Alcoholic liver disease. *Are there any differences between China and Western countries in clinical features?*

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ABSTRACT

Objectives: To investigate the clinical features of alcoholic liver disease (ALD) in hospitalized Chinese patients, and their differences compared with western countries.

Methods: Four hundred and eight hospitalized patients with ALD at First Affiliated Hospital of Zhejiang University College of Medicine, Hangzhou, from January 2008 to December 2010 were studied retrospectively. Clinical data were analyzed and compared with western countries through literature review.

Results: The patients with ALD accounted for 7.8% of all hospitalized patients with liver diseases. These patients comprised 400 men and 8 women, aged between 45 and 55 years. Among the patients, there were 318 patients with alcoholic cirrhosis (77.9%), 48 patients with alcoholic hepatitis (11.8%), 9 patients with fatty liver (2.2%), and 33 patients with mild alcoholic injury (8.1%). The abstinence rate in these patients was 37.7%. Logistic-regression analysis showed that daily intake amount, duration of drinking, drinking hard liquors and smoking were the risk factors for alcoholic cirrhosis, but abstinence was the favorable factor for treatment. Compared with western countries, Chinese patients had a lower constituent ratio of ALD among liver diseases, lower proportions of females, and rate of concomitant hepatitis C infection; but the drinking status, clinical manifestations, and abstinence rate were similar between them.

Conclusion: There are differences as well as similarities between China and western countries in the clinical features of ALD.

Alcoholic liver disease (ALD) is a common liver disease caused by excessive alcohol consumption, and encompasses several conditions: fatty liver, alcoholic hepatitis, alcoholic liver fibrosis, and cirrhosis. Massive hepatic necrosis or liver failure may also be seen in some heavy alcohol drinkers. Alcoholic liver disease is the major cause of liver disease in western countries. In recent years, with the improved living standards, its incidence has increased greatly in China. Due to the culture and custom differences between China and western countries, there are differences in the incidences of ALD. However, few reports are seen concerning the differences in the features of ALD between China and western countries. In the present study, we retrospectively analyzed 408 hospitalized patients with ALD, and compared the clinical features of ALD between China and western countries through literature review.

Methods. This is a retrospective study including 408 consecutive patients with ALD admitted to the First Affiliated Hospital of Zhejiang University College of Medicine, Hangzhou, China between January 2008 and December 2010. Diagnosis was made according to guidelines for the diagnosis and treatment of ALD established by the Chinese Medical Association (2010 revision).[1] Patients with incomplete medical history were excluded from the study. This study complies with the principles of the Helsinki Declaration. Medical record numbers of patients with liver diseases were searched in the hospital medical records information management system, and the medical records were investigated. Data were collected, including general information (gender, age, occupation, marital status, educational level, and length of hospital stay, and so forth), smoking, drinking (daily intake amount, duration of drinking, abstinence, and duration of abstinence, and so forth), clinical manifestations, laboratory data (blood routine test, liver function test, and so forth), and clinical outcomes. Alcohol content calculation formula: alcohol content = intake amount (ml) × alcohol degree (%) × 0.8. The alcohol degree for liquor is 40%, for rice wine and red wine is 15%, and for beer is 4%.

Data were analyzed using the Statistical Package for Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA). The rates (for example, ALD, alcoholic cirrhosis) and averages (for example, age, daily alcohol consumption) were calculated. Multivariate logistic-regression (stepwise) models were developed, and odds ratios (ORs) were used to evaluate risk factors associated with alcoholic cirrhosis. Variables (age, gender, occupation, education level, smoking, drinking types, daily intake amount, duration of drinking, and abstinence) were defined as independent variables, and alcoholic cirrhosis was defined as a dependent variable. *P*-values less than 0.05 with a 95% confidence interval were considered statistically significant.

Results. There were 408 patients who were diagnosed with ALD and included in the study. They accounted for 7.8% (408/5231) of total hospitalized patients with liver diseases over the same period, and comprised 400 men and 8 women with a male-female ratio of 50:1. The mean age was 55.2 years (range: 23-83 years) and most were aged between 45 and 55 years (36.8%). The educational levels of most patients were classified as elementary school (41.4%) and junior high school (32.8%). The mean length of hospital stay was 17.1 days (range: 1-125 days). Two hundred and sixty-five patients had a history of smoking (65.0%), 7 patients underwent liver transplantation, and 14 patients died. Among the 408 patients, there were 318 patients with alcoholic cirrhosis (77.9%) who accounted for 11.6% of total patients with liver cirrhosis, and there were 48 patients with alcoholic hepatitis (11.8%), 9 patients with fatty liver (2.2%), and 33 patients with mild alcoholic injury (8.1%). Thirty-six patients (8.8%) also had hepatitis virus infection: hepatitis B virus (HBV), 32 patients (7.8%), hepatitis C virus (HCV), 2 patients (0.5%), and hepatitis D virus, 2 patients (0.5%).

