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Original Article

Characteristics of pathogenic bacteria in intra-abdominal infection and risk factors for septic shock in patients with liver cirrhosis

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Abstract: Objective: To explore the characteristics of pathogenic bacteria in intra-abdominal infection and the risk factors for septic shock in patients with liver cirrhosis. Methods: This retrospective study analyzed the clinical data of patients with cirrhosis admitted to the Department of Infectious Diseases of the 910th Hospital of Chinese People's Liberation Army, who were divided into an intra-abdominal infection group (n=145) and non-infection group (n=100). We analyzed the risk factors for intra-abdominal infection in patients with liver cirrhosis, and further conducted bacterial culture for patients with intra-abdominal infection to investigate the distribution of pathogenic bacteria and analyzed the risk factors for septic shock. Results: Multivariate regression analysis found that age (P=0.005), length of hospital stay (P=0.024), invasive operation (P=0.002), and hypoproteinemia (P=0.026) were risk factors for intra-abdominal infection in patients with cirrhosis. 65 of the 145 patients with intra-abdominal infection were tested to be pathogen-positive, with a positivity rate of 44.83%. A total of 118 strains were isolated from the samples of 65 patients with positive test results. Among the 118 strains, 74 of them were gram-negative bacteria (62.71%), 41 were gram-positive bacteria (34.75%), and 3 were fungus (2.54%). Multivariate regression analysis found that age (P=0.003), length of stay (P=0.001), invasive operations (P=0.024) and hypoproteinemia (P=0.001) were all risk factors for septic shock in patients with liver cirrhosis combined with intra-abdominal infection. Conclusion: Age, length of hospital stay, invasive operation, and hypoproteinemia are risk factors for intra-abdominal infection and septic shock in patients with cirrhosis, and gram-negative bacteria are the main pathogens in associated intra-abdominal infection.

Keywords: Liver cirrhosis, intra-abdominal infection, characteristics of pathogenic bacteria, septic shock, risk factors

Introduction

Liver cirrhosis is a chronic and progressive disease. The patients often have weakened immune function and less ability to resist infection from foreign pathogens, making patients prone to infections [1, 2]. Intra-abdominal infection is the most common infection in patients with liver cirrhosis. This infection can easily aggravate the disease condition and affect the prognosis [3]. Therefore, how to effectively control the intra-abdominal infection associated with liver cirrhosis has become the key to treatment. At present, most of the patients with cirrhosis complicated by intra-abdominal infection are treated with antibiotics. With the widespread use of antibacterial drugs, drug-resistant bacteria have become increasingly common, resulting in poor clinical efficacy of antibiotics; also, the drug-resistant bacteria can be different in patients and countries [4, 5]. A study found that the pathogenic bacteria of intra-abdominal infection in patients with cirrhosis were mainly Gram-negative bacteria, with Escherichia coli and Klebsiella pneumoniae in the majority [6]. However, another study showed that the infection of patients with cirrhosis and ascites complicated with spontaneous bacterial peritonitis were mainly caused by gram-positive bacteria [7]. The pathogens of liver cirrhosis combined with intra-abdominal infection are varied. Therefore, understanding the distribution of pathogens is conducive to the selection of antibiotics in clinical treatment.

Furthermore, one of the most serious complications of liver cirrhosis combined with intra-abdominal infection is septic shock, showing a mortality of up to 50% without timely treatment [8]. Analysis of risk factors for septic shock benefits prevention, thereby improving the prognosis of patients. Therefore, this study included patients with liver cirrhosis and intra-abdominal infection to explore the distribution of pathogenic bacteria and to further analyze the risk factors for septic shock. Understanding the influencing factors of cirrhosis combined with intra-abdominal infection and septic shock is helpful for prevention and early intervention to improve survival. Discussing the pathogenic bacteria distribution allows selection of clinical targeted drugs and improves efficacy.

Materials and methods

General data

This retrospective study analyzed clinical data of patients with liver cirrhosis admitted to the Department of Infectious Diseases of the 910th Hospital of Chinese People's Liberation Army from January 2017 to August 2021. The patients were divided into two groups according to whether the patients had the complication of intra-abdominal infection: infection group (n=145) and non-infection group (n=100). The patients were aged 25-78 years old, with an average age of 62.4±9.7 years old. This study was approved by the Ethics Committee of the 910th Hospital of Chinese People's Liberation Army.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients who met the diagnostic criteria for liver cirrhosis which was confirmed by biochemical and imaging examinations [9]. (2) Patients who met the diagnostic criteria for intra-abdominal infection according to *Hospital Infection Diagnostic Criteria* [10] and confirmed by bacterial culture. (3) Patients with an age over 18 years old; (4) Patients with no history of intra-abdominal infection at admission; (5) Patients with complete data.

