective and accurate in evaluating the liver reserve function of cirrhotic patients.

Limitation

The Sample size was a small and single-center study

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