PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

World J Gastroenterol 2004;10(6):899-902
World Journal of Gastroenterology
 ISSN 1007-9327

• CLINICAL RESEARCH •

Clinical features and risk factors of patients with fatty liver in Guangzhou area

Qi-Kui Chen, Hai-Ying Chen, Kai-Hong Huang, Ying-Qiang Zhong, Ji-Ao Han, Zhao-Hua Zhu, Xiao-Dong Zhou

Qi-Kui Chen, Kai-Hong Huang, Ying-Qiang Zhong, Ji-Ao Han, Zhao-Hua Zhu, Department of Gastroenterology, The Second Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510120, Guangdong Province, China
Hai-Ying Chen, Department of Gastroenterology, The People' s Hospital of Zhongshan City, Zhongshan, 528400, Guangdong Province, China
Xiao-Dong Zhou, The Medical Research Center, The Second Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510120, Guangdong Province, China
Supported by the National Natural Science Foundation of China, No.30270371
Correspondence to: Dr. Qi-Kui Chen, Department of Gastroenterology, The Second Affiliated Hospital, Sun Yat-Sen University, 107 West Yanjiang Road, Guangzhou 510120, Guangdong Province, China. qkchen@21cn.com
Telephone: +86-20-81332598 **Fax:** +86-20-81332244
Received: 2003-10-31 **Accepted:** 2003-12-22

Abstract

AIM: There is still no accepted conclusion regarding the clinical features and related risk factors of patients with fatty liver. The large-scale clinical studies have not carried out yet in Guangzhou area. The aim of the present study was to investigate the clinical features and related risk factors of patients with fatty liver in Guangzhou area.

METHODS: A total of 413 cases with fatty liver were enrolled in the study from January 1998 to May 2002. Retrospective case-control study was used to evaluate the clinical features and related risk factors of fatty liver with logistic regression.

RESULTS: Obesity (*OR*: 21.204), alcohol abuse (*OR*: 18.601), type 2 diabetes mellitus (*OR*: 4.461), serum triglyceride (TG) (*OR*: 3.916), serum low-density lipoprotein cholesterol (LDL-C) (*OR*: 1.840) and fasting plasma glucose (FPG) (*OR*: 1.535) were positively correlated to the formation of the fatty liver. The levels of serum alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT) increased mildly in the patients with fatty liver and were often less than 2-fold of the normal limit. The higher abnormalities of aspartate aminotransferase (AST) levels (42.9%) with AST/ALT more than 2(17.9%) were found in patients with alcoholic fatty liver (AFL) than those with nonalcoholic fatty liver (NAFL) (16.9% and 5.0% respectively). The elevation of serum TG, cholesterol (CHOL), LDL-C was more common in patients with NAFL than with AFL.

CONCLUSION: Obesity, alcohol abuse, type 2 diabetes mellitus and hyperlipidemia may be independent risk factors of fatty liver. The mildly abnormal hepatic functions can be found in patients with fatty liver. More obvious damages of liver function with AST/ALT usually more than 2 were noted in patients with AFL.

Chen QK, Chen HY, Huang KH, Zhong YQ, Han JA, Zhu ZH, Zhou XD. Clinical features and risk factors of patients with fatty liver in Guangzhou area. *World J Gastroenterol* 2004; 10(6): 899-902
http://www.wjgnet.com/1007-9327/10/899.asp

INTRODUCTION

Fatty liver is a condition of hepatic steatosis caused by many risk factors and may progress to liver fibrosis and cirrhosis. Generally, the diagnosis of fatty liver should be based on the history, clinical manifestation, laboratory investigation and medical imaging. Liver biopsy should be taken if necessary. After to know the possible related risk factors of fatty liver existed in the history, the abnormal degree of the biochemical and imaging features can provide a clue for early diagnosis. Although the related risk factors and laboratory features have already been reported, there is still no well-accepted conclusion[1-3]. The large-scale clinical studies have not carried yet in Guangzhou area, southern China[4].

Retrospective case-control study was used to analyze fatty liver. The age, gender, obesity, type 2 diabetes mellitus, hyperlipidemia, alcohol abuse, smoking, and history of drugs or toxins and so on were recorded to evaluate the effects of these variables on fatty liver and investigate the related risk factors. The liver function and other serum biochemical levels were compared to find out the difference of laboratory abnormalities, so that they could provide a scientific foundation for the diagnosis, prevention and treatment of fatty liver.

