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ORIGINAL ARTICLE

Retrospective Cohort Study

Clinical impact of multidrug-resistant organisms in liver cirrhosis: A retrospective cohort study in the intensive care setting

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Abstract

BACKGROUND

Colonization with multidrug-resistant organisms (MDROs) is frequently observed in critically ill patients with liver cirrhosis admitted to intensive care units (ICUs). However, whether colonization directly leads to infections or adversely impacts clinical outcomes remains unclear. Clarifying this relationship may help determine the prognostic significance of colonization in these patients.

AIM

To evaluate the clinical relevance of MDRO colonization and infection at ICU admission in patients with cirrhosis.

METHODS

This retrospective single-center cohort study included 107 ICU admissions of patients with liver cirrhosis at a tertiary care center (2018-2024). Colonization was

assessed by rectal and nasal/pharyngeal swabs within 48 hours of ICU admission. Outcomes analyzed included MDRO infection during ICU stay, concordance between colonizing and infecting strains, organ support requirements, and 28-day transplant free survival. Multivariable logistic regression and Kaplan-Meier analyses were used to evaluate predictors of infection and mortality.

RESULTS

Nearly one-third (29.9%) of patients were colonized with MDROs on admission, more commonly in the acute-on-chronic liver failure phenotype than those with acute decompensation (34.5 *vs* 10.0%, P = 0.033). Although infections were established in the majority (85%) of cases, of which 17.6% due to MDROs, colonization alone did not independently predict these infections [odds ratio (OR) = 2.18, P = 0.383] nor influenced short-term mortality (OR = 1.14, P = 0.813). However, once MDRO infection occurred, an 82% concordance was observed between colonizing and infecting strains. MDRO infections, unlike colonization, significantly increased the need for organ-support interventions, including mechanical ventilation and vasopressor therapy and prolonged ICU stays. Only severity of organ dysfunction, quantified by the Sequential Organ Failure Assessment score, independently predicted 28-day mortality (OR = 1.38, P = 0.024).

CONCLUSION

MDRO colonization at ICU admission is frequent among critically ill patients with cirrhosis, particularly those with acute-on-chronic liver failure. While colonization alone does not predict infection or early mortality, its clinical value emerges in guiding empirical antibiotic treatment once infection is suspected. Ultimately, short-term survival appears to be more strongly influenced by the severity of organ failure than by either MDRO colonization or infection.

Key Words: Liver cirrhosis; Acute-on-chronic liver failure; Critical care; Multidrug-resistant organisms; Colonization; Infection

Core Tip: This retrospective intensive care unit cohort study evaluated the impact of multidrug-resistant colonization in patients with liver cirrhosis. While colonization was common, especially in those with acute-on-chronic liver failure, it was not independently linked to infection or short-term mortality. However, high concordance between colonizing and infecting strains supports its role in guiding empirical antibiotic therapy once infection is suspected. These findings highlight the importance of early screening, local resistance data, and tailored empirical treatment to improve outcomes of critically ill patients with cirrhosis.

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INTRODUCTION

Bacterial infections are a frequent and serious complication in patients with cirrhosis, often triggering clinical deterioration and progression to organ failure[1-3]. These infections remain the predominant trigger of acute decompensation (AD) and acute-on-chronic liver failure (ACLF), particularly among patients admitted to intensive care units (ICU)[1,2,4]. Prompt recognition and antibiotic administration are critical, as even short delays can worsen clinical outcomes and increase mortality risk[5,6]. However, the rising prevalence of multidrug-resistant organisms (MDROs) significantly complicates effective empirical therapy and poses substantial clinical challenges in these critically ill patients[1,4,7-9]. Recent global studies report an increasing burden of MDRO infections in patients with cirrhosis, with an overall prevalence around 34% among hospitalized individuals and similar or slightly higher rates (23%-47%) in ICU settings[1,10]. Over the last two decades, there has been a notable shift toward more healthcare-associated infections, driven by recurrent hospitalizations and antibiotic exposure, along with evolving pathogen profiles characterized by increased detection of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), particularly in Western countries[1,10,11]. The rising prevalence and changing epidemiology pose substantial challenges to ICU management and liver transplantation, including increased risk of treatment failure, organ dysfunction, transplant delisting, graft loss, and mortality[1,3,10-13].

Colonization with MDROs, particularly at rectal and nasal sites, is prevalent among critically ill patients with cirrhosis, with reported rates between 32% and 47%[14,15]. Colonization strongly predicts subsequent infection, with studies consistently reporting a concordance of 76%-82% between colonizing and infecting strains[14,16,17]. Risk factors include

prior antibiotic exposure, overuse of prophylactic antibiotics, and repeated healthcare contact[18-20]. Beyond traditional risk factors, cirrhosis-associated immune dysfunction may could facilitate MDRO colonization and infection. Cirrhosis-associated immune dysfunction involves systemic inflammation alongside impaired innate and adaptive immunity, worsened by gut dysbiosis, increased intestinal permeability, and defective phagocytic function, all promoting bacterial translocation and colonization[6,20-23]. Additionally, patients with ACLF display immune profiles similar to those seen in sepsis, including decreased monocyte human leukocyte antigen-D related expression and impaired tumor necrosis factor-α production, consistent with a state of immune paralysis[24].

Notably, the prevalence and spectrum of colonizing organisms vary substantially across regions[25]. While oxacillinase (OXA)-48-producing *Klebsiella pneumoniae* (*K. pneumoniae*) and *Acinetobacter baumannii (A. baumanii)* predominate in some centers, others report higher rates of vancomycin-resistant enterococci or extended-spectrum beta-lactamases (ESBL)-producing *Escherichia coli* (*E. coli*)[6,15,26]. These epidemiological variations emphasize the need for robust local microbiological surveillance to guide empiric therapy and infection control. MDRO infections are associated with poorer outcomes, including increased organ support organ support needs and higher short-term mortality[1,15,16]. These adverse outcomes likely result from delayed initiation of effective antimicrobial therapy, more severe baseline disease, and greater risk of septic complications[1,15,16]. Despite this, standardized approaches to screening and managing MDRO colonization in cirrhosis remain inconsistent and debated[1,27].

Given the existing controversy about the prognostic implications of MDRO colonization in critically ill patients with cirrhosis, this study aims to clarify whether colonization at ICU admission independently predicts subsequent MDRO infection or influences short-term survival[15,16,28]. By contributing region-specific data from Southeastern Europe, a region underrepresented in prior research, we intend to address a critical gap regarding local MDRO epidemiology and clinical outcomes. We hypothesized that MDRO colonization upon ICU admission is associated with higher rates of subsequent infection and adverse clinical outcomes. Our primary objective was: To determine whether colonizing MDRO strains identified at ICU admission were concordant with subsequent infecting pathogens. Our secondary objectives were: (1) To describe the local epidemiology of MDRO colonization and infection in critically ill cirrhotic patients within our ICU setting; (2) To compare colonization and infection patterns between patients presenting with AD and ACLF phenotypes; and (3) To evaluate the clinical impact of MDRO colonization and infection, specifically regarding short-term mortality and organ support requirements. Integrating colonization data into clinical decision-making may help refine risk stratification, support appropriate empiric antibiotic selection, and enable earlier intervention in this high-risk population[14,29].

MATERIALS AND METHODS

Study design and setting

This single-center, retrospective cohort study was conducted at the University Hospital Centre Zagreb, Croatia. The study included critically ill patients with liver cirrhosis admitted to the medical ICU between January 1, 2018 and December 31, 2024.

Study population

Eligible participants (Figure 1) were adults with established liver cirrhosis who had an ICU stay of at least 48 hours due to liver-related complications. Exclusion criteria included prior solid organ transplantation/cirrhosis of the liver graft, advanced hepatocellular carcinoma (beyond Milan criteria), or ICU admission unrelated to liver disease (*e.g.*, myocardial infarction). For patients with multiple ICU admissions, only admissions separated by more than two months were included as distinct events.

Data collection

Data were extracted from the electronic medical records and included demographic variables, liver disease aetiology, and comorbidities (diabetes, cardiovascular, respiratory, renal diseases). Pre-admission variables included prior hospitalization, antibiotic exposure, and medication use (*e.g.*, norfloxacin prophylaxis, non-selective beta-blockers, proton pump inhibitors). Clinical and laboratory data at ICU admission included vital signs, need for organ support (mechanical ventilation, vasopressors, renal replacement therapy), and laboratory parameters [white blood cell count (WBC), platelets, bilirubin, creatinine, sodium, albumin, international normalized ratio, liver enzymes, C-reactive protein, procalcitonin]. Disease severity was assessed using Model for End-Stage Liver Disease (MELD), MELD-Na, Sequential Organ Failure Assessment (SOFA), chronic liver failure (CLIF)-organ failure, and CLIF-ACLF/CLIF-AD, as appropriate.

