



Clinical predictors and outcomes of *Klebsiella pneumoniae* bacteraemia in a regional hospital in Hong Kong

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SUMMARY

Background: *Klebsiella pneumoniae* (KP) infection is associated with high morbidity and mortality. Multidrug resistance, especially extended-spectrum β -lactamase (ESBL) production, in KP is endemic worldwide.

Aim: To evaluate the clinical characteristics and outcomes of patients with KP bacteraemia in critical care and general ward settings.

Methods: Adult patients admitted to a regional hospital in Hong Kong from January 1st, 2009 to June 30th, 2016 (7.5 years) with KP bacteraemia were included. Demographics, clinical features, microbiological characteristics, and outcomes were analysed.

Findings: Among 853 patients, 178 (20.9%) required critical care and 176 (20.6%) died within 30 days of hospital admission. Thirty-day survivors were younger ($P < 0.001$), had milder disease (defined by Sequential Organ Failure Assessment score) ($P < 0.001$), presented with hepatobiliary sepsis ($P < 0.001$) or urosepsis ($P < 0.001$), less septic shock ($P = 0.013$), fewer invasive organ supports ($P < 0.001$), and had appropriate empirical antibiotics ($P < 0.001$). Cox regression analysis showed that respiratory tract infection (hazard ratio: 2.99; 95% confidence interval: 2.061–4.337; $P \leq 0.001$), gastrointestinal tract infection (excluding hepatobiliary system) (2.763; 1.761–4.337; $P \leq 0.001$), mechanical ventilation (2.202; 1.506–3.221; $P \leq 0.001$), medical case (1.830; 1.253–2.672; $P = 0.002$), inappropriate empirical antibiotics (1.716; 1.267–2.324; $P \leq 0.001$), female (1.699; 1.251–2.307; $P < 0.001$), age > 65 years (1.692; 1.160–2.467; $P = 0.006$), and presence of solid tumour (1.457; 1.056–2.009; $P = 0.022$) were independent risk factors for 30-day mortality. Unexpectedly, diabetes mellitus was associated with better 30-day survival ($P = 0.002$). A total of 102 patients (12.0%) had infections with ESBL-producing strains, which were not associated with higher 30-day mortality.

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Conclusion: KP bacteraemia is associated with high 30-day mortality. Site of infection, patients' comorbidities and appropriate use of empirical antibiotic are important predictors of patients' outcomes.

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Introduction

Klebsiella pneumoniae (KP) bacteraemia is associated with high mortality in both general wards and intensive care units (ICUs) [1], with a significant number of patients dying within two days of admission [2].

The emergence of multidrug-resistant KP infections, notably carbapenemase-producing (CP) and extended spectrum β -lactamase (ESBL)-producing strains, is an increasing threat, being associated with significant morbidity and mortality worldwide [3–9]. In endemic countries such as Greece, 10% of patients admitted to ICU were found to have CP-KP infection [10]. CP-KP bacteraemia has been associated with four times greater mortality than non-CP-KP bacteraemia [11].

Local data have suggested that patients with malignancy or liver disease tend to have worse outcomes when contracting KP [12]. Wider literature review suggests that advanced age, respiratory tract infection and inappropriate antimicrobial therapy are predictors of mortality in community-acquired KP bacteraemia [5]. Early appropriate antimicrobial use significantly improves clinical outcome [13]. Efforts have been made to identify a mortality risk score for KP bacteraemia; however, further refinement and validation in clinical practice is required [14]. There is a scarcity of evidence for reproducible clinical predictors of KP bacteraemia upon which to develop risk scores, and the problem is compounded by the increasing proportion of KP isolates that are antibiotic resistant.

Our study aimed to evaluate the incidence, clinical characteristics and outcomes of patients with KP bacteraemia in critical care and general ward settings in a regional hospital in Hong Kong.

Methods

Study design and data collection

Adult patients with KP bacteraemia admitted to Pamela Youde Nethersole Eastern Hospital, a 1700-bed regional hospital in Hong Kong that provides comprehensive services except cardiothoracic surgery, transplant surgery and burns, within the period from January 1st, 2009 to June 30th, 2016 were included. Patients aged <18 years were excluded. The medical records, data in clinical management systems and clinical information systems (IntelliVue Clinical Information Portfolio, Philips Medical, Amsterdam, Netherlands) were reviewed retrospectively. Demographics, past medical histories, diagnoses, clinical parameters, microbiological data, and drug information were identified.

Disease severity was quantified using the Sequential Organ Failure Assessment (SOFA) score [15,16]. Clinical data included the use of invasive organ supports including inotropic use, mechanical ventilation and renal replacement therapies, ICU and hospital length of stay, together with mortality.

Primary outcome was 30-day mortality and secondary outcomes were ICU and hospital mortality as well as ICU and hospital length of stay.

Definitions

Klebsiella pneumoniae bacteraemia was defined as one or more blood cultures growing KP. If more than one positive blood culture was obtained from any patient, only the first one was included.

Empiric antimicrobial was defined as the antimicrobial used within 24 h of the culture being taken. Appropriate empirical antimicrobial was defined as at least one of the empirical antimicrobials matching the in-vitro susceptibility pattern [17–19]. Prior steroid use was defined as oral or intravenous administration of steroid within 30 days before the index positive blood culture. Chemotherapy use was defined as biological agents or chemotherapy administered within 30 days before the index positive blood culture. Any antibiotics use within 30 days before the index hospital admission was regarded as prior antibiotics use.

Microbiology

Blood cultures were incubated and processed, and KP identified, using standard methods. Antibiotic susceptibility testing was based on the Clinical and Laboratory Standards Institute interpretive criteria [20–26]. ESBL testing was based on Clinical and Laboratory Standards Institute testing criteria [20–26] or used the double-disk synergy test described by Jarlier *et al.* [27]. Carbapenem-resistant (CR) KP isolates were sent to the Public Health Laboratory Centre of Hong Kong (PHLC) for confirmatory genetic testing.

Ethics

This study was approved by the hospital ethics committee and written informed consent was waived.

Statistical analysis

Comparisons were performed between (i) survivors and non-survivors, and (ii) ESBL-producing and non-ESBL-producing KP. Results were expressed as mean \pm standard deviation (SD) or as number of cases and percentages as appropriate. Univariate analysis for categorical variables was compared using Pearson χ^2 -tests or Fisher's exact test as appropriate. Student's *t*-test or Mann–Whitney *U*-test was used to compare continuous variables. Variables with $P < 0.2$ in univariate analysis or with clinical significance from previous studies were included within the multivariate analysis. Cox regression analysis (forward stepwise approach) was used to assess independent predictors for 30-day mortality. Logistic regression analysis was used to assess independent predictors for the presence of ESBL KP infection. All

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