DOI：10.6314/JIMT.202608_37(4).01 內科學誌 2026：37：227-237

Clinical Characteristics and Microbiological Features of Serotype K54 Klebsiella pneumoniae Bacteremia: A Single-Center Retrospective Study from Taiwan

Ming-Hang Tsai[1], Ching-Hsun Wang[2], Feng-Yee Chang[2], L. Kristopher Siu[3], Jung-Chung Lin[2], Esther Yip-Mei Liu[2], Sheng-Kang Chiu[4], Kuan-Yu Chen[2]

[1]Division of Infectious, Department of Medicine, Tri-Service General Hospital Song Shan Branch, National Defense Medical University, Taipei, Taiwan.
[2]Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical University, Taipei, Taiwan
[3]Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Miaoli, Taiwan
[4]Division of Infectious Diseases, Department of Internal Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan.

Abstract

Serotype K54 *Klebsiella pneumoniae* is one of the major serotypes causing invasive community-acquired (CA) bacteremia in Taiwan while limited studies reported. This study utilized a 9-year (2014–2022) bacteremia patients database from our hospital to analyze the clinical characteristics of patients infected with K54 *K. pneumoniae* and microbiologic features of corresponding strains comparing with those by K1 *K. pneumoniae.* During the study period, a total of 772 bacteremia inpatients infected by *K. pneumoniae* were screened. Among these, 33 isolates (4.2%) were identified as K54, while 97 (12.5%) were K1. Patients with K54 bacteremia more frequently had liver cirrhosis ($p = 0.013$) and a higher Charlson Comorbidity Index score ($p = 0.044$). Disease severity was greater in the K54 group, as indicated by a higher SOFA score ($p = 0.002$), whereas intra-abdominal infection was less frequent compared to those by K1 *K. pneumoniae* ($p = 0.016$). The 28-day mortality did not differ significantly between groups. The prevalence of hypervirulent strains and antimicrobial resistance profiles was similar between K54 and K1 strains. In subgroup analyses of K54 *K. pneumoniae* isolates stratified by CA and hospital-acquired (HA) infections, isolates from CA infections showed a higher prevalence of hypervirulent strains and lower levels of antimicrobial resistance compared with those from HA infections. In conclusion, K54 *K. pneumoniae* bacteremia patients were associated with greater comorbidity burden and disease severity than K1 *K. pneumoniae* infection. K54 *K. pneumoniae* isolates from CA and HA infections exhibited distinct microbiologic features, suggesting divergent evolutionary trends under different environmental pressures.

Key Words: *Klebsiella pneumoniae*, K54, hypervirulence, K1, bacteremia

Reprint requests and correspondence：Kuan-Yu Chen
Address：Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical University No. 325, Section 2, Cheng-Kung Road, Neihu 114, Taipei, Taiwan