MATERIALS AND METHODS

Clinical data

The data of 413 cases of fatty liver in this hospital from January 1998 to May 2002 were collected. Fatty liver was diagnosed according as the standard by Chinese Association of Medicine and Sherlock[5-7] The 200 cases without fatty liver during the same period were selected randomly as control. Age, gender, serum lipids, fasting plasma glucose (FPG), obesity (body mass index, BMI$\geqslant$25), alcohol abuse, smoking, type 2 diabetes mellitus, history of drugs and toxins, hepatitis virus infection (HCV and HBV), pregnancy, jejuno-ileal bypass surgery and total parenteral nutrition were recorded in fatty liver group and non fatty liver group respectively.

The laboratory data of serum triglyceride (TG), cholesterol (CHOL), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein AI (Apo AI), apolipoprotein B (Apo B), uric acid (UA), aspartate aminotransferase (AST), alanine aminotransferase (ALT), the ratio of AST/ALT, albulin (ALB), globin (GLB), ratio of A/G, gamma-glutamyltransferase (GGT) and total bilirubin were collected in two groups respectively. The serum biochemical indexes were examined by an autoanalyzer based on a standard protocol.

Statistical analysis

All data analysis was performed with EXCEL 97 and SPSS 10.0 /PC statistical package. A P value less than 0.05 (2-tailed) was considered to be statistically significant. The frequency was compared using Chi-squared (χ^2) test. The univariate and multivariate stepwise logistic regression was used to select the independent variables. Data with normal distribution were expressed as mean±SD. The differences between groups were analyzed for statistical significance using Student' s t test. Data

with abnormal distribution were expressed as median and interquartile range.

RESULTS

General condition

Among 413 fatty liver cases, the gender ratio (M/F) was 1.02:1. The age ranged from 8 to 83 years. The median age was 57 years. No significant differences in age and gender were found between the fatty liver group and non-fatty liver group. The possible causes of fatty liver are showed in Table 1.

Table 1 Possible causes of fatty liver and its comparison with non-fatty liver group (%)

Factors	Fatty liver group (n=413)	Non-fatty liver group (n=200)
Alcohol abuse	51(12.4)[b]	7(3.5)
Obesity	244(59.1)[b]	17(8.5)
Type 2 diabetes mellitus	206(49.9)[b]	15(7.5)
Hyperlipidemia	276(66.8)[b]	63(31.5)
Hypertriglyceridemia	92(22.3)[b]	17(8.5)
Hypercholesterolemia	64(15.5)	35(17.5)
Mixed Hyperlipidemia	120(29.1)[b]	11(5.5)
HBV infection	50(12.1)	31(15.5)
HCV infection	34(8.2)	10(5.0)
History of drugs and toxins	6(1.5)	2(1.0)

[b]P<0.001, *vs* Non-fatty liver group.

Analysis of independent risk factors of patients with fatty liver

Analysis of univariate logistic regression was performed among 20 variables, such as age, gender, obesity, alcohol abuse, smoking, type 2 diabetes mellitus, TG, CHOL, HDL-C, LDL-C, Apo AI, Apo B, FPG, HCV and HBV infection, history of drugs and toxins, pregnancy, jejuno-ileal bypass surgery and total parenteral nutrition. TG, CHOL, HDL-C, LDL-C, Apo B, FPG, obesity, alcohol abuse, smoking, type2 diabetes mellitus were positively correlated to fatty liver respectively (odds rate, OR>1, P<0.05), while Apo AI was negatively correlated to it (OR<1, P<0.05). Multivariate stepwise logistic regression was used to select the variables independently associated with fatty liver. Obesity, alcohol abuse, type 2 diabetes mellitus, TG, LDL-C and FPG were entered the model of logistic regression as the independent risk factors of fatty liver. In contrast, Apo B was negatively correlated to it (Table 2).