Microbiological and outcome data

Routine surveillance for MDRO colonization was preformed *via* nasal/pharyngeal and rectal swabs within 48 hours of ICU admission. In contrast, infections were identified throughout the ICU stay, based on clinical suspicion and confirmed by targeted cultures obtained during ICU hospitalization. Outcomes included ICU and hospital length of stay, organ support requirements, and 28-day transplant-free survival, ICU survival, and overall hospital survival.

Definitions

Cirrhosis was diagnosed based on histological findings or a combination of clinical indicators, such as variceal bleeding, ascites, or hepatic encephalopathy, along with imaging and laboratory results supportive of the diagnosis. Organ failures

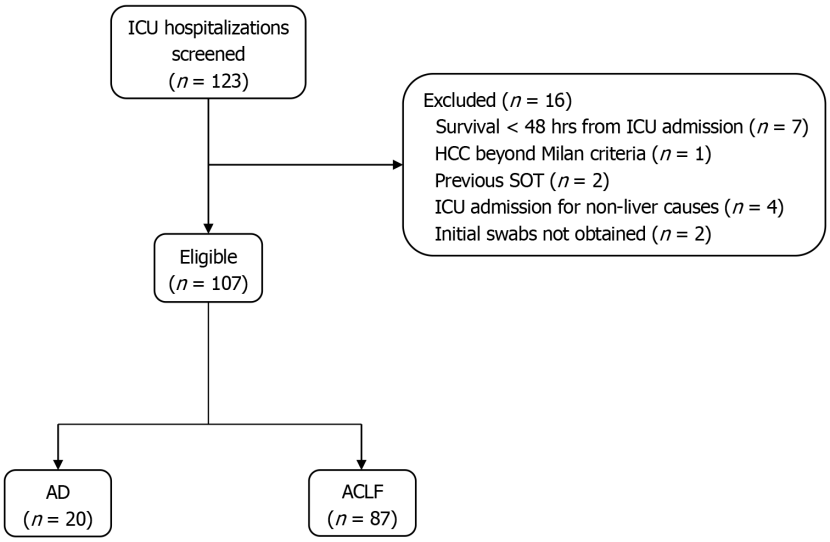

Figure 1 Study flow diagram. Of 123 intensive care unit hospitalizations screened, 16 were excluded due to early mortality, non-liver related intensive care unit admission, prior transplantation, advanced hepatocellular carcinoma, or missing swabs at admission. The final cohort included 107 patients, categorized as acute decompensation (*n* = 20) or acute-on-chronic liver failure (*n* = 87). AD: Acute decompensation; ACLF: Acute-on-chronic liver failure; ICU: Intensive care unit; HCC: Hepatocellular carcinoma; SOT: Solid organ transplant.

and ACLF were defined according to CLIF Consortium criteria[30]. MDRO colonization was defined as a positive screening swab for methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus spp*., extended-spectrum beta-lactamase-producing *Enterobacterales*, or carbapenem-resistant Gram-negative bacteria. MDRO infections were infections caused by organisms resistant to ≥ 1 agent in ≥ 3 antimicrobial classes.

The distinction between colonization and infection was based on clinical presentation and microbiological findings. Infection was diagnosed when patients exhibited signs or symptoms consistent with infection (*e.g*., fever, hypotension, elevated inflammatory markers, leukocytosis) together with positive cultures from typically sterile or clinically relevant sites. Infections were further categorized according to antimicrobial susceptibility into those caused my MDROs and dose caused by susceptible organisms. Colonization was defined by the presence of MDROs in screening cultures (*e.g*., rectal, nasopharyngeal swabs) without accompanying clinical or laboratory evidence of active infection at the time of sampling. Patients who met criteria for both, *i.e*., had clinical signs of infection and MDROs identified in both screening and diagnostic cultures, were classified as both colonized and infected.

Infections were defined as follows: (1) Urinary tract infection required the presence of > 10 Leukocytes per high-power field in urinary sediment and positive urine culture, or uncountable leukocytes per field with negative culture; (2) Pneumonia or upper respiratory tract infection required clinical signs of infection with new infiltrates on chest radiography, or clinical signs of infection and a positive sputum or bronchoalveolar lavage culture; (3) Hepatic or intra-abdominal infection was defined by clinical signs of infection with radiological evidence of infected non-solid intra-abdominal or hepatic collections; (4) Surgical wound or soft tissue infection was identified by clinical signs including swelling, erythema, warmth, and tenderness; (5) Bacteremia was defined by the presence of viable bacteria in ≥ set of blood cultures; (6) Cholangitis required cholestasis, right upper quadrant pain and/or jaundice, and radiological evidence of biliary obstruction; (7) *Clostridioides* infection required compatible clinical symptoms (diarrhoea) and a positive nucleic acid amplification test or stool culture; (8) Spontaneous bacterial peritonitis was defined as bacterial infection of ascitic fluid in the absence of any surgically correctable intra-abdominal infection source, and an ascitic neutrophil count of ≥ 250/mm^3; and (9) Unproven bacterial infection was defined by fever ≥ 38 °C and leucocytosis (WBC ≥ 12000/mm^3), initiating antibiotic therapy without an identified source.

No targeted decontamination interventions (*e.g*., selective digestive tract contamination, topical chlorhexidine bathing) were performed based on colonization results. Colonized patients were managed with standard institutional infection-control precautions, including isolation or cohorting and strict adherence to hand hygiene and contact precautions. Empiric antibiotic therapy was guided by clinical suspicion, severity of illness and clinical judgement of treating physicians.

Statistical analysis

All analyses were conducted using IBM SPSS statistics (version 29.0.0.0). Descriptive statistics were reported as medians (interquartile range) or frequencies (%). Group comparisons used χ^2 or Fisher's exact tests for categorical variables, and *t*-tests or Mann-Whitney *U* tests for continuous variables based on Shapiro-Wilk normality testing.

Two multivariable logistic regression models evaluated whether MDRO colonization predicted: (1) Subsequent infection; and (2) 28-day transplant-free mortality. Both models adjusted for MELD-Na, SOFA, CLIF-ACLF scores, age and sex. MELD was excluded due to collinearity with MELD-Na. Covariates were selected a priori based on their known clinical relevance and prognostic significance in critically ill patients with cirrhosis. MELD-Na, SOFA, and CLIF-ACLF scores reflect liver disease severity and organ dysfunction, while age and sex are recognized demographic predictors[31,

32]. Prior to model fitting, multicollinearity was formally assessed using variance inflation factor. All predictor variables demonstrated acceptable variance inflation factor values (< 2), indicating no significant multicollinearity. Model adequacy was further evaluated using convergence diagnostics and pseudo-R^2 measures as indicators of model fit. Assumptions were checked *via* convergence diagnostics and variance estimates.

Kaplan-Meier survival analyses assessed 28-day survival from ICU admission to death or censoring (discharge or day 28). Unadjusted survival curves were stratified by colonization and infection status between AD and ACLF subgroups, and compared using the log-rank test. A predefined missing data strategy was applied. Variables with more than 50% missing data were excluded. For variables with less than 10% missing data, complete case analysis was used. Cases missing survival or phenotype status were excluded from subgroup analyses. A two-tailed alpha of 0.05 was used, and $P < 0.05$ was considered statistically significant. No correction for multiple testing was applied due to the exploratory nature of the study.

Ethical considerations

The study was approved by the Institutional Review Board of the University Hospital Centre Zagreb (Approval No: 02/013 AG). All study procedures were conducted in accordance with the principles of the Declaration of Helsinki, Good Clinical Practice, and the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies. Given the retrospective design and anonymized data collection, the requirement for individual informed consent was waived.

RESULTS

Cohort characteristics and baseline comparisons

A total of 107 ICU admissions from 105 patients with liver cirrhosis were included in the final cohort. The median age was 60 years (interquartile range: 53-67), and 69.2% were male. Most patients were admitted with ACLF (81.3%), while the remainder presented with AD (18.7%). The most common etiology of cirrhosis was alcohol-associated liver disease (82.2%), followed by chronic viral hepatitis (10.3%) and metabolic dysfunction associated steatotic liver disease (5.6%). Multiple etiologies could be assigned per patient where applicable. Baseline characteristics of the cohort are shown in Table 1.

MDRO colonization at ICU admission was identified in 32 patients (29.9%). Compared to non-colonized patients, those with colonization had significantly lower platelet counts (76.5×10^9/L *vs* 100.0×10^9/L, $P = 0.004$), lower enzyme levels (alanine aminotransferase, $P = 0.039$; gamma-glutamyl transpeptidase, $P = 0.011$), and a higher prevalence of diabetes mellitus (37.5% *vs* 17.3%, $P = 0.045$). Infection was more frequently the reason for ICU admission in colonized patients (53.1% *vs* 24.0%, $P = 0.007$), and ACLF was more common in this group (93.8% *vs* 76.0%, $P = 0.033$). No significant differences were observed in MELD-Na, SOFA, or CLIF-ACLF scores, nor in most other comorbidities. When comparing patients with AD and ACLF, those with ACLF had significantly higher inflammatory markers (WBC: 12.7×10^9/L *vs* 9.8×10^9/L, $P = 0.034$; procalcitonin: 1.2 ng/mL *vs* 0.5 ng/mL, $P = 0.003$), as well as greater disease severity reflected by higher MELD-Na (29.2 *vs* 19.7, $P < 0.001$) and SOFA scores (9.0 *vs* 5.5, $P < 0.001$). Short-term outcomes were significantly worse in ACLF patients, including lower transplant- free survival (39.1% *vs* 75%, $P = 0.008$), ICU survival (43.7% *vs* 85.0%, $P = 0.001$), and overall hospital survival (34.5% *vs* 75.0%, $P = 0.002$).

