

ORIGINAL ARTICLE

## PREVALENCE OF BACTERIAL RESISTANCE IN HOSPITALIZED CIRRHOTIC PATIENTS IN SOUTHERN BRAZIL: A NEW CHALLENGE

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### SUMMARY

**Background & Aims:** An increased frequency of infections by multiresistant bacteria has been described in hospitalized patients. The aim of this study was to evaluate the bacterial resistance profile in cirrhotic patients. **Methods:** This is a retrospective observational study. We assessed the antimicrobial susceptibility of 5,839 bacterial isolates from patients with and without cirrhosis. Regarding the multidrug resistance, we evaluated 4,505 bacterial isolates from 2,180 patients. **Results:** Two hundred and fifty-one patients had cirrhosis (mean age  $57.6 \pm 11$  years; 61.8% were male, 47.8% of cases associated with hepatitis C virus). Of the isolates of patients with and without cirrhosis, 174/464 (37.5%) and 1,783/4,041 (44.1%) were multiresistant, respectively ( $p = 0.007$ ). *E. coli* was the most common multiresistant bacteria in both groups. Approximately 20% of *E. coli* and *Klebsiella* sp. isolates were ESBL-producers and 44% of *S. aureus* isolates were methicillin-resistant in cirrhotic patients. In cirrhotic patients admitted to the emergency department, hospital ward, and intensive care unit, 28.3%, 50% and 40% had multiresistant isolates, respectively. In patients with and without cirrhosis, 36.2% and 33.5% of isolates were resistant to third-generation cephalosporins, respectively. **Conclusions:** The empirical treatment of infections in hospitalized patients using broad-spectrum antibiotics should consider the observed pattern of bacterial resistance.

**KEYWORDS:** Hepatic cirrhosis; Bacterial infections; Multi-drug resistance.

### INTRODUCTION

Bacterial infections are a major clinical event in cirrhotic patients. Infections may be present on admission or appear throughout hospitalization in 25 to 35% of cirrhotic patients<sup>1,2</sup>, an incidence that is four to five times higher than in the general population and that has been increasing over the past few years<sup>3,4</sup>. Infections in cirrhotic patients are associated with a mortality rate of 38%, which represents a four-fold increase compared to individuals without cirrhosis or without any infection. Of the infected patients, 30% die within one month, and another 30% die within one year<sup>5</sup>. Currently, infections are considered the leading cause of death in patients with decompensated cirrhosis<sup>6</sup>.

Bacterial translocation is the main factor involved in the pathogenesis of infections in cirrhotic patients; bacterial overgrowth, increased intestinal permeability, and immune changes constitute the key factors related to its development. The severity of liver disease and the occurrence of upper gastrointestinal bleeding have an important role in the development of infections in this population. A different mechanism is probably involved in the pathogenesis of bacterial translocation in patients without chronic liver disease<sup>7-9</sup>.

The most common bacterial infections in cirrhotic patients are spontaneous bacterial peritonitis (SBP) and urinary tract infection (UTI), followed by respiratory infection (RI), skin and soft tissue infection, and bloodstream infection (bacteremia)<sup>3,10</sup>. In our setting, 541 hospital admissions of 426 patients with cirrhosis were evaluated, and 135 episodes of bacterial infections were identified, most frequently being the ICU (31.1%), SBP (25.9%), and RI (25.2%)<sup>11</sup>. Gram-negative aerobic bacteria were the most commonly found pathogens in SBP and ICU, while gram-positive bacteria were predominantly found in RI and in procedure-related bloodstream infections (bacteremia episodes)<sup>1,12,13</sup>. There was association between the presence of infection and the alcoholic etiology of liver disease, as well as between the Child-Pugh classification and the occurrence of upper gastrointestinal bleeding. In-hospital mortality was significantly higher in infected patients and was associated with the degree of hepatocellular dysfunction<sup>11</sup>.

Enterobacteria and non-enterococcal streptococci were the causative agents of most spontaneous bacterial infections in cirrhotic patients. Third-generation cephalosporins used to be first choice antimicrobial treatment for SBP and many other infections in cirrhotic patients, as they are active against these bacteria and are also well tolerated<sup>14,15</sup>. However,

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important changes in the epidemiology of bacterial infections in cirrhotic patients have occurred in the last decade, possibly associated to the use of prophylactic antibiotic treatment and the increment of invasive procedures in these patients<sup>16</sup>. Higher frequencies of spontaneous and secondary infections caused by multiresistant pathogens have been reported in several countries, especially in nosocomial episodes, associated to treatment failure, septic shock and hospital mortality<sup>1,10,17-31</sup>.