Table 2 Multivariate stepwise logistic regression

Variables	β	*SE*	*OR*	95%*CI*	*P*-value
Obesity	3.054	0.354	21.204	10.539-42.429	0.000
Alcohol abuse	2.923	0.509	18.601	6.585-50.432	0.000
Type 2 diabetes mellitus	1.495	0.354	4.461	2.228-8.952	0.022
TG	1.365	0.268	3.916	2.316-6.621	0.000
LDL-C	0.610	0.184	1.840	1.283-2.640	0.001
FPG	0.429	0.094	1.535	1.278-1.846	0.000
Apo B	-1.590	0.530	0.204	0.072-0.576	0.003

β: partial regression coefficient; *SE*: standard error of partial regression coefficient; *OR*: odds ratio; *CI*: confidence interval.

Abnormal liver function in patients with fatty liver

Using χ^2 test, the abnormal frequencies of ALT, AST/ALT and GGT showed significant differences between the patients with and without fatty liver (Table 3).

Comparison of serum biochemical features between alcoholic fatty liver (AFL) group and nonalcoholic fatty liver (NAFL) group

The abnormal frenquencies of serum TG, CHOL, LDL-C and ApoB were higher in NAFL group than those in AFL group. The proportion of HDL-C≤1.0, AST≥40 and AST/ALT≥2 were higher in patients with AFL than with NAFL (Table 4).

Table 3 Abnormal liver function in the patients with fatty liver and non-fatty liver (%)

Liver function	Fatty liver group (n=413)	Non-fatty liver group (n=200)
AST (≥40 U)	85(20.6)	38(19.0)
(40-80 U)	65(15.7)	26(13.0)
(≥80 U)	20(4.8)	12(6.0)
ALT (≥40 U)	129(31.2)[a]	37(18.5)
(40-80 U)	84(20.3)[a]	26(13.0)
(≥80 U)	45(10.9)[a]	11(5.5)
AST / ALT (<1)	161(39.0)[a]	28(14.0)
(≥2)	23(5.6)[a]	54(27.0)
ALB (≤35 g / L)	16(3.9)	15(7.5)
GLB (≥30 g / L)	42(10.2)	29(14.5)
A / G (≤1.5)	84(20.3)	47(23.5)
GGT (≥50 U / L)	145(35.1)[a]	46(23.0)
TBIL (≥17.1 μmol / L)	75(18.2)	39(19.5)

[a]P<0.05, *vs* Non-fatty liver group.

Table 4 Comparison of laboratory abnormalities among AFL, NAFL and control groups (%)

Biochemical Index	AFL group (n=28)	NAFL group (n=301)	Control group (n=163)
TG (≥1.7 mmol / L)	2(7.1)[a]	169(56.2)[c]	27(17.7)
CHOL (≥5.2 mmol / L)	2(7.1)[a]	148(49.2)[c]	35(22.9)
HDL-C (≤1.0 mmol / L)	9(32.1)[a]	35(11.6)	27(17.7)
LDL-C (≥2.6 mmol / L)	12(42.9)[a]	214(71.1)	97(63.4)
Apo AI (≤1.2 mmol / L)	13(46.4)	118(39.2)	45(29.4)
Apo B (≥1.1 mmol / L)	4(14.3)[ac]	149(49.5)[e]	53(34.6)
UA (≥452 mg / dL)	5(17.9)	89(29.6)[e]	18(11.8)
AST (≥40 U)	12(42.9)[ac]	51(16.9)	24(15.7)
ALT (≥40 U)	10(35.7)[c]	87(28.9)[e]	26(17.0)
AST / ALT (<1)	11(39.3)[c]	168(55.8)[e]	31(20.3)
(≥2)	5(17.9)[a]	15(5.0)[e]	40(26.1)
ALB (≤35 g / L)	3(10.7)	9(3.0)	7(4.6)
GLB (≥30 g / L)	3(10.7)	32(10.6)	20(13.1)
A / G (≤1.5)	7(25.0)	64(21.3)	31(20.3)
GGT (≥50 U / L)	10(35.7)	95(31.6)[e]	30(19.6)
TBIL (≥17.1 μmol / L)	6(21.4)	50(16.6)	30(19.6)

[a]P<0.05, *vs* NAFL group; [c]P<0.05, *vs* control group; [e]P<0.05, *vs* control group.

