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EVALUATION OF THE EFFICACY OF A PHAGE COCKTAIL AGAINST GENTAMICIN-RESISTANT *Klebsiella pneumoniae*

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Abstract: The bacteria *Klebsiella pneumoniae* is one of top aetiological agents associated with nosocomial infection, and it has gained its notoriety with the emergence of multidrug resistance strains. In this study, we evaluated the effect of lytic bacteriophage cocktail isolated from our local sewage as potential antimicrobial candidate against Gentamicin-resistant *Klebsiella pneumoniae*. A total of five clinical-acquired *K. pneumoniae* isolates including a carbapenem-resistant *K. pneumoniae* (CRKP) strain showed resistance towards gentamicin (GN). Phages were isolated using double-layer agar method against clinical- and community-acquired *K. pneumoniae* as host strains. Phage characterization using PCR partial sequencing of different viral genes; Lysin, Major Capsid Protein (g23) and Tail Fiber Protein has suggested that these phages possibly belonged to Myoviridae (ϕKPaV04, ϕKPaV08, ϕKPaV12) and Podoviridae (ϕKPaV03, ϕKPaV10). The characterized phages was selected for cocktail have exhibited high titer and broad host range with 22-44% lysis towards a panel of 18 *K. pneumoniae* strains. The antimicrobial efficacy of a single phage cocktail administration showed 80% growth suppression of GN-resistant *K. pneumoniae* after 18 h of incubation. Suggesting the possibility of phage cocktail to be used against nosocomial infections by multidrug resistant bacteria including being an alternative to antibiotic GN in the treatment of CRKP infections.

Keywords: Gentamicin-resistant, bacteriophage, *Klebsiella pneumoniae*.

Introduction

Nosocomial infections, also known as hospital-acquired infections refer to any systemic or localized conditions in patients that result from the reaction caused by an infectious agent or toxin contracted within a hospital environment (Kouchak & Askarian, 2012). The most common type of infections includes bloodstream infections (BSI), catheter-associated urinary tract infections (UTI), surgical site infections (SSI) and ventilator-associated pneumonia (VAP) (Khan *et al*., 2017). Pathogens referred to as the 'ESKAPE' bugs with growing multidrug resistance and virulence are responsible for the majority of nosocomial infections. These ESKAPE pathogens consist of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. (Rice, 2008). Antimicrobial resistance in these pathogens causing high risk of mortality and morbidity are among the 12 bacteria listed by the World Health Organization (WHO) to urgently directed the research and development of new antibiotics (Tacconelli *et al*., 2018).

Klebsiella pneumoniae is a gram-negative encapsulated bacillus that belong to the Enterobacteriaceae family. *K. pneumoniae* is commonly found in the human gastrointestinal tract but instead, is frequently linked to lower respiratory tract infection and catheter-associated urinary tract infection (Navidinia, 2008). The emergence of *K. pneumoniae* exhibiting multidrug resistance phenotypes has made the nosocomial infections difficult to treat. K. *pneumoniae* is progressively resistant towards penicillin and ampicillin caused by genes classified as ESBL (extended-spectrum