Microbiological Characteristics and Antibiotic Susceptibility in Liver Cirrhosis Patients With Nosocomial Spontaneous Bacterial Peritonitis Caused by Escherichia coli: A Multicenter Study

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Abstract

Escherichia coli is a prevalent causative pathogen of spontaneous bacterial peritonitis (SBP). In this retrospective study, we investigated the microbiological characteristics and antibiotic susceptibility of E. coli clinical isolates obtained from liver cirrhosis patients suffering from nosocomial SBP. Our results showed that extended-spectrum β-lactamase (ESBL)-producing E. coli accounted for 47% of the cases, while 62% of the isolates were multi-drug resistant (MDR) pathogens. ESBL-producing and MDR isolates showed high incidences of resistance to third-generation cephalosporins, but they displayed susceptibility to carbapenems, β-lactamase inhibitors, and aminoglycosides. Importantly, liver cirrhosis patients with MDR E. coli SBP showed a significantly higher death rate than patients with non-MDR infections (P = 0.021). The 30-day mortality of nosocomial SBP was independently correlated with female gender (odds ratio (OR) = 5.200, 95% confidence interval (CI) = 1.194–22.642), liver failure (OR = 9.609, 95% CI = 1.914–48.252), hepatocellular carcinoma (OR = 8.176, 95% CI = 2.065–32.364), hepatic encephalopathy (OR = 8.176, 95% CI = 2.065–32.364), model of end-stage liver disease score (OR = 1.191, 95% CI = 1.053–1.346), white blood cell count (OR = 0.847, 95% CI = 0.737–0.973), and ascites polymorphonuclear (OR = 95.903, 95% CI = 3.410–2697.356). In conclusion, third-generation cephalosporins may be inappropriate for empiric treatment of nosocomial SBP caused by E. coli, due to the widespread presence of ESBLs and high incidence of MDR pathogens.

Keywords: spontaneous bacterial peritonitis; Escherichia coli; liver cirrhosis; extended spectrum beta-lactamases; multidrug resistance

Introduction

Liver cirrhosis is characterized by diffuse fibrosis and the formation of regenerative nodules, leading to irreversible liver damages.1,2 A variety of risk factors have been confirmed for liver cirrhosis, including chronic hepatitis virus infections, alcohol abuse, accumulation of fat in liver cells, alterations in inflammation, and other metabolic disorders.3,4 Liver cirrhosis may lead to several fatal complications, such as hepatocellular carcinoma (HCC), hepatopulmonary syndrome, coagulation disorders, and bacterial infections.5 Bacterial infections are a major cause for liver cirrhosis-related death, increasing the mortality by four-fold.6 Unfortunately, liver cirrhosis patients show high susceptibility to bacterial infections due to their immune dysregulation.7 Spontaneous bacterial peritonitis (SBP) is a serious complication and common cause of death in liver cirrhosis patients with ascites, and its prevalence ranges between 10% and 30% in hospitalized cirrhotic patients.8 SBP can contribute to aggressive disease progression and severe complications in liver cirrhosis patients, consequently leading to long hospital stays, high costs, and poor prognosis.9,10 Antimicrobial treatment should be timely and empirically performed for SBP cases without knowledge of the pathogens and drug sensitivity;11 Gram-negative enteric bacteria such as Escherichia coli are considered as the leading group of pathogens involved in SBP, and third-generation cephalosporins are the first-line recommended treatment.12,13 However, treatment failure with empiric antimicrobials is increasing, leading to high mortality in SBP cases.14 The wide prevalence of multidrug-resistant (MDR) pathogens represents a leading cause for
therapeutic failure.15,16 Extended-spectrum β-lactamase (ESBL) production is the most important antimicrobial resistance mechanism leading to treatment failure of E. coli,17 because the ESBLs are able to hydrolyze broad-spectrum cephalosporins.18 Most of the SBP patients are diagnosed during hospitalization and confirmed as nosocomial SBP. Patients diagnosed with nosocomial SBP show a high incidence of drug-resistant infections, leading to high mortality.16,19 Therapeutic failure of third-generation cephalosporins is observed in 33%–75% of the nosocomial SBP cases.20,21 Therefore, microbiological characterization of nosocomial SBP in cirrhosis patients is urgently required to improve empiric treatment. In this study, we investigated the microbiological characteristics and antibiotic management in nosocomial SBP caused by E. coli among liver cirrhosis patients.