Exclusion criteria: (1) Patients complicated with other infections; (2) Patients with malignant tumors; (3) Patients with severe heart, brain or kidney diseases; (4) Patients with immunodeficiency; (5) Patients with pregnancy or in lactation; (6) Patients who received antifungal treatment; (7) Patients with infection at multiple sites; (8) Patients who had immunomodulators; (9) Patients with shock caused by other reasons.

Methods

The ascites fluid of patients with intra-abdominal infection was cultured on the first day of admission. For the bacterial culture and drug sensitive test, 10 mL of ascites was collected following the ascites puncture. The ascites sample was cultivated in broth agar at a constant room temperature for 24 h. Then, the positive samples were transferred to blood agar for continuous culture. The VITEK2 Compact automatic bacterial identification and drug susceptibility analysis system (Mérieux, France) was used to identify the positive strains and test the drug susceptibility. The experiment and the operation process were carried out in strict accordance with the *National Clinical Laboratory Operation Regulations*. The infection condition was identified according to the results of bacterial culture.

The occurrence of septic shock in patients with liver cirrhosis and intra-abdominal infection was recorded. Clinical data including age, gender, etiology, length of stay, with or without invasive operations, Child-Pugh score, and complications were used for statistical analysis.

Outcome measures

(1) Risk factors for intra-abdominal infection were analyzed in patients with liver cirrhosis. (2) The distribution of pathogenic bacteria was investigated in patients with cirrhosis and intra-abdominal infection with positive results in bacterial culture of ascites. (3) Risk factors for septic shock in patients with liver cirrhosis and intra-abdominal infection were statistically analyzed.

Statistical methods

Statistical software SPSS 17.0 was used to analyze the data. Continuous variables that conformed to normal distribution and homogeneity of variance were presented as mean ± standard deviation ($\overline{x}$±sd) and processed using independent sample t-test for inter-group com-

Table 1. Risk factors for intra-abdominal infection in patients with liver cirrhosis

Item	Liver cirrhosis with intra-abdominal infection group (n=145)	Liver cirrhosis without intra-abdominal infection group (n=100)	χ^2/t	P
Gender				
Male	88 (60.69%)	62 (62.00%)	0.043	0.836
Female	57 (39.31%)	38 (38.00%)		
Age (Y)				
≥60	83 (57.24%)	38 (38.00%)	8.776	0.003
<60	62 (42.76%)	62 (62.00%)		
Etiology				
Hepatitis cirrhosis	78 (53.79%)	40 (40.00%)	4.510	0.034
Others	67 (46.21%)	60 (60.00%)		
Length of hospital stay				
≥2 weeks	91 (62.76%)	47 (47.00%)	5.579	0.015
<2 weeks	54 (37.24%)	53 (53.00%)		
Invasive operations				
Yes	66 (45.52%)	20 (20.00%)	16.916	<0.001
No	79 (54.48%)	80 (80.00%)		
Child-Pugh class				
A-B	76 (52.41%)	66 (66.00%)	4.483	0.034
C	69 (47.59%)	34 (34.00%)		
Upper gastrointestinal bleeding				
Yes	36 (24.83%)	15 (15.00%)	3.468	0.063
No	109 (75.17%)	85 (85.00%)		
Diabetes				
Yes	40 (27.59%)	16 (16.00%)	4.506	0.034
No	105 (72.41%)	84 (84.00%)		
Hypoproteinemia				
Yes	65 (44.83%)	30 (30.00%)	5.481	0.019
No	80 (55.17%)	70 (70.00%)		
Chronic obstructive pulmonary disease				
Yes	36 (24.83%)	22 (22.00%)	0.262	0.609
No	109 (75.17%)	78 (78.00%)		

parison, denoted by t, while those not conforming to normal distribution and homogeneity of variance were presented as M (P25, P75) and processed using rank-sum test, denoted by F. The counted data were expressed as percentage and processed using Pearson's chi-square test, denoted by χ^2. Logistic regression was used to analyze the risk factors. The variables with differences in univariate analysis were selected, and the stepwise forward selection (Wald) was used for variable screening. The inclusion level was P<0.1, and the exclusion level was ≥0.1. The risk for intra-abdominal infection and septic shock in patients was expressed by the adjusted odds ratio (OR value). A difference of P<0.05 was considered significant.

