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Research Article

The Auxiliary Diagnostic Value of Serum Total Bile Acids in Liver Cirrhosis at Clinical Test

Changxiu Sun, Qi Zhu*

Department of Clinical Laboratory, The Affiliated People's Hospital of Jiangsu University, Zhenjiang, China

Abstract

Objective: To investigate the auxiliary diagnostic value of serum total bile acid (TBA) in clinical testing of liver cirrhosis (LC). *Methods:* A total of 85 patients with LC and 77 patients with hepatitis who were treated in the Affiliated People's Hospital of Jiangsu University from June 2023 to April 2025 were included as the observation group, and 81 healthy people who underwent physical examination in this hospital during the same period were randomly selected as the control group. LC patients comprise 44 cases in the compensated stage and 41 cases in the decompensated stage. The general information of the respondents was collected, and the serum levels of TBA, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Prealbumin (PA), Gamma-Glutamyltransferase (GGT), Alkaline Phosphatase (ALP), and Adenosine Deaminase (ADA) were measured for patients in each group. Logistic regression was used to analyze the influencing factors of LC. The receiver operating characteristic (ROC) curve was used to evaluate the auxiliary diagnostic value of serum TBA level for LC. *Results:* Compared with the control group, the levels of TBA, AST, GGT, ALT, ALP, ADA in the LC group were significantly increased, while the level of PA was significantly decreased ($p<0.05$). Compared with patients in the compensated stage of LC, those in the decompensated stage exhibited a significantly elevated level of serum TBA and a notably reduced level of serum Prealbumin (PA) ($P<0.05$), while no significant differences were observed in the levels of other serum indicators. Logistic regression showed that TBA (*OR*=1.018, 95%*CI*: 1.002~1.034, *P*<0.05) was an independent risk factor for LC, while PA (*OR*=0.984, 95%*CI*: 0.978~0.989, *P*<0.01) was an independent protective factor for LC. The area under the receiver operating characteristic (ROC) curve (AUC) of serum TBA level in LC patients was 0.892, the 95% confidence interval (CI) was 0.851 to 0.933, and the corresponding sensitivity and specificity were 88.2% and 76.6%, respectively. The AUC of serum TBA level in patients with decompensated cirrhosis was 0.924, the 95% CI was 0.887-0.961, and the corresponding sensitivity and specificity were 97.6% and 74.1%, respectively. *Conclusion:* The detection of TBA in serum can be used as an auxiliary examination for patients with liver disease, which can provide a certain value for the diagnosis of LC.

Keywords

Liver Cirrhosis, TBA, Auxiliary Diagnosis, Laboratory Tests

1. Introduction

The liver is an important organ for human metabolism and biotransformation. It has a variety of physiological functions, such as secreting bile, participating in digestion, detoxification, immunity, and decomposing and synthesizing proteins.

*Corresponding author: 975370925@qq.com (Qi Zhu)

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LC is a common chronic liver disease, which can lead to liver dysfunction. At the same time, the liver of patients will also change its metabolic mode according to changes in the human environment [1]. The etiology of LC is multifactorial, including viral hepatitis, chronic alcohol consumption, cholestasis, genetic diseases, chemical toxins, and autoimmune diseases. The main cause of LC in China is viral infection [2, 3]. When the human body is infected with hepatitis virus, viral hepatitis can regularly activate the host immune system, but the virus can not be cleared during this process, which can lead to diffuse damage to the liver, progressing to liver fibrosis, cirrhosis, and even liver cancer [4]. The number of liver cancer deaths caused by viral hepatitis in China is about 400,000 every year, accounting for more than 40% of the global total. China has a high incidence rate of viral hepatitis [5].

Due to the strong compensatory ability of the liver, cirrhosis can be divided into compensatory cirrhosis and decompensated cirrhosis. In the early stage of cirrhosis, the patient's liver does not lose compensatory function, so there will be no obvious clinical symptoms [6]. However, with the development of the disease, the burden on multiple systems of the patient's body increases, and the symptoms gradually appear. Upon progression to decompensated LC, the structure and function of the liver are severely damaged. A large number of liver cells undergo degeneration and necrosis, leading to complications such as ascites, esophageal and gastric varices, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, and cancer, which seriously endanger the patient's life [7]. Because of the lack of obvious clinical manifestations in compensated LC, missed diagnosis and delayed treatment occur from time to time [8]. Many patients are found to have reached the late stage of cirrhosis when they have symptoms, losing the precious opportunity of liver histological reversal, and resulting in poor prognosis.