Results

Patient baseline information

According to inclusion criteria, 211 E. coli nosocomial SBP cases in liver cirrhosis patients were included in our study. The mean age of patients was 50 years and the majority of cases were male (n = 176, 83%) (Table 1). The main cause for liver cirrhosis was a hepatitis B virus infection (n = 135, 64%) and most patients were confirmed at Child-Pugh stage C (n = 185, 88%), with a mean model of end-stage liver disease (MELD) score of 20.7 and a mean onset temperature of 38.8°C. The most common complications included liver failure (n = 99, 47%), hepatic encephalopathy (HE; n = 59, 28%), and renal dysregulation (n = 54, 26%). Laboratory examinations showed that white blood cell (WBC) counts were in the normal range (6.95 ± 4.42 × 10^9/L) and further analysis of ascites specimens showed average WBC counts and percentage of neutrophils were 12531.58/mm^3 and 0.67 ± 0.26, respectively. The majority of patients displayed high polymorphonuclear leukocyte count values (≥250/mm^3; n = 151, 72%). Microbiological tests showed that 99 (47%) patients were infected by ESBL-producing E. coli, while 130 (62%) isolates were confirmed as MDR E. coli. Finally, 58 patients died within 30 days after hospital admission, indicating a mortality rate of 27%.

Effects of ESBLs and MDR status on drug susceptibility

In vitro antibiotic susceptibility analysis showed that ESBL-producing E. coli displayed high incidences of resistance to penicillins (ampicillin: 100%; piperacillin: 98%) and quinolones (gatifloxacin: 75.0%; levofloxacin: 66%) (Table 2). Moreover, besides cefmetazole, their resistant rate to cephalosporins was higher than 50%. Importantly, ESBL-producing isolates were largely susceptible to minocycline, carbapenems, β-lactamase inhibitors, aminoglycosides, furadantin, and fosfomycin (Table 2). MDR-status was also a key factor for antibiotic susceptibility. In our study, over 40% of the MDR pathogens showed resistance to major cephalosporins, except for cefmetazole (Table 2). Furthermore, MDR E. coli displayed high incidences of resistance to penicillins (ampicillin: 100%; piperacillin: 83%) and quinolones (gatifloxacin: 78%; levofloxacin: 69%). The MDR pathogens displayed low incidences of resistance to minocycline, carbapenems, β-lactamase inhibitors, aminoglycosides, furadantin, and fosfomycin. In addition, it is noteworthy that one ESBL-producing isolate showed resistance to all tested antibiotics. This pathogen was carried by a 24-year-old male, who was diagnosed at Child stage C and a MELD score of 52. Unfortunately, without effective antibiotics this patient finally died.

Table 1

| Parameters | Patients (n = 211, %) |
|------------|---------------------|
| Demographic data | |
| Age (years) | 50.69 ± 12.45 |
| Gender Male | 176 (83.41) |
| Female | 35 (16.59) |
| Clinical characteristics | |
| Etiology of cirrhosis | |
| Hepatitis C viral | 14 (6.63) |
| Hepatitis B viral | 135 (63.98) |
| Autoimmune | 10 (4.74) |
| Alcohol | 31 (14.69) |
| Others | 21 (9.95) |
| Child-Pugh stage | |
| B | 26 (12.32) |
| C | 185 (87.68) |
| MELD | 20.72 ± 8.27 |
| onset temperature (°C) | 38.79 ± 0.86 |
| Complications | |
| Liver failure | 99 (46.02) |
| HCC | 36 (17.06) |
| HE | 59 (27.06) |
| Diabetes mellitus | 18 (8.53) |
| Renal dysregulation | 54 (25.59) |
| Pneumonia | 10 (4.74) |
| UGB | 20 (9.48) |
| Hematological factors | |
| WBC (×10^9/L) | 6.95 ± 4.42 |
| Neutrophil (100%) | 0.80 ± 0.096 |
| Ascites examinations | |
| Leukocyte (×10^3/mm^3) | 6290.93 ± 12531.58 |
| Polymorphonuclear (100%) | 0.67 ± 0.26 |
| PMN (×10^3/mm^3) | 5317.48 ± 11264.13 |
| PMN stage | |
| ≥250/mm^3 | 150 (71.09) |
| <250/mm^3 | 61 (28.91) |
| Microbiological examinations | |
| ESBL | |
| Negative | 112 (53.08) |
| Positive | 99 (46.92) |
| MDR | |
| Yes | 130 (61.61) |
| No | 81 (38.39) |
| Clinical outcomes | |
| Non-survivors | 58 (27.49) |
| Improved | 144 (68.25) |
| Invalid | 9 (4.26) |

ESBL: extended-spectrum β-lactamase; HCC: hepatocellular carcinoma; HE: hepatic encephalopathy; MDR: multi-drug-resistant; MELD: model for end-stage liver diseases; PMN: polymorphonuclear leukocyte count; UGB: upper gastrointestinal bleeding; WBC: white blood cell count.