Results

Risk factors for intra-abdominal infection in patients with liver cirrhosis

As compared to patients with liver cirrhosis but without intra-abdominal infection, those with both liver cirrhosis and intra-abdominal infection showed older age, higher rate of hepatitis cirrhosis, Child-Pugh class C, diabetes and hypoproteinemia, longer length of hospital stay, and higher number of invasive operations received (all P<0.05). Age, etiology, length of hospital stay, invasive operations, Child-Pugh class, diabetes, and hypoproteinemia were the risk factors for intra-abdominal infection in patients with liver cirrhosis, **Table 1**.

Table 2. Multivariate logistic regression analysis of intra-abdominal infection occurrence in patients with liver cirrhosis

Factor	OR value (95% CI)	P
Age (Y)	1.762 (1.231-2.765)	0.005
Etiology	2.372 (0.562-10.723)	0.291
Length of stay (d)	3.322 (1.922-9.291)	0.024
Invasive operations	1.922 (1.265-2.865)	0.002
Child-Pugh class	2.456 (0.872-12.912)	0.135
Upper gastrointestinal bleeding	3.453 (0.861-11.221)	0.234
Diabetes	0.862 (0.234-3.723)	0.762
Hypoproteinemia	5.234 (1.567-22.833)	0.026

Note: Age ≤60 years old was assigned as 1, age >60 years old as 0; for etiology, hepatitis cirrhosis was assigned as 1, others as 0; length of hospital stay ≥2 weeks was assigned as 1, <2 weeks as 0; for invasive operations, yes was assigned as 1, no as 0; for Child-Pugh class, C was assigned as 1, A-B as 0; for upper gastrointestinal bleeding, yes was assigned as 1, no as 0; for diabetes, yes was assigned as 1, no as 0; for hypoalbuminemia, yes was assigned as 1, no as 0.

Table 3. Distribution of pathogenic bacteria in patients with liver cirrhosis and intra-abdominal infection

Pathogenic bacteria	Number of stains (n)	Composition ratio (%)
Gram-negative bacteria (n=74)	74	62.71
Escherichia Coli	30	25.42
Klebsiella pneumoniae	23	19.49
Pseudomonas aeruginosa	11	9.32
Citrobacter freundii	7	5.93
Enterobacter aerogenes	2	1.69
Enterobacter cloacae	1	0.85
Gram-positive bacteria (n=41)	41	34.75
Staphylococcus epidermidis	14	11.86
Streptococcus pneumoniae	12	10.17
Enterococcus faecalis	9	7.63
Staphylococcus aureus	4	3.39
Staphylococcus haemolyticus	2	1.69
Fungus (n=3)	3	2.54
Candida albicans	3	2.54

Multivariate logistic regression analysis of the risk factors for intra-abdominal infection in patients with liver cirrhosis

Multivariate regression analysis found that age (OR value (95% CI): 1.762 (1.231-2.765), P=0.005), length of stay (OR value (95% CI): 3.322 (1.922-9.291), P=0.024), invasive operation (OR value (95% CI): 1.922 (1.265-2.865), P=0.002) and hypoproteinemia (OR value (95% CI): 5.234 (1.567-22.833), P=0.026) were risk factors for intra-abdominal infection in patients with liver cirrhosis, **Table 2**.

Distribution of pathogenic bacteria in patients with liver cirrhosis and intra-abdominal infection

The pathogenic bacteria were tested in the 145 patients with liver cirrhosis combined with intra-abdominal infection, and 65 patients were found to be positive, with a positivity rate of 44.83%. A total of 118 strains were isolated from the sample collected from 65 patients with positive test results. Among the 118 strains, 74 of them were gram-negative bacteria (62.71%), 41 were gram-positive bacteria (34.75%), and 3 strains were fungus (2.54%), **Table 3**.