Given the poor prognosis of patients with both cirrhosis and infection, especially when inappropriated empiric antibiotic treatment is started, along with the evidence of a new bacterial resistance profile in these patients in several hospitals from Europe<sup>1,18,19,21,22,27,28</sup>, Asia<sup>17,20,23,25,29-31</sup>, and the USA<sup>10</sup>, the assessment of the microbiological profile in a tertiary referral hospital in Latin America is relevant.

The aim of this study was to assess the resistance profile of bacteria isolated from cirrhotic patients admitted to a referral hospital in Southern Brazil.

## MATERIAL AND METHODS

This is a retrospective observational study. All clinical samples that presented bacterial growth in cultures from patients hospitalized in the emergency department, intensive care unit (ICU) and internal medicine ward at the Hospital of Santa Clara, Irmandade Santa Casa de Misericórdia de Porto Alegre were selected, in the period between January the 1<sup>st</sup>, 2009 and December the 31, 2011. Therefore 6,548 bacterial isolates from 2,780 patients were selected. Of these, 72 bacterial isolates from 40 patients were excluded from the study due to insufficient data in medical records. Additionally, 637 bacterial isolates from 88 patients were excluded from the analysis because the bacterial isolates were recovered from biological materials of lower clinical and/or epidemiological interest (skin or wound secretions, oropharynx and nasopharynx secretions, stool samples, genital secretions and other tissues). Thus, we included in the analysis 5,839 bacterial isolates from 2,652 patients, recovered from biological materials of greater clinical and epidemiological relevance: blood samples, respiratory secretions (sputum, tracheal aspirate, bronchial lavage and bronchoalveolar lavage), urine samples, ascites and other intra-abdominal fluids or abscesses.

For the evaluation of bacterial multiresistance, coagulase-negative *Staphylococcus* sp. was excluded because it is often a contaminant<sup>10,20</sup>. Consequently, 4,505 bacterial isolates from 2,180 patients were analyzed.

Patients with and without cirrhosis diagnosis were identified through a chart review. The diagnosis of cirrhosis was established according to clinical, laboratory and ultrasonographic features of patients and/or through liver biopsy.

The microorganisms' susceptibility to antimicrobials was assessed through the disk diffusion method in accordance with the Clinical and Laboratory Standards Institute's (CLSI) criteria<sup>32</sup>. In cases of methicillin-resistant *S. aureus* (MRSA) identification, complementary tests such as the E-test was performed to establish the susceptibility to vancomycin. The following bacteria were considered multiresistant: MRSA, *E. faecium* and *E. faecalis* resistant to vancomycin (VRE), extended-spectrum beta-lactamases (ESBL) producing *E. coli* and *Klebsiella* sp., and all bacteria resistant to at least three of the main antibiotic classes<sup>33</sup>.

The antimicrobial susceptibility profile of isolated bacteria was evaluated, in addition to the occurrence of multiresistance. We also assessed the patients' age and gender; cirrhosis diagnosis; etiology of cirrhosis, date of diagnosis; type of biological material (blood, respiratory secretions, urine, ascites, and other intra-abdominal fluid collections); and place of hospitalization at the time the clinical sample was collected (emergency department, hospital ward, ICU).

The number of days between the date of admission and the date of sample collection was divided into categories (0-2 days, 3-7 days, 8-15 days, 16-30 days and  $\geq 31$  days). The trend test was used to determine the increment or decrement of multiresistant bacteria episodes according to the time interval between the date of admission and the date of biological material collection, in both groups.

Regarding the analysis of bacterial resistance in different biological materials, the following bacteria were considered the main multiresistant ones: ESBL-producing *E. coli* and *Klebsiella* sp., MRSA, VRE, *Acinetobacter* sp., *P. aeruginosa*, *A. xylosoxidans*, *B. cepacia* and *S. maltophilia*.

