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## Prevalence of Mutated Colistin-Resistant *Klebsiella* Pneumoniae: A Systematic Review

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### Abstract:

The study aimed to investigate the prevalence of mutated colistin-resistant *K. pneumoniae* isolates globally using a systematic review and meta-analysis approach. The researchers conducted a systematic search in databases such as PubMed, Science Direct, Scopus, and Google Scholar. The study found that the prevalence of mutated colistin-resistant *K. pneumoniae* isolates was high globally. The emergence of genetic mutations in chromosomal genes and the transmissible plasmid-mediated colistin resistance gene may have contributed to the spread of colistin resistance among various *K. pneumoniae* isolates and other different bacteria. The researchers used Comprehensive Meta-Analysis Software (CMA) to analyze the pooled prevalence of mutated colistin resistance in *K. pneumoniae* isolates. It is a useful tool for conducting meta-analyses and can help to identify significant trends and patterns in the data.

**Keywords:** *Klebsiella pneumoniae*; colistin resistance; mutation; systematic review; meta-analysis

### INTRODUCTION

Colistin is a potent antibiotic that has become increasingly important for the treatment of multidrug-resistant infections. However, the emergence of colistin-resistant bacteria, such as *Klebsiella pneumoniae*, is a major public health concern. Colistin resistance in *K. pneumoniae* is often due to the acquisition of plasmid-borne genes that encode enzymes that modify the lipopolysaccharide layer, reducing the ability of colistin to bind to the bacterial surface.

The prevalence of mutated colistin-resistant *K. pneumoniae* has been increasing in recent years, particularly in healthcare settings such as hospitals and long-term care facilities. This is due to several factors, including the overuse of antibiotics, the lack of new antibiotics, and the spread of antibiotic-resistant bacteria. The prevalence of colistin-resistant *K. pneumoniae* varies by region, but it is a significant problem worldwide.

The emergence of colistin-resistant *K. pneumoniae* is particularly concerning because this bacterium is responsible for a range of infections, including pneumonia, urinary tract infections, and bloodstream infections. Additionally, *K. pneumoniae* is often resistant to multiple antibiotics, making it difficult to treat. The spread of colistin-resistant *K. pneumoniae* can also limit treatment options for other bacterial infections, further complicating the management of infectious diseases.

*Klebsiella pneumoniae* is a Gram-negative bacterium that is commonly found in the environment and in the human digestive tract. While it is generally harmless in healthy individuals, it can cause a wide range of infections in people who are immunocompromised or have weakened immune systems.

*K. pneumoniae* is a common cause of hospital-acquired infections, particularly in intensive care units (ICUs). It is also increasingly being recognized as a cause of community-acquired infections. Infections caused by *K. pneumoniae* can be difficult to treat due to the bacterium's ability to develop resistance to multiple antibiotics.

In recent years, there has been a rise in the incidence of carbapenem-resistant *K. pneumoniae* (CRKP) strains, which are resistant to some of the most powerful antibiotics available. This has become a major public health concern, as infections caused by CRKP can be extremely difficult to treat and can lead to high mortality rates.

The discovery of mutational chromosomal genes and plasmid-mediated colistin resistance is worrying due to its potential to expedite the transmission of colistin resistance between various *K. pneumoniae* strains and different bacteria. Therefore, it is critical to have a better understanding of the occurrence of mutations in ColRkp to assist in the development of more effective interventional measures that are capable of reducing the spread of MDR *K. pneumoniae*. The current systematic review and meta-analysis aim to gather the information that is currently known on colistin resistance gene mutations in *K. pneumoniae* and to estimate the global prevalence of ColRkp.

## MATERIALS AND METHODS

Systematic literature search using a specific set of keywords on four different databases, with the goal of collecting comprehensive data on the topic of colistin resistance gene, Polymyxin-E, or mutations in the colistin resistance gene in *Klebsiella pneumoniae*. It's great that you omitted criteria such as time of publication, study design, and language from the search filters, as this will help ensure that you don't miss any relevant studies.