Risk factors for septic shock in patients with liver cirrhosis and intra-abdominal infection

Among the 145 patients with liver cirrhosis and intra-abdominal infection, the incidence of septic shock was 27.59% (40 cases). As compared to patients without septic shock, those with septic shock received more invasive operations and had older age, longer hospital stays, and higher rate of upper gastrointestinal bleeding, diabetes, and hypoproteinemia (all P<0.05), suggesting that age, length of hospital stay, invasive operations, upper gastrointestinal bleeding, diabetes, and hypoalbuminemia were risk factors for septic shock, **Table 4**.

Multivariate logistic regression analysis of risk factors for septic shock in patients with liver cirrhosis and intra-abdominal infection

Multivariate regression analysis found that age (OR value 4.283 (2.242-5.782), P=0.001), length of hospital stay (OR value (95% CI): 4.392 (3.176-5.627), P=0.003), invasive operations (OR Value (95% CI): 2.431 (1.458-4.382) P=0.021) and hypoproteinemia (OR value (95% CI): 5.829 (3.562-8.273), P=0.001) were risk factors for septic shock in patients with liver cirrhosis combined with intra-abdominal infection, **Table 5**.

Discussion

Liver cirrhosis can be the late stage of various liver diseases, often accompanied by decline of

Table 4. Risk factors for septic shock in patients with liver cirrhosis and intra-abdominal infection

Item	Septic shock group (n=40)	Non-septic shock group (n=105)	χ^2/t	P
Gender				
Male	28 (70.00%)	60 (57.14%)	2.007	0.152
Female	12 (30.00%)	45 (42.86%)		
Age (Y)				
≥60	30 (75.00%)	53 (50.48%)	7.117	0.008
<60	10 (25.00%)	52 (49.52%)		
Etiology				
Hepatitis cirrhosis	22 (55.00%)	56 (53.33%)	0.032	0.857
Others	18 (45.00%)	49 (46.67%)		
Length of hospital stay				
≥2 weeks	32 (80.00%)	59 (56.19%)	7.026	0.008
<2 weeks	8 (20.00%)	46 (43.81%)		
Invasive operations				
Yes	25 (62.50%)	41 (39.05%)	6.424	0.011
No	15 (37.50%)	64 (60.95%)		
Child-Pugh class				
A-B	20 (50.00%)	56 (53.33%)	0.129	0.719
C	20 (50.00%)	49 (46.67%)		
Upper gastrointestinal bleeding				
Yes	15 (37.50%)	21 (20.00%)	4.753	0.029
No	25 (62.50%)	84 (80.00%)		
Diabetes				
Yes	16 (40.00%)	24 (22.86%)	4.261	0.039
No	24 (60.00%)	81 (77.14%)		
Hypoproteinemia				
Yes	27 (67.50%)	38 (36.19%)	11.481	0.001
No	13 (32.50%)	67 (63.81%)		
Chronic obstructive pulmonary disease				
Yes	10 (25.00%)	26 (24.76%)	0.001	0.976
No	30 (75.00%)	79 (75.24%)		

Table 5. Multivariate logistic regression analysis of septic shock occurrence in patients with liver cirrhosis and intra-abdominal infection

Factor	OR value (95% CI)	P
Age (Y)	4.283 (2.242-5.782)	0.001
Length of stay (d)	4.392 (3.176-5.627)	0.003
Invasive operations	2.431 (1.458-4.382)	0.021
Upper gastrointestinal bleeding	0.865 (0.192-3.674)	0.652
Diabetes	3.412 (0.892-10.023)	0.135
Hypoproteinemia	5.829 (3.562-8.273)	0.001

Note: Age ≤60 years old was assigned as 1, age >60 years old as 0; length of hospital stay ≥2 weeks was assigned as 1, <2 weeks as 0; for invasive operations, yes was assigned as 1, no as 0; for Child-Pugh class, C was assigned as 1, A-B as 0; for upper gastrointestinal bleeding, yes was assigned as 1, no as 0; for diabetes, yes was assigned as 1, no as 0; for hypoalbuminemia, yes was assigned as 1, no as 0.

liver function and may induce liver cancer [11, 12]. Intestinal permeability in patients with liver cirrhosis is increased due to gastrointestinal edema, intestinal mucosal degeneration and other factors, which makes it easy for pathogenic bacteria to enter the abdominal cavity from the intestine. Furthermore, decline in immune function also makes patients with liver cirrhosis more prone to intra-abdominal infection [13, 14]. This study included liver cirrhosis patients with or without intra-abdominal infection as the research subjects. Multivariate regression analy-

sis showed that age, length of hospital stay, invasive operations and hypoproteinemia were risk factors for intra-abdominal infection in patients with liver cirrhosis. With an increase in age, organ function declines. Coupled with the poor immunity of patients with liver cirrhosis, the risk of infection is significantly increased [15, 16]. Invasive operations can cause oxidative stress, which also increases the risk of exogenous infections [17]. Patients with liver cirrhosis are prone to hypoalbuminemia due to the decline of protein synthesis ability, which reduces the immunity of patients and induces infection [18].

