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Serum lipid profiling in decompensated patients with Hepatitis B virus -related cirrhosis

Changzhi Xu[1], Yanhua Yi[2], Zhizhi Xie[1], Donglin Zhu[1], Zhu Wang[3]*, Yun Xi[1]*

[1]Department of Laboratory Medicine, Third Affiliated Hospital of Sun Yat-sen university, Guangzhou, Guangdong 510530, P.R.China

[2]Department of Emergency, Third Affiliated Hospital of Sun Yat-sen university, Guangzhou, Guangdong 510530, P.R.China

[3]Department of Urology, Affiliated Longhua People's Hospital, Southern Medical University, Shenzhen, Guangdong 510080, P.R.China

* Correspondence: xiyun1993@163.com; wangzhu@smu.edu.cn;

Xi Yun and Wang Zhu are co-corresponding authors

SUMMARY

Background: The association of lipid profile with decompensation in patients with liver cirrhosis has not been clarified. The present study aimed to investigate the impact of Hepatitis B virus (HBV) infection on the lipid profile in decompensated patients with hepatitis B cirrhosis.

Methods: A total of 178 HBV-related decompensated cirrhosis (HBV-DeCi) patients were included in this retrospective analysis. The included patients were subdivided into 4 groups: 24 patients with HBsAg, HBeAg and HBcAb positive were set as group Ia; 14 patients with HBsAg, HBeAg ,HBeAb and HBcAb positive were set as group Ib;112 patients with HBsAg, HBeAb and HBcAb positive were set as group II; 28 patients with HBsAb, HBeAb and

HBcAb positive were set as group III. Lipid profile included total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein- cholesterol (LDL-c), triglycerides (TG), and lipoprotein(a) (Lpa) were analyzed respectively. The difference between mentioned groups and the HBV infection were characterized respectively.

Results: Our data showed that the values of TG in group Ia was 1.2181 ± 0.1898 (mmol/L), in Ib was 1.306 ± 0.1702 (mmol/L), in Ia+Ib was 1.29 ± 0.1338 (mmol/L), and in group III was 0.8950±0.07200 (mmol/L). There were significant differences between group Ia and III (P=0.0498), Ib and III (P=0.0125) and also between group Ia+Ib and III (P=0.0217).

Conclusions: Serum TG levels are closely related to the HBV infection in HBV-DeCi patients. It may be used as a new indicator of advanced liver disease and cirrhosis recompensation.

Keywords: hepatitis B virus, decompensated cirrhosis, Lipid profile

Introduction

Liver, a major organ for the production of cholesterol and lipoprotein, plays a vital role in maintaining the body's lipid metabolism [1]. In ongoing hepatocyte damage, such as progressive fibrosis of the liver, glycogen reserves are reduced, increasing the lipid catabolism [2]. Decreased levels in specific components of lipid profile indicate more decompensation events, worse liver function, and reduced survival in liver cirrhosis [3]. Chronic hepatitis B virus (HBV) infection is the leading cause of liver-related morbidity and mortality in Asia. Up to 40% of chronic HBV carriers develop serious complications such as hepatic decompensation during their lifetime [4]. Untreated patients with HBV-related decompensated cirrhosis (HBV-DeCi) were previously reported to have poor prognosis, with a five-year survival rate of only 14% to 35% [5, 6]. The pathogenesis of complications of decompensated hepatitis B cirrhosis is very complicated.

As a series of studies, our study explored the influence of HBV on conventional coagulation parameters and blood parameters in HBV-DeCi patients [7,8]. However, the difference among the lipid profile in patients of the same period with HBV-DeCi is still unknown. The hepatitis virus damages liver function; does it also disrupt the metabolism of lipids in the liver? It is necessary to further explore them, in order to provide reference for clinical diagnosis and treatment.

Materials and Methods

We continuously analyzed 178 hospitalized HBV DeCi patients between January 2019 to November 2021 in the Third Affiliated Hospital of Sun Yat-sen university. The 178 patients meeting all of the following requirements were enrolled: (1) between 7-80 years old; (2) no previous liver or other organ transplantation; (3) confirmation of chronic HBV infection (HBsAg positive for ≥6 months, or HBsAb and HBcAb positive); (4) clinical manifestations included symptoms such as ascites, hepatic encephalopathy (HE) and/or variceal bleeding and/or jaundice; (5) confirmation cirrhosis stage: Child-Pugh class B.

Exclusion criteria: (1) co-infected with HIV, HCV, HDV and HEV; (2) HBV infection with alcoholic liver disease or non-alcoholic fatty liver disease; (3) pregnancy; (4) death, discharge within 48 hours after admission.