The average daily alcohol consumption was 144.3 g (range: 40-960 g), and the mean duration of drinking was 26.2 years (range: 1-60 years). The drinking types included liquor (278 patients, 68.1%), rice wine (83 patients, 20.3%), red wine (4 patients, 1%), beer (14 patients, 3.4%) and mixed (29 patients, 7.1%). One hundred and fifty-four patients had stopped drinking, and the abstinence rate was 37.7%.

The symptoms in these patients included abdominal distension (207 patients), fatigue (178 patients), dark urine (104 patients), anorexia (101 patients), yellowish skin (80 patients), edema of lower extremity (63 patients), bleeding (53 patients: melena 30 patients, hematemesis 38 patients, and bleeding gums 5 patients), abdominal pain (38 patients), fever (32 patients), oliguria (29 patients), nausea and vomiting (21 patients), and diarrhea (12 patients). The physical signs observed in these patients included hepatic facies (185 patients), anemia (184 patients), ascites (166 patients), jaundice (165 patients), spider angioma (87 patients), liver palms (65 patients), splenomegaly (62 patients), edema of lower extremity (63 patients), unconsciousness or coma (17 patients), asterixis (11 patients) and abdominal tenderness (9 patients). Complications that occurred in these patients included electrolyte disturbance (241 patients: hyponatremia 98 patients, hypokalemia 98 patients, hypocalcemia 166 patients), spontaneous peritonitis (64 patients), hepatic encephalopathy (39 patients), upper gastrointestinal hemorrhage (38 patients), hepatorenal syndrome (27 patients), esophageal and gastric fundal varices (20 patients) and hepatopulmonary syndrome (4 patients). The average values of serum alanine aminotransferase (ALT) (67.8 g/L, normal <50 g/L), aspartate aminotransferase (AST) (111.3 g/L, normal <40 g/L), total bilirubin (97.6 μmol/L, normal<22 μmol/L), direct bilirubin (57.7 μmol/L, normal<7 μmol/L) and mean corpuscular volume (102.1 fL, normal 79～101 fL), were all higher than the normal range, but albumin (33.39 g/L, normal 35.0～55.0 g/L) and albumin/globulin ratio (1.32, normal 1.5-2.5) were lower than the normal range. There were 195 patients (47.8%) with the ratio of AST/ALT ≥ 2.

As shown in **Table 1**, logistic-regression analysis indicated that daily intake amount, duration of drinking, drinking hard liquors, and smoking were the risk factors for alcoholic cirrhosis, but abstinence was the favorable factor for treatment of ALD. To characterize the clinical features of ALD in the Chinese population, we combined our data with domestic multicenter study data,[2,3] and compared this with western countries. As shown in **Table 2**, Chinese patients had a lower constituent ratio of ALD among liver diseases, lower proportion of females, and rate of concomitant hepatitis C infection; but the peak onset age and abstinence rate were similar between them.

Discussion. Alcoholic liver disease is a major health problem in the western countries. In China, with the improvement of living standards, alcohol consumption

Table 1 - Results of logistic-regression analysis of risk factors for alcoholic cirrhosis among Chinese alcoholic liver disease patients.

Variables	Coefficient	Standard error	Wald	*P*-value	OR	95% CI
Hard liquors	0.607	0.287	4.471	0.034	1.836	1.045-3.223
Daily intake amount	0.008	0.002	10.776	0.001	1.008	1.003-1.012
Duration of drinking	0.043	0.016	7.236	0.007	1.044	1.012-1.077
Smoking	0.858	0.374	5.258	0.022	2.358	1.133-4.907
Abstinence	-0.952	0.284	11.239	0.001	0.386	0.221-0.673

OR - odds ratio, CI - confidence interval

Table 2 - Comparison of alcoholic liver disease data in Chinese domestic multicenters and western countries.

