

INPLASY PROTOCOL

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Corresponding author:
Mohan Ju

08301010203@fudan.edu.cn

Author Affiliation:
Huashan Hospital North,
Fudan University

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No conflicts of interest.

Predictors of mortality in patients infected with carbapenem-resistant *Klebsiella pneumoniae*: A systematic review and meta-analysis

Qian, Y¹; Bi, Y²; Liu, S³; Ju, M⁴.

Review question / Objective: What risk factors are associated with mortality in patients infected with carbapenem-resistant *Klebsiella pneumoniae*?

Condition being studied: Some previous researches reported that patients infected with carbapenem-resistant *Klebsiella pneumoniae* have higher mortality rate compared with those with carbapenem-susceptible *Klebsiella pneumoniae*. Identification of risk factors for death caused by CRKP infection is crucial for early implementation of an appropriate therapy and improving patients' outcome. Many studies have attempted to identify all risk factors, However, studies investigating predictors of mortality in patients infected with CRKP produced inconsistent results. Therefore, we conducted a systematic review and meta-analysis to evaluate the relation between possible risk factors and mortality inpatients with CRKP infection.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 October 2020 and was last updated on 11 October 2020 (registration number INPLASY2020100037).

INTRODUCTION

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with carbapenem-resistant *Klebsiella pneumoniae* have higher mortality rate compared with those with carbapenem-susceptible *Klebsiella pneumoniae*. Identification of risk factors for death caused by CRKP infection is crucial for early implementation of an appropriate therapy and improving patients' outcome. Many studies have attempted to identify all

risk factors, However, studies investigating predictors of mortality in patients infected with CRKP produced inconsistent results. Therefore, we conducted a systematic review and meta-analysis to evaluate the relation between possible risk factors and mortality inpatients with CRKP infection.

METHODS

Search strategy: Two independent examiners (MH.J. and YY.Q.) performed a comprehensive search in the MEDLINE, Cochrane Library, and EMBASE databases from their inception to May 31, 2020 to identify potentially relevant studies. The initial search strategy includes terms related to ‘Klebsiella pneumoniae’ OR ‘K pneumoniae infection’ OR ‘Klebsiella) AND ‘resistance’ AND (‘carbapenem’ OR ‘imipenem’ OR ‘meropenem’ OR ‘ertapenem’ OR ‘doripenem’) AND (‘mortality’ OR ‘fatality’ OR ‘lethality’ OR ‘prognosis’ OR ‘predictor’ OR ‘survival’). In addition, the reference lists cited by eligible retrieved articles were manually searched to maximize inclusion of relevant data. We did not perform grey literature searches or systematically search for unpublished data. Only articles written in English were reviewed.

Participant or population: Adults with infection caused by carbapenem-resistant *Klebsiella pneumoniae*.

Intervention: Risk factors associated with mortality in patients infected with carbapenem-resistant *Klebsiella pneumoniae*.

Comparator: Survivors of patients infected with CRKP.

Study designs to be included: Studies reporting risk factors of mortality in patients infected with CRKP were included in this meta-analysis.

Eligibility criteria: In this meta-analysis, observational studies reporting mortality and associated risk factors of patients infected with CRKP were included. Carbapenem resistance was defined as

resistance to carbapenems, such as imipenem, meropenem, ertapenem, or doripenem, irrespective of susceptibility to other antibiotics. The primary outcome was mortality. On the other hand, after reviewing by 2 independent examiners, non-original articles, such as reviews, meta-analyses, etc., case reports, in vitro or experimental animal studies, or pediatric researches were not included. Researches in which CRKP status (infection/colonization) was not clarified were also excluded.

Information sources: Pubmed, Embase and Cochrane library.

Main outcome(s): Mortality of patients with CRKP infection.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale score (NOS), ranging from 0-9 for quality assurance, was used for the methodological quality assessment of articles included. Two independent examiners (MH.J. and YY.Q.) performed NOS for each study. Inconsistencies between the two investigators were extensively discussed until agreement was achieved. Studies with NOS score of 5 or greater underwent further analysis, while others were excluded because of the potential high risk of bias.

Strategy of data synthesis: Statistical analyses were performed using Review Manager (version 5.3 software). We tested between study heterogeneity with the Q statistic (significant when $p < 0.10$) and quantified the extent of heterogeneity with the I² statistic. It is common practice to interpret I² > 50% as representing substantial inconsistency or significant statistical heterogeneity. The pooled odds ratio (OR) and 95% confidence interval (CI) were calculated to express binary outcome results, while weighted mean difference (WMD) and 95% CI were used for the expression of continuous outcome results.

Subgroup analysis: It is common practice to interpret I² > 50% as representing substantial inconsistency or significant

statistical heterogeneity. If this happens, a subgroup analysis may be performed.

Sensibility analysis: The sensitivity analysis on the literature included, it was through eliminating one study at a time in the process of meta-analysis to observe the change of merging effect, so as to illustrate the stability and accuracy of the results. The publication bias was identified by the funnel plots.

Language: English.

Country(ies) involved: China.

Keywords: Carbapenem resistance; *Klebsiella pneumoniae*; Risk factors; Mortality.

Contributions of each author:

Author 1 - Yiyi Qian.

Author 2 - Yingmin Bi.

Author 3 - Shuang Liu.

Author 4 - Mohan Ju.