

# Characteristics of symptom in patients with hepatic cirrhosis of different etiologies

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## Research article

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# Abstract

**Backgrounds:** The complications of hepatic cirrhosis are responsible for death and hospitalization. We aimed to analyze the clinical characteristics in cirrhotic symptom according to etiology.

**Methods:** A total of 1,573 admissions of decompensated hepatic cirrhosis in the hospital were enrolled between September 2014 and August 2019. We described the relationships between major symptoms and cirrhotic etiologies. We assessed the secondary hepatic encephalopathy for each cirrhotic etiology.

**Results:** Among all complications, the constituent ratio of gastrointestinal hemorrhage was 37.87%, followed by ascites and jaundice with 23.70% and 11.40%, respectively. Gastrointestinal hemorrhage was more presented in hepatitis B and hepatitis C than in alcoholic cirrhosis (57.59%, 47.86% and 42.19%,  $p < 0.05$ ). No significant difference was found between hepatitis B and hepatitis C for all symptoms. Jaundice was the major symptom in primary biliary cirrhosis and autoimmune cirrhosis. Alcoholic cirrhotic patients had a higher rate to develop secondary encephalopathy than other etiologies (13.51%,  $p < 0.05$ ).

**Conclusions:** Gastrointestinal hemorrhage was the main symptom for hospitalization in decompensated cirrhotic patients. Patients of hepatitis cirrhosis were more likely to have gastrointestinal hemorrhage than those of alcohol cirrhosis. Patients of alcohol cirrhosis were likely to develop a secondary encephalopathy following the presentation of other symptoms.

## 1. Introduction

Hepatic cirrhosis is a common chronic disease worldwide, especially in Asia [1]. Decompensated hepatic cirrhosis is the late stage of cirrhosis with complications such as ascites, gastrointestinal hemorrhage, jaundice and encephalopathy [2]. Among these manifestations, encephalopathy is usually more serious than others [3, 4]

Although these complications are commonly seen in clinical practice, there were few studies extensively illustrating the characteristics of the major symptom for each cirrhotic etiology. Moreover, the encephalopathy secondary to other symptoms in decompensated cirrhotic patients was rarely studied.

We retrospectively analyzed hepatic cirrhotic patients hospitalized in past 5 years. We tried to analyze the main symptom of each etiology. We further investigated the presence of secondary hepatic encephalopathy following other symptoms.

## 2. Materials And Methods

### *Patients*

China Medical University Affiliated Shengjing Hospital is the second

largest hospital in Northeast China. A total of 1,573 admissions of decompensated hepatic cirrhosis were enrolled between September 2014 and August 2019. If the same patient was readmitted with the same symptom, the repeated data were excluded, and the final sample size was 1,227.

### **Definition**

The diagnosis of decompensated hepatic cirrhosis was based on the clinical manifestation, laboratory test and image examination such as computer tomography (CT) or magnetic resonance image (MRI).

The major symptom was the main manifestation for patients to hospitalize. For the patients with more than one cirrhotic symptom, the most prominent symptom was recorded as the major symptom. The patients with secondary hepatic encephalopathy referred to those who presented hepatic encephalopathy after the presentation of other major symptoms, while the patients with primary hepatic encephalopathy referred to those whose major symptom was hepatic encephalopathy. The gastrointestinal symptom referred to the diarrhea, nausea, disgusting with greasy food, abdominal discomfort and so on. The patients of ascites included those of peritonitis.

The etiology of hepatic cirrhosis was determined based on the clinical history, manifestation and serology tests. Alcoholic cirrhosis was defined as consumption of over 40 g per day in men or over 20 g per day in women for at least 5 years [5].

All the clinical data were collected from the records of hospital information system. The study was approved by the ethics committee of China Medical University Affiliated Shengjing Hospital.

### Statistical analysis

Descriptive statistics were calculated for all variables. Continuous variables were expressed as mean values and standard deviations. Categorical variables were analyzed using Pearson's Chi-square test. Data were analyzed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and Microsoft Office Excel 2007. A p-value less than 0.05 (two-sided) was considered significant.

## 3. Results

Figure 1 showed the annual admissions for cirrhosis and all cause in gastroenterology department. The admissions for all cause remained stable while the number of inpatients with hepatic cirrhosis decreased annually.