Prevalence and patterns of colonization and infection

In the 107 ICU admissions, 38 distinct MDRO colonizing strains were identified in 32 patients (29.9%), indicating some had harbored multiple organisms. The most common were MRSA (26.3%), *A. baumanii* (21.1%), and OXA-48-producing *K. pneumoniae* (21.1%), while VRE was found in 10.5% of cases (Table 2; Figure 2). Infection occurred in 91 patients (85.0%), with a total of 56 distinct MDRO strains identified in 16 MDRO-positive infection episodes, suggesting some infections involved multiple sites and/or multiple resistant organisms. The most frequently infecting pathogens were *A. baumanii* (37.5% of MDRO infections), *K. pneumoniae* with various resistance profiles (approximately 28.6%), and MRSA (16.1%). Some organisms such as ESBL-producing *E. coli* and certain *Klebsiella spp.* were detected exclusively during infection and not colonization, highlighting gaps in routine surveillance (Table 2). Overall, the distribution of specific MDROs did not significantly differ between colonization and infection ($P > 0.1$ for all comparisons). However, the variety of resistance mechanisms observed across isolates highlights the clinical complexity of managing infections in these populations.

Patterns of MDRO colonization and infection varied by clinical phenotype. Colonization with *A. baumanii* and OXA-48-producing *K. pneumoniae* was more frequently observed in patients with ACLF than AD (87.5% *vs* 12.5%, $P = 0.508$), although subgroup comparisons did not reach statistical significance. Notably, nearly all isolates of ESBL and OXA-48 *K. pneumoniae*, VRE, and MRSA were identified in ACLF patients (Supplementary Tables 1 and 2). The spectrum of infection types also differed between phenotypes. Pneumonia was the most common infection in both groups (72.4% in ACLF *vs* 60.0% in AD), followed by urinary tract infections and bacteriaemia. Skin and soft tissue infections and intra-abdominal infections were rare and observed exclusively in ACLF patients. However, none of these phenotype specific differences reached statistical significance (Supplementary Table 3).

Clinical outcomes by colonization and infection status

Clinical outcomes differed by MDRO infection status but were less influenced by colonization alone. In colonized patients, there were no statistically significant differences in major outcomes compared to non-colonized peers; rates of mechanical ventilation (59.4% *vs* 50.7%, $P = 0.539$), renal replacement therapy (40.6% *vs* 30.7%, $P = 0.438$), vasopressor use

Table 1 Baseline clinical and laboratory characteristics of intensive care unit patients with cirrhosis, stratified by multidrug-resistant organism colonization and decompensation phenotype (acute decompensation *vs* acute-on-chronic liver failure), *n* (%)/median (interquartile range)

Characteristics	Total (*n* = 107)	Without MDRO colonization (*n* = 75)	With MDRO colonization (*n* = 32)	*P* value[1]	AD (*n* = 20)	ACLF (*n* = 87)	*P* value[1]
Clinical and laboratory data							
Age (years), median	60.0 (53.0, 67.0)	59 (53.0, 66.0)	61.0 (52.5, 69.0)	0.343	56.0 (50.3, 63.0)	61.0 (53.0, 68.0)	0.118
Gender				0.123			0.475
Male	74 (69.2)	48 (64.0)	26 (81.2)		12 (60.0)	62 (71.3)	
Female	33 (30.8)	27 (36.0)	6 (18.8)		8 (40.0)	25 (28.7)	
Hospital admission within last 3 months	40 (37.4)	25 (33.3)	15 (46.9)	0.268	7 (35.0)	33 (37.9)	1
ICU admission within last 3 months	12 (11.2)	7 (9.3)	5 (15.6)	0.542	4 (20.0)	8 (9.2)	0.231
Systemic antibiotics within last 3 months	38 (35.5)	23 (30.7)	15 (46.9)	0.167	5 (25.0)	33 (37.9)	0.406
Long-term norfloxacin prophylaxis	3 (2.8)	3 (4.0)	0 (0)	0.553	1 (5.0)	2 (2.3)	0.466
NSBB	41 (38.3)	27 (36.0)	14 (43.8)	0.591	9 (45.0)	32 (36.8)	0.67
IPP prior to hospital	58 (54.2)	39 (52.0)	19 (59.4)	0.659	12 (60.0)	46 (52.9)	0.774
IPP prior to ICU	76 (71.0)	50 (66.7)	26 (81.2)	0.197	15 (75.0)	61 (70.1)	0.872
TIPSS	8 (7.5)	5 (6.7)	3 (9.4)	0.694	1 (5.0)	7 (8.0)	1
WBC ($\times 10^9$/L)	12.2 (7.8, 16.8)	12.4 (7.2, 17.8)	11.6 (9.2, 14.3)	0.498	9.8 (5.1, 12.1)	12.7 (8.3, 17.2)	0.034
Platelets ($\times 10^9$/L)	88.0 (57.5, 122.0)	100.0 (64.0, 132.0)	76.5 (45.0, 100.0)	0.004	101.0 (76.3, 138.0)	84.0 (55.5, 118.5)	0.166
Serum creatinine (μmol/L)	150.0 (84.0, 278.5)	150.0 (88.0, 305.5)	140.5 (79.8, 220.0)	0.586	67.5 (59.5, 100.5)	185.0 (101.0, 317.0)	0.094
Serum sodium (mmol/L)	134.0 (130.0, 138.0)	134.0 (130.5, 138.0)	135.0 (129.0, 138.0)	0.751	136.5 (129.8, 142.8)	134.0 (130.0, 137.5)	0.246
Serum albumin (g/L)	26.0 (22.7, 29.5)	26.0 (22.4, 29.3)	26.0 (23.3, 30.0)	0.935	27.5 (22.0, 31.3)	26.0 (23.0, 29.0)	0.584
Serum bilirubin (μmol/L)	102.0 (45.0, 219.0)	100.0 (47.6, 207.0)	139.5 (42.5, 213.0)	0.586	69.5 (37.5, 94.3)	114.0 (49.0, 280.5)	0.094
INR	1.7 (1.4, 2.2)	1.6 (1.3, 2.2)	1.77 (1.6, 2.4)	0.156	1.4 (1.3, 1.5)	1.8 (1.5, 2.4)	0
CRP (mg/L)	36.1 (17.0, 73.5)	32.4 (15.4, 75.1)	36.6 (21.3, 68.9)	0.617	37.5 (13.0, 55.1)	35.0 (17.4, 80.5)	0.29
PCT (ng/mL)	1.1 (0.5, 2.8)	1.1 (0.5, 2.8)	1.2 (0.6, 2.2)	0.824	0.5 (0.1, 1.1)	1.3 (0.6, 2.9)	0.003
AST (U/L)	97.0 (49.0, 214.0)	110.0 (49.0, 262.0)	79.5 (50.0, 133.8)	0.187	76.0 (42.8, 130.8)	106.0 (52.0, 228.0)	0.303
ALT (U/L)	48.0 (21.0, 117.5)	60.0 (22.0, 141.0)	29.5 (18.3, 79.5)	0.039	39.5 (22.0, 101.5)	49.0 (20.50, 117.50)	0.851
GGT (U/L)	67.0 (34.0, 162.5)	80.0 (39.0, 225.0)	47.5 (24.0, 87.8)	0.011	141.5 (51.8, 564.5)	60.0 (30.5, 119.5)	0.01
ALP (U/L)	108.0 (87.0, 154.5)	109.0 (86.5, 179.5)	106.0 (90.8, 129.0)	0.492	100.0 (82.5, 187.3)	109.0 (87.0, 144.5)	0.876
Cirrhosis etiology							
ALD	88 (82.2)	64 (85.3)	24 (75.0)	0.315	16 (80.0)	72 (82.8)	0.752
Chronic viral hepatitis	11 (10.3)	9 (12.0)	2 (6.2)	0.5	1 (5.0)	10 (11.5)	0.685