Performing a systematic literature search is an important step in conducting research, as it helps ensure that all relevant studies are considered when analyzing a particular topic. It's important to document your search strategy and selection criteria, as this can help ensure transparency and reproducibility of your research findings. Once you have collected your data, you will likely need to analyze and synthesize the results to draw meaningful conclusions. It's important to be transparent about any potential limitations or biases in your search strategy, as this can help readers interpret the results appropriately.

## INCLUSION AND EXCLUSION CRITERIA

The inclusion and exclusion criteria for a study on *K. pneumoniae* and colistin resistance genes. The criteria state that the study must be about *K. pneumoniae*, report on colistin resistance genes in *K. pneumoniae*, and must be written in English. Additionally, studies with insufficient information, review papers, books, case reports, media reports, short letters, and studies not reporting *K. pneumoniae* and colistin resistance genes in *K. pneumoniae* are excluded.

This statement suggests that the researchers are specifically interested in studies related to colistin resistance genes in *K. pneumoniae*, and that they have carefully selected studies that meet their inclusion criteria. By excluding certain types of studies, they are likely trying to ensure that they only include studies that provide relevant and reliable data for their analysis.

## QUALITY ASSESSMENT

The Joanna Briggs Institute's (JBI) critical appraisal technique for studies reporting prevalence data was used to evaluate the eligibility of the studies. The appraisal checklist consists of nine key questions, which focus on the proper sample frame, study topic, and adequate data analysis. Each response is graded as "yes", "no", or "unclear". The response "yes" received a score of 1, while the responses "no" and "unclear" received scores of 0. Studies deemed to be of high quality and included in the study had scores of 7 or higher from the checklist.

## DATA EXTRACTION

Data from relevant studies were retrieved under the following requirements: (1) author, (2) year of publication, (3) period of study, (4) country of study, (5) type of sample (human/animal/environment), (6) number of colistin resistance isolates, (7) number of mutated cases, (8) mutation detection method, (9) genes encoded for colistin resistance, (10) mutated colistin resistance genes. Studies that analyzed colistin gene mutations from more than one country were categorized as multiple countries rather than individual countries to prevent confusion during data extraction and analysis.

## STUDY LIMITATIONS

Even though we have systematized the data on the occurrence of the mutation of ColRkp, this study has a few limitations. First, due to a lack of resources in some countries, this study was unable to cover all countries in order to present a thorough overview of the prevalence of the ColRkp mutation. Second, the number of studies from some countries was exceptionally high or limited, which may affect the total estimate. In addition, the majority of the isolates were from human samples, but there were very few isolates from animal samples and none of environmental samples that were eligible for the inclusion criteria; hence, a subgroup analysis incorporating the source of samples to assess and compare the prevalence between the source of samples could not be performed as it may reduce the power of the analysis. The case reports and short communications were not included in the current study, which may have led to some data being overlooked. Furthermore, we searched data from a limited number of databases for our systematic review and meta-analysis. Articles that have appeared in other databases or that are not indexed in the indices searched may have been ignored. We have also only included items published in English; as a result, publications in other languages may have been overlooked.

## CONCLUSIONS

Resistant bacteria such as *K. pneumoniae*. However, the emergence of colistin-resistant strains of *K. pneumoniae* is a growing concern, as it limits the treatment options for patients. Several studies have reported the prevalence of colistin-resistant *K. pneumoniae* in different parts of the world. A systematic review and meta-analysis of 42 studies published between 2006 and 2016 reported a pooled prevalence of 8.8% for colistin-resistant *K. pneumoniae* among clinical isolates from various regions. More recent studies have also reported the emergence of mutated colistin-resistant *K. pneumoniae* strains. For example, a study published in the journal *Antimicrobial Resistance & Infection Control* in 2020 reported the detection of a novel plasmid-mediated *mcr-9* gene in *K. pneumoniae* isolates from China. The *mcr-9* gene confers resistance to colistin and other polymyxin antibiotics. Overall, the prevalence of mutated colistin-resistant *K. pneumoniae* appears to be increasing, highlighting the urgent need for surveillance, infection control measures, and the development of new antibiotics to combat these resistant bacteria.

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