Introduction

Historically, *Klebsiella pneumoniae* has been regarded as a typical nosocomial pathogen, primarily affecting immunocompromised patients and those with multiple comorbidities[1,2]. Hospital-acquired (HA) infections caused by *K. pneumoniae* encompass a broad spectrum of clinical syndromes, including urinary tract infections, pneumonia, bloodstream infections, and wound infections[3]. In addition to nosocomial infections, *K. pneumoniae* is also capable of causing community-associated infections, most commonly pneumonia, which predominantly occurs in patients with alcoholism or diabetes mellitus[4]. In the mid-1980s and 1990s, several case series from Taiwan described a distinctive invasive clinical syndrome caused by *K. pneumoniae* infection[5-7]. This syndrome is typically characterized by pyogenic liver abscess accompanied by potential metastatic complications, including meningitis and endophthalmitis[8,9]. Although early cases were mainly reported in the Asia–Pacific region, an increasing number of cases have subsequently been documented worldwide[10,11]. Subsequent studies demonstrated that *K. pneumoniae*–associated invasive syndrome is predominantly linked to a limited number of capsular serotypes, including K1, K2, K5, K20, K54, and K57, which not simply distinguish strains within the same species; rather, they reflect distinct phenotypic characteristics of the organism, ranging from hypervirulence and invasive potential to differences in antimicrobial resistance[12]. Among these, the K1 capsular serotype accounts for the majority of cases, followed by K2 and other serotypes[13]. In Taiwan, multiple surveillance studies have similarly shown that K1 and K2 capsular serotypes have remained the two most prevalent serotypes among bloodstream isolates over the past decades, whereas other virulent serotypes, such as K5, K20, K54, and K57, consistently rank below K1/K2[14-16]. K1 represents the predominant capsular serotype among hypervirulent *K. pneumoniae* strains responsible for the invasive syndrome in Taiwan, and is thus regarded as the prototype for hypervirulent K. pneumoniae and has been extensively investigated[8,17]. In contrast, relatively limited information is available regarding other hypervirulent capsular serotypes capable of causing similar invasive infections. To address this knowledge gap, we focused on serotype K54, an established but insufficiently characterized virulence-associated serotype in Taiwan. The present study aimed to describe the clinical characteristics and outcomes of patients with K54 *K. pneumoniae* bacteremia and to compare them with those of patients with K1 *K. pneumoniae* bacteremia. In addition, we compared the virulence and antimicrobial resistance profiles of the corresponding K54 *K. pneumoniae* bloodstream isolates with those of K1 *K. pneumoniae* isolates.

Method

Study design and patients

This study was conducted at a 1,800-bed tertiary teaching hospital in Taipei, Taiwan, and was approved by the Institutional Review Board (TSGHIRB No. B202405019).

K. pneumoniae bloodstream isolates have been consecutively collected for antimicrobial resistance surveillance since 2014 and stored at –80 °C in lysogeny broth with 20% glycerol. Adult inpatients with *K. pneumoniae* bacteremia identified between 2014 and 2022 were included if complete clinical data and stored isolates were available. Only the first bacteremic episode per patient was analyzed. The study population was restricted to patients with serotype K54 or K1 *K. pneumoniae* bacteremia; patients younger than 18 years, with incomplete hospitalization records, transferred before completion of treatment, or with non-K1/K54 bacteremia were excluded.

Clinical data collection and definition

Clinical data for patients with *K. pneumoniae* bacteremia were retrospectively extracted from electronic medical records. Variables included demographics, comorbidities, infection source, disease severity at bacteremia onset, treatments, and outcomes. Community acquired (CA)- and HA infections were defined as previously described[18]. Comorbidities present at admission were recorded, and comorbidity burden was assessed using the Charlson Comorbidity Index[19]. Disease severity was evaluated using the Sequential Organ Failure Assessment score, and septic shock was defined according to the Sepsis-3 criteria[20]. Infection sources were determined based on National Healthcare Safety Network definitions[21]. Local abscess was defined by culture confirmation or radiological evidence. Appropriate empirical antibiotic therapy was defined as receipt of at least one active agent within 48 hours of bacteremia onset. Source control included catheter removal, abscess drainage, or surgical debridement. Twenty-eight–day mortality was defined as death within 28 days of bacteremia onset.

Microbiology

From 2012 to 2015, *K. pneumoniae* isolates were identified using the VITEK 2 automated system (bioMérieux, France); from 2016 onward, identification was performed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (VITEK MS; bioMérieux). Antimicrobial susceptibility testing for amikacin, gentamicin, piperacillin–tazobactam, ceftazidime, cefepime, ceftriaxone, imipenem/cilastatin, doripenem, ciprofloxacin, levofloxacin, trimethoprim/sulfamethoxazole, colistin, and tigecycline was conducted using the VITEK 2 system. Susceptibility breakpoints were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) 2022 guidelines, except for tigecycline and colistin, which were interpreted using U.S. Food and Drug Administration and 2022 European Committee on Antimicrobial Susceptibility Testing criteria, respectively.

