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Bacteremic community-acquired infections due to *Klebsiella pneumoniae*: clinical and microbiological presentation in New Caledonia, 2008–2013

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SUMMARY

Objectives: To provide data on severe bacteremic community-acquired infections due to *Klebsiella pneumoniae* in New Caledonia.
Methods: All patients admitted with bacteremic community-acquired infections due to *K. pneumoniae* at the only tertiary medical center in New Caledonia, from 2008 to 2013, were included retrospectively in this study. Clinical and microbiological characteristics were analyzed, as well as risk factors for mortality.
Results: The characteristics of 119 patients were analyzed. The most common clinical presentation was urinary tract infection (40 cases, 33%), followed by pneumonia (28 cases, 23%), deep abscesses (15 cases, 13%), liver abscess (12 cases, 9%), meningitis in (five cases, 4%), and endophthalmitis (two cases, 1%). Multiple localizations were reported in 18 cases (15%) and isolated bacteremia was reported in 22 cases (18%). The overall mortality rate was 22% (26/119) and the mortality rate in the intensive care unit was 33% (14/42). Renal impairment, chronic liver disease, pneumonia, and isolated bacteremia were independent risk factors for mortality.
Conclusions: *K. pneumoniae* is a dominant cause of severe community-acquired bacteremic infection in New Caledonia. Physicians should be aware of the poor prognosis of any patient with a bacteremic *K. pneumoniae* infection and should monitor patients presenting with risk factors closely.

1. Introduction

Klebsiella pneumoniae is a common Gram-negative bacterium with worldwide distribution, classically causing nosocomial infections, community-acquired pneumonia, liver abscess, and urinary tract infections, mostly in patients with underlying diseases.[1–4] However, in specific regions such as Taiwan, *K. pneumoniae* bacteremia is more likely to be community-acquired compared with the USA, Australia, South Africa, Europe, and Argentina.[5] Moreover, this pathogen has recently emerged as a major cause of a severe infectious syndrome including liver abscess without underlying hepatobiliary disease, potentially associated with metastatic localizations such as meningitis or endophthalmitis.[6,7] This syndrome is considered a serious public health problem in Southeast Asia.[8] Risk factors for such infections include diabetes mellitus and a potential genetic predisposition.[6] The *K. pneumoniae* isolates from severe invasive infections are often hypermucoviscous and frequently belong to the capsular serotype K1 or K2.[9,10]

To date, severe community-acquired *K. pneumoniae* infections have not been explored in New Caledonia. The aim of the present study was to report the epidemiology, clinical presentations, microbiological features, and outcomes through a retrospective cohort study of adult patients admitted to the only tertiary referral hospital for bacteremic community-acquired infections due to *K. pneumoniae* in New Caledonia.

2. Methods

2.1. Patient selection

Microbiology records were used to identify consecutive patients with bacteremia due to *K. pneumoniae* admitted between January 2008 and December 2013 to the Centre Hospitalier

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Territorial, the only tertiary referral center in New Caledonia. The medical records of patients with a community-acquired bacteremic infection were reviewed. Community-acquired infection was defined as the acquisition of the infection outside a hospital, long-term care facility, or nursing home. Bacteremia was defined as the presence of at least one blood culture sampled within 48 h of presentation in the hospital yielding a pathogen presumed to be the cause of the infection. The diagnosis was confirmed by two infectious diseases specialists. The institutional review board of New Caledonia approved this study.

2.2. Data collection and definition

The following data were collected for each patient: demographic characteristics, underlying diseases or risk factors, clinical variables present at admission, laboratory data, empirical and concordant antibiotics received, admission to the intensive care unit (ICU), days of hospitalization, and in-hospital death. Concordant antibiotic therapy was defined as the initial antibiotic therapy including any antibiotic to which the infecting organism was sensitive based on the microbiology report.

2.3. Microbiology laboratory procedures

The VITEK 2 system (bioMérieux, Marcy l'Etoile, France) was used to confirm bacterial identifications. The antimicrobial susceptibility of *K. pneumoniae* was tested by disk diffusion method and results were interpreted in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI; M100-S17 2007). Extended-spectrum beta-lactamase (ESBL) production was determined using a double-disk potentiation test with amoxicillin–clavulanic acid and cefotaxime, ceftazidime, or cefepime using the ESBL-positive results of the VITEK 2 N131 card.

