Section: General Medicine

Original Research Article

ASSESSMENT OF THE VALUE OF SERUM CHOLINESTERASE AS A LIVER FUNCTION TEST IN PATIENT WITH LIVER DISEASES

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Abstract

Background: Liver function is influenced by cholinesterase enzymes, which hydrolyse acetylcholine to choline and acetic acid. Serum cholinesterase activity decreases with liver dysfunction due to reduced synthesis, suggesting that it may be a more specific indicator of liver dysfunction than traditional liver function tests. This study aimed to assess serum cholinesterase levels and liver function, examine the correlation, and grade the severity of liver dysfunction based on cholinesterase levels in patients with chronic liver disease. **Materials and Methods:** A cross-sectional observational study was conducted in Government Rajaji Hospital Madurai on 50 chronic liver diseases of outpatients and inpatients for six months, from March 2021 to August 2021. After selecting the cases, thorough history-taking and clinical examination were performed. Tests including serum albumin, serum globulin, prothrombin time, INR, ultrasonography of the abdomen, upper GI endoscopy, blood count, erythrocyte sedimentation rate, and C-reactive protein were performed. **Result:** Chronic liver disease was more common among patients aged 31–40 years, and it was more common in males. High bilirubin levels, coagulopathy, and elevated INR levels were significantly positively correlated with serum albumin and serum cholinesterase levels. Conversely, patients with lower albumin levels have lower serum cholinesterase levels. Serum cholinesterase levels also correlate with the severity of chronic liver disease, with patients with reduced cholinesterase levels having elevated SGOT levels. SGPT levels are also significantly correlated with low serum cholinesterase levels. **Conclusion:** The present study concludes that Serum cholinesterase can be considered an alternative biomarker for diagnosing and assessing the severity and prognosis of patients with chronic liver diseases.

INTRODUCTION

The liver is a vital organ, accounting for 2–3% of the average body weight. It has two lobes and is protected by a rib cage and ligamentous attachment. The liver receives a dual blood supply, with 75% coming from the portal vein and 25% from the hepatic artery. The hepatic artery has alpha and beta-adrenergic receptors, and flow through it is controlled by the splanchnic nerves of the autonomic nervous system.[1-3] Diseases involving the hepatobiliary system are a major cause of mortality and morbidity in developing countries.[1,4] Liver function tests assess serum total bilirubin, protein, albumin, globulin, SGOT, ALT, and ALP. These tests often show changes in patients with nonhepatic diseases. However, these tests have limitations, such as vitamin K deficiency, anticoagulant treatment, clotting factor deficiency, haemolytic anaemia, and alkaline phosphatase in other organs. Damage to cell membranes can also cause abnormal levels of LDH and aminotransferase.[5,6]

Serum albumin levels may be altered due to nonhepatic causes, such as malnutrition, malabsorption, and kidney diseases. Albumin is a major component of plasma proteins produced by liver polyribosomes bound to the rough endoplasmic reticulum and then secreted into the plasma. A reduction in serum albumin levels reflects reduced synthesis by hepatocytes. However, serum albumin level changes depend on plasma volume and losses, for instance, in the gut or urine, which may be responsible for developing hypoalbuminemia.[7-9] Therefore, there is a need for a specific and sensitive test for liver disease. Serum cholinesterase has been studied for decades as a biomarker to assess the liver's synthetic, excretory, and metabolic functions. Hepatocytes produce serum cholinesterase; hence,

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they reflect the liver function. Serum cholinesterase values are not affected by transfusion of albumin or transfusion of blood products such as fresh frozen plasma.[10,11]

Previous studies have shown that serum cholinesterase levels might help diagnose liver diseases and aid in assessing the severity and prognosis of liver diseases. Cholinesterase belongs to the enzymatic group, which helps break down the esters of choline and thiocholine. Serum cholinesterases are synthesised by the hepatic parenchyma and are released into the circulation.[12,13] Multiple studies in the past have shown an excellent correlation with the currently available routine liver function tests such as serum albumin, PT INR, Bilirubin, and aminotransferases.

AIM

This study aimed to assess serum cholinesterase levels and liver function, examine the correlation, and grade the severity of liver dysfunction based on cholinesterase levels in patients with chronic liver disease.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in Government Rajaji Hospital Madurai on 50 chronic liver diseases of outpatients and inpatients for six months from March 2021 to August 2021. The study received institutional ethics committee approval and informed consent before initiation.

Inclusion Criteria

Patients with confirmed chronic liver disease and abnormal results in at least four out of five specific liver function tests were included.