Serotyping and virulence-associated genes detection via PCR method

Genomic DNA of isolates from stored isolates was extracted by boiling methods and tested by PCR for the presence of capsular serotype-specific (cps) genes K1 and K54 as well as other major serotypes (K2, K5, K20, and K57) were tested which we performed before[14]. Recent study by Russo et al indicates that the presence of five virulence genes—*peg-344, iroB, iucA, rmpA,* and *rmpA2*—provides the most accurate means of distinguishing hvKp from classic *K. pneumoniae* (cKp), and has been suggested as the working definition for hvKp[22-24]. Therefore, we tested the virulence genes *peg-344, iroB, iucA, rmpA,* and *rmpA2* identified among identified K54/K1 *K. pneumoniae* isolates using the primers and related protocols listed before[23].

Statistical analysis

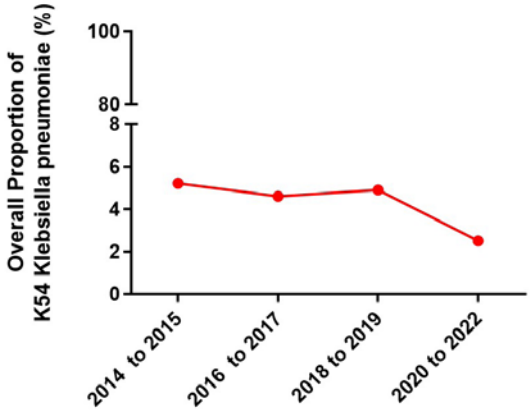
Statistical analyses were performed using SPSS version 21.0 (SPSS Inc., USA). Categorical variables were expressed as numbers (percentages) and compared using the chi-squared test or Fisher's exact test, as appropriate. Continuous variables were presented as mean ± standard deviation and compared using Student's t test or the Mann–Whitney U test, depending on data distribution. Logistic regression analysis was conducted to identify factors associated with 28-day mortality. Variables considered clinically relevant to outcomes were first assessed using univariable logistic regression. Variables with a p value ≤ 0.10 in univariable analysis were subsequently included in the multivariable logistic regression model. To evaluate whether infection with K54 *K. pneumoniae* was associated with increased mortality compared with K1 *K. pneumoniae*, infection with K54 versus K1 *K. pneumoniae* was forced into the multivariable model regardless of its statistical

significance in univariable analysis. All statistical tests were two-tailed, and a p value <0.05 was considered statistically significant.

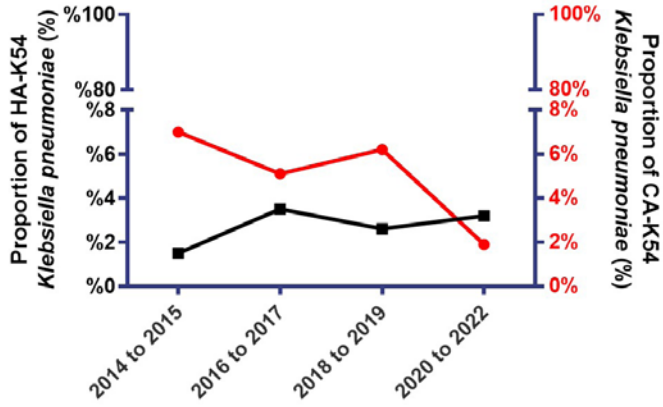
Results

During the study period (2014–2022), a total of 772 *K. pneumoniae* isolates were collected from adult hospitalized patients with bloodstream infections, with each isolate obtained from a unique patient. Among these isolates, 33 (4.2%) were identified as K54 *K. pneumoniae*. Other major serotypes K1, K2, K5, K20, K57 were 97(12.5%), 80(10.3%), 20(2.5%), 27(3.4%) and 11(1.4%). Of the 33 K54 isolates, 8 were derived from hospital-acquired infections, whereas 25 were obtained from community-acquired infections. The proportion of K54 *K. pneumoniae* among all *K. pneumoniae* isolates showed a decreasing trend over time. Further analysis demonstrated that the prevalence of K54 *K. pneumoniae* among patients with community-acquired *K. pneumoniae* bacteremia declined, whereas a gradual increasing trend was observed among patients with hospital-acquired infections. (Figure 1A and 1B)