MASLD	6 (5.6)	3 (4.0)	3 (9.4)	0.361	2 (10.0)	4 (4.6)	0.312
PSC/PBC	1 (0.9)	1 (1.3)	0 (0)	1	1 (5.0)	0 (0)	0.187
AIH	1 (0.9)	1 (1.3)	0 (0)	1	1 (5.0)	0 (0)	0.187
Cryptogenic	8 (7.5)	5 (6.7)	3 (9.4)	0.694	0 (0)	8 (9.2)	0.347
HCC	3 (2.8)	1 (1.3)	2 (6.2)	0.212	1 (5.0)	2 (2.3)	0.466
Comorbidities							
Diabetes mellitus	25 (23.4)	13 (17.3)	12 (37.5)	0.045	5 (25.0)	20 (23.0)	1
Cardiovascular diseases	50 (46.7)	33 (44.0)	17 (53.1)	0.513	7 (35.0)	43 (49.4)	0.359
Respiratory diseases	15 (14.0)	9 (12.0)	6 (18.8)	0.537	2 (10.0)	13 (14.9)	0.732
Chronic kidney diseases	13 (12.1)	8 (10.7)	5 (15.6)	0.692	2 (10.0)	11 (12.6)	1
Chronic hemodialysis	1 (0.9)	1 (1.3)	0 (0)	1	0 (0)	1 (1.1)	1
Disease severity at admission							
MELD score	12.0 (10.0, 13.0)	11.0 (10.0, 13.0)	12.0 (10.8, 13.3)	0.365	10.0 (8.0, 11.0)	12.0 (10.5, 13.0)	0
MELD-Na score	27.4 (21.3, 33.5)	27.0 (21.4, 34.0)	29.08 (20.9, 32.6)	0.979	19.7 (16.0, 23.3)	29.3 (24.2, 35.2)	0
SOFA score	8.0 (6.0, 11.0)	8.0 (6.0, 10.0)	8.5 (7.0, 11.0)	0.247	5.5 (4.0, 7.0)	9.0 (7.0, 11.0)	0
CLIF ACLF score	61.0 (53.8, 66.0)	61.0 (56.0, 65.8)	58.0 (53.3, 65.8)	0.558	71.0 (71.0, 71.0)	61.0 (53.5, 65.5)	0.168
Type of ICU admission							
Organ failure	48 (44.9)	36 (48.0)	12 (37.5)	0.431	9 (45.0)	39 (44.8)	1
Bleeding	11 (10.3)	9 (12.0)	2 (6.2)	0.5	5 (25.0)	6 (6.9)	0.046
Infection	35 (32.7)	18 (24.0)	17 (53.1)	0.007	2 (10.0)	33 (37.9)	0.017
Other	13 (12.1)	12 (16.0)	1 (3.1)	0.103	4 (20.0)	9 (10.3)	0.259
ACLF at ICU admission	87 (81.3)	57 (76.0)	30 (93.8)	0.033	0 (0.0)	87 (100.0)	0
Organ support at admission	63 (58.9)	44 (58.7)	19 (59.4)	1	7 (35.0)	56 (64.4)	0.031
Mechanical ventilation	45 (42.1)	30 (40.0)	15 (46.9)	0.656	7 (35.0)	38 (43.7)	0.647
Vasopressors	45 (42.1)	32 (42.7)	13 (40.6)	1	0 (0.0)	45 (51.7)	0
Outcomes							
Mechanical ventilation	57 (53.3)	38 (50.7)	19 (59.4)	0.539	9 (45)	48 (55.2)	0.566
Acute RRT	36 (33.6)	23 (30.7)	13 (40.6)	0.438	1 (5)	35 (40.2)	0.003
Vasopressors	52 (48.6)	34 (45.3)	18 (56.2)	0.41	1 (5)	51 (58.6)	0
28-day transplant free survival	49 (45.8)	37 (49.3)	12 (37.5)	0.361	15 (75)	34 (39.1)	0.008
Overall ICU survival	55 (51.4)	41 (54.7)	14 (43.8)	0.41	17 (85)	38 (43.7)	0.001
Overall hospital survival	45 (42.1)	35 (46.7)	10 (31.2)	0.206	15 (75)	30 (34.5)	0.002
ICU LOS	8.0 (4.0, 16.0)	8.0 (4.0, 14.0)	10.0 (3.0, 18.3)	0.513	5.0 (3.0, 10.5)	9.0 (5.0, 17.0)	0.084
Hospital LOS	22.0 (12.0, 36.0)	21.0 (12.0, 31.0)	27.0 (17.8, 47.0)	0.083	20.5 (11.8, 37.0)	24.0 (12.0, 36.0)	0.946

[1]*P* values were calculated using Fisher's exact or Mann-Whitney *U* test, as appropriate.

ICU: Intensive care unit; NSBB: Non-selective beta-blockers; IPP: Infection prevention protocol; TIPSS: Transjugular intrahepatic portosystemic shunt; WBC: White blood cell count; INR: International normalized ratio; CRP: C-reactive protein; PCT: Procalcitonin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; ALD: Alcohol-associated liver disease; MASLD: Metabolic dysfunction-associated steatotic liver disease; PSC: Primary sclerosing cholangitis; PBC: Primary biliary cholangitis; AIH: Autoimmune hepatitis; HCC:

Hepatocellular carcinoma; MELD: Model for End-Stage Liver Disease; SOFA: Sequential Organ Failure Assessment; CLIF: Chronic liver failure; ACLF: Acute-on-chronic liver failure; RRT: Renal replacement therapy; LOS: Length of stay; AD: Acute decompensation; MDRO: Multidrug-resistant organism.

(56.2% *vs* 45.3%, $P = 0.410$), and 28-day transplant free survival (37.5% *vs* 49.3%, $P = 0.361$) were similar between groups. ICU and hospital survival were also not statistically different (ICU: 43.8% *vs* 54.7%, $P = 0.410$; hospital 32.2% *vs* 46.7%, $P = 0.206$) neither were median ICU or hospital lengths of stay (Table 3). In contrast, MDRO infection was associated with significantly worse outcomes. Patients with documented MDRO infections had higher rates of mechanical ventilation (59.3% *vs* 18.8%, $P = 0.005$) and vasopressor use (53.8% *vs* 18.8%, $P = 0.013$) compared to non-infected patients. ICU length of stay was longer (median 9.0 days *vs* 5.0 days, $P = 0.003$), as was hospital length of stay (24.0 days *vs* 14.0 days, $P = 0.030$). Hospital survival was significantly lower in infected patients (37.4% *vs* 68.8%, $P = 0.038$), while ICU and 28-day transplant-free survival was also lower, but did not reach statistical significance (Table 3).

Predictors of infection and mortality

Two multivariable logistic regression models were constructed to evaluate whether MDRO colonization at ICU admission predicted adverse clinical outcomes, specifically subsequent MDRO infection and 28-day transplant-free mortality. In the first model ($n = 87$), colonization was not independently associated with infection [odds ratio (OR) = 2.18; 95% confidence internal (CI): 0.47-10.10; $P = 0.383$]. None of the included covariates, MELD-Na score, SOFA score, CLIF-ACLF score, age or sex, were statistically significant predictors of infection. CLIF-ACLF score approached significance ($P = 0.066$), and male sex appeared to have a protective association (OR = 0.17), but this did not reach statistical significance (Table 4). In the second model evaluating predictors of 28-day mortality, colonization again showed no significant association with outcome (OR = 1.14; 95%CI: 0.37-3.50; $P = 0.813$). However, SOFA score emerged as a significant predictor, with higher scores associated with increased risk of death (OR = 1.38; 95%CI: 1.04-1083; $P = 0.024$). CLIF-ACLF score also neared significance ($P = 0.062$). MELD-Na, age, and sex were not significant in this model (Table 5).

Stratified outcomes by AD vs ACLF status

Outcomes were further examined according to decompensation phenotype. MDRO colonization was significantly more common among patients with ACLF compared to those with AD (34.5% *vs* 10.0%, $P = 0.033$). Although MDRO infection was prevalent in both groups (86.2% in ACLF *vs* 80.0% in AD) the difference was not statistically significant ($P = 0.494$). In patients who developed infection, strain concordance with colonization was observed in all AD cases (2/2) and in 81.8% of ACLF cases (18/22; $P = 1.000$). Clinical outcomes were worse in the ACLF subgroup. Patients with ACLF had significantly lower 28-day transplant-free survival (39.1% *vs* 75.0%, $P = 0.002$) compared to those with AD. Although ICU length of stay was longer in the ACLF patients (median 9.0 days *vs* 5.0 days), this did not reach statistical significance ($P = 0.084$). Hospital length of stay was similar between two groups ($P = 0.946$; Table 6).

Kaplan-Meier survival analysis

Kaplan-Meier analysis revealed no statistically significant differences in 28-day survival based on colonization or infection status in either AD or ACLF groups. Kaplan-Meier was conducted to assess 28-day transplant free survival stratified by MDRO colonization and infection status within both AD and ACLF subgroups. In patients with ACLF, MDRO infection was associated with a lower survival probability over the 28-day period compared to non-infected peers. However, the difference did not reach statistical significance ($P = 0.257$). A similar pattern was observed in AD patients, where those with MDRO infection had worse survival, however, again not statistically significant ($P = 0.225$). MDRO colonization status did not significantly impact 28-day survival in either clinical group. In ACLF patients, survival curves for colonized and non-colonized individuals were nearly superimposable ($P = 0.956$). Among AD patients, no survival difference by colonization was observed ($P = 0.542$; Figure 3).