Early diagnosis and detection of cirrhosis are very important for patients, as they can not only enhance treatment efficacy, delay cirrhosis and its complications, but also improve patient survival rates and quality of life. Liver biopsy is the gold standard for the diagnosis of LC and the assessment of liver fibrosis [9]. However, due to its high cost, potential trauma to patients, and risks such as subcapsular bleeding and biliary peritonitis, patients have a lower willingness to accept this method, which also limits the application of liver biopsy in clinical diagnostic practice [10]. Therefore, it is very important to find non-invasive early diagnostic indicators that can accurately reflect the degree of liver damage and metabolic function, and serological related indicator tests can provide more auxiliary diagnostic methods for early clinical detection of liver diseases. The synthesis and secretion of TBA are completed by the liver, which contributes to intestinal nutrient absorption and biliary cholesterol secretion. TBA is the main component of bile and is closely related to lipid digestion. As a signal molecule, TBA plays an important role in maintaining metabolic homeostasis and protecting liver [11, 12]. When LC occurs, many normal liver cells will be destroyed, and the number of functional liver cells decreases, which will be reflected in the change of serum TBA level [13]. Therefore, it is of great clinical value to explore the practical application of serological examination represented by TBA in the early diagnosis of LC.

2. Research Objects and Methods

2.1. Research Objects

This retrospective study enrolled 85 patients diagnosed with LC (cirrhosis case group), 77 patients with viral hepatitis (hepatitis case group), and 81 healthy individuals undergoing routine physical examinations (healthy control group) admitted to the Affiliated People's Hospital of Jiangsu University between June 2023 and April 2025.

Inclusion criteria: (1) The LC case group was in line with the clinical diagnostic criteria of LC by clinical and imaging examination [14]. (2) The hepatitis case group met the diagnostic criteria for hepatitis patients through clinical and laboratory tests [15]. (3) The health control group consists of health examination personnel who have not been diagnosed with any liver disease or other serious chronic diseases. (4) Based on the Child-Pugh scoring system results, patients with LC were categorized into compensated stage (Class A) and decompensated stage (Classes B and C) [16]. Exclusion criteria: (1) Patients with liver cancer or other types of malignant tumors. (2) Suffering from other severe organ failure. (3) Have undergone liver surgery or liver transplantation within the past 6 months. (4) Recent taking drugs that affect liver function indicators. (5) Suffering from kidney disease or cardiovascular diseases.

2.2. Research Methods

2.2.1. Clinical Data Collection

Basic data such as age, gender, and disease status of the subjects were collected. Laboratory serological tests were performed, including TBA, AST, ALT, PAB, GGT, ALP, and ADA. The Reagents were purchased from Meikang Biotechnology Co., Ltd. The Beckman AU5800 automatic biochemical analyzer was purchased from Beckman Kurt Co., Ltd. KDC-2046 low-speed refrigerated centrifuge was purchased from Anhui Zhongke Zhongjia Scientific Instrument Co., Ltd. The measurement of TBA was performed using the enzymatic cycling method. The inter-assay and intra-assay coefficients of variation for the biochemical tests were ≤5.7% and ≤4.1%, respectively. All subjects were fasted for 8~10h, and fasting blood samples were taken from the elbow vein using a vacuum negative pressure tube in the early morning of the next day (7:00-9:00). Blood samples (5 mL) were collected using

separator tubes, allowed to stand at room temperature for 30 minutes, and then centrifuged at 4,000 rpm for 10 minutes to extract the upper plasma. All laboratory related indicators were detected by the laboratory of this hospital within 4h of the day.

2.2.2. Statistical Analysis Method

SPSS 22.0 software was used to analyze the sample data. Normality test was performed on the laboratory test data. The measurement data conforming to the normal distribution were expressed as mean ± standard deviation (x ± s). Single factor analysis of variance is used for inter group comparisons, and LSD-t test is used for pairwise comparisons. The measurement data that did not conform to the normal distribution were expressed as [M(P25-P75)]. The Kruskal-Wallis H test was used for comparison among multiple groups, and the Kruskal-Wallis single factor analysis of variance was used for pairwise comparison. The count data were expressed as the number of cases (%), and the $\chi 2$ test was used for comparison among groups. Logisitc regression was used to analyze the related influencing factors of cirrhosis, and the ROC curve was drawn. P<0.05 indicated that the difference was statistically significant.