Exclusion Criteria

Patients aged <30 or >60 years with acute abdominal diseases, anaemia, protein-energy malnutrition, chronic infection, chronic illness such as thyroid disorders, Diabetes, Bronchial asthma, Myasthenia Gravis, seizure disorder, postoperative subjects, organophosphorus poisoning, pregnancy, oral contraceptive pills, MAO inhibitors, cyclophosphamide, caffeine, theophylline, morphine, phenothiazine derivatives, codeine and procaine hydrochloride, malignancy, extensive burns, and chronic debilitating illness were excluded.

After selecting the cases, thorough history-taking and clinical examination were performed. Investigations were performed using the following methods: serum cholinesterase was measured using the DGKC method, and total and direct bilirubin levels were estimated using the DMSO method 3. NADH, the Kinetic UV method, and IFCC were used to estimate alanine aminotransferase. Aspartate aminotransferase (AST) levels were measured using NADH, kinetic UV, and IFCC. Total protein was estimated using the biuret method. Alkaline phosphatase by p-nitrophenyl phosphate, kinetic method DGKC, and Serum albumin were measured using the Bromocresol Green method 8. Serum Globulin, Prothrombin time and INR, Ultrasonography of the abdomen, Upper GI endoscopy, Complete blood count using automated haematology analyser, Erythrocyte sedimentation rate by Westergren method, C-Reactive protein by latex enhanced nephelometry were performed.

Statistical Analysis

The collected data were analysed using SPSS software and expressed as frequencies and percentages. The Pearson correlation coefficient and P-value were calculated to determine the study's correlation and statistical significance. Statistical significance was set at $p<0.05$.

RESULTS

In our study population, chronic liver diseases mostly occurred in patients aged 31–40 and 41–50 years, with a slight increase in incidence in the age group of 31–40 years, which is the productive age group of the country rather than 41–50 years. It is less common in patients aged < 30 years and >50 years. Females are more commonly affected than their male counterparts. There is a slight rise in incidence in females in the age group of 41 to 50 years, whereas 31 to 40 years and 51 to 60 years have an equal incidence of chronic liver disease.

Of the 50 participants, 84% of males and 16% of females had chronic liver disease. The primary cause was alcohol intake, accounting for 70% of the cases, followed by Hepatitis B (18%) and Hepatitis B (12%). The most common aetiology of chronic liver disease was alcohol consumption [Table 1].

Twenty% of patients had serum cholinesterase levels >3000 units/L, 24% between 1500 and 3000 units/L, and 56% <1500 units/L. Regarding serum total bilirubin levels, 18% had values <5 mg/dl, 24% between 5 and 10 mg/dl, and 58% had values >10 mg/dl. Regarding SGOT levels, 20% had levels <120IU/L, 20% between 120 and 240IU/L, and 60% had levels >240IU/L.

The distribution of SGPT levels was as follows: 20% <120 IU/L, 14% between 120 and 240 IU/L, and 66% >240 IU/L. Regarding serum albumin levels, 18% were between 2.6 and 3.5 g/dl, 24% between 2 and 2.5 g/dl, and 58% were <2.0 g/dl. For INR values, 16% were between 1 and 1.5, 24% were between 1.6 and 2, and 60% were >2 [Table 2].

A significant negative correlation was observed between serum cholinesterase levels and SGOT, SGPT, INR, and serum bilirubin levels. In addition, serum cholinesterase levels were significantly positively correlated with serum albumin levels. This suggests that serum cholinesterase could serve as an alternative biomarker reflecting synthetic liver function in patients with chronic liver disease [Table 3].

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Table 1: Demographic data of the study

		Frequency
Age	20-30	1
	31-40	21
	41-50	20
	51-60	8
Sex	Male	42(84)
	Female	8(16)
Aetiology	Alcohol	35(70)
	HBS Ag positive	9(18)
	HCV positive	6(12)

Table 2: Biochemical parameters of the study population

		Frequency	Percentage
Cholinesterase	>3000	10	20
	1500-3000	12	24
	<1500	28	56
Bilirubin	<5	9	18
	5-10	12	24
	>10	29	58
SGOT levels	<120	10	20
	120-240	10	20
	>240	30	60
SGPT (IU/L) levels	<120	10	20
	120-240	7	14
	>240	33	66
Serum albumin levels (g/dl)	2.6-3.5	9	18
	2.0-2.5	12	24
	<2.0	29	58
INR (International Normalised Ratio) levels	1-1.5	8	16
	1.6-2	12	24
	>2	30	60

Table 3: Correlation between SGOT, SGPT, serum albumin, INR, and total bilirubin in the study population

		Sr. Cholinesterase (U/L)			P-value
		>3000	1500-3000	<1500	
SGOT (IU/L)	<120	10	0	0	<0.0001
	120-240	0	10	0	
	>240	0	2	28	
SGPT (IU/L)	<120	10	0	0	<0.0001
	120-240	0	7	0	
	>240	0	5	28	
Sr. Albumin (g/dl)	2.6-3.5	9	0	0	<0.0001
	2.0-2.5	1	11	0	
	<2.0	0	1	28	
INR	1-1.5	8	0	0	<0.0001
	1.6-2	2	10	0	
	>2	0	2	28	
Total bilirubin (mg/dl)	<5	9	0	0	<0.0001
	5-10	1	11	0	
	>10	0	1	28	