DISCUSSION

This study explored the clinical relevance of MDRO colonization at ICU admission in patients with cirrhosis, with a particular focus on its relationship to subsequent infection, patient outcomes, and local epidemiological patterns. While colonization at ICU admission was frequent and often concordant with the organisms' causing infection, it was not independently associated with MDRO infection or short-term mortality. These findings diverge from previous reports and suggest that, in a population with advanced liver disease and high baseline infection rates, the prognostic significance of colonization may be limited. They also emphasize the importance of interpreting colonization data in the light of timing, host immune status, and regional resistance profiles.

We observed a high concordance (approximately 82%) between colonizing and infecting strains, aligning with previous studies that emphasize the predictive value of colonization in anticipating subsequent infection strains[14,17]. This observation supports the consideration of colonization data when selecting empiric antibiotic regimens, particularly when infection is clinically suspected and prior MDRO colonization has been documented. However, the absence of certain pathogens, such as ESBL-producing *E. coli*, in screening samples indicates that reliance on colonization data alone could lead to incomplete empirical coverage. Thus, clinicians should consider colonization status alongside local microbiological data and clinical suspicion rather than as an isolated guide.

Table 2 Multidrug-resistant organism species identified in colonization and infection episodes at intensive care unit admission, *n* (%)

MDRO species	Total (*n*)	Colonized	Infected	*P* value[1]
MDR *A. baumanii*	29	8 (21.1)	21 (37.5)	0.142
Escherichia coli, ESBL	2	0 (0.0)	2 (3.6)	0.513
Escherichia coli, ESBL and OXA-48	1	0 (0.0)	1 (1.8)	1
Klebsiella oxytoca, OXA-48	1	1 (2.6)	0 (0.0)	0.404
Klebsiella pneumoniae, ESBL	3	1 (2.6)	2 (3.6)	1
Klebsiella pneumoniae, ESBL and OXA-48	5	3 (7.9)	2 (3.6)	0.391
Klebsiella pneumoniae, KPC	3	1 (2.6)	2 (3.6)	1
Klebsiella pneumoniae, OXA-48	19	8 (21.1)	11 (19.6)	0.925
MDR *Pseudomonas spp.*	2	2 (5.3)	0 (0.0)	0.161
VRE	10	4 (10.5)	6 (10.7)	1
MRSA	19	10 (26.3)	9 (16.1)	0.341

[1]*P* values were calculated using Fisher's exact test.
MDRO: Multidrug-resistant organism; *A. baumanii*: *Acinetobacter baumannii*; ESBL: Extended-spectrum beta-lactamase; OXA-48: Oxacillinase-48; KPC: *Klebsiella pneumoniae* carbapenemase; MDR: Multidrug-resistant; VRE: Vancomycin-resistant *Enterococcus spp.*; MRSA: Methicillin-resistant *Staphylococcus aureus*.

Table 3 Clinical outcomes stratified by multidrug-resistant organism colonization and infection status, *n* (%)/median (interquartile range)

Outcome	Colonized patients (*n* = 32)	Non-colonized (*n* = 75)	*P* value[1]	Infected patients (*n* = 91)	Non-infected (*n* = 16)	*P* value[1]
Mechanical ventilation	19 (59.4)	38 (50.7)	0.539	54 (59.3)	3 (18.8)	0.005[a]
Renal replacement therapy	13 (40.6)	23 (30.7)	0.438	31 (34.1)	5 (31.2)	1
Vasopressor use	18 (56.2)	34 (45.3)	0.41	49 (53.8)	3 (18.8)	0.013[b]
ICU LOS	10.0 (15.2)	8.0 (10.0)	0.513	9.0 (12.0)	5.0 (2.2)	0.003[c]
28-day transplant free survival	12 (37.5)	37 (49.3)	0.361	38 (41.8)	11 (68.8)	0.084
ICU survival	14 (43.8)	41 (54.7)	0.41	44 (48.4)	11 (68.8)	0.217
Hospital survival	10 (31.2)	35 (46.7)	0.206	34 (37.4)	11 (68.8)	0.038[d]
Hospital LOS (days)	27.0 (29.2)	21.0 (19.0)	0.083	24.0 (26.5)	14.0 (15.0)	0.03[e]

[a]$P < 0.01$ for mechanical ventilation in infected *vs* non-infected patients.
[b]$P < 0.05$ for vasopressor use in infected *vs* non-infected patients.
[c]$P < 0.01$ for intensive care unit length of stay in infected *vs* non-infected patients.
[d]$P < 0.05$ for hospital length of stay in infected *vs* non-infected patients.
[e]$P < 0.05$ for hospital survival in infected *vs* non-infected patients.
[1]*P* values were calculated using Fisher's exact or Mann-Whitney *U* test, as appropriate.
LOS: Length of stay; ICU: Intensive care unit.

MDRO colonization at ICU admission was observed in nearly 30% of our cohort, consistent with rates reported in critically ill patients with cirrhosis[16]. However, the predominant colonizing strains in our population, MRSA, *A. baumanii*, and OXA-48-producing *K. pneumoniae*, differ from those reported in Western European centers, where ESBL-producing *E. coli* and VRE are more frequently observed[6,15,26]. The spectrum of MDROs varies widely across regions, and local surveillance data are essential for guiding empirical therapy and infection control[6,11]. Regional data from Eastern Europe suggest a particularly high prevalence of carbapenem-resistant organisms in ICU-admitted patients with cirrhosis, which is reflected in our cohort by the predominance of *A. baumanii* and OXA-48 producing *K. pneumoniae*[33].

Infection was identified in 85% of patients, with 17.6% of these involving MDROs. This is comparable to the prevalence reported in other ICU cohorts of patients with cirrhosis[16]. However, the spectrum of infecting organisms also showed some divergence. In our cohort, Gram-negative non-fermenters such as *A. baumanii* were particularly prominent, an observation consistent with Eastern and Southern European epidemiology[1,34]. The overall severity of illness in our

Table 4 Multivariable logistic regression model predicting multidrug-resistant organism infection during intensive care unit admission (*n* = 87)

Predictor	OR	95%CI	*P* value[1]
MDRO colonization	2.18	0.47-10.10	0.383
MELD-Na score	0.94	0.82-1.08	0.321
SOFA score	1.03	0.68-1.54	0.394
CLIF-ACLF score	1.11	0.99-1.23	0.903
Age	0.94	0.86-1.02	0.066
Sex (male *vs* female)	0.17	0.02-1.61	0.152

[1]*P* values based on Wald test.
MDRO: Multidrug-resistant organism; MELD: Model for End-Stage Liver Disease; SOFA: Sequential Organ Failure Assessment; CLIF: Chronic liver failure; ACLF: Acute-on-chronic liver failure; OR: Odds ratio; CI: Confidence interval.

Table 5 Multivariable logistic regression model predicting 28-day transplant-free mortality in intensive care unit patients with cirrhosis (*n* = 87)

Predictor	OR	95%CI	*P* value[1]
MDRO colonization	1.14	0.37-3.50	0.813
MELD-Na score	0.99	0.91-1.08	0.829
SOFA score	1.38	1.04-1.83	0.024[a]
CLIF-ACLF score	1.07	1.00-1.16	0.062
Age	1.04	0.98-1.10	0.241
Sex (male *vs* female)	1.66	0.53-5.19	0.387

[a]$P < 0.05$ for Sequential Organ Failure Assessment score as predictor of 28-day transplant-free mortality.
[1]*P* values based on Wald test.
MDRO: Multidrug-resistant organism; MELD: Model for End-Stage Liver Disease; SOFA: Sequential Organ Failure Assessment; CLIF: Chronic liver failure; ACLF: Acute-on-chronic liver failure; OR: Odds ratio; CI: Confidence interval.

cohort, reflected in high CLIF-ACLF, MELD-Na, and SOFA scores, confirms a critically ill population with substantial baseline risk[6]. MDRO colonization was notably more frequent in patients with ACLF, potentially reflecting the immunological dysfunction inherent to this phenotype[20,21]. This association persisted even when global severity scores were comparable, supporting the notion that ACLF-related immune derangements may predispose patients to microbial colonization independently of liver function. However, despite the high prevalence of colonization and MDRO infection, we did not observe a statistically significant association between colonization at ICU admission and MDRO infection nor short-term mortality in either group. These findings contrast with previous studies that report a clearer link between colonization and infection[14,16,17]. Several factors may account for this discrepancy, including the fact that over 80% of patients in our cohort were already infected at ICU admission limiting opportunities to detect new infections and potentially reducing the colonization's predictive value. Additionally, the predominance of patients with advanced liver disease and high baseline severity may have diminished the independent prognostic importance of colonization.