Quantitative variables were described as mean and standard deviation, and categorical variables were described by means of absolute and relative counts. Comparisons between patients with and without cirrhosis and between the bacterial isolates from these two groups were performed using the Student's t-test for quantitative variables, and the chi-square or Fisher's exact test for categorical variables. Differences were considered significant at the level of 0.05. All data were processed and analyzed using the Statistical Package for the Social Sciences (SPSS) 18.0.

This study was approved by the ethics committee of the hospital Irmandade Santa Casa de Misericórdia de Porto Alegre (protocol number 90.420).

## RESULTS

### Bacterial isolates and patient characteristics

The antimicrobial susceptibility profile of 5,839 bacterial isolates from 2,652 patients was analyzed.

The mean age of patients was  $59.4 \pm 16.8$  years. Approximately half of the patients (49.9%) were male.

Of the 2,652 patients, 251 (9.5%) presented a diagnosis of cirrhosis. The mean age of patients with cirrhosis was  $57.6 \pm 11$  years, and the mean age of patients without cirrhosis was  $59.6 \pm 17.3$  years ( $p = 0.01$ ). The majority of cirrhotic patients (61.8%) were males, while less than half of the patients without cirrhosis (48.7%) were male ( $p < 0.001$ ).

Among patients with cirrhosis, the most frequent cause of liver disease was infection by hepatitis C virus (HCV, 47.8%), followed by alcohol (21.1%) and HCV-alcohol combination (11.1%).

Five hundred and seventy-six bacterial isolates from 251 patients with cirrhosis were identified. Approximately half of the bacterial isolates (50.9%) were gram-negative, the most frequent bacteria being *E. coli* (26.6%) and coagulase-negative *Staphylococcus* sp. (19.4%).

Five thousand, two hundred and thirty-six bacterial isolates from patients without cirrhosis were identified. More than half of the isolates (58.4%) were gram-negative, the most frequent bacteria being coagulase-negative *Staphylococcus* sp. (23.2%) and *E. coli* (18.8%).

**Bacterial resistance in clinical samples of patients with and without cirrhosis**

To evaluate the bacterial multiresistance, coagulase-negative *Staphylococcus* sp. isolates were excluded, corresponding to 112 excluded isolates in cirrhotic patients and 1,222 isolates in patients without cirrhosis.

Among cirrhotic patients, of the 464 bacterial isolates analyzed according to antibiotic resistance, 174 (37.5%) were multiresistant.

Among patients without cirrhosis, of the 4,041 bacterial isolates, 1,783 (44.1%) were multiresistant ( $p = 0.007$ ).

The frequency of multiresistant bacteria, evaluated according to genus and species, in the clinical samples of patients with and without cirrhosis is shown in Table 1.

Among 206 isolates of *E. coli* and *Klebsiella* sp. in cirrhotic patients, 98 (47.6%) were resistant to three or more antibiotics. Of these, 42 (42.8%) were ESBL producers. Among the 1,481 isolates of *E. coli* and *Klebsiella* sp. in patients without cirrhosis, 775 (52.3%) were resistant to three or more antimicrobials. Of these, 286 (36.9%) were ESBL producers.

Among 61 isolates of *S. aureus* in cirrhotic patients, 29 (47.5%) were resistant to three or more antimicrobials. Of these, 27 (93.1%)

**Table 1**  
Frequency of isolated multiresistant bacteria in clinical samples from patients with and without cirrhosis

Bacteria	With cirrhosis		Without cirrhosis	
	Total n	MR n (%)	Total n	MR n (%)
<b>Gram-positive †</b>				
<i>S. aureus</i>	61	29 (16.7)	469	211 (11.8)
<i>Enterococcus</i> sp.	43	1 (0.6)	169	5 (0.4)
<i>S. viridans</i>	18	1 (0.6)	50	1 (<0.1)
Other Gram-positive bacteria	31	0	165	0
<i>E. faecium</i>	10	7 (4.0)	56	46 (2.6)
<i>E. faecalis</i>	8	0	59	3 (0.2)
<b>Gram-negative</b>				
<b>Enterobacteria</b>				
<i>E. coli</i>	153	70 (40.2)	992	553 (31.0)
<i>K. pneumoniae</i>	53	28 (16.1)	434	201 (11.3)
<i>Enterobacter</i> sp.	22	9 (5.2)	266	119 (6.7)
Other enterobacteria	9	0	99	22 (1.2)
<i>Proteus</i> sp.	8	3 (1.7)	143	26 (1.4)
<i>Serratia</i> sp.	4	1 (0.6)	128	18 (1.0)
<i>K. oxytoca</i>	0	0	52	21 (1.2)
<b>Nonfermenting Gram-negative Bacilli</b>				
<i>P. aeruginosa</i>	12	7 (4.0)	482	219 (12.3)
<i>Acinetobacter</i> sp.	12	10 (5.7)	253	238 (13.3)
Other Nonfermenting Gram-negative Bacilli	11	1 (0.6)	115	52 (2.9)
<i>S. maltophilia</i>	4	4 (2.3)	44	44 (2.5)
<i>A. xylooxidans</i>	3	3 (1.7)	4	4 (0.2)
Other Gram-negative Bacteria	2	0	61	0
<b>Total of evaluated bacteria</b>	<b>464</b>	<b>174 (100)</b>	<b>4,041</b>	<b>1,783 (100)</b>