DISCUSSION

In recent years, the prevalence of fatty liver is constantly increasing along with the improvement of life-style, the change of dietetic structure, the aged population and the application of new diagnostic technique. The incidence of fatty liver in 3432 Japanese adults thorough medical examination was 21.8%[2]. In China, fatty liver affected 10.2% of cadres in Nanjing[8] with 11.4% of male and 6.8% of female. There were no data to show the prevalence of fatty liver in the southern China. Because of distinct life-style and climate feature in Guangzhou, the pattern

of fatty liver could be different from other area. Among 413 patients with fatty liver, the gender ratio (M/F) was 1.02:1. The age ranged widely. The median age was 57 years.

Fatty liver may be an independent disease, but more generally, it is a lesion of the liver in certain systemic diseases. Fatty liver may be caused by many diseases and risk factors, and can progress from mild steatohepatitis to severe fibrosis and cirrhosis[9]. The etiological prevention is very important because of the lack of effective therapy. Although the etiology of hepatic steatosis is explored extensively, the complicated and multi-factor pathogenesis make it remain poorly understood. The possible related risk factors include: alcohol abuse, diabetes mellitus, obesity, hyperlipidemia, drugs and toxins, hepatitis virus infection (especially HCV), rapid weight loss, jejuno-ileal bypass surgery, total parenteral nutrition, pregnancy and so on[10-16].

413 patients with fatty liver were diagnosed mainly according to the history, clinical manifestations, laboratory and ultrasound examination. Liver biopsy was the best method of diagnosing fatty liver. But it was difficult to carry out in large sample of populations. This was the possible limitations of the study.

Our data from 413 patients with fatty liver showed that obesity, alcohol abuse, type 2 diabetes mellitus, hyperlipidemia and elevation of fasting plasma were independent risk factors confirmed by a multivariate logistic analysis. These correlations were similar to the researches at home and abroad[3,4]. It suggested that the pathogenesis of fatty liver in southern China might have a similar pattern to other area in China and abroad.

Obesity was easily accompanied with fatty liver[17]. The percentage of the obese patients with fatty liver (59.1%) was significantly higher than controls (8.5%). Obesity is a very common phenomenon in the developed countries. 60-100% patients of non-alcoholic steatohepatitis (NASH) were proved to have obesity[18]. This situation was also found in developing country, especially in China. According to the data in 11 provinces/autonomous regions/municipalities of China from July 1995 to July 1997, the prevalence rate of overweight and obesity among 42 751 Chinese adults aged 20-74 years were 21.51% and 2.92% respectively[19]. There were about 200-300 million of overweight and 30-40 million of obese populations in China. With the odds ratio of 21.204, obesity was a predictor of fatty liver. The practice of prevention for overweight and obesity was very important for control of fatty liver.

Alcohol liver disease was the major medical complications of alcohol abuse. Alcohol abuse was one of the major causes of fatty liver and cirrhosis in the Western countries. At least 80% of heavy drinkers developed fatty liver, 10-35% of alcoholic hepatitis, and approximately 10% cirrhosis[20]. Alcohol drinkers were not as common in southern China as in northern China[19]. Based on our data, there were only 12.4% patients with alcohol abuse and 6.8% of them with alcoholic fatty liver among 413 patients with fatty liver according to diagnostic standard of China in 2002. But, the proportion of alcoholic abuse was still higher in patients with fatty liver than those without fatty liver. Alcoholic abuse contributed to a risk factor of fatty liver.

Type 2 diabetes mellitus usually accompanied insulin resistance[12,21]. Both peripheral and hepatic insulin resistance were present in almost all patients with nonalcoholic fatty liver disease, irrespective of the coexistence of related risk factors[21]. Above findings, together with the associated hyperlipidemia, obesity, hypertension and herperurisemia, were considered as the manifestations of the metabolic syndrome that was associated with insulin resistance[22,23]. In this study, either type 2 diabetes or elevation of fasting plasma glucose was related to fatty liver. It suggested that insulin resistance might be a risk factor of fatty liver.

The role of serum lipids in fatty liver remained controversial[16,24]. Some researches showed that the effects of hyperlipidemia on fatty liver were complicated and difficult to be disassociated with obesity and type 2 diabetes mellitus. Among the 413 patients with fatty liver, the total incidence of hyperlipidemia was 66.8%, which consisted of 22.3% of hypertriglyceridemia, 15.5% of hypercholesterolemia and 29.1% of mixed hyperlipidemia. TG and LDL-C were independent risk factors and ApoB was a protective factor confirmed by multivariate logistic analysis. TG and LDL-C stimulated the proliferation and collagen synthesis of hepatic stellate (HSC) and increased deposition of extracellular matrix (ECM) in the liver by means of lipid peroxidation[25,26]. This process was relative to hepatic fibrosis and effected prognosis of patients with fatty liver.