Clinically, these findings suggest phenotype-specific considerations: In ACLF patients, characterized by higher MDRO colonization rates, empirical therapy might need broader initial coverage informed by local MDRO profiles. Repeated colonization screening during prolonged hospital stays or pre-ICU admission could enhance detection and tailor empirical treatment, although prospective validation of such strategies is needed. Regarding infection control, although standard isolation and contact precaution protocols were employed for MDRO-colonized patients, our study did not specifically investigate transmission events, and no targeted decontamination strategies (*e.g.*, selective digestive decontamination or chlorhexidine bathing) were implemented. Enhanced surveillance using molecular typing could potentially clarify transmission dynamics and further refine infection control measures.

This study has several limitations. The retrospective, single-center design limits generalizability, and its observational nature precludes causal inference. In particular, our findings reflect a Southeastern European resistance profile, limiting direct applicability to settings with different epidemiological patterns. Additionally, the lack of molecular strain typing prevented definitive confirmation of colonizing and infecting strain concordance. Another limitation was the inability to clearly differentiate colonization timing relative to infection onset, particularly since many patients were infected at ICU admission. Thus, the exact predictive window and causal relationships remain uncertain. Nonetheless, this study offers

Table 6 Clinical outcomes stratified by decompensation phenotype (acute decompensation *vs* acute-on-chronic liver failure), *n* (%)/median (interquartile range)

Outcome	AD (*n* = 20)	ACLF (*n* = 87)	*P* value[1]
MDRO colonized	2 (10.0)	30 (34.5)	0.033[a]
Total infections	16 (80.0)	75 (86.2)	0.494
Strain-concordant infection	2 (100.0)	18 (81.8)	1.000
ICU length of stay (days)	5.0 (7.5)	9.0 (12.0)	0.084
28-day transplant-free survival	15 (75.0)	34 (39.1)	0.008[b]
ICU survival	17 (85.0)	38 (43.7)	0.001[c]
Hospital survival	15 (75.0)	30 (34.5)	0.002[d]
Hospital LOS (days)	20.5 (25.2)	24.0 (24.0)	0.946

[a]$P < 0.05$ for multidrug-resistant organism colonization (acute-on-chronic liver failure *vs* acute decompensation).
[b]$P < 0.01$ for 28-day transplant-free survival (acute-on-chronic liver failure *vs* acute decompensation).
[c]$P < 0.01$ for intensive care unit survival (acute-on-chronic liver failure *vs* acute decompensation).
[d]$P < 0.01$ for hospital survival (acute-on-chronic liver failure *vs* acute decompensation).
[1]*P* values were calculated using Fisher's exact or Mann-Whitney *U* test, as appropriate.
MDRO: Multidrug-resistant organism; ICU: Intensive care unit; LOS: Length of stay; AD: Acute decompensation; ACLF: Acute-on-chronic liver failure.

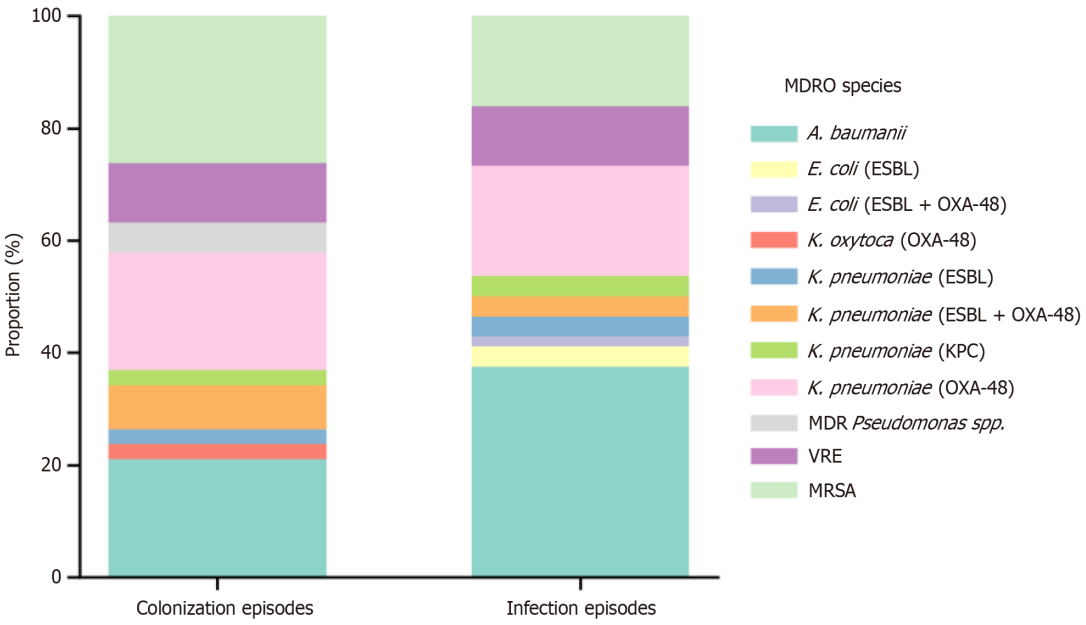

Figure 2 Distribution of multidrug-resistant organism species in colonization and infection episodes among intensive care unit admissions. Stacked bar shows the proportions of bacterial species in colonization's episodes (left) and infection episodes (right). MDRO: Multidrug-resistant organism; *E. coli*: *Escherichia coli*; ESBL: Extended-spectrum beta-lactamase; OXA-48: Oxacillinase-48; *K. pneumoniae*: *Klebsiella pneumoniae*; KPC: *Klebsiella pneumoniae* carbapenemase; MDR: Multidrug-resistant; VRE: Vancomycin-resistant *Enterococcus spp.*; MRSA: Methicillin-resistant *Staphylococcus aureus*.

several notable strengths. It focuses on a relatively homogeneous, well-characterized population of critically ill patients with cirrhosis, minimizing heterogeneity in baseline liver disease and clinical trajectories. Microbiological data were obtained from systematic screening and diagnostic cultures, enabling a detailed comparison between colonizing and infecting strains. Additionally, outcomes were stratified by both colonization and decompensation phenotype (AD *vs* ACLF), offering insights into host-pathogen interactions across different immunological states. Compared to earlier studies, our data contribute region-specific evidence from a high-risk ICU-setting with a distinct MDRO profile, underlining the value of tailored surveillance and empiric therapy in local practice contexts.