Ethics statement

The procedures were approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen university[No. (2022) 02-318-01]. Written informed consent was acquired from all participants.

Clinical data extraction

Patients' demographics and histories, clinical data and laboratory variables were obtained from medical records retrospectively. The laboratory parameters included examination of Lipid profile: total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein- cholesterol (LDL-c), triglycerides (TG), and lipoprotein(a)(Lpa); aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBil) and direct bilirubin (DBil), HBV serological markers and HBV viral load. Liver function test: AST, ALT, TBil, DBil and Lipid profile were analyzed by automatic analyzer (Hitachi 7600, Japan). HBV serological markers were examined by Abbot i4000 Automatic chemiluminescence immune analyzer (USA). HBV viral load (quantification values) was determined through HBV-DNA PCR by using ABI2000 (USA).

Statistical analysis

GraphPad prism 9 (https://www.graphpad.com) was used for statistical analysis. The continuous variables following normal distribution were reported as the mean ± SEM, and

assessed by unpaired t-test. Non-normally distribution was expressed as the median of the interquartile interval (IQR) and assessed using the Mann-Whitney U test. $P < 0.05$ was considered as statistical significance.

Results

Demographic and clinical data characteristics.

A total of 178 patients with HBV-DeCi (age 51.2±11.2 years, 18.5% women) were included. Based on different serological markers, the included patients were divided into 4 groups: 24 patients with HBsAg, HBeAg and HBcAb positive were set as group Ia; 14 patients with HBsAg, HBeAg, HBeAb and HBcAb positive were set as group Ib, group Ia and group Ib (patients 38 cases) were set as Group I; 112 cases with HBsAg, HBeAb, HBcAb positive were set as Group II and 28 patients with HBsAb, HBeAb and HBcAb positive were set as Group III. Patients in both Group I and Group II received anti-viral treatment for over 6 months. There was no significant difference in sex, age, AST, ALT, TBil, DBil or HBV DNA load were observed (P>0.05). Details of the demographic, clinical, and laboratory characteristics of the participants are presented in Table 1.

Table1. Clinical characteristics between HBsAg positive and negative patients

Terms	Group I(Ia+Ib)	Group II	Group III
Number	38	112	28
Gender(F/M)	5/33	21/91	7/22
Age,years (7-74) P value	45.8(21-67) P=0.1544	53.1(29-74) P=0.2598	50.7(7-70)
AST, U/L (0-40) P value	187.4±97.28 P=0.2770	58.77±6.25 P=0.7804	62.56±10.44
ALT, U/L (0-40) P value	164.6±73.57 P=0.1782	50.26±9.66 P=0.8170	45.64±9.38
TBil,μmol/L (3.4-17.1) P value	48.31±10.57 P=0.1413	62.35±8.99 P=0.3854	80.39±20.63
DBil,μmol/L (0-6.8) P value	*27.31±7.57* P=0.1264	35.27±5.68 P=0.2277	51.87±15.39
HBV DNA P* value	104154673±103401725 P*=0.0868	516135±276795	

HBV DNA indicates HBV viral load； P value : *versus* Group III; P* value: Group I *versus* Group II

HBV infection and the lipid profile

The lipid profile from the multivariate analysis presented in Table 2 show that HBV-DeCi patients with HBsAg, HBeAg and HBcAb positive maybe have a higher TG level, which

indicated that only TG levels were associated with HBV infection and replication. And then, group I was subdivided into two groups: 24 patients with HBsAg, HBeAg and HBcAb positive were set as group Ia; 14 patients with HBsAg, HBeAg, HBeAb and HBcAb positive were set as group Ib. TG levels of them were compared and analyzed, both of group Ia and Ib had a higher TG level which compared with group III as presented in Fig.1.There was no difference between group Ia and Ib (1.281±0.1898 versus 1.306±0.1702, P=0.93)

Table2.The difference of lipid profile between different groups (*, P<0.05)

Variables	Group I	Group II	Group III	P value		
				I VS II	II VS III	I VS III
HDL-c	0.7032±0.06452	0.8248±0.04629	0.8482±0.08233	0.1687	0.8178	0.1645
LDL-c	2.054 ± 0.1476	2.023 ± 0.0984	2.145±0.2310	0.8730	0.6328	0.7800
APoA	0.8366 ± 0.0535	0.9346 ± 0.0392	0.9171±0.05965	0.1889	0.8360	0.3220
APoB	0.715 ± 0.03772	0.721 ± 0.03410	0.6529±0.04660	0.9240	0.3468	0.2996
TC	3.674 ± 0.1882	3.749 ± 0.1315	3.603±0.3048	0.7669	0.6317	0.8350
TG	1.290 ± 0.1338	1.113 ± 0.0829	0.8950±0.07200	0.2766	0.2029	0.0217
Lpa	73.84 ± 15.81	93.76 ± 12.80	67.43±10.92	0.4050	0.3173	0.7576