Data are presented as the number of samples obtained by direct counting (percentage). MR: multiresistant. † Coagulase-negative *Staphylococcus* sp. isolates were excluded.

were resistant to methicillin. Among 469 isolates of *S. aureus* in patients without cirrhosis, 211 (45%) were resistant to three or more antimicrobials. Of these, 201 (95.3%) were resistant to methicillin.

The frequency of the main multiresistant bacteria according to the type of biological material in patients with and without cirrhosis are shown in Table 2 and Table 3, respectively.

No statistically significant differences were found when the proportions of the main multiresistant bacteria in different biological materials were compared in patients with and without cirrhosis.

**Bacterial resistance according to number of days between admission and sample collection**

An increment in the incidence of multidrug-resistant bacteria according to number of days between admission and sample collection was found in patients with ( $p < 0.001$ ) and without cirrhosis ( $p < 0.001$ ).

In clinical samples collected within the first two days of hospitalization, 27.2% and 34.3% of isolates from patients with and without cirrhosis were multiresistant, respectively. In clinical samples collected after 31 days of hospitalization, 64.4% and 61.5% of isolates from patients with and without cirrhosis were multiresistant, respectively.

**Bacterial resistance in emergency department, hospital ward, and ICU**

In cirrhotic patients, 28.3%, 50%, and 40% of isolates were multiresistant in the emergency department, hospital ward, and ICU, respectively. In patients without cirrhosis, 35.4%, 47.8% and 52.4% of isolates were multiresistant, respectively.

**Resistance to third-generation cephalosporins**

Of the 464 analyzed isolates from cirrhotic patients, 168 (36.2%) were resistant to third-generation cephalosporins. Of the 4,041 isolates

**Table 2**  
Main multiresistant bacteria isolated in clinical samples from cirrhotic patients according to the type of biological sample

Bacteria	Blood	Respiratory secretions	Urine	Ascitic fluid	Other abdominal collections
Total multiresistant bacteria	64/166	15/52	69/188	25/51	1/7
ESBL-producing <i>E. coli</i> and <i>Klebsiella</i> sp.	11/55	0/9	25/119	6/20	0/3
Methicillin-resistant <i>S. aureus</i>	14/36	4/10	3/6	6/9	-/-
Vancomycin-resistant <i>E. faecium</i>	5/8	-/-	1/1	1/1	-/-
Vancomycin-resistant <i>E. faecalis</i>	0/5	-/-	-/-	0/1	0/2
Multiresistant <i>Acinetobacter</i> sp.	4/6	4/4	1/1	1/1	-/-
Multiresistant <i>P. aeruginosa</i>	3/3	3/6	-/-	1/3	-/-
<i>S. maltophilia</i>	4/4	-/-	-/-	-/-	-/-
<i>A. xylosoxidans</i>	1/1	-/-	-/-	2/2	-/-
<i>B. cepacia</i>	-/-	-/-	-/-	-/-	-/-

Data are presented as the number of resistant isolates by the total number of isolates. *ESBL*: extended spectrum beta-lactamases.