Impact of ESBL-producing and MDR E. coli infections on clinical and laboratory characteristics of SBP in liver cirrhosis patients

To analyze the impact of ESBL and MDR on clinical and laboratory characteristics and outcome, we compared the clinical and laboratory information of the SBP cases according to the presence of ESBL and MDR status. Our results demonstrated that MDR status was significantly correlated with the ESBL production (P < 0.001) (Table 3). Furthermore, while basic patient and laboratory characteristics were not significantly
correlated with ESBL producing or MDR E. coli, patients suffering from SBP caused by MDR E. coli showed a significantly higher death rate than non-MDR infections ($P=0.021)$ (Table 3). Therefore, it appears that multidrug resistance had a significant impact on the clinical outcome of SBP in liver cirrhosis patients.

**Multivariate analysis for 30-day mortality**

Logistic regression analysis was performed to identify independent indicators for 30-day mortality in liver cirrhosis patients with nosocomial SBP. Our results demonstrated that mortality of the study population was independently correlated with female gender ($P=0.028$), liver failure ($P=0.006$), HCC ($P=0.029$), HE ($P=0.003$), high MELD score ($P=0.005$), low WBC ($P=0.019$), and high ascites polymorphonuclear ($P=0.007$) (Table 4).

**Discussion**

Nosocomial SBP is one of the commonly observed bacterial infections in hospitalized patients, posing a great threat to human life. Timely antibiotic treatment is an effective way to reduce the mortality of patients with SBP. However, therapeutic failures may occur. In order to improve the efficacy of empirical treatments, we investigated the microbiological characteristics and antibiotic sensitivity of E. coli isolates obtained from nosocomial SBP cases in liver cirrhosis patients.

In our study, 88% of the cases were diagnosed at Child-Pugh stage C, which is consistent with a previous study that reported 87% of the E. coli SBP cases at Child-Pugh stage C. ESBL-producing E. coli was isolated from 47% of the cultures, while the rate of MDR infections was 62% in our study. We investigated the clinical characteristics of SBP in liver cirrhosis patients, caused by ESBL-producing and MDR infections. Our analysis demonstrated that ESBL-producing and MDR infections were not associated with clinical symptoms of SBP, but MDR infections might result in higher mortality.

ESBL-producing and MDR are two major reasons for treatment failure in E. coli SBP. In our study, we found that ESBL-producing and MDR E. coli showed significantly higher resistance to cephalosporins, penicillins, quinolones, tobramycin, and SMZCO. Importantly, over 40% of the isolated pathogens showed resistance to third-generation cephalosporins, which is similar to a previous study that reported a resistance rate to the third-generation cephalosporins of 48% in E. coli isolated from SBP specimens. Chon et al. indicated that antibiotic switching and mortality were higher in patients with nosocomial SBP during hospitalization, thereby revealing high therapeutic failure of third-generation cephalosporin. Therefore, third-generation cephalosporins might be inappropriate for empiric treatment of
nosocomial SBP. The isolated pathogens in our study showed high sensitivity to carbapenems, β-lactamase inhibitors, and aminoglycoside antibiotics. Carbapenems, such as imipenem and meropenem, are effective antibiotics for liver cirrhosis patients presenting infections, particularly for those cephalosporin-resistant cases. However, wide application of carbapenems may stimulate the bacteria develop carbapenemase-producing ability, leading to poor therapeutic efficacy based on the current antibiotics. Moreover, due to the abuse of broad-spectrum antibiotics in clinics and transfection of antibiotic resistance genes, the prevalence of PDR appears to be increasing. PDR infections pose a great challenge to the current antibiotic management. Therefore, it is urgent to explore new antibiotics for PDR infections. In addition, rapid pathogen identification and targeted therapy may decrease the occurrence of PDR infections.

