LETTER TO THE EDITOR

Author Response

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We thank Salotagi S et al.[1] for their interest in our study. We have noted the reader's concerns regarding antibiotic selection and are hereby addressing their queries. It's essential to clarify that although a single dose of aminoglycosides or fosfomycin is conventionally reserved for managing uncomplicated lower urinary tract infections (UTIs), our study uniquely focused on patients admitted to the intensive care unit, manifesting signs of severe sepsis and septic shock. Furthermore, the severity of illness among these patients was underscored by a mean sequential organ failure assessment (SOFA) score was 7, indicative of a higher risk of ICU mortality estimated at around 30%.

In our study, samples exhibiting carbapenem resistance underwent testing using the VITEK 2 automated system, adhering to ISO standards to determine minimum inhibitory concentrations (MICs). The GeneXpert system, utilizing PCR technology detects the presence of carbapenem-resistant (CARBA-R) genes, including NDM, OXA-48, Imipenemase (IMP-1), and KPC. The interaction between CAZ-AVI and AZT was evaluated through a double-disk sandwich diffusion method. However, it's important to note that the genotypic and phenotypic correlation of CARBA-R *Enterobacteriaceae* falls outside the scope of our study's objectives.[2] We acknowledge the viewpoint expressed by our readers regarding the reserved use of ceftazidime-avibactam with aztreonam as a last-resort treatment for severe invasive infections. Notably, none of our patients received this combination therapy as an empirical option. Approximately 50% of patients were administered ceftazidime-avibactam with aztreonam as early targeted therapy following CARBA-R results, while the remainder received it after the final sensitivity report.[3,4]

The main study outcomes included evaluating clinical success on day 14 and the microbiological response. Clinical success was a composite outcome defined by various factors including patient survival, hemodynamic stability, and improvement in SOFA score. To analyze this composite outcome, a cox multivariate regression model was employed, adjusting for baseline SOFA score and existing comorbidities. Unlike univariate methods, the cox model enables simultaneous assessment of multiple factors, providing a thorough evaluation of their influence on survival time.[5]

Despite the promising results, it's crucial to acknowledge the limitations of our study, including the influence of clinician discretion in antibiotic selection and the potential for bias in patient allocation. We agree with the readers' suggestion that a well-structured randomized controlled trial would provide more robust evidence to address these limitations and offer clearer insights into treatment outcomes. Moving forward, further research is warranted to explore optimal treatment strategies for CARBA-R *Enterobacteriaceae* infections, taking into account factors such as infection severity, antibiotic resistance patterns, and individual patient characteristics. By continuing to advance our understanding of these complex infections, we can enhance patient outcomes and contribute to the global effort in combating antimicrobial resistance.

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