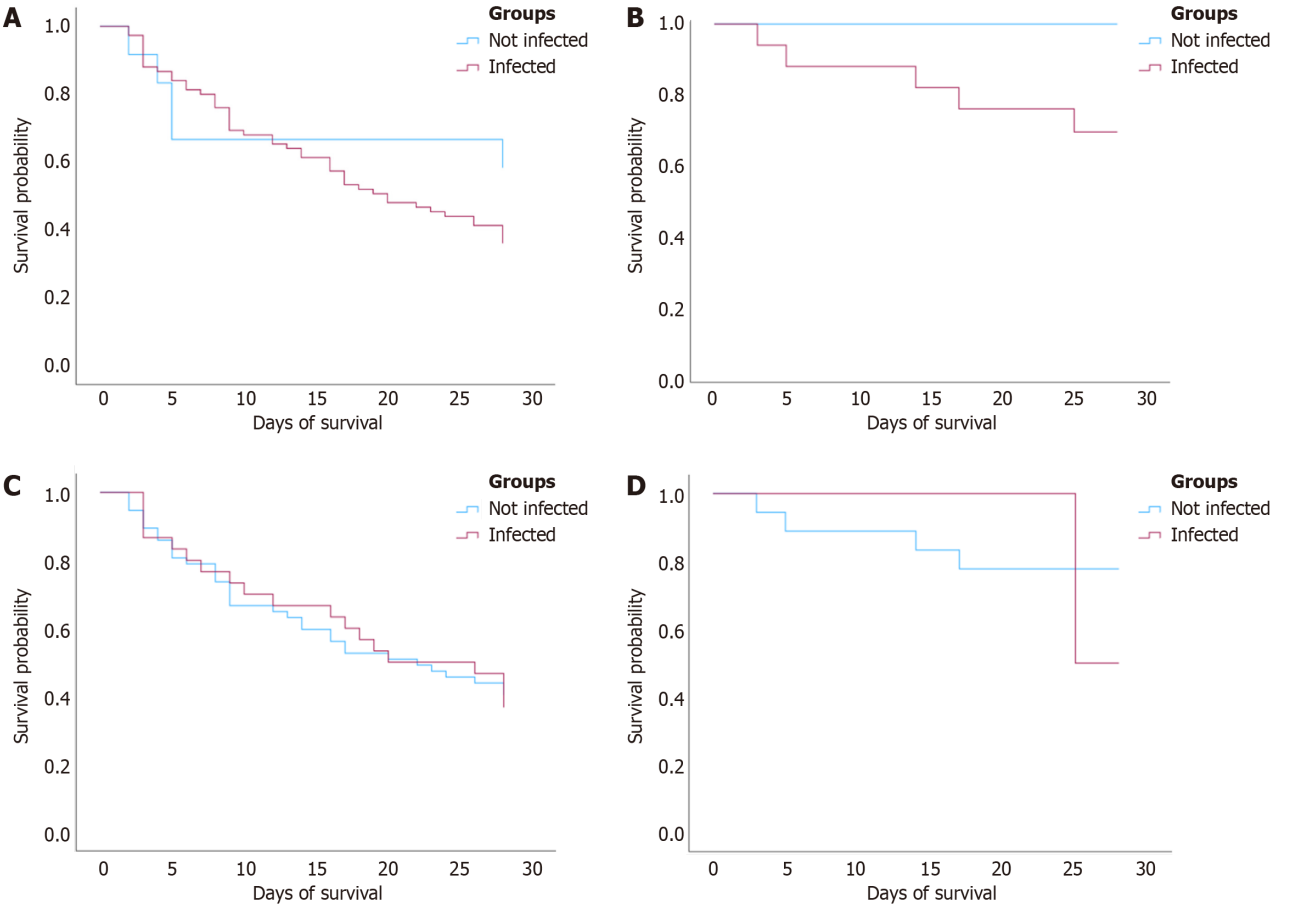

Figure 3 Kaplan-Meier curves for 28-day transplant-free survival in intensive care unit patients with cirrhosis, stratified by multidrug-resistant organism status and clinical phenotype. A: 28-day survival of acute-on-chronic liver failure patients without and multidrug-resistant organism (MDRO) infection (P = 0.257); B: 28-day survival of acute decompensation patients without and with MDRO infection (P = 0.225); C: 28-day survival of acute-on-chronic liver failure patients without and with MDRO colonization at intensive care unit admission (P = 0.956); D: 28-day survival of acute decompensation patients without and with MDRO colonization at intensive care unit admission (P = 0.542).

CONCLUSION

In critically ill patients with cirrhosis, especially those with ACLF, colonization with MDROs at ICU admission is common but not independently associated with short-term mortality or subsequent infection, highlighting the complexity of infection risk in this population. The high concordance between colonizing and infecting strains supports the clinical value of colonization data for guiding empirical therapy when infection is clinically suspected. MDRO infections were associated with significantly higher resource utilization, including increased need for mechanical ventilation, vasopressors, and renal replacement therapy, emphasizing their clinical impact despite the limited predictive value of colonization status alone. Our findings highlight that short-term mortality is more strongly driven by the extent of organ dysfunction than by MDRO colonization status, suggesting that physiological status remains the dominant factor in early outcome prediction.

Given that infections are the leading ICU admission trigger, incorporating earlier MDRO screening, phenotype-tailored empirical therapy, and enhanced surveillance might improve clinical management. Local epidemiological insight, targeted surveillance, and region-adapted empirical strategies are essential to support timely, effective treatment. However, caution is warranted to avoid overinterpreting colonization as a standalone determinant for empirical coverage, given its limited predictive performance demonstrated herein. Prospective studies that incorporate antimicrobial susceptibility profiling and track infection dynamics over time are warranted to refine screening strategies and improve microbiological precision in this at-risk population.

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REFERENCES

1 **Terra C**, de Mattos ÂZ, Chagas MS, Torres A, Wiltgen D, Souza BM, Perez RM. Impact of multidrug resistance on the management of bacterial infections in cirrhosis. *World J Clin Cases* 2023; **11**: 534-544 [*RCA*] [PMID: 36793638 DOI: 10.12998/wjcc.v11.i3.534] [FullText] [Full Text(PDF)]

2 **Wong F**, Piano S, Singh V, Bartoletti M, Maiwall R, Alessandria C, Fernandez J, Soares EC, Kim DJ, Kim SE, Marino M, Vorobioff J, Barea RCR, Merli M, Elkrief L, Vargas V, Krag A, Singh SP, Lesmana LA, Toledo C, Marciano S, Verhelst X, Intagliata N, Rabinowich L, Colombato L, Kim SG, Gerbes A, Durand F, Roblero JP, Bruns T, Yoon EL, Girala M, Pyrsopoulos NT, Kim TH, Yim SY, Juanola A, Gadano A, Angeli P; International Club of Ascites Global Study Group. Clinical features and evolution of bacterial infection-related acute-on-chronic liver failure. *J Hepatol* 2021; **74**: 330-339 [*RCA*] [PMID: 32781201 DOI: 10.1016/j.jhep.2020.07.046] [FullText]

3 **Ferrarese A**, Senzolo M, Cattelan AM, Sasset L, Battistella S, Zanetto A, Germani G, Russo FP, Gambato M, Pelizzaro F, Vio S, Bassi D, Cillo U, Burra P. Bacterial Infections in End-Stage Liver Disease: Implications for Liver Transplantation. *Transplantology* 2024; **5**: 129-139 [*RCA*] [DOI: 10.3390/transplantology5030013] [FullText]

4 **Martin Mateos R**, Albillos A. Sepsis in Patients With Cirrhosis Awaiting Liver Transplantation: New Trends and Management. *Liver Transpl* 2019; **25**: 1700-1709 [*RCA*] [PMID: 31408581 DOI: 10.1002/lt.25621] [FullText]

5 **Chen G**, To U. Inpatient management of bacterial infections in patients with cirrhosis: A clinical review. *Clin Liver Dis (Hoboken)* 2024; **23**: e0214 [*RCA*] [PMID: 38952696 DOI: 10.1097/CLD.0000000000000214] [FullText]

6 **Fernández J**, Prado V, Trebicka J, Amoros A, Gustot T, Wiest R, Deulofeu C, Garcia E, Acevedo J, Fuhrmann V, Durand F, Sánchez C, Papp M, Caraceni P, Vargas V, Bañares R, Piano S, Janicko M, Albillos A, Alessandria C, Soriano G, Welzel TM, Laleman W, Gerbes A, De Gottardi A, Merli M, Coenraad M, Saliba F, Pavesi M, Jalan R, Ginès P, Angeli P, Arroyo V; European Foundation for the Study of Chronic Liver Failure (EF-Clif). Multidrug-resistant bacterial infections in patients with decompensated cirrhosis and with acute-on-chronic liver failure in Europe. *J Hepatol* 2019; **70**: 398-411 [*RCA*] [PMID: 30391380 DOI: 10.1016/j.jhep.2018.10.027] [FullText]

7 **Fernández J**, Piano S, Bartoletti M, Wey EQ. Management of bacterial and fungal infections in cirrhosis: The MDRO challenge. *J Hepatol* 2021; **75** Suppl 1: S101-S117 [*RCA*] [PMID: 34039482 DOI: 10.1016/j.jhep.2020.11.010] [FullText]

8 **Piano S**, Bunchorntavakul C, Marciano S, Rajender Reddy K. Infections in cirrhosis. *Lancet Gastroenterol Hepatol* 2024; **9**: 745-757 [*RCA*] [PMID: 38754453 DOI: 10.1016/S2468-1253(24)00078-5] [FullText]

9 **Ferguson Toll J**, Solà E, Perez MA, Piano S, Cheng A, Subramanian AK, Kim WR. Infections in decompensated cirrhosis: Pathophysiology, management, and research agenda. *Hepatol Commun* 2024; **8**: e0539 [*RCA*] [PMID: 39365139 DOI: 10.1097/HC9.0000000000000539] [Full Text]

10 **Onorato L**, Monari C, Capuano S, Grimaldi P, Coppola N. Prevalence and Therapeutic Management of Infections by Multi-Drug-Resistant

Organisms (MDROs) in Patients with Liver Cirrhosis: A Narrative Review. *Antibiotics (Basel)* 2022; **11**: 232 [*RCA*] [PMID: 35203834 DOI: 10.3390/antibiotics11020232] [FullText] [Full Text(PDF)]

11 **Trad N**, Mohamed G, Bizid S, Abdallah HB, Bouali R, Abdelli MN. Clinical impact of multidrug-resistant bacterial infections in patients with cirrhosis. *Future Sci OA* 2024; **10**: FSO945 [*RCA*] [PMID: 38813115 DOI: 10.2144/fsoa-2023-0160] [FullText]

12 **Ferrarese A**, Senzolo M, Burra P. Multidrug-Resistant Bacterial Infections before and after Liver Transplantation. *OBM Transplant* 2020; **4**: 110 [*RCA*] [DOI: 10.21926/obm.transplant.2002110] [FullText]

13 **Incicco S**, Tonon M, Zeni N, Gambino C, Gagliardi R, Calvino V, Barone A, Zilio G, Feltracco P, Burra P, Cillo U, Angeli P, Piano S. Impact of bacterial infections prior to liver transplantation on post-transplant outcomes in patients with cirrhosis. *JHEP Rep* 2023; **5**: 100808 [*RCA*] [PMID: 37534231 DOI: 10.1016/j.jhepr.2023.100808] [FullText] [Full Text(PDF)]