In the current study, we also analyzed the risk factors for mortality among the study population. Multivariate analysis revealed that the onset temperature (°C), leukocyte count; UGB: upper gastrointestinal bleeding; WBC: white blood cell count.

Table 3

Comparison of clinical and laboratory data of the study subjects according to their microbiological examinations

| Parameters               | ESBL-producing E. coli (n = 99) | ESBL-negative E. coli (n = 112) | P     | MDR E. coli (n = 130) | Non-MDR E. coli (n = 81) | P     |
|-------------------------|---------------------------------|---------------------------------|-------|-----------------------|--------------------------|-------|
| Demographic data        |                                 |                                 |       |                       |                          |       |
| Age (years)             | 49.93 ± 12.18                   | 51.13 ± 12.07                   | 0.484 | 50.47 ± 12.30         | 50.73 ± 12.75            | 0.883 |
| Gender                  |                                 |                                 | 0.339 |                       |                          |       |
| Males                   | 80 (80.81)                      | 96 (85.71)                      |       | 108 (83.08)           | 68 (83.95)               | 0.868 |
| Females                 | 19 (19.19)                      | 16 (14.29)                      |       | 22 (16.92)            | 13 (16.05)               |       |
| Clinical characteristics |                                 |                                 | 0.906 |                       |                          | 0.988 |
| Hepatitis B virus        | 5 (5.05)                        | 9 (8.04)                        |       | 9 (6.92)              | 5 (6.17)                 |       |
| Autimmune               | 63 (63.64)                      | 72 (64.29)                      | 0.684 | 82 (63.08)            | 53 (65.43)               |       |
| Alcohol                 | 5 (5.05)                        | 5 (4.46)                        |       | 6 (4.61)              | 4 (4.94)                 |       |
| OTHERS                   | 16 (16.16)                      | 15 (13.39)                      |       | 19 (14.61)            | 12 (14.81)               |       |
| Child-Pugh stage        |                                 |                                 | 0.933 |                       |                          |       |
| B                       | 12 (12.12)                      | 14 (12.50)                      |       | 15 (11.54)            | 11 (13.58)               | 0.661 |
| C                       | 87 (87.81)                      | 88 (87.50)                      |       | 115 (88.46)           | 70 (86.42)               |       |
| MELD                    | 20.82 ± 8.64                    | 20.63 ± 7.97                    | 0.872 | 20.04 ± 7.80          | 21.15 ± 8.56             | 0.345 |
| onsets temperature (°C) | 38.83 ± 0.85                    | 38.76 ± 0.88                    | 0.570 | 38.89 ± 0.84          | 38.72 ± 0.88             | 0.192 |
| Complications           |                                 |                                 |       |                       |                          |       |
| Liver failure           | 46 (46.46)                      | 53 (47.32)                      | 0.901 | 61 (46.92)            | 38 (46.91)               | 0.999 |
| HCC                     | 18 (18.18)                      | 18 (16.07)                      | 0.684 | 26 (20.00)            | 10 (12.35)               | 0.151 |
| HE                      | 32 (32.52)                      | 27 (24.11)                      | 0.184 | 41 (31.54)            | 19 (22.22)               | 0.143 |
| Diabetes mellitus       | 9 (9.09)                        | 9 (8.04)                        | 0.784 | 11 (8.46)             | 7 (8.64)                 | 0.964 |
| Renal dysregulation     | 24 (24.24)                      | 30 (26.79)                      | 0.673 | 36 (27.69)            | 18 (22.22)               | 0.376 |
| Pneumonia               | 5 (5.05)                        | 5 (4.46)                        | 0.841 | 8 (6.15)              | 2 (2.47)                 | 0.221 |
| UGB                     | 10 (10.10)                      | 10 (8.93)                       | 0.772 | 14 (10.77)            | 6 (7.41)                 | 0.417 |
| Hematological factors   |                                 |                                 |       |                       |                          |       |
| WBC (×10^9/L)           | 7.31 ± 4.66                     | 6.62 ± 4.18                     | 0.284 | 7.27 ± 4.90           | 6.43 ± 3.49              | 0.207 |
| Neutrophil (100%)       | 0.81 ± 0.008                    | 0.79 ± 0.006                    | 0.322 | 0.81 ± 0.009          | 0.79 ± 0.009             | 0.221 |
| Asceres examinations    |                                 |                                 |       |                       |                          |       |
| Leukocyte (×10^9/m^3)   | 5971.96 ± 7961.63               | 6572.88 ± 1523.17               | 0.729 | 7207.60 ± 14955.53    | 4819.74 ± 6092.91        | 0.179 |
| Polymorphonuclear (100%)| 0.70 ± 0.25                     | 0.65 ± 0.27                     | 0.114 | 0.70 ± 0.25           | 0.63 ± 0.27              | 0.074 |
| PMN (×10^9/m^3)         | 5057.76 ± 7513.6                 | 5547.05 ± 1964.92               | 0.754 | 6177.57 ± 13351.69    | 3937.07 ± 5888.20        | 0.160 |
| PMN stage              | 0.850                           |                                 |       |                       |                          | 0.621 |
| ≥250/mm^3              | 71 (71.71)                      | 79 (70.54)                      | 0.94  | 72 (72.37)            | 56 (69.14)               |       |
| <250/mm^3              | 28 (28.29)                      | 32 (29.46)                      | 0.36  | 27 (27.69)            | 25 (30.86)               |       |
| Microbiological examinations |                            |                                 |       |                       |                          |       |
| ESBL                    |                                 |                                 |       |                       |                          |       |
| ESBL-producing E. coli  | –                               | –                               |       | 98 (75.38)            | 1 (1.23)                 | <0.001|
| ESBL-negative E. coli   | –                               | –                               |       | 32 (24.62)            | 80 (98.76)               |       |
| MDR                     | <0.001                          | –                               |       | –                     | –                        |       |
| MDR-E. coli             | 98 (98.99)                      | 32 (28.57)                      |       | –                     | –                        |       |
| MDR-negative E. coli    | 1 (0.1)                         | 80 (71.43)                      |       | –                     | –                        |       |
| Clinical outcomes      |                                 |                                 |       |                       |                          |       |
| Survival status        | 0.139                           |                                 |       |                       |                          | 0.021 |
| Non-survivors           | 32 (32.32)                      | 26 (23.21)                      | 0.43  | 33 (30.88)            | 15 (18.52)               |       |
| Survivors               | 67 (67.68)                      | 86 (76.79)                      | 0.87  | 86 (66.93)            | 66 (81.48)               |       |