**Table 3**  
Main multiresistant bacteria isolated in clinical samples from patients without cirrhosis according to the type of biological material

Bacteria	Blood	Respiratory secretions	Urine	Ascitic fluid	Other abdominal collections
Total multiresistant bacteria	344/977	580/1,281	785/1,576	6/10	68/197
ESBL-producing <i>E. coli</i> and <i>Klebsiella</i> sp.	38/286	48/210	191/894	-/-	9/91
Methicillin-resistant <i>S. aureus</i>	76/218	106/214	12/28	1/1	6/8
Vancomycin-resistant <i>E. faecium</i>	15/20	-/-	19/19	0/3	12/14
Vancomycin-resistant <i>E. faecalis</i>	2/43	-/-	1/1	-/-	0/15
Multiresistant <i>Acinetobacter</i> sp.	52/58	150/157	33/35	-/-	3/3
Multiresistant <i>P. aeruginosa</i>	21/54	124/283	73/129	-/-	1/16
<i>S. maltophilia</i>	2/2	30/30	8/8	3/3	1/1
<i>A. xylosoxidans</i>	-/-	4/4	-/-	-/-	-/-
<i>B. cepacia</i>	5/5	7/7	1/1	-/-	-/-

Data are presented as the number of resistant isolates by the total number of isolates. *ESBL*: extended spectrum beta-lactamases.

from patients without cirrhosis, 1,355 (33.5%) were resistant to these antibiotics ( $p = 0.26$ ).

In cirrhotic patients, of the 166 bacterial isolates from blood cultures, 59 (35.5%) were resistant to third-generation cephalosporins. Of the 52 bacterial isolates from respiratory secretions, 13 (25%) were resistant to these antibiotics. In urine, 75 out of 188 (39.9%) isolates were resistant. In ascitic fluid samples, 19 out of 51 (37.3%) isolates were resistant. In other intra-abdominal fluid samples or abscesses (secondary bacterial peritonitis), two out of seven (28.6%) isolates were resistant.

When comparing the proportions of bacteria that are resistant to third-generation cephalosporins in different biological materials of patients with and without cirrhosis, no statistically significant differences were found.

In cirrhotic patients, 24.9%, 50% and 42.7% of bacterial isolates from the emergency department, hospital ward and ICU were resistant to third-generation cephalosporins, respectively. In patients without cirrhosis, 21.5%, 41.8% and 43.2% were resistant to these antibiotics.

## DISCUSSION

In face of an increased occurrence of multiresistant bacteria in infections of cirrhotic patients, we evaluated the profile of bacterial resistance in clinical samples from patients admitted to a tertiary hospital in Southern Brazil. To the best of our knowledge, this is the first study published in Latin America in this setting.

We evaluated the microbiological profile of isolated bacteria from cirrhotic patients, mostly with associated HCV infection, similarly to other studies<sup>10,19</sup>. Half of these bacteria were gram-negative. In these patients, among the gram-negative bacteria, the most common one was *E. coli*, while among gram-positive bacteria the most frequent one was coagulase-negative *Staphylococcus* sp. These results are in agreement with the current literature<sup>1,19,30</sup>.

High levels of multiresistance were found among cirrhotic patients, as well as among other patients, suggesting that the current high prevalence of these bacteria is mainly related to an epidemiological change in hospital infections, which is often not dependent on the patient's underlying disease. Multiresistant bacteria accounted for 31% of the isolated microorganisms in infections of cirrhotic patients in a Spanish study<sup>1</sup>. In other studies carried out in Asia<sup>30</sup> and the USA<sup>10</sup>, nearly half of the infections in cirrhotic patients were caused by bacteria resistant to antibiotics. Nosocomial infections, long-term prophylaxis with norfloxacin, infection by multiresistant bacteria in the past six months, and use of beta-lactam antibiotics in the last three months were identified as risk factors for the occurrence of infections by multiresistant bacteria in cirrhotic patients<sup>1</sup>.

In this study, *E. coli* was the most common multiresistant bacteria in cirrhotic, followed by *S. aureus*, *K. pneumoniae*, and *Acinetobacter* sp. Additionally, *P. aeruginosa* was also one of the most frequent multiresistant bacteria, especially in patients without cirrhosis. In a Spanish study<sup>1</sup>, ESBL-producing enterobacteria were the main multiresistant microorganisms, followed by *P. aeruginosa*, MRSA, and *E. faecium*.

We found a high prevalence of ESBL-producing *E. coli* and *Klebsiella* sp. and of MRSA in cirrhotic patients. The possibility that these pathogens might be involved in infections in these patients in our medical center should be considered during the evaluation of the empirical therapy to be prescribed, especially in hospital episodes.