3. Results

3.1. Basic Information of Investigated Objects

The age distribution of the investigated objects is shown in Table 1. There were 52 males and 33 females in the LC case group, aged from 22 to 77 years old, with an average age of (56.96 ±9.71) years. There were 38 males and 39 females in the hepatitis case group, aged from 27 to 77 years old, with an average age of (54.16 ±10.80) years. There were 41 males and 40 females in the health control group, aged from 27 to 78 years old, with an average age of (54.65 ±12.07) years. There was no statistically significant difference in gender and age among the three research groups (P>0.05), which was comparable.

Table 1. *Age distribution of survey subjects.*

Age (ears)	LC Case Group (n=85)		Hepatitis Case Group (n=77)		Health control group (n=81)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
21~30	1	1.2%	1	1.3%	2	2.5%
31~40	1	1.2%	7	9.1%	9	11.1%
41~50	16	18.8%	20	26.0%	17	21.0%
51~60	41	48.2%	30	39.0%	27	33.3%
61~70	19	22.4%	14	18.2%	18	22.2%
71~80	7	8.2%	5	6.5%	8	9.9%

3.2. Clinical Data Analysis

Compared with the healthy control group, the levels of TBA, AST, ALT, ALP and ADA in the LC case group and the hepatitis case group were significantly increased, while the level of PA was significantly decreased, and the differences were statistically significant (P<0.05). Meanwhile, the GGT level in the LC case group was significantly higher than that in the healthy control group (P<0.05). Compared with the hepatitis case group, the levels of TBA, AST, GGT, ALP and ADA in the LC case group were significantly increased, while the level of PA was significantly decreased, and the differences were statistically significant (P < 0.05). There was no statistically significant difference in age and gender ratio among the three groups (P>0.05). The statistical results are shown in Table 2. According to the results of clinical diagnosis, there were 44 patients with compensated cirrhosis and 41 patients with decompensated cirrhosis. Compared with patients with compensated cirrhosis, the level of TBA in patients with decompensated cirrhosis was significantly increased, while the level of PA was significantly decreased, and the differences were statistically significant (P <0.05). There was no significant difference in the levels of AST, ALT, GGT, ALP, and ADA between these two groups (P>0.05). The statistical results are shown in Table 3.

Table 2. Comparison of serum index levels in each group of subjects.

Variable	LC case group (n=85)	hepatitis case group (n=77)	healthy control group (n=81)	*F*-value	*P*-value
Age (years)	56.96±9.71	54.16±10.80	54.65±12.07	1.562	0.212
male/female	52/33	38/39	41/40	2.804	0.246
TBA (umol/L)	30 (11.75 ~ 77.7)[a,b]	4.8 (2.7 ~ 13.65)[a]	1.4 (1.1 ~ 1.8)	150.28	<0.001
AST (u/L)	37 (25.5 ~ 53.5)[a,b]	24 (20 ~ 37.5)[a]	20 (16.5 ~ 24)	68.967	<0.001
ALT (u/L)	28 (19 ~ 45)[a]	27 (18 ~ 44)[a]	17 (12.5 ~ 25.5)	27.88	<0.001
PA (mg/L)	151.80±64.23[a,b]	243.35±68.42[a]	313.74±46.99	116.54	<0.001
GGT (u/L)	52 (29 ~ 113.5)[a,b]	25 (16 ~ 58.5)	22 (15 ~40)	37.01	<0.001
ALP (u/L)	110 (84 ~ 164)[a,b]	84 (64.5 ~ 116)[a]	72 (60.5 ~ 86)	43.27	<0.001
ADA (u/L)	23.3 (16.8 ~ 32.2)[a,b]	12.8 (9.8 ~ 17.3)[a]	7.6 (6.6 ~ 8.9)	142.39	<0.001

a: $P<0.05$ compared with the healthy control group. b: $P<0.05$ compared with the hepatitis case group.

Table 3. Comparison of serum index levels in patients with LC.