Clinical characteristics of patients with K54 *K. pneumoniae* bacteremia were compared with those with K1 bacteremia (n=97, Table 1). Age, sex distribution, acquisition setting, and polymicrobial infection rates were similar between groups. Patients with K54 bacteremia more frequently had liver cirrhosis (27.3% vs. 8.2%, p=0.013) and a higher Charlson Comorbidity Index score (median 3 [IQR, 1–5.5] vs. 2 [IQR, 0.5–3], p=0.044). At bacteremia onset, disease severity was greater in the K54 group, as indicated by a higher SOFA score (median 4 [IQR, 3–9] vs. 2 [IQR, 1–5], p=0.002). Respiratory tract infection was more common among K54 cases (33.3% vs. 9.3%, p=0.004), whereas intra-abdominal infection was less frequent (30.3% vs. 54.6%, p=0.016). Immediate appropriate antimicrobial therapy and mortality outcomes did not differ significantly between groups. In the subgroup analysis of K54 bacteremia, the CA and HA subgroup showed comparable comorbidity burden, disease severity, and sources distribution. All patients from the CA subgroup received immediate appropriate antimicrobial therapy, compared with 75% of those from the HA group, indicating a trend



1A



1B

Figure legend.

Figure 1A. Temporal trend in the proportion (%) of serotype K54 *Klebsiella pneumoniae* among all *Klebsiella pneumoniae* blood isolates.

Figure 1B. Temporal trend in the proportion (%) of serotype K54 *Klebsiella pneumoniae* from community acquired or hospital acquired setting among all *Klebsiella pneumoniae* blood isolates.

Table 1. Clinical characteristics comparisons of *Klebsiella pneumoniae* bacteremia patients by K1 and K54.

Variable, n (%)	K54			K1	*p* value[b]	*p* value[c]
	Total (n=33)	CA-subgroup (n=25)	HA-subgroup (n=8)	Total (n=97)		
Age in years[a]	65 (55–82.5)	64 (55.0–82.5)	66 (54.75–83.0)	64 (56–73.5)	0.477	0.951
Male sex	23 (69.7)	18 (72.0)	5 (62.5)	68 (70.1)	0.965	0.673
Community acquired	25 (75.8)	-	-	81 (83.5)	0.322	
Polymicrobial infection	4 (12.1)	2 (8.0)	2 (25.0)	4 (4.1)	0.112	0.241
Co-morbidity						
Previous cerebral disease	2 (6.1)	2 (8.0)	0 (0)	10 (10.3)	0.729	1.000
Renal insufficiency	8 (24.2)	7 (28.0)	1 (12.5)	16 (16.5)	0.322	0.643
Chronic obstructive pulmonary disease	1 (3.0)	1 (4.0)	0 (0)	1 (1.0)	0.445	1.000
Liver cirrhosis	9 (27.3)	8 (32.0)	1 (12.5)	8 (8.2)	0.013	0.394
Heart failure	3 (9.1)	3 (12.0)	0 (0)	3 (3.1)	0.171	0.560
Type 2 diabetes mellitus	16 (48.5)	14 (56.0)	2 (25.0)	40 (41.2)	0.468	0.225
Malignancy	9 (27.3)	6 (24.0)	3 (37.5)	20 (20.6)	0.428	0.651
Dementia	2 (6.1)	1 (4.0)	1 (12.5)	2 (2.1)	0.267	0.432
Peptic ulcer	4 (12.1)	3 (12.0)	1 (12.5)	12 (12.4)	1.000	1.000
Autoimmune	1 (3.0)	0 (0)	1 (12.5)	2 (2.1)	1.000	0.242
Charlson Comorbidity Index score [a]	3 (1–5.5)	3 (1–5)	2.5 (0.25–5.75)	2 (0.5–3)	0.044	0.606
Clinical condition at onset						
SOFA score[a]	4 (3-9)	4 (3-9)	3.5 (1.25–11.0)	2 (1–5)	0.002	0.606
ICU stay	7 (21.2)	6 (24.0)	1 (12.5)	13 (13.4)	0.283	0.652
Primary source of bacteremia						
Respiratory tract infection	11 (33.3)	7 (28.0)	4 (50.0)	9 (9.3)	0.004	0.391
Intra-abdominal infection	10 (30.3)	9 (36.0)	1 (12.5)	53 (54.6)	0.016	0.382
Skin and soft tissue infection	0 (0)	0 (0)	0 (0)	7 (7.2)	0.190	-
Central line associated infection	1 (3.0)	0 (0)	1 (12.5)	6 (6.2)	0.678	0.242
Unidentified	3 (9.1)	2 (8.0)	1 (12.5)	6 (6.2)	0.692	1.000
Urinary tract infection	8 (24.2)	7 (28.0)	1 (12.5)	14 (14.4)	0.194	0.643
Others	0 (0)	0 (0)	0 (0)	2 (2.1)	1.000	-
Local abscess formation	8 (24.2)	7 (28.0)	1 (12.5)	42 (43.3)	0.052	0.643
Immediate appropriate antimicrobial use	31 (93.9)	25 (100)	6 (75)	96 (99.0)	0.158	0.053
28-day mortality	8 (24.2)	7 (28.0)	1 (12.5)	16 (16.5)	0.322	0.643
In-hospital mortality	9 (27.3)	7 (28.0)	2 (25.0)	18 (18.6)	0.286	1.000