In cirrhotic patients, 28.3%, 50%, and 40% of isolates from the emergency department, hospital ward, and ICU were multiresistant, respectively. Additionally, more than one third of isolates recovered during the first two days of hospitalization in patients with and without cirrhosis was multiresistant. It is worth noting that the occurrence of multiresistant bacteria is significant, even among patients admitted to the emergency department. It is possible that the majority of infections diagnosed in this setting could be classified as HCA and nosocomial infections, but for the moment, we cannot confirm this information.

As third-generation cephalosporins were the first choice empirical antibiotics against SBP and other infections<sup>14,15</sup>, the bacterial resistance to these antibiotics was evaluated and 36.2% of isolates from cirrhotic patients were resistant. Among isolates recovered from ascitic fluid samples, 37% were resistant. Bacteria resistant to third-generation cephalosporins were identified in 21.5% to 57% of SBP cases in Europe<sup>21,27,28</sup>. The empirical therapy with these antimicrobials was efficient in only 67% of SBP cases in Europe<sup>1</sup> and in 62.8% of SBP cases in Asia<sup>31</sup>.

Due to the high frequency of multiresistant organisms and to the increased mortality when infections are identified in cirrhotic patients, changes in clinical practice have begun to take place around the world. In Spain, a new protocol for the empirical treatment of infections was implemented, consisting of the use of carbapenems combined or not with a glycopeptide in nosocomial infections, and also in infections associated to the systemic inflammatory response syndrome<sup>1</sup>. New and similar recommendations are also being made for the treatment of healthcare-associated infections (those diagnosed within the first 48 hours of hospitalization in a patient who has had a recent contact with the healthcare system<sup>34</sup>), due to the similarities between the microbiological profiles<sup>6</sup> in these two medical settings.

The Special Conference on Bacterial Infections held by the European Association for the Study of the Liver (EASL)<sup>3</sup> established new guidelines for the empirical treatment of infections in cirrhotic patients. In general, third-generation cephalosporins continue to be recommended as the empirical therapy for community-acquired infections; however, piperacillin-tazobactam or meropenem, associated or not to a glycopeptide, should be used in nosocomial infections. Healthcare-associated pneumonia taking place in ICU should be treated as nosocomial infections, whereas the treatment of healthcare-associated cellulitis and spontaneous infections should be based on the severity of the infection and on local pattern of bacterial resistance. The use of piperacillin-tazobactam in nosocomial infections should be restricted to areas of low prevalence of multiresistant bacteria, and carbapenems would be indicated when the coverage of ESBL-producing bacteria is necessary. Vancomycin and teicoplanin should be prescribed in areas with a high prevalence of MRSA and vancomycin-susceptible enterococci<sup>3</sup>, and replaced by linezolid or daptomycin in areas with a high prevalence of VRE<sup>35</sup>.

In the present study, it was not possible to analyze the clinical response to treatment. However, the knowledge of the local microbiological profile is fundamental for the prescription of the most effective antibiotics. This study has indicated a specific pattern of bacterial resistance in a Southern Brazilian medical center, but these data cannot be extrapolated to other hospitals, and this is in accordance with worldwide evidence of a high frequency of multiresistant bacteria in cirrhotic patients and also with the ineffectiveness of empirical therapy with third-generation cephalosporins for the treatment of infections in these patients, especially in nosocomial episodes. A recent study in our hospital setting has shown a hospital mortality of 40% in SBP cases<sup>36</sup>. Thus, we recommend the use of broad-spectrum antibiotics, such as carbapenems, associated or not to glycopeptides, not only in the initial treatment of nosocomial infections, but also in healthcare-associated infections whenever severity signs or risk factors for multiresistant bacteria are present. In the case of SBP, 48 hours after the beginning of treatment, a diagnostic paracentesis should be performed and a reduction of at least 25% in the number of polymorphonuclear cells should be observed<sup>3,14</sup>.

Early and effective antimicrobial treatment is essential in the management of cirrhotic patients with bacterial infections. The administration of an inappropriate therapy is associated to an increased mortality<sup>14</sup>. The choice of the empirical therapy should be based not only on the severity and the origin of the infection, but also on the local microbiological profile. Epidemiological patterns of bacterial resistance in Latin American hospitals should be evaluated, and broad-spectrum antibiotics should be used properly in order to minimize the impact of infections on the prognosis of cirrhotic patients<sup>3,6</sup>.

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