Table 1 showed the baseline characteristics of patients with decompensated hepatic cirrhosis according to major symptoms. The mean age was  $57.34 \pm 12.32$  years and the ratio of male to female was 779:448. Among all the major symptoms, gastrointestinal hemorrhage occupied 37.87%, followed by ascites and jaundice with 23.70% and 11.40%.

Table 1  
Baseline characteristics of cirrhotic patients for major symptoms.

	N (%)	Male: Female	Age (year)
Gastrointestinal hemorrhage	465 (37.87%)	310:154	$56.29 \pm 11.92$
Ascites	291 (23.70%)	185:106	$59.97 \pm 12.43$
Jaundice	140 (11.40%)	82:58	$54.33 \pm 12.96$
Primary hepatic encephalopathy	71 (5.78%)	53:18	$59.01 \pm 11.68$
Lower limb edema	39 (3.18%)	24:15	$59.59 \pm 10.26$
Gastrointestinal symptom	93 (7.57%)	55:38	$57.62 \pm 11.86$
Liver function abnormal	28 (2.28%)	13:22	$55.34 \pm 12.29$
Infection	23 (1.87%)	14:9	$57.00 \pm 11.71$
Others	71 (5.78%)	43:28	$57.15 \pm 13.67$
Total	1227	779:448	$57.34 \pm 12.32$

The major symptoms according to cirrhotic etiology were presented in Table 2. Comparing those of hepatitis B or hepatitis C cirrhosis, patients of alcoholic cirrhosis had a lower proportion of gastrointestinal hemorrhage (135/320 and 167/290,  $p < 0.05$ ; 135/320 and 42/70,  $p < 0.05$ ) and a higher proportion of jaundice (55/320 and 22/290,  $p < 0.05$ ; 55/320 and 1/70,  $p < 0.05$ ). Although patients of alcoholic cirrhosis had a higher proportion of ascites than those of hepatitis B cirrhosis, the difference was not significant (100/135 and 84/167,  $p > 0.05$ ). For all the symptoms, no significant difference was found between hepatitis B and hepatitis C cirrhosis.

Table 2  
The major symptom for admissions according to hepatic cirrhosis etiology.

	Alcohol (N = 320)	Hepatitis B(N = 290)	Cryptogenic(N = 175)	Hepatitis C(N = 70)	PBC(N = 53)	Autoimmune(N = 37)	Others(N = 22)
Gastrointestinal hemorrhage	135 (135/320)	167 (167/290)	82 (82/175)	42 (42/70)	15 (15/53)	16 (16/37)	8 (8/22)
Ascites	100 (100/320)	84 (84/290)	54 (54/175)	21 (21/70)	15 (15/53)	8 (8/37)	9 (9/22)
Jaundice	55 (55/320)	22 (22/290)	26 (26/175)	1 (1/70)	22 (22/53)	12 (12/37)	2 (2/22)
Primary encephalopathy	30 (30/320)	17 (17/290)	13 (13/175)	6 (6/70)	1 (1/53)	1 (1/37)	3 (3/22)
PBC: Primary biliary cirrhosis							

Patients of primary biliary cirrhosis (PBC) and those of autoimmune cirrhosis had a high proportion of jaundice, but there was no difference between patients of PBC and autoimmune cirrhosis (22/57 and 12/37,  $p > 0.05$ ). The difference of primary hepatic encephalopathy was not significant between alcoholic cirrhosis and other etiologies.

Table 3 presented the secondary encephalopathy for each etiology. Patients of alcoholic cirrhosis were more likely to develop into hepatic encephalopathy following the presentation of other symptoms (13.5%,  $p < 0.05$ ).

Table 3  
The presentation of secondary encephalopathy for different cirrhotic etiology.

	Alcohol		HBV		Cryptogenic		HCV		PBC		Immune	
Secondary encephalopathy (N = 120)	47	P < 0.05	36	P = 0.78	21	P = 0.948	7	P = 0.62	5	P = 0.16	4	P = 0.67
No encephalopathy (N = 1099)	301		328		179		72		83		46	

## 4. Discussion

This study showed a gradual decline in the incidence of hepatic cirrhosis from the perspective of admissions. The major symptoms according to cirrhotic etiology were studied. The patients of alcoholic cirrhosis were likely to develop into encephalopathy following the presentation of other symptoms.