CA, community acquired; HA, hospital acquired; SOFA, Sequential Organ Failure; ICU, intensive care unit
[a]Data are presented as median (interquartile range).
[b]Comparison between patient with K54 and K1 *Klebsiella pneumoniae* bacteremia
[c]Comparison between CA- and HA- K54 *Klebsiella pneumoniae* bacteremia patients

toward delayed appropriate therapy in patient with HA-K54 bacteremia. No significant differences were observed in 28-day or in-hospital mortality between the CA and HA subgroups. Logistic regression then was performed as shown in Table 2. In the univariable analysis, higher Charlson Comorbidity Index score, respiratory tract infection, higher SOFA score, and intensive care unit admission were associated with increased 28-day mortality, whereas intra-abdominal infection was associated with lower mortality. In multivariable analysis, only the SOFA score remained independently associated with 28-day mortality (adjusted OR, 1.440 per point increase; 95% CI, 1.173–1.769; $p<0.001$). Infection caused by K54 strains, compared with K1 strains, was not independently associated with 28-day mortality after controlling confounding variables. The distribution of virulence factors and antimicrobial resistance profiles between K54 and K1 *K. pneumoniae* isolates were shown in Table 3. Overall, K54 isolates exhibited comparable prevalence of hypervirulence-associated genes compared with K1 isolates. In contrast, within the K54 subgroup, community-acquired isolates demonstrated significantly higher carriage rates of *peg-344*, *iroB*, *rmpA*, *rmpA2*, *iucA,* and the hypervirulence genotype than hospital-acquired isolates. Regarding antimicrobial susceptibility, resistance to cefazolin was more frequently observed in K54 isolates than in K1 isolates. Among K54 strains, HA isolates showed higher

Table 2. Logistic regression analysis of factors associated with 28-day mortality in patients with bacteremia by K54 and K1 *Klebsiella pneumoniae*