Group	TBA (umol/L)	AST (u/L)	ALT (u/L)	PA (mg/L)	GGT (u/L)	ALP (u/L)	ADA (u/L)
Compensatory Phase (n=44)	25.2 (11 ~ 58.2)	37.5 (27 ~ 53.5)	35.5 (22 ~ 48.8)	193 (101.8 ~ 248.8)	55 (34.8 ~ 122.5)	116.5 (93 ~ 161)	23.2 (14.9 ~ 31.6)
Decompensated Phase (n=41)	44.3 (14.5 ~ 137.1)*	37 (24.5 ~ 59)	25 (16 ~ 40.5)	105 (68.5 ~ 162)**	47 (27.5 ~ 103)	97 (72 ~ 177)	24 (18.3 ~ 33.9)

*P <0.05, **P <0.01, compared with compensatory phase.

Binary Logistic regression was performed with LC as the dependent variable to analyze the clinical influencing factors of LC. The regression results showed that both TBA and PA were independent influencing factors for the occurrence of LC, with TBA being a risk factor and PA being a protective factor (P<0.05), as shown in Table 4.

Table 4. Logistic regression analysis of influencing factors of LC.

Influence Factor	*B*	S.E.	Wald χ^2	*P* value	*OR*	95%*CI*
TBA	0.18	0.008	5.084	0.024	1.018	1.002~1.034
PA	-0.16	0.003	34.128	<0.001	0.984	0.978~0.989

3.3. ROC Curve of TBA

The ROC curve showed that the area under the ROC curve (AUC) of serum TBA levels in the cirrhosis case group was 0.892, with a 95% confidence interval of 0.851~0.933, and the sensitivity and specificity were 88.2% and 76.6%, respectively, as shown in Figure 1. The AUC of serum TBA levels in patients with decompensated cirrhosis was 0.924, with a 95% confidence interval of 0.887~0.961, and the sensitivity and specificity were 97.6% and 74.1%, respectively, as shown in Figure 2. The results show that serum TBA has important reference value in the auxiliary diagnosis of cirrhosis, and its auxiliary diagnostic effect for decompensated LC is better.

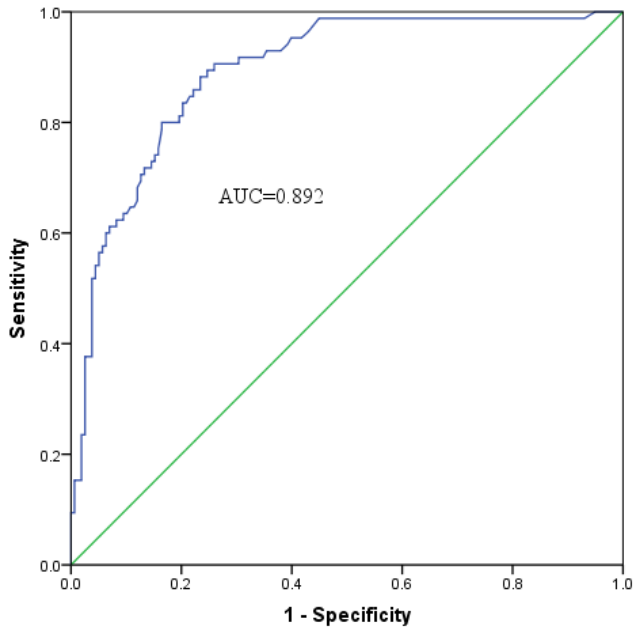

Figure 1. ROC curve of TBA distribution in LC patients.

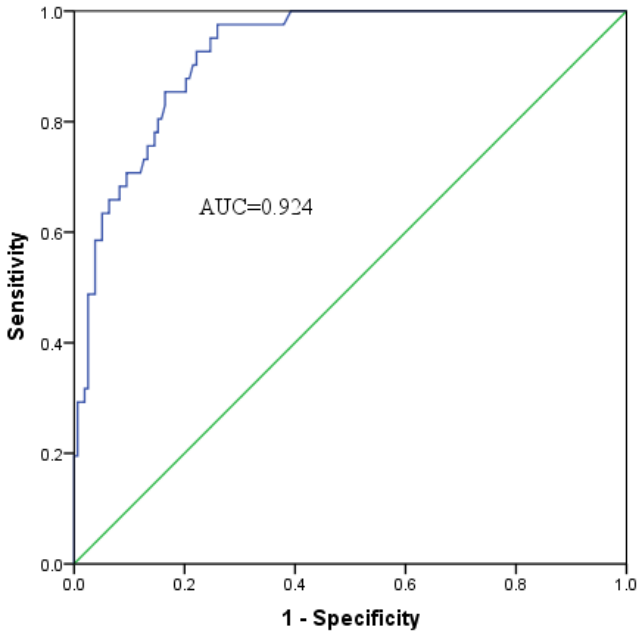

Figure 2. ROC curve of TBA distribution in decompensated LC patients.