14 **Prado V**, Hernández-Tejero M, Mücke MM, Marco F, Gu W, Amoros A, Toapanta D, Reverter E, Peña-Ramirez C, Altenpeter L, Bassegoda O, Mezzano G, Aziz F, Juanola A, Rodríguez-Tajes S, Chamorro V, López D, Reyes M, Hogardt M, Kempf VAJ, Ferstl PG, Zeuzem S, Martínez JA, Vila J, Arroyo V, Trebicka J, Fernandez J. Rectal colonization by resistant bacteria increases the risk of infection by the colonizing strain in critically ill patients with cirrhosis. *J Hepatol* 2022; **76**: 1079-1089 [*RCA*] [PMID: 35074475 DOI: 10.1016/j.jhep.2021.12.042] [FullText]

15 **Verma N**, Divakar Reddy PV, Vig S, Angrup A, Biswal M, Valsan A, Garg P, Kaur P, Rathi S, De A, Premkumar M, Taneja S, Ray P, Duseja A, Singh V. Burden, risk factors, and outcomes of multidrug-resistant bacterial colonisation at multiple sites in patients with cirrhosis. *JHEP Rep* 2023; **5**: 100788 [*RCA*] [PMID: 37484213 DOI: 10.1016/j.jhepr.2023.100788] [FullText] [Full Text(PDF)]

16 **Kim M**, Cardoso FS, Pawlowski A, Wunderink R, Ladner DP, Abraldes JG, Karvellas CJ. The impact of multidrug-resistant microorganisms on critically ill patients with cirrhosis in the intensive care unit: a cohort study. *Hepatol Commun* 2023; **7**: e0038 [*RCA*] [PMID: 36669500 DOI: 10.1097/HC9.0000000000000038] [FullText] [Full Text(PDF)]

17 **Pouriki S**, Alexopoulos T, Vasilieva L, Vrioni G, Alexopoulou A. Rectal colonization by resistant bacteria is associated with infection by the colonizing strain and high mortality in decompensated cirrhosis. *J Hepatol* 2022; **77**: 1207-1208 [*RCA*] [PMID: 35643207 DOI: 10.1016/j.jhep.2022.05.013] [FullText]

18 **Crocombe D**, O'Brien A. Antimicrobial prophylaxis in decompensated cirrhosis: friend or foe? *Hepatol Commun* 2023; **7**: e0228 [*RCA*] [PMID: 37655979 DOI: 10.1097/HC9.0000000000000228] [FullText]

19 **Kutmutia R**, Tittanegro T, China L, Forrest E, Kallis Y, Ryder SD, Wright G, Freemantle N, O'Brien A. Evaluating the Role of Antibiotics in Patients Admitted to Hospital With Decompensated Cirrhosis: Lessons From the ATTIRE Trial. *Am J Gastroenterol* 2023; **118**: 105-113 [*RCA*] [PMID: 35970815 DOI: 10.14309/ajg.0000000000001937] [FullText] [Full Text(PDF)]

20 **Liakina V**. Antibiotic resistance in patients with liver cirrhosis: Prevalence and current approach to tackle. *World J Clin Cases* 2023; **11**: 7530-7542 [*RCA*] [PMID: 38078132 DOI: 10.12998/wjcc.v11.i31.7530] [FullText] [Full Text(PDF)]

21 **Hasa E**, Hartmann P, Schnabl B. Liver cirrhosis and immune dysfunction. *Int Immunol* 2022; **34**: 455-466 [*RCA*] [PMID: 35792761 DOI: 10.1093/intimm/dxac030] [FullText]

22 **McGettigan B**, Hernandez-Tejero M, Malhi H, Shah V. Immune Dysfunction and Infection Risk in Advanced Liver Disease. *Gastroenterology* 2025; **168**: 1085-1100 [*RCA*] [PMID: 39927926 DOI: 10.1053/j.gastro.2024.08.046] [FullText]

23 **Tranah TH**, Kronsten VT, Shawcross DL. Implications and Management of Cirrhosis-Associated Immune Dysfunction Before and After Liver Transplantation. *Liver Transpl* 2022; **28**: 700-716 [*RCA*] [PMID: 34738724 DOI: 10.1002/lt.26353] [FullText]

24 **Wasmuth HE**, Kunz D, Yagmur E, Timmer-Stranghöner A, Vidacek D, Siewert E, Bach J, Geier A, Purucker EA, Gressner AM, Matern S, Lammert F. Patients with acute on chronic liver failure display "sepsis-like" immune paralysis. *J Hepatol* 2005; **42**: 195-201 [*RCA*] [PMID: 15664244 DOI: 10.1016/j.jhep.2004.10.019] [FullText]

25 **Piano S**, Singh V, Caraceni P, Maiwall R, Alessandria C, Fernandez J, Soares EC, Kim DJ, Kim SE, Marino M, Vorobioff J, Barea RCR, Merli M, Elkrief L, Vargas V, Krag A, Singh SP, Lesmana LA, Toledo C, Marciano S, Verhelst X, Wong F, Intagliata N, Rabinowich L, Colombato L, Kim SG, Gerbes A, Durand F, Roblero JP, Bhamidimarri KR, Boyer TD, Maevskaya M, Fassio E, Kim HS, Hwang JS, Gines P, Gadano A, Sarin SK, Angeli P; International Club of Ascites Global Study Group. Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide. *Gastroenterology* 2019; **156**: 1368-1380.e10 [*RCA*] [PMID: 30552895 DOI: 10.1053/j.gastro.2018.12.005] [Full Text]

26 **Kremer WM**, Gairing SJ, Kaps L, Ismail E, Kalampoka V, Hilscher M, Michel M, Siegel E, Schattenberg JM, Galle PR, Sprinzl MF, Wörns MA, Nagel M, Labenz C. Characteristics of bacterial infections and prevalence of multidrug-resistant bacteria in hospitalized patients with liver cirrhosis in Germany. *Ann Hepatol* 2022; **27**: 100719 [*RCA*] [PMID: 35460883 DOI: 10.1016/j.aohep.2022.100719] [FullText]

27 **Revelli L**, Dirchwolf M. Editorial: Terlipressin and MDRO colonisation in cirrhosis-Is there a causal link? *Aliment Pharmacol Ther* 2024; **59**: 1284-1285 [*RCA*] [PMID: 38652777 DOI: 10.1111/apt.17940] [FullText]

28 **Roy A**, Premkumar M. Progress in Hepatology-rectal Colonization by Resistant Bacteria Increases the Risk of Infection by the Colonizing Strain in Critically Ill Patients with Cirrhosis. *J Clin Exp Hepatol* 2022; **12**: 1574-1575 [*RCA*] [PMID: 36340315 DOI: 10.1016/j.jceh.2022.07.004] [FullText]

29 **Santoro-Lopes G**, de Gouvêa EF, Monteiro RC, Branco RC, Rocco JR, Halpern M, Ferreira AL, de Araújo EG, Basto ST, Silveira VG, Ribeiro-Filho J. Colonization with methicillin-resistant Staphylococcus aureus after liver transplantation. *Liver Transpl* 2005; **11**: 203-209 [*RCA*] [PMID: 15666377 DOI: 10.1002/lt.20338] [FullText]

30 **Jalan R**, Saliba F, Pavesi M, Amoros A, Moreau R, Ginès P, Levesque E, Durand F, Angeli P, Caraceni P, Hopf C, Alessandria C, Rodriguez E, Solis-Muñoz P, Laleman W, Trebicka J, Zeuzem S, Gustot T, Mookerjee R, Elkrief L, Soriano G, Cordoba J, Morando F, Gerbes A, Agarwal B, Samuel D, Bernardi M, Arroyo V; CANONIC study investigators of the EASL-CLIF Consortium. Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. *J Hepatol* 2014; **61**: 1038-1047 [*RCA*] [PMID: 24950482 DOI: 10.1016/j.jhep.2014.06.012] [FullText]

31 **Zhang C**, Zhang X, Sun Z, Liu X, Shen B. MetaSepsisBase: a biomarker database for systems biological analysis and personalized diagnosis of heterogeneous human sepsis. *Intensive Care Med* 2023; **49**: 1015-1017 [*RCA*] [PMID: 37329364 DOI: 10.1007/s00134-023-07126-4] [Full Text]

32 **D'Amico G**, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006; **44**: 217-231 [*RCA*] [PMID: 16298014 DOI: 10.1016/j.jhep.2005.10.013] [FullText]

33 **Lingiah VA**, Pyrsopoulos NT. Bacterial Infections in Cirrhotic Patients in a Tertiary Care Hospital. *J Clin Transl Hepatol* 2021; **9**: 32-39 [*RCA*] [PMID: 33604253 DOI: 10.14218/JCTH.2020.00076] [FullText] [Full Text(PDF)]

34 **Fischer P**, Pandrea S, Dan Grigorescu M, Stefanescu H, Tefas C, Hadade A, Procopet B, Ionescu D. The threat of carbapenem resistance in Eastern Europe in patients with decompensated cirrhosis admitted to intensive care unit. *Dig Liver Dis* 2022; **54**: 1385-1391 [*RCA*] [PMID: 35732546 DOI: 10.1016/j.dld.2022.05.011] [FullText]

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