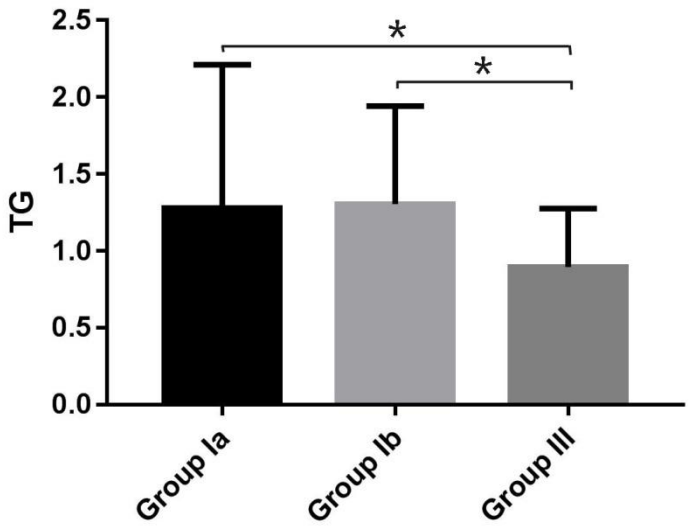

Figure 1. Comparison of TG between the subgroup I and group III (*, P<0.05).

Discussions

The liver plays an undeniably important role in lipid metabolism. Accumulating clinical studies suggested that chronic HBV infection was associated with lower levels of serum total cholesterol and TG compared to non HBV-infected controls [9-11]. Interestingly, in present

study we found that HBV-DeCi patients with positive HBsAg had a higher TG level than negative group, which showed a reversed pattern as compared to previous reports.

An essential explanation for these controversial results is due to the different control groups applied in different studies. It well known that the levels of cholesterol, TG, and lipoprotein(a) were significantly lower in patients with liver cirrhosis than those without liver cirrhosis [3,12,13]. Patients with decompensated cirrhosis usually suffer from intestinal microbial dysbiosis, which will reduce the digestion and absorption of lipid, and then present with hypocholesterolemia [14,15]. Among the patients with acute gastrointestinal bleeding, hemodilution secondary to blood loss can be manifested as hypocholesterolemia [16]. Therefore, even for the same set of data, controversial conclusions may be obtained according to the different control groups.

Secondly, there were some potential mechanisms has been proposed to explain the association of lipid profile with hepatic decompensation. HBx protein overexpression in hepatocytes decreased ApoB secretion, increased the intracellular levels of ApoB, TG, and cholesterol, and interfered with VLDL/LDL assembly or secretion [17]. ApoC3 acted as an inhibitor of lipoprotein lipase (LPL), which was a crucial enzyme in TG lipoprotein catabolism [18]. HBV inhibited the synthesis and secretion of ApoC3[19]. Therefore, during chronic HBV infection, a decrease in ApoC3 expression would increase LPL activity, decrease VLDL synthesis and secretion, and increase TG decomposition. In present study, our findings may indicate a different mechanism in TG synthesis and decomposition in HBV-DeCi patients.

In summary, our data showed that in HBV-DeCi patients, HBV infection might lead to a higher TG level. However, due to the small sample size and limitation of retrospective study, the available data are far from conclusive, there is still a long way to go before clarifying the complex interaction between HBV infection and hepatic lipid metabolism.

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Abbreviations

HBV-related decompensated cirrhosis (HBV-DeCi); Hepatitis B surface antigen (HBsAg);

Hepatitis B surface antibody (HBsAb); Hepatitis B e antigen (HBeAg); Hepatitis B e antibody (HBeAb); Hepatitis B core antibody (HBcAb); aspartate aminotransferase to platelet ratio index (APRI); fibrosis index based on four factors (FIB-4); gamma-glutamyl transpeptidase to platelet ratio (GPR), albumin-bilirubin score (ALBI); aspartate aminotransferase (AST); alanine aminotransferase (ALT); total bilirubin (TBil); direct bilirubin (DBil). total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein- cholesterol (LDL-c), triglycerides (TG).

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