Variables	Male-female ratio	Peak onset age (years)	Average daily intake amount (g)	Average duration of drinking (years)	Constituent ratio among liver diseases (%)	Hepatitis B infection (%)	Hepatitis C infection (%)	Abstinence rate (%)
Combined domestic	76:1	40-55	128.9-144.3	22.4-26.2	4.3-7.8	7.8-28.3	0.12-3.4	37.7
Western countries	3-4.7:1[6,7]	45-55[8]	129-150[6,10]	14-24.5[6,11]	36.8-53[4,5]	8.1[13]	14-20.8[4,14]	20-34[16]

has increased and there is an increasing trend in the incidence of ALD. In the present study, the combined domestic data showed that the constituent ratio of ALD among liver diseases was 4.3-7.8%, which is much lower than those in western countries (36.8-53%).[4,5] However, among the spectrum of ALD, alcoholic liver cirrhosis accounted for the largest proportion (50%), which is similar to western countries (68-78.7%).[6,7] In addition, the ages of patients with ALD ranged from 23 to 83 years, and the peak onset age was between 40 and 55 years, both of which are similar to western countries.[8]

Studies have shown that women develop ALD more rapidly and to a greater extent than men while consuming less alcohol, suggesting that women are more vulnerable to developing ALD.[9] However, in the present study, the combined domestic data showed that the male-female ratio was only 76:1. The reason for the fact may be due to extremely less women with excessive drinking in China. To the contrary, there are many more women with excessive drinking in western countries, and reports have shown that the male-female ratio was 3-4.7:1.[6,7]

By logistic-regression analysis, we showed that daily intake amount and duration of drinking are the risk factors for alcoholic cirrhosis. In the present study, the average daily intake amount and duration of drinking in patients with ALD were 128.9-144.3 g and 22.4-26.2 years in the combined domestic data, which are comparable to western countries (129～150 g and 14～24.5 years).[6,10,11] Due to the wide range of average daily intake amount and duration of drinking in patients with ALD, different thresholds of daily intake amount and duration of drinking are set for the diagnosis of ALD in different countries. Drinking types and dietary habits are related to ALD. Drinking hard liquors and drinking on an empty stomach are risk factors for ALD. Our study indicated that hard liquors were the risk factors for alcoholic cirrhosis. Due to the cultural differences, drinking on an empty stomach and drinking hard liquors are common in western countries, but in China, most drinkers drink with food. These different drinking patterns may explain the large difference between western countries and China in the incidence of ALD. Our study also indicated that smoking was a risk factor for alcoholic cirrhosis. Smoking is an important risk factor for a variety of diseases, including lung cancer, oral cancer, and cardiovascular diseases. Smoking may increase the severity of liver diseases. Bailey et al[12] reported that combined exposure to ethanol and tobacco increased hepatic steatosis and hypoxia in the hypercholesterolemic apoE(-/-) mouse, suggesting that smoking may accelerate and exacerbate ALD.

Concomitant infection with HBV or HCV viruses contributes to the progression of ALD. Alcohol and hepatitis viruses may exert synergistic liver toxicity. In the present study, the combined domestic data showed that the rate of concomitant HBV infection was 7.8-28.3% in patients with ALD, but the rate of concomitant HCV infection was only 0.12-3.4%. However, due to higher prevalence of HCV than HBV in western countries, 14-20.8% of alcoholics had concomitant HCV infection, but only 8.1% had concomitant HBV infection.[4,13,14]

Abstinence is the cornerstone of management of ALD, and it may improve hepatic fibrosis and reduce mortality in patients with alcoholic cirrhosis.[15] In the present study, we showed that abstinence was the favorable factor for treatment of ALD. However, due to the toxic effect on the central nervous system, alcohol recidivism is more likely to occur following abstinence and the relapse rates range from 67% to 81%.[15] The abstinence rate is low in both China and western countries.[16] Therefore, the importance of abstinence in the treatment of ALD should be emphasized; when necessary, medications may be used to help sustain abstinence.

The limitations in our study are that analyzed data were based on a single center, and the sample size was relatively small, which may not allow extrapolation to all Chinese patients with ALD. However, we combined domestic multicenter study data with our present data to analyze the clinical features of ALD in China, and

to compare them with western countries. In addition, we analyzed the risk factors associated with alcoholic cirrhosis, to help preventing occurrence of more severe liver diseases. A large multicenter clinical study is required to further characterize the clinical features of ALD in China.