Like most Asian countries, China used to be a country dominated by hepatitis B [6]. However, with the widespread use of vaccine in recent 30 years, the incidence of hepatitis B has gradually decreased [7], which led to a decline in the incidence of cirrhosis. Some studies of epidemiology in China reported the decreasing trend in hepatitis B, which was consistent to our study from the view of admissions [8].

Some studies in western countries reported that the patients of alcoholic cirrhosis were still increasing [9, 10]. Considering the improvement of living condition and the increased intake of alcohol in China, we should pay attention to the growth of alcoholic cirrhosis while reducing the number of hepatitis B.

Ascites and gastrointestinal varices are direct complications of portal hypertension. In most western countries, ascites is reported as the main cause of admission for patients of decompensated hepatic cirrhosis [11,12,13]. However, our study found that gastrointestinal bleeding was the main symptom. Through further study, we found that the incidence of gastrointestinal bleeding was higher in hepatitis cirrhotic patients than that in alcoholic cirrhotic patients. Considering the higher proportion of hepatitis B in our country, it makes sense that the gastrointestinal bleeding is most common in China while ascites is most common in western countries. However, there are different conclusions in some other studies. A study in India suggested that all the symptoms including gastrointestinal bleeding, ascites, encephalopathy and jaundice were more obvious in patients with alcoholic cirrhosis than in patients with nonalcoholic cirrhosis [14]. Another study in Portugal reported that fluid retention was more common in viral cirrhosis, whereas encephalopathy and variceal bleeding was more frequent in alcoholic cirrhosis [15]. Part of the reasons for different conclusions may lie in the different criteria of symptoms between studies. Because gastrointestinal bleeding is relatively urgent and more life-threatening, as we focused on the main symptom for admission, some bleeding patients with ascites were not classified into ascites group. Moreover, ascites is not so emergent as gastrointestinal bleeding, many patients are used to apply diuretics at home by themselves. But whether there are differences in racial or pathophysiology, more studies are needed.

The proportion of jaundice in alcoholic cirrhosis is higher than hepatitis B or C cirrhosis. A guideline in USA pointed out that patients tend to have acute alcoholic hepatitis once they have jaundice symptoms, and this situation is very dangerous [16]. Our clinical experience tells that if the patients of alcoholic cirrhosis come to hospital with the aggravation of jaundice, they had a high possibility of developing into acute-on-chronic liver failure in a short period of time. Many studies have found that although patients of alcohol cirrhosis had a lower rate of having liver cancer than hepatitis, the mortality is higher [17, 18]. Rapid aggravation of jaundice in a short period of time might be the beginning of deterioration in alcoholic cirrhotic patients, which should be paid attention to.

No significant difference in all the symptoms was found between hepatitis B and hepatitis C cirrhosis. This shows that there are many common clinical features for hepatitis cirrhosis, even though the types are different.

Jaundice is the main symptom for patients of primary biliary cirrhosis and those of autoimmune hepatic cirrhosis, which is consistent with the clinical characteristics and pathophysiology [19]. Both of them are mainly due to intrahepatic cholestasis which leads to the jaundice and pruritus. With the development of the disease, it is often accompanied by jaundice rather than portal hypertension.

Hepatic encephalopathy is a common complication in patients with decompensated hepatic cirrhosis. There are several theories for the hepatic encephalopathy, such as portosystemic shunt, plasma ammonia and pseudo-transmitters [3]. For patients of alcoholic cirrhosis, there are many studies illustrating the direct and indirect effects of alcohol on brain nerves, which increase the risk of encephalopathy [20, 21]. In our study, although the alcoholic cirrhosis inpatients did not present the hepatic encephalopathy at first, after the presentation of other symptoms, the patients turned to develop hepatic encephalopathy. Most of them showed mild hepatic encephalopathy symptoms, such as day and night reversal, decreased ability of calculation and so on. But this is not the case in patients of other cirrhotic etiologies. Therefore, we

determined that for patients with alcoholic cirrhosis, other decompensated symptoms might induce some factors leading to the aggravation of brain damage caused by chronic alcohol injury.

There are limitations in our study. To avoid invasive test, we did not do liver biopsy to confirm cirrhotic etiology. For the patients with gastrointestinal bleeding, to avoid inducing the recurrence of gastrointestinal bleeding due to the severe esophageal varices, not all the patients were taken the endoscopy to identify the bleeding cause.