HCC: hepatocellular carcinoma; ESBL: extended-spectrum β-lactamase; HE: hepatic encephalopathy; MDR: multidrug-resistant; MELD: model for end-stage liver diseases; PMN: polymorphonuclear leukocyte count; UGB: upper gastrointestinal bleeding; WBC: white blood cell count.
indicated that female gender, presentation of liver failure, HCC and HE, high MELD score, WBC, and polymorphonuclear were independent risk factors for mortality in liver cirrhosis patients suffering from *E. coli* SBP. The effects of gender on mechanisms of liver cirrhosis have rarely been reported. Tommaso et al. reported that the interaction between hepatitis virus infection and alcohol might contribute to greater liver damage in females than that in males. Their study might explain the results obtained in our study. Besides, the presentation of liver failure, HCC and HE, as well as high MELD score contributed to high mortality in nosocomial SBP. These results might reveal that not only the disease itself, but also the related complications could influence the clinical outcomes in SBP patients. In addition, we also found that polymorphonuclear in ascitic fluid was independently associated with mortality of SBP. In our SBP cases, the function of neutrophils in ascites was severely impaired, which might explain their high susceptibility to infections and high levels of polymorphonuclear. Polymorphonuclear in ascitic fluid might be an effective biomarker for disease progression and clinical outcomes in SBP patients.

Our study has several limitations. Firstly, the study was retrospective in design and the sample size was relatively small, which reduces its statistical power. Secondly, the analysis results might be affected by the ascitic fluid culturing technique. Therefore, further well-designed prospective studies with extended sample size are required to improve our analysis.

### Conclusions

Due to the widespread nature of ESBL-producing and MDR *E. coli*, β-lactamase inhibitors and carbapenem antibiotics may be appropriate alternatives for third-generation cephalosporins for empirical treatment of nosocomial SBP in liver cirrhosis patients. The mortality of nosocomial SBP appeared to be independently correlated with female gender, liver failure, HCC and HE, high MELD score, as well as WBC, and ascites polymorphonuclear. These results may be helpful for improvement of empirical treatment guidelines for nosocomial SBP caused by *E. coli*, and for improvement of therapeutic efficacy and clinical outcomes.