4. Discussion

LC is a diffuse injury of the liver caused by a long-term or repeated action of a certain cause. The histopathological manifestations were massive necrosis of liver cells, nodular regeneration of residual liver cells and formation of fibrous septa, leading to the destruction of hepatic lobule structure and the formation of pseudolobules [17]. The liver is the only place where bile acids are synthesized and TBA is taken up from the portal vein. TBA is secreted from the liver to the bile and discharged into the intestinal cavity with the bile, which acts on the digestion and absorption of fat. After the action of bacteria in the intestinal cavity, more than 95% of the bile acid is absorbed by the intestinal wall and returned to the liver through the portal vein blood, forming the enterohepatic circulation of bile acid [18]. Therefore, the normal human serum TBA concentration is very low. When liver disease occurs, due to the destruction of a large number of normal liver cells, its anabolic function is impaired, and the liver's intake of TBA in portal vein blood is reduced. At this time, the collateral circulation is formed, and the bile acid bypasses the liver directly into the blood through the portal vein system, resulting in an increase in serum bile acid levels [19]. In addition, decompensated cirrhosis is often accompanied by intrahepatic cholestasis, and intrahepatic bile duct obstruction, causing a large amount of bile reflux into the blood, which further promotes the increase of TBA level in patients with LC [20]. Excessive alcohol intake upregulates hepatic bile acid synthesis enzyme expression, leading to increased bile acid production and subsequent intrahepatic cholestasis, thereby elevating serum bile acid levels [21]. Dysregulation of lipid metabolism and hepatic steatosis serve as precursor factors for NAFLD. Bile acids, acting as both metabolic and signaling molecules in the liver and extrahepatic tissues, participate in systemic lipid metabolism through the enterohepatic circulation pathway. Studies have demonstrated elevated TBA levels in patients with NAFLD [22]. Serum PA is a protein synthesized by liver cells with a short half-life of only 1.9 days. It can sensitively reflect the liver synthesis, reserve, and metabolic functions of patients, and therefore has important value in clinical laboratory diagnosis [23]. When the liver is subjected to continuous chronic injury, the synthesis of PA and transport capacity of hepatocytes decrease. When the human body suffers from viral hepatitis or cirrhosis, liver cell necrosis produces toxic substances. As a non-specific defense substance, PA is consumed to clear the toxic substances, which can also lead to a decrease in serum PA levels [24]. Previous studies have found a certain correlation between TBA elevation and LC progression. Following the onset of liver cirrhosis, hepatocytes demonstrate impaired capacity for efficient bile acid uptake and metabolic clearance. Concurrently, the normal portal vein access to the systemic circulation is blocked, so a large amount of bile acids can only be excreted through the portosystemic collateral vessels, bypassing the liver and directly entering the systemic circulation, resulting in increased serum TBA levels. In addition, LC may also be associated with damage to the intrahepatic bile-blood barrier, which can also aggravate the increase of serum TBA [25-27]. For patients with decompensated cirrhosis, serum TBA can be significantly increased even if the liver cell damage is small, and these changes are earlier than the changes of transaminases, indicating that serum TBA level has important clinical value for understanding the liver function of patients. The results of this study showed that the TBA level in the LC case group was significantly higher than that in the hepatitis

case group and the health control group, suggesting that high levels of TBA may be closely related to the occurrence of cirrhosis. Through logistic regression analysis, it was further confirmed that TBA is an independent risk factor for cirrhosis, while PA is an independent protective factor for cirrhosis. This suggests that individuals with elevated serum TBA levels and decreased PA levels are more likely to have cirrhosis.