In conclusion, gastrointestinal hemorrhage was the main symptom for hospitalization in decompensated cirrhotic patients. Patients of hepatitis cirrhosis were more likely to have gastrointestinal hemorrhage than those of alcohol cirrhosis. Patients of alcohol cirrhosis were likely to develop a secondary encephalopathy following the presentation of other symptoms.

## 5. List Of Abbreviations

Primary biliary cirrhosis (PBC)

## 6. Declarations

### *Ethics approval and consent to participate*

The study protocol was approved by the Institutional Review Board of Shengjing Hospital (Approval No. 2017PS159K).

### *Consent for publication*

The present study was a retrospective study. It only used the objective data from Hospital Information System and the information of all the patients were confidential. The data were from the treating process of the patients, instead of clinical trial. The Exemption from Informed Consent was permitted by the Board. The specialist of the Board concluded that the present study is in accordance with the World Medical Association Declaration of Helsinki.

### *Availability of data and materials*

The clinical data are from Hospital Information System which is our clinical working system. All the data were the objective records of patients' conditions in the treating process. We retrospectively reviewed the clinical data for the past 5 years and conducted the present study.

### *Competing interests*

Not applicable

### *Funding*

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### *Authors' contributions*

Xin Guan: Study concept and design, data analysis and interpretation; drafting of the manuscript; Data collection.

Fei Xing: Critical revision of the manuscript for important intellectual content. Statistical analysis. Data collection

Mengchun Wang: Data collection and analysis.

Yan Li: Corresponding author. Study concept and design.

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### ***Authors' information (optional)***

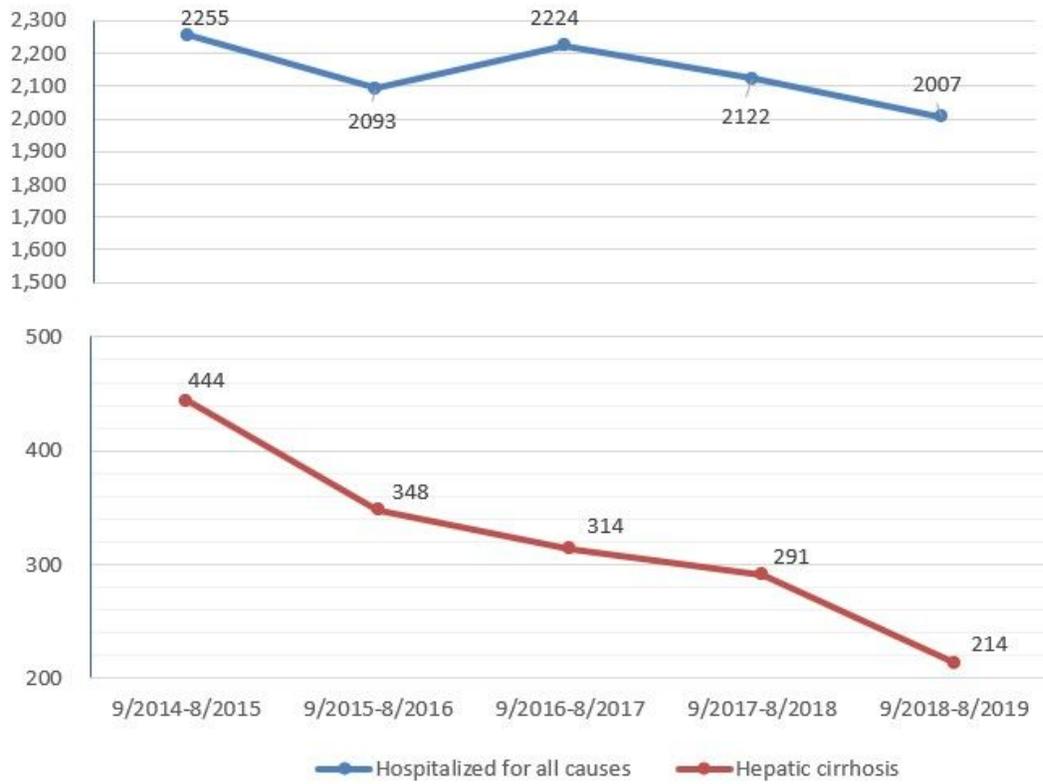
Not applicable

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## Figures



**Figure 1**

Hospital admissions for hepatic cirrhosis and all causes from Sep 2014 to Aug 2019.