### Materials and methods

#### Study population and inclusion criteria

The present study was a multicenter retrospective study of *E. coli* SBP in liver cirrhosis patients at the Beijing 302 Hospital and Beijing You’an Hospital from January 2015 to December 2018. The patients came from several provinces and cities in China. The patients included in our study were recruited based on the following criteria: (1) adult population; (2) diagnosed with liver cirrhosis combined with nosocomial SBP; (3) aerobic and anaerobic cultures of bedside inoculation were both positive; (4) *E. coli* was the only pathogen isolated from their ascitic cultures; (5) patients had available medical records. In addition, all the participants were primarily diagnosed with SBP, and those with evidences for a secondary peritonitis were excluded from our observational study.

#### Diagnosis standards

Liver cirrhosis was defined according to clinical examinations, laboratory tests, and histological and imaging evidences, and the disease severity was evaluated by Child-Pugh stage and MELD scores. Diagnosis of SBP was made according to the criteria defined by the American Association for the Study of Liver Diseases and European Association for the Study of the Liver, as follows: (1) presence of the typical signs or symptoms: abdominal pain, fever, diarrhea, tenderness, and/or rebound pain; (2) positive ascitic fluid bacterial culture; (3) no signs for other infections. Nosocomial SBP was defined as an infection occurring later than 48 hours after hospital admission. Antibiotic susceptibility testing was performed by disk diffusion method, and the results were analyzed based on the Clinical Laboratories Standards Institute criteria. *E. coli* ATCC 25922 was included in all tests as quality control. Isolated pathogens showing resistance to three or more antibiotics from different classes were confirmed as MDR. The clinical outcome was analyzed by the 30-day mortality.

#### Statistical analysis

The continuous variables were expressed as mean ± standard deviation, and compared between two groups using Student *t*-test (normal distribution) or the rank sum test (abnormal distribution). The categorical variables were recorded as case number and percentages, and their comparisons were performed by Chi-square test. The baseline characteristics of the study subjects were compared according to the presence of ESBL and MDR status. In addition, logistic regression was performed to identify the independent indicators of the study population for 30-day mortality. All analyses were performed using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). P values ≤ 0.05 were considered as statistically significant.

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**Table 4**

| Factors                | OR (95% CI) | P  |
|------------------------|-------------|----|
| Gender                 | 5.200 [1.194–22.642] | 0.028 |
| Age                    | 0.999 [0.954–1.045]  | 0.956 |
| Hepatitis B viral      | 1.677 [0.094–29.796] | 0.725 |
| Autoimmune             | 6.333 [0.212–189.057] | 0.287 |
| Alcohol                | 1.194 [0.047–30.529]  | 0.915 |
| Others                 | 1.679 [0.086–32.758]  | 0.732 |
| Liver failure          | 9.699 [0.914–48.229]  | 0.066 |
| HCC                    | 12.644 [1.299–123.065] | 0.029 |
| HE                     | 8.176 [2.065–32.364]  | 0.003 |
| Diabetes mellitus      | 2.651 [0.164–42.932]  | 0.493 |
| Renal dysregulation    | 3.233 [0.838–12.476]  | 0.089 |
| Pneumonia              | 0.463 [0.059–3.625]   | 0.463 |
| UGB                    | 3.026 [0.553–16.559]  | 0.202 |
| Child-Pugh stage       | 0.121 [0.007–2.183]   | 0.152 |
| MELD                   | 1.191 [1.053–1.346]   | 0.005 |
| Onset temperature      | 0.670 [0.350–1.283]   | 0.227 |
| WBC                    | 0.847 [0.737–0.973]   | 0.019 |
| Neutrophil             | 54.467 [1.070–20891.047] | 0.207 |
| Leukocyte              | 0.999 [0.999–1.000]   | 0.166 |
| Polymorphonuclear      | 95.903 [3.410–2697.356] | 0.007 |
| PMN                    | 1.001 [1.000–1.001]   | 0.262 |
| ESBL                   | 1.070 [0.238–4.803]   | 0.930 |
| MDR                    | 1.664 [0.345–8.024]   | 0.526 |

HCC: hepatocellular carcinoma; ESBL: extended-spectrum β-lactamase; HE: hepatic encephalopathy; MDR: multidrug-resistant; MELD: model for end-stage liver diseases; PMN: ascites polymorphonuclear leukocyte count; UGB: upper gastrointestinal bleeding; WBC: white blood cell count.
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