The serological indicators detected in the laboratory have significant clinical value in the diagnosis of liver diseases. AST in hepatocytes mainly exists in mitochondria. When the liver is damaged, AST will be released into the blood due to the destruction of mitochondria, resulting in an increase in serum AST levels [28]. ALT is widely present in various organs of the human body, with the highest content in the liver, and most of these ALT are found in the cytoplasm. When the liver cells are continuously damaged, the permeability of the liver cell membrane will change, causing ALT to overflow from the cells into the blood, thereby increasing the serum ALT level [29]. ALT is often used to assess the degree of liver inflammation, but its relationship with liver fibrosis is still controversial. GGT in serum is a microsomal enzyme, which is abundant in human liver. GGT in the liver is mainly present in the cytoplasm of hepatocytes and intrahepatic bile duct epithelium, which is an essential enzyme for glutathione synthesis. Patients with LC are prone to hyperfunction of intrahepatic synthesis or obstruction of bile exclusion, which will lead to an increase in serum GGT levels, so that GGT can be used as a serum marker of liver injury [30]. ALP is a metabolic enzyme that is widely present in the liver and is generally not released under normal conditions. When the human body experiences bile stasis, cirrhosis, and other conditions, there will be severe biliary compression obstruction around the liver lesion. Liver cells will increase the synthesis of ALP to cope with bile flow disorders, and bile will also reflux into the bloodstream, resulting in a significant increase in serum ALP levels [31]. ADA is a cytoplasmic enzyme that exists in liver cells and is associated with cellular immune activity. When liver injury occurs, the cell membrane permeability increases significantly, and ADA penetrates the tissue blood barrier, resulting in an increase in ADA content in the blood [32]. The results of this study showed that the levels of AST, ALT, ALP, and ADA in the LC and hepatitis case groups were significantly higher than those in the healthy control group, and the GGT level in the LC case group was significantly higher than that in the healthy control group. Meanwhile, the levels of AST, GGT, ALP and ADA in the LC case group were significantly higher than those in the hepatitis case group. This indicates that there is a strong correlation between serum indicators and the occurrence and severity of liver diseases.

Liver biopsy is an important standard for the diagnosis of LC, but due to the risks associated with this invasive procedure, the diagnosis and early warning ability of LC is limited [33]. Therefore, it is of great clinical value to assist the diagnosis of LC by serological indicators. The FIB-4 index, a non-invasive diagnostic model for LC assessment, demonstrates favorable diagnostic performance. Studies indicate that while FIB-4 exhibits a relatively high AUC value in diagnosing LC, its diagnostic sensitivity remains below 50%, necessitating further investigation to validate its efficacy as a non-invasive diagnostic tool [34]. The APRI serves as a significant indicator for assessing LC severity. Similar to the FIB-4 index, both models are influenced by multiple confounding factors. Existing studies reveal that cirrhotic patients may present with APRI scores below 1, which contradicts the conventional diagnostic threshold of APRI≥2 [35]. This discrepancy underscores the necessity of incorporating complementary diagnostic methodologies. The results of this study showed that the area under the ROC curve of serum TBA in patients with LC was 0.892, and the AUC of serum TBA in patients with decompensated cirrhosis was 0.924, indicating that TBA has a certain value in the auxiliary diagnosis of patients with LC. At the same time, serum TBA is more accurate for the auxiliary diagnosis of decompensated cirrhosis, which can better diagnose liver disease and reflect the progress of the disease in clinical application. Undeniably, the utility of TBA as an auxiliary diagnostic tool for LC presents certain limitations. Studies have demonstrated significantly elevated serum TBA levels in patients with acute suppurative cholangitis who do not exhibit concurrent LC [36]. This clinical scenario may compromise the diagnostic specificity of TBA in cirrhosis assessment.

5. Conclusion

In summary, this study demonstrates that patients with LC exhibit elevated serum TBA levels and reduced prealbumin (PA) levels, which correlate with the clinical manifestations of LC. In clinical diagnosis and treatment, close attention should be paid to serum TBA levels in order to detect the occurrence of LC early and effectively control the progression of the disease. In future studies, it is necessary to further expand the sample size and explore the intrinsic correlation between various serum indicators and the occurrence of LC.

Abbreviations

TBA	Total Bile Acid
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
PA	Prealbumin
GGT	Gamma Glutamyltransferase
ALP	Alkaline Phosphatase
ADA	Adenosine Deaminase

Author Contributions

Changxiu Sun: Data curation, Formal Analysis, Investigation, Software, Visualization, Writing – original draft

Qi Zhu: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

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