Variable	Unadjusted OR (95% CI)	*p* value	Adjusted OR (95% CI)	*p* value
Age	0.994 (0.963–1.025)	0.694		
Male sex	1.794 (0.618–5.212)	0.282		
Polymicrobial infection	1.515 (0.286–8.013)	0.625		
Charlson Comorbidity Index score	1.291 (1.108–1.504)	0.001	1.213 (0.983–1.498)	0.072
Source of infection				
Respiratory tract infection	5.182 (1.840–14.597)	0.002	2.922 (0.467–18.273)	0.252
Intra-abdominal infection	0.110 (0.031–0.390)	<0.001	0.597 (0.115–3.113)	0.541
Skin and soft tissue infection	1.836 (0.334–10.087)	0.484		
Central line associated infection	3.643 (0.759–17.491)	0.106		
Unidentified	1.286 (0.250–6.615)	0.764		
Urinary tract infection	1.378 (0.453–4.195)	0.573		
Disease severity				
SOFA score	1.461 (1.260–1.694)	<0.001	1.440 (1.173–1.769)	<0.001
ICU stay	16.714 (5.508–50.722)	<0.001	1.627 (0.256–10.351)	0.606
Multiple drug resistant *Klebsiella pneumoniae*	2.020 (0.482–8.461)	0.336		
Hypervirulence genotype[a]	0.628 (0.248–1.591)	0.326		
K54 vs K1 *Klebsiella pneumoniae*	1.620 (0.620–4.230)	0.325	0.209 (0.029–1.515)	0.121

CI, confidence interval; OR, odds ratio
[a]Concurrent five virulence genes carriage: *peg-344, iroB, rmpA, rmpA2* and *iucA*

Table 3. Virulence profile and antimicrobial resistance comparison between K54 and K1 *Klebsiella pneumoniae.*

Variable, n (%)	K54			K1	*p* value[a]	*p* value[b]
	Total (n=33)	CA-subgroup (n=25)	HA-group (n=8)	Total (n=97)		
Virulence factors distribution						
peg-344	21 (63.6)	20 (80.0)	1 (12.5)	73 (75.3)	0.197	0.001
iroB	21 (63.6)	20 (80.0)	1 (12.5)	73 (75.3)	0.197	0.001
rmpA	20 (60.6)	19 (76.0)	1 (12.5)	74 (76.3)	0.082	0.003
rmpA2	20 (60.6)	19 (76.0)	1 (12.5)	73 (75.3)	0.107	0.003
iucA	20 (60.6)	19 (76.0)	1 (12.5)	74 (76.3)	0.082	0.003
Hypervirulence genotype[c]	20 (60.6)	19 (76.0)	1 (12.5)	72 (74.2)	0.137	0.003
Antibiotic resistance						
Cefazolin	5 (15.2)	1 (4.0)	4 (50.0)	4 (4.1)	0.046	0.008
Gentamicin	2 (6.1)	0 (0)	2 (25.0)	0 (0)	0.063	0.053
Amikacin	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Ciprofloxacin	2 (6.1)	1 (4.0)	1 (12.5)	4 (4.1)	0.643	0.432
Levofloxacin	1 (3.0)	0 (0)	1 (12.5)	2 (2.1)	1.000	0.242
Ceftriaxone	2 (6.1)	1 (4.0)	1 (12.5)	3 (3.1)	0.601	0.432
Ceftazidime	2 (6.1)	0 (0)	2 (25.0)	3 (3.1)	0.601	0.053
Cefepime	1 (3.0)	0 (0)	1 (12.5)	2 (2.1)	1.000	0.242
Imipenem/cilastatin	1 (3.0)	0 (0)	1 (12.5)	0 (0)	0.254	0.242
Doripenem	1 (3.0)	0 (0)	1 (12.5)	0 (0)	0.254	0.242
Piperacillin/tazobactam	1 (3.0)	0 (0)	1 (12.5)	1 (1.0)	0.445	0.242
Trimethoprim/ sulfamethoxazole	4 (12.1)	1 (4.0)	3 (37.5)	6 (6.2)	0.273	0.036
Colistin	1 (3.0)	0 (0)	1 (12.5)	0 (0)	0.254	0.242
Tigecycline	0 (0)	0 (0)	0 (0)	1 (1.0)	1.000	-
Multiple drug resistance	5 (15.2)	2 (8.0)	3 (37.5)	5 (5.2)	0.122	0.078