Intra-abdominal infection is a common infection in patients with liver cirrhosis, with an incidence of about 60%, and the pathogenic bacteria of the infection have been reported differently in different regions [19, 20]. Previous studies have shown a general low positive rate of ascites culture during abdominal infection. A study showed that 20 of 98 patients with cirrhosis complicated by intra-abdominal infection were positive for ascites pathogen culture, with a positive rate of 20.41% [21]. An analysis of the distribution and drug resistance of bacteria isolated from patients with abdominal infection showed that the positive rate for pathogen culture in patients with abdominal infection was 15-55%, which is similar to the result (44.83%) of our study [22]. This study showed that the majority of pathogenic bacteria detected were gram-negative, and most of them were Escherichia coli and Klebsiella pneumoniae, which is consistent with previous studies [23, 24]. Clinically, third generation cephalosporins and quinolones are often used for the treatment of gram-negative bacteria. With the raised use of antibiotics, multi-drug-resistant bacteria and gram-positive bacteria are increasing. So, it is necessary to select sensitive antibiotics based on the results of drug culture. Therefore, ascites culture should be conducted in the early period for patients with liver cirrhosis and intra-abdominal infection to determine the pathogenic bacteria. For those with a low positive rate in ascites culture, a comprehensive evaluation should be conducted with the results of other laboratory examinations. For patients with liver cirrhosis and intra-abdominal infection who had poor efficacy after antimicrobial therapy, the treatment regimen should be adjusted considering there might be multi-drug-resistant bacteria or gram-positive bacterial infections.

Septic shock in patients with liver cirrhosis can easily lead to multiple organ failure and increase mortality [24]. Therefore, analysis of the risk factors for septic shock in patients with liver cirrhosis combined with intra-abdominal infection is beneficial to the early prevention of septic shock. This study showed that age, length of hospital stay, invasive operations and hypoproteinemia were risk factors for septic shock caused by liver cirrhosis and intra-abdominal infection. Older age can lead to decline of organ function, which makes the elderly more vulnerable to infection. Patients with liver cirrhosis have poor immunity [25]. Therefore, elderly patients with liver cirrhosis should be given more attention in preventing septic shock. Moreover, prolonged hospital stay increases the risk of infection. Patients are prone to nosocomial infections, as well as gram-positive bacteria and multi-drug resistant bacteria infections, leading to an increase in the incidence of septic shock [26]. Invasive operation itself can increase the risk of infection. So, for patients with liver cirrhosis and intra-abdominal infection, the risk of infection is significantly increased after invasive operations, which also increase the possibility of multi-drug resistant bacteria infection and septic shock [17]. Hypoalbuminemia is closely related to the decline in immunity. A study has shown that hypoalbuminemia can lead to a poor anti-infectious treatment effect by decreasing the plasma concentration of antibacterial drugs [27]. A study showed that the incidence of septic shock in patients with hypoalbuminemia and liver cirrhosis was 17.5% [28]. It was reported that anti-infection and albumin supplementation for patients with liver cirrhosis and intra-abdominal infection could significantly reduce the mortality comparing to antibacterial drugs alone [18].

Limitations and prospects: This is a single-center study with a small sample size. Multi-center studies with expanded sample size should be conducted to further explore the distribution of pathogens and risk factors for septic shock in patients with liver cirrhosis and intra-abdominal infection. Also, this is a retrospective study, and the included clinical data are not comprehensive, so prospective studies should be carried out in the future for further research.

In summary, age, length of hospital stay, invasive operation, and hypoproteinemia are risk factors for intra-abdominal infection and septic shock in patients with liver cirrhosis, and gram-negative bacteria are the main pathogens in liver cirrhosis and intra-abdominal infection.

Disclosure of conflict of interest

None.

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