2.4. Statistical analysis

Contingency data were analyzed by two-tailed Chi-square test or Fisher's exact test, and continuous data were analyzed by Student *t*-test or the Mann–Whitney *U*-test. A *p*-value of <0.05 was considered to be statistically significant, and all probabilities were two-tailed. Variables with *p*-values of <0.10 on univariate analysis were subsequently entered into the multivariate analysis. The multivariate logistic regression model was used to evaluate risk factors for mortality in bacteremic infections caused by *K. pneumoniae*. All statistical analyses were performed using Stata version 12.0 software (StataCorp LP, College Station, TX, US).

3. Results

The characteristics of 119 patients were analyzed. Demographic characteristics and clinical presentations are shown in Table 1. A majority (55%) of the patients were younger than 65 years of age. The most common clinical presentation was urinary tract infection (40 cases, 33%), followed by pneumonia (28 cases, 23%), deep abscesses (15 cases, 13%), liver abscess (12 cases, 9%), meningitis (five cases, 4%), and endophthalmitis (two cases, 1%). Multiple localizations were reported in 18 cases (15%) and isolated bacteremia was reported in 22 cases (18%) (Table 2).

The mean duration of hospitalization was 15 days (95% confidence interval (CI) 10–22 days) and the mean duration between the onset of symptoms and hospitalization was 2 days (95% CI 1–4 days). Forty-two (35%) patients were admitted to the ICU. The mean duration of stay in the ICU was 32 days (95% CI 12–44 days). Twenty-three (19%) patients presented with septic shock. Concordant antibiotic treatment was given to 85 (90%) patients with bacteremic *K. pneumoniae* infection according to the results of susceptibility testing. ESBL-related resistance phenotypes were identified in four (3%) cases. The overall mortality rate was 22% (26/119) and the mortality rate in the ICU was 33% (14/42). Factors associated with mortality in bacteremic *K. pneumoniae* infection are listed in Table 3. Renal impairment (odds ratio (OR) 2.7, 95% CI 1.1–3.5; $p = 0.03$), chronic liver disease (OR 2.9, 95% CI 2.1–5.3; $p < 0.001$), pneumonia (OR 2.9, 95% CI 2.0–5.9; $p < 0.001$), and isolated bacteremia (OR 2.5, 95% CI 1.2–5.1; $p = 0.02$) were independent risk factors for mortality.

Table 1
Clinical characteristics at presentation and outcome of patients with bacteremic infection due to *Klebsiella pneumoniae*, New Caledonia 2008–2013

Variables ($N = 119$)	*n* (%) or mean (range)
Sex	
Male	51 (43)
Female	68 (57)
Age, years	58 (44–70)
Ethnicity	
Melanesian	57 (48)
Asian	9 (7)
Other	34 (45)
Comorbidities	
Diabetes mellitus	45 (38)
Renal impairment	11 (9)
Chronic liver disease	17 (14)
Immunosuppressive treatment	11 (9)
Outcome	
Death	26 (22)
Use of vasopressors	23 (19)
ICU length of stay, days	8 (2–13)
Duration of hospitalization, days	15 (7–60)

ICU, intensive care unit.

3.1. Susceptibility testing

Out of the 119 *K. pneumoniae* isolates, 64 (54%) showed uniform resistance to ampicillin, ticarcillin, and piperacillin and susceptibility to a number of classes of antibiotic, including clavulanic acid, quinolones, cephalosporins, co-trimoxazole, macrolides, and aminoglycosides (defining the wild phenotype). Four (3%) isolates showed ESBL production.

4. Discussion

K. pneumoniae is a major cause of infection worldwide, including in New Caledonia. The present study further highlights the role of *K. pneumoniae* as a dominant pathogen in community-acquired bacteremic infections in the Pacific Region. Although conducted in a single institution, the findings of the present study are compatible with those of previous studies conducted in the

Table 2
Site of infection among patients with *Klebsiella pneumoniae* identified in blood culture, New Caledonia 2008–2013

Site of infection ($N = 119$)	*n* (%)
Urinary tract infection	40 (33)
Pneumonia	28 (23)
Deep abscess	15 (13)
Liver abscess	12 (9)
Meningitis	5 (4)
Endophthalmitis	2 (1)
Soft tissue infection	4 (3)
Multiple localizations	18 (15)
Isolated bacteremia	22 (18)

