prospective cohort with predefined radiological assessment, and ideally with a TKI-treated control arm.

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**Authors’ contributions**
All authors contributed to the design, writing, and final review of the paper.

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**Association of rectal colonisation by MDROs with new infection in cirrhosis**

*To the Editor:*

We read with interest the study by Prado et al. regarding the increased risk of rectal colonisation by multidrug resistant organisms (MDROs) in critically ill patients with cirrhosis, resulting in new clinical infections and poor short-term outcomes.¹ The study also depicted the differences in MDROs based on local epidemiological patterns. In practice, the routine use of rectal colonisation patterns, if validated in further prospective studies, may influence the use of early antibiotic prophylaxis to prevent potentially life-threatening new infections by MDROs in patients with cirrhosis. Certain issues require further consideration.

First, in the Barcelona study cohort, patients with cirrhosis in comparison to no cirrhosis had higher rates of MDRO colonisation at admission. This was expected due to the presence of well-established risk factors for MDRO colonisation in the cirrhosis group, such as recent hospitalisation (53.5% vs. 28.9%; p <0.01) and ICU admission (20.9% vs. 5.6%; p <0.01) within the prior 3 months and high rates of mechanical ventilation requirement. Interestingly, neither new colonisation rates during ICU stay nor new infection rates by colonising strains were different in patients with cirrhosis and no cirrhosis, respectively. More frequent rectal swabs (e.g. once in 3 days) may be more appropriate in sick patients with cirrhosis without rectal colonisation by baseline MDROs to best determine the time lag between rectal colonisation and new infections.²

Second, colonisation in the rectum could be commensals with different microbiological patterns in different regions worldwide. To establish the connection between a colonising strain and the infection causing strain, we need to do molecular typing to establish whether the same colonising bacteria from stool in each patient are also responsible for common peripheral infections, e.g. respiratory, urinary tract or spontaneous bacterial peritonitis. Species sub-classification is also essential to distinguish pathogenic from non-pathogenic strains.³

Third, patients with cirrhosis often require proton pump inhibitor (PPI)- and lactulose-based therapy during ICU stay. It is known that PPIs and lactulose affect gut colonisation and increase the risk of bacterial infections. The influence of these important risk factors on colonisation and infection rates in the present study is not known.⁴

Finally, the study should have elaborated on the influence of severity and etiology of liver disease on MRDO colonisation and infection rate. In the Barcelona cohort, there were 60 (46%) patients with acute-on-chronic liver failure (ACLF). Being a highly inflammatory and rapidly progressing liver state, recent studies have shown that patients with ACLF harbour highly pathogenic bacteria adding to the advanced nature of illness and sepsis with multi-organ dysfunction. The current study does not address the difference between colonising bacteria in patients with or

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**Keywords:** Rectal colonisation; MDRO; Cirrhosis; Infections.

**References**


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without ACLF. Further, it is not clearly described whether these patients with ACLF received steroids or other effective therapies as disease-modifying agents.

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**Authors’ contributions**
Both SPS and AJ contributed equally in manuscript writing and final editing.

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**Reply to: “Association of rectal colonisation by MDROs with new infection in cirrhosis”**

To the Editor:

We read with interest the letter by Dr. Singh et al.1 on our recent manuscript2 and we thank the authors for their thoughtful comments. Still, we think that some of the raised points deserve further clarification.

Firstly, our study does not support the authors conclusion that epidemiological surveillance in critically ill patients with cirrhosis could guide early antibiotic prophylaxis to prevent life-threatening new infections by MRDOs. We believe that our study suggests that data on rectal colonization could be used to delineate and de-escalate broad-spectrum empirical antibiotic strategies in this setting, as infections occurring in colonized patients are mainly caused by the colonizing resistant strain.

Secondly, colonization at ICU admission was higher in patients with cirrhosis, a feature that was directly correlated with the presence of well-established risk factors for antibiotic resistance. Recent hospitalization, ICU admission and systemic antibiotic exposure were much more prevalent in the cirrhotic population, a finding that explains the higher rate of MDRO rectal colonization at baseline. As pointed out by Dr. Singh et al., rates of new colonization during ICU stay and of new bacterial infections by MDROs during hospitalization were similar between critically ill patients with and without cirrhosis, a finding that was in some way unexpected considering the higher risk of nosocomial infections described in the literature in the cirrhotic population. Also, the patients without cirrhosis were critically ill and therefore at high risk of colonization and infection with MDROs. Epidemiological surveillance swabs were performed weekly following local practice guidelines. A higher frequency may be an interesting approach, though the potential benefit is probably outweighed by the associated costs.

Thirdly, Dr. Singh et al. raised a point regarding the potential benefit of molecular typing that ensures the concordance between the colonizing bacteria and the strain responsible for infection in our study. These techniques, which we have used in other studies, are still very costly and too complex to be easily applicable to clinical practice. We believe that, similar to other confirmatory studies carried out in populations other than cirrhosis,1–4 decisions based on classical microbiology are useful in clinical practice, since colonization by MDROs is associated with increased risk of infection by the colonizing bacteria.

Fourthly, we agree that the administration of proton pump inhibitors and lactulose can modify intestinal microbiota and therefore increase the risk of colonization by MDROs. Regrettfully, none of these variables was specifically investigated in our prospective dataset. However, patients with hepatic encephalopathy at ICU