The correlation between hepatitis virus infection (especially HCV) and hepatic steatosis was found[27]. Although the incidence of chronic HBV and HCV infection in China remained the highest proportion in the world, there was no significant difference in the incidence of HBV or HCV infection between patients with and without fatty liver. The infection of HBV and HCV was excluded from the model of multivariate stepwise logistic regression.

The clinical and laboratory features varied greatly with different causes and degree of hepatic steatosis in patients with fatty liver[28]. The elevation of serum TG, CHOL and LDL-C was more common in patients with NAFL than those with AFL. Most patients with fatty liver had no obvious symptoms and signs of liver disease at the time of diagnosis. But a higher proportion of patients with cryptogenic cirrhosis shared many of the clinical and demographic features of patients with fatty liver. NASH played an under-recognized role in many patients with cryptogenic cirrhosis[29]. Mild elevation usually less than 2 folds of the normal limit of serum ALT and GGT was showed in this investigation. The mitochondria was the most likely source of the reactive oxygen species (ROS) leading to lipid peroxidation in patients with fatty liver[30]. AST, a mitochondrial enzyme, was more easily affected by ethanol[31]. Among the abnormal hepatic functions, the higher AST levels with AST/ALT more than 2 were found in those with AFL. The increases of serum lipids and AST/ALT ratio might be useful in differentiating NAFL from AFL.

ACKNOWLEDGMENTS

We greatly thank Dr. Jie Yan from the Department of Medical Statistics of Sun Yat-Sen University for statistical analysis.

REFERENCES

1 **Angulo P.** Nonalcoholic fatty liver disease. *N Engl J Med* 2002; **346**: 1221-1231
2 **Omagari K,** Kadokawa Y, Masuda J, Egawa I, Sawa T, Hazama H, Ohba K, Isomoto H, Mizuta Y, Hayashida K, Murase K, Kadota T, Murata I, Kohno S. Fatty liver in non-alcoholic non-overweight Japanese adults: incidence and clinical characteristics. *J Gastroenterol Hepatol* 2002; **17**: 1098-1105
3 **Angulo P,** Lindor KD. Non-alcoholic fatty liver disease. *J Gastroenterol Hepatol* 2002; **17**: S187-190
4 **Fan JG.** Studies on fatty liver in China. *Shijie Huaren Xiaohua Zazhi* 2001; **9**: 6-10
5 **Sherlock S,** Dooley J. Diseases of the liver and biliary system. 10ed.Oxford: *Blackwell Sci Pub* 1997: 427-433
6 **Fatty Liver and Alcoholic Liver Disease Study Group of Chinese Liver Disease Association.** Diagnostic criteria of nonalcoholic fatty liver disease. *Zhonghua Ganzangbing Zazhi* 2003; **11**: 71
7 **Fatty Liver and Alcoholic Liver Disease Study Group of Chinese Liver Disease Association.** Diagnostic criteria of alcoholic fatty liver disease. *Zhonghua Ganzangbing Zazhi* 2003; **11**: 72
8 **Wang H,** Chen J. Epidemiological studies of fatty livers. *Xin*

Xiaohuabingxue Zazhi 1997; **5**: 100-101

9 **Bacon BR,** Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: An expanded clinical entity. *Gastroenterology* 1994; **107**: 1103-1109

10 **James O,** Day C. Non-alcoholic steatohepatitis: another disease of affluence. *Lancet* 1999; **353**: 1634-1636

11 **Pares A,** Tresserras R, Nurez L, Cerralbo M, Plana P, Pujol FJ, Massip J, Caballeria L, Bru C, Caballeria J, Vidal J, Salleras L, Rodes J. Prevalence and factors associated to the presence of fatty liver in apparently healthy adult men. *Med Clin* 2000; **114**: 561-565

12 **Marchesini G,** Brizi M, Morselli-Labate AM, Bianchi G, Bugianesi E, McCullough AJ, Forlani G, Melchionda N. Association of nonalcoholic fatty liver disease with insulin resistance. *Am J Med* 1999; **107**: 450-455