In conclusion, there are many differences as well as similarities between China and western countries in the clinical features of ALD.

Received 12th December 2013. Accepted 8th April 2014.

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References

1. Li YM; the Chinese National Workshop on Fatty Liver and Alcoholic Liver Disease for the Chinese Liver Disease Association. Guidelines for management of alcoholic liver disease: an updated and revised edition. ***Chin J Intern Med*** 2010; 49:357-359. Chinese
2. Chi BR, Sun Y, Zhou D, Huo JR, Wang BY, Bai WY, et al. A multicenter study of alcoholic liver disease in China. ***Chin J of Dig*** 2007; 27: 231-234. Chinese. Available from: http://www.cnki.com.cn/Article/CJFDTotal-ZHHX200704010.htm
3. Wang BY, Yu JH. [The clinical characteristics of alcoholic patients with hepatitis virus infection]. ***Zhonghua Gan Zang Bing Za Zhi*** 2009; 17: 809-811. Chinese
4. Said A, Williams J, Holden J, Remington P, Musat A, Lucey MR. The prevalence of alcohol-induced liver disease and hepatitis C and their interaction in a tertiary care setting. ***Clin Gastroenterol Hepatol*** 2004; 2: 928-934.
5. Haukeland JW, Lorgen I, Schreiner LT, Frigstad SO, Brandsaeter B, Bjøro K, et al. Incidence rates and causes of cirrhosis in a Norwegian population. ***Scand J Gastroenterol*** 2007; 42: 1501-1508.
6. Hourigan KJ, Bowling FG. Alcoholic liver disease: a clinical series in an Australian private practice. ***J Gastroenterol Hepatol*** 2001; 16: 1138-1143.
7. Tao N, Sussman S, Nieto J, Tsukamoto H, Yuan JM. Demographic characteristics of hospitalized patients with alcoholic liver disease and pancreatitis in Los Angeles county. ***Alcohol Clin Exp Res*** 2003; 27: 1798-1804.
8. Thomson SJ, Westlake S, Rahman TM, Cowan ML, Majeed A, Maxwell JD, et al. Chronic liver disease--an increasing problem: a study of hospital admission and mortality rates in England, 1979-2005, with particular reference to alcoholic liver disease. ***Alcohol Alcohol*** 2008; 43: 416-422.
9. Sharma MR, Polavarapu R, Roseman D, Patel V, Eaton E, Kishor PB, et al. Increased severity of alcoholic liver injury in female verses male rats: a microarray analysis. ***Exp Mol Pathol*** 2008; 84: 46-58.
10. Naveau S, Giraud V, Ganne N, Perney P, Hastier P, Robin E, et al. [Patients with alcoholic liver disease hospitalized in gastroenterology. A national multicenter study]. ***Gastroenterol Clin Biol*** 2001; 25: 131-136. French
11. Campollo O, Martínez MD, Valencia JJ, Segura-Ortega J. Drinking patterns and beverage preferences of liver cirrhosis patients in Mexico. ***Subst Use Misuse*** 2001; 36: 387-398.
12. Bailey SM, Mantena SK, Millender-Swain T, Cakir Y, Jhala NC, Chhieng D, et al. Ethanol and tobacco smoke increase hepatic steatosis and hypoxia in the hypercholesterolemic apoE(-/-) mouse: implications for a "multihit" hypothesis of fatty liver disease. ***Free Radic Biol Med*** 2009; 46: 928-938.
13. Stroffolini T, Cotticelli G, Medda E, Niosi M, Del Vecchio-Blanco C, Addolorato G, et al. Interaction of alcohol intake and cofactors on the risk of cirrhosis. ***Liver Int*** 2010; 30: 867-870.
14. Bialek SR, Redd JT, Lynch A, Vogt T, Lewis S, Wilson C, et al. Chronic liver disease among two American Indian patient populations in the southwestern United States, 2000-2003. ***J Clin Gastroenterol*** 2008; 42: 949-954.
15. O'Shea RS, Dasarathy S, McCullough AJ; Practice Guideline Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Alcoholic liver disease. ***Hepatology*** 2010; 51: 307-328.
16. Trabut JB, Plat A, Thepot V, Fontaine H, Vallet-Pichard A, Nalpas B, et al. Influence of liver biopsy on abstinence in alcohol-dependent patients. ***Alcohol Alcohol*** 2008; 43: 559-563.

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