DISCUSSION

The suggestion to estimate the level of activity of serum cholinesterase as a means to differentiate hepatic from post-hepatic jaundice was first put forth by McArdle (1940) and has since been found to be a useful indicator of liver function in patients with liver disease.[14] In China, cholinesterase has been incorporated into scoring systems used to assess the severity of hepatitis.[15] The current study analysed the 50 participants to assess serum cholinesterase concentration as a liver disease biomarker. In our study, most patients were in the 31-40 age group (80%). This showed that chronic liver disease was most seen in 31-40 years of age in our study population. Forty-two patients were males (84%), and the remaining eight (16%) were females. Among 50 patients with chronic liver disease, the most common aetiology of chronic liver disease was alcohol consumption in 35 patients (70%), followed by Hepatitis B virus infection, which accounted for approximately 18% (9 patients), and Hepatitis C virus infection which causes chronic liver disease in 6 patients (12%). A similar study was reported by Meng et al., in which 866 cirrhotic patients presented with elevated cholinesterase levels. The study observed a consistent elevation of cholinesterase in patients undergoing liver diseases such as cirrhosis, hepatitis, and ascites.[12]

Among the 50-study population, ten patients had serum cholinesterase levels >3000 U/L, which accounted for 20% of the patients. Twelve patients

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(24%) had serum cholinesterase levels between 1500 and 3000 U/L, and 28 patients (56%) had serum cholinesterase levels <1500 U/L. This shows that the majority of the population has severely reduced cholinesterase levels. Of the 50 patients, nine patients (18%) had total bilirubin levels <5 mg/dl, 12 patients (24%) had total bilirubin levels between 5 and 10 mg/dl, and 29 patients (58%) had a total bilirubin level >10 mg/dl. Thirty patients (60%) had an INR level >2. Thus, most of the patients had coagulopathy. In comparison to Meng et al., findings the cholinesterase levels were significantly similar to our study, where group A patients (cirrhosis and hepatitis) were reported with cholinesterase levels of 5368.04±1657.32 U/l, followed by group B (2943.06±1212.84 U/l) and group C (1832.51±710.68 U/l).12 Gu and Zhong also reported similar in-line results.[16] Furthermore, Prakash et al. also reported comparable findings about the serum bilirubin levels of Group A (5978±535 U/l), Group B (3957±454 U/l), and Group C (2267±332 U/l). It is important to note that the Child-Pugh score incorporates five clinical measures of liver disease, two of which, ascites and hepatic encephalopathy, are subjective in nature.[17]

Our study examined the association between serum albumin and cholinesterase levels. Our findings indicate a positive correlation between the two, with a highly significant p-value of <0.0001. In addition, serum total bilirubin levels were significantly negatively correlated with serum cholinesterase levels in patients with chronic liver disease (p <0.0001). Furthermore, INR values were negatively correlated with serum cholinesterase values, which was also statistically significant (p < 0.0001). This result is consistent with previous studies conducted by Meng et al.[12] The study by Mohamed et al. in 150 patients reported similar findings where cholinesterase was significantly associated with liver disease. In addition, the cholinesterase activity was positively correlated with prothrombin time, and a negative correlation was seen with serum albumin concentrations.[18]

In our study population, SGOT values were negatively correlated with serum cholinesterase values, which was also statistically significant (p<0.0001). In our study population, SGPT values were negatively correlated with serum cholinesterase values, which was also statistically significant (p<0.0001). Aygun et al. also reported a negative correlation, where a decreased level of cholinesterase was reported with elevated SGPT and SGOT levels.[19]

CONCLUSION

In conclusion, this study revealed that chronic liver diseases are most prevalent among individuals aged 31–40 years, with a peak in the productive age group. Females are more commonly affected than men and alcohol consumption is the primary cause. Serum cholinesterase levels significantly correlated with liver function markers, suggesting its potential as a biomarker for assessing synthetic liver function in patients with chronic liver disease. These findings align with previous research and emphasise the importance of considering demographic factors in understanding liver diseases. Further validation may enhance the clinical utility of serum cholinesterase for liver disease assessment.

Limitations

The study population was small, and it was a single-centre study. All the subjects were from the same centre. Therefore, race, dietary habits, and environmental factors may also play a role in the pathogenesis of liver disease. Individuals with congenital deficiency of serum cholinesterase in southern India were excluded from the study. A liver biopsy was not performed to identify the pathological cause of chronic liver disease.

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