13 **Falchuk KR,** Fiske SC, Haggitt RC, Federman M, Trey C. Pericentral hepatic fibrosis and intracellular hyaline in diabetes mellitus. *Gastroenterology* 1980; **78**: 535-541

14 **Rinella ME,** Alonso E, Rao S, Whitington P, Fryer J, Abecassis M, Superina R, Flamm SL, Blei AT. Body mass index as a predictor of hepatic steatosis in living liver donors. *Liver Transpl* 2001; **7**: 409-414

15 **Powell EE,** Cooksley WG, Hanson R, Searle J, Halliday JW, Powell LW. The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. *Hepatology* 1990; **11**: 74-80

16 **Assy N,** Kaita K, Mymin D, Levy C, Rosser B, Minuk G. Fatty infiltration of liver in hyperlipidemic patients. *Dig Dis Sci* 2000; **45**: 1929-1934

17 **Gray DS.** Diagnosis and prevalence of obesity. *Med Clin North Am* 1989; **73**: 1-13

18 **Sheth SG,** Gordon FD, Chopra S. Nonalcoholic steatohepatitis. *Ann Intern Med* 1997; **126**: 137-145

19 **Wang WJ,** Wang KA, Li TL, Xiang HD, Ma LM, Fu ZY, Chen JS, Liu ZY, Bai J, Fong JG, Jin SX, Li YQ, Qing NL, Chen H. A study on the epidemiological characteristics of obesity in Chinese Adults. *Zhonghua Liuxingbingxue Zazhi* 2001; **22**: 129-132

20 **Walsh K,** Alexander G. Alcoholic liver disease. *Postgrad Med J* 2000; **76**: 280-286

21 **Marceau P,** Biron S, Hould FS, Marceau S, Simard S, Thung SN, Kral JG. Liver pathology and the metabolic syndrome X in severe obesity. *J Clin Endocrinol Metab* 1999; **84**: 1513-1517

22 **Marchesini G,** Brizi M, Bianchi G, Tomassetti S, Bugianesi E, Lenzi M, McCullough AJ, Natale S, Forlani G, Melchionda N. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. *Diabetes* 2001; **50**: 1844-1850

23 **Luyckx FH,** Lefebvre PJ, Scheen AJ. Non-alcoholic steatohepatitis: association with obesity and insulin resistance, and influence of weight loss. *Diabetes Metab* 2000; **26**: 98-106

24 **Neuschwander-Tetri BA,** Bacon BR. Nonalcoholic steatohepatitis. *Med Clin North Am* 1996; **80**: 1147-1166

25 **Lu LG,** Zeng MD, Li JQ, Hua J, Fan JG, Fan ZP, Oiu DK. Effect of lipid on proliferation and activation of rat hepatic stellate cells (I). *World J Gastroenterol* 1998; **4**: 497-499

26 **Lu LG,** Zeng MD, Li JQ, Hua J, Fan JG, Oiu DK. Study on the role of free fatty acids in proliferation of rat hepatic stellate cells (II). *World J Gastroenterol* 1998; **4**: 500-502

27 **Rubbia-Brandt L,** Leandro G, Spahr L, Giostra E, Quadri R, Male PJ, Negro F. Liver steatosis in chronic hepatitis C: a morphological sign suggesting infection with HCV genotype 3. *Histopathology* 2001; **39**: 119-124

28 **Itoh S,** Yougel T, Kawagoe K. Comparison between nonalcoholic steatohepatitis and alcoholic hepatitis. *Am J Gastroenterol* 1987; **82**: 650-654

29 **Caldwell SH,** Oelsner DH, Iezzoni JC, Hespenheide EE, Battle EH, Driscoll CJ. Cryptogenic cirrhosis: clinical characterization and risk factors for underlying diseaas.*Hepatology* 1999; **29**: 664-669

30 **Day CP.** Non-alcoholic steatohepatitis (NASH): where are we now and where are we going? *Gut* 2002; **50**: 585-588

31 **French SW.** Mechanisms of alcoholic liver injury. *Can J Gastroenterol* 2000; **14**: 327-332

Edited by Zhang JZ **Proofread by** Xu FM