Table 3
Risk factors associated with mortality among patients with *Klebsiella pneumoniae* identified in blood culture, New Caledonia 2008–2013

Variable	Univariate analysis		Multivariate analysis	
	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value
Age	3.1 (0.6–4.9)	0.33		
Sex	1.0 (0.8–1.9)	0.67		
Diabetes	0.3 (0.1–2.2)	0.59		
Renal impairment	2.5 (1.2–5.1)	0.04	2.7 (1.1–3.5)	0.03
Chronic liver disease	3.4 (2.8–5.9)	<0.001	2.9 (2.1–5.3)	<0.001
Pneumonia	3.6 (2.9–6.9)	<0.001	2.9 (2.0–5.9)	<0.001
Isolated bacteremia	2.2 (1.3–5.0)	0.02	2.5 (1.2–5.1)	0.02
ESBL phenotype	1.2 (0.7–2.9)	0.77		
Concordant antibiotherapy	0.7 (0.5–3.9)	0.8		

RR, relative risk; CI, confidence interval; ESBL, extended-spectrum beta-lactamase.

Pacific Region, and again reflect the highly endemic nature of *K. pneumoniae* infections in this area.[11]

Similarly to the present study, other studies have described steatosis and liver cirrhosis as the main risk factors for Klebsiella primary liver abscesses.[12,13] Moreover, bacteremic community-acquired pneumonia due to *K. pneumoniae* is significantly associated with alcoholism.[5] Another study has found alcoholism to be a risk factor for a poor outcome of bacteremic community-acquired pneumonia due to *K. pneumoniae*.[14] Although chronic alcoholism was reported in only seven patients in the present study, with no association with mortality, it is likely that this comorbidity was under-reported since chronic alcoholism is endemic in New Caledonia.[15]

Another striking finding is that isolated bacteremia was an independent risk factor for mortality. This result suggests that the underlying cause of bacteremia should be scrutinized with attention, including liver abscess. The mortality rate from bacteremic infection due to *K. pneumoniae* in those admitted to the ICU was high (33%) in this study, despite appropriate empiric antibiotics and supportive care being provided in most cases. A previous study found that the first 48 h in the development of community-acquired pneumonia are critical.[16] Importantly, the time lag between symptom onset and the initiation of antibiotherapy was found to be significantly associated with mortality, which has been proposed as a major determinant of the outcome in severe infections.[17] Likewise, physicians should be aware of the high mortality rate in patients with bacteremic infections due to *K. pneumoniae* and should monitor patients more closely. Knowledge of the different characteristics of *K. pneumoniae* bacteremia infection is of great importance for physicians in endemic areas such as New Caledonia. It is also vital for the medical community in which physicians are constantly faced with the diagnostic and prognostic challenges of severely infected patients with uncommon pathogens.

A few limitations of this study deserve careful consideration. First, due to the retrospective nature of the study, there were some missing data, as illustrated by the lack of information related to past medical history. Second, therapeutic strategies (including antimicrobial therapy) were not standardized. Third, it was not possible to study the phenotypic and genotypic characteristics of the *K. pneumoniae* in this analysis (including K1 and K2 serotypes, hypermucoviscosity phenotype, and the aerobactin rmpA genes), and strain specificities seem to be a major element of metastatic localization[10] and severity of infection.[9] This requires specific investigations, which were not performed routinely. As not all of the patients were admitted to the ICU, the interest of such predictor tools remains to be demonstrated in the context of bacteremia due to *K. pneumoniae*.

In conclusion, *K. pneumoniae* is a dominant cause of severe bacteremic infection in the study tertiary-care hospital in New Caledonia. Bacteremia infections due to *K. pneumoniae* are associated with a high mortality, despite an excellent proportion of initial adequate antibiotherapy in New Caledonia. Physicians should be aware of the poor prognosis of any patient with a bacteremic *K. pneumoniae* infection and should monitor these patients closely. In the future, the determination of factors related to the host, i.e., genetic susceptibility, and to bacteria, i.e., virulence, is likely to be crucial for a better understanding of the pathophysiology of invasive infections due to *K. pneumoniae*.

Conflict of interest: None declared.

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