In vitro Antimicrobial Activity of Ceftazidime-Avibactam Tested against Carbapenem Resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* Clinical Isolates

Thesis

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Summary

There is growing complexity surrounding the treatment of MDR Gram-negative infections, with the necessity to understand both national and local epidemiology, how to provide adequate empiric coverage, and have sufficient surveillance to identify opportunities to treat bacteria and minimize emerging resistance mechanisms with new agents.

The overwhelming prevalence of antibiotic resistance is a critical public health problem. MDR Gram-negative bacteria, particularly those resistant to carbapenems become a global threat as their Infections are associated with high morbidity and mortality rates, especially in patients with serious underlying diseases or ICUs patients.

Carbapenem resistant organisms are resistant to almost all β -lactams leaving only few available options for treatment. These limited therapeutic options are highlighting the need for new antibiotics to treat serious infections caused by these resistant strains.

Ceftazidime/avibactam is a semisynthetic non β -lactam β -lactamaes that was launched worldwide which demonstrated to be effective and safety in patients with gram-negative infections and it was FDA and EMA approved for complicated urinary infections complicated intra-abdominal infection and hospital associated pneumonia including ventilator-associated pneumonia and other infections due to aerobic gram-negative bacteria when there are limited treatment options .

This suggests that ceftazidime-avibactam can be used in the treatment of infections caused by MDR pathogens including CRO organisms.

In this study we aimed to assess the in vitro activity of ceftazidime-avibactam against carbapenem-resistant *Enterobacteraece* and *pseudomonas aeurginosa* isolates, also to determine Prevalence of carbapenem resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* clinical isolates.

We found Prevalence of carbapenem resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* clinical isolates was 72.6%

Thirty hundred twenty CRO isolates were collected from different clinical samples at microbiology unit of CUSPH Ceftazidime-avibactam susceptibility testing was done using disk diffusion method and and the presence of carbapenemases was detected by mCIM and multiplex PCR tests in 170 CRO .

In our study, mCIM was positive in 92.4% of the isolates, and $bla_{\rm NDM}$ gene was the most frequently detected carbapenemase gene in 70.0% of the isolates, followed by $bla_{\rm OXA-48}$ gene in 67.6% and $bla_{\rm KPC}$ gene in 16.5%. ceftazidime-avibactam was active against 30.0% of the isolates and it showed the highest sensitivity compared to the other tested antibiotics.