CA, community acquired; HA, hospital acquired.
[a]Comparison between patient with K54 and K1 *Klebsiella pneumoniae* bacteremia
[b]Comparison between CA- and HA- K54 *Klebsiella pneumoniae* bacteremia patients
[c]Concurrent five virulence genes carriage: *peg-344, iroB, rmpA, rmpA2* and *iucA*

resistance rates to several antibiotics, including cefazolin and trimethoprim/sulfamethoxazole, compared with CA isolates. Multidrug resistance was more common among HA K54 isolates, although this difference did not reach statistical significance. Four isolates exhibited resistance to ceftriaxone, and one isolate was resistant to imipenem/cilastatin; however, none of these isolates harbored any of the virulence genes tested in the current study.

Discussion

In the present study, we conducted a longitudi-

nal observational study to characterize the clinical features of patients with K54 *K. pneumoniae* bacteremia and the microbiological characteristics of the corresponding K54 isolates, and to compare these findings with those of patients infected with K1 *K. pneumoniae*, which has been regarded as a prototype of hvKp. During the study period, the prevalence of K54 among the overall *K. pneumoniae* bacteremia cohort decreased from 5.2% to 2.5%, which was consistent with nationwide data during the corresponding period [14]. Further analysis revealed that this decline was primarily driven by cases originating from the community, whereas the prevalence of HA K54 *K. pneumoniae* gradually increased. Given the relatively small sample size of the current study, continued surveillance is warranted to confirm these observations. In addition, several notable findings from the study were observed. First, marked differences in clinical characteristics were identified between patients with K54 and K1 bacteremia, including underlying comorbidities, disease severity at onset, and sources of infection. In contrast, the virulence gene profiles and antimicrobial resistance patterns of K54 isolates were largely comparable to those of K1 isolates. Second, further subgroup analysis of patients with K54 bacteremia stratified by CA- and HA infection revealed that K54 isolates from the HA subgroup harbored virulence genes less frequently but exhibited higher levels of antimicrobial resistance compared with those from the CA subgroup.

Although K54 *K. pneumoniae* is a common serotype among hvKp, reports describing the clinical presentations of infected patients remain limited and most published studies have been confined to case reports[25-28]. Only two relevant clinical cohort studies were identified in the literature[29,30]. The first study, conducted by Jiehui Q. et al., demonstrated that patients with K54 *K. pneumoniae* infections had a higher prevalence of underlying hepatobiliary disease, whereas other clinical characteristics, including outcomes, were comparable to those of patients infected with non-K54 strains[30]. Another study by Alka H. et al suggested that patients with K54 *K. pneumoniae* were at increased risk of presenting with respiratory tract infections[29]. Our findings are consistent with previous reports, showing that patients with K54 *K. pneumoniae* bacteremia more frequently had underlying liver cirrhosis and a respiratory tract source of infection. Moreover, the higher Charlson Comorbidity Index observed in patients with K54 infection compared with those with K1 *K. pneumoniae* infection may have contributed to greater disease severity in our cohort. Based on these findings, clinicians should maintain a high index of suspicion for abscess formation in patients with underlying hepatobiliary tract diseases, in addition to diabetes mellitus, which is more commonly observed in patients with K1 *K. pneumoniae* infection, as early drainage procedures have been shown to prevent metastatic complications and improve clinical outcomes[31].

Accurately defining hvKp remains challenging. Based on recent studies by Thomas A.R. et al., the presence of five virulence-associated genes (*iucA*, *iroB*, *peg-344*, *rmpA*, and *rmpA2*), detected using a PCR-based platform, has been developed and validated as a highly accurate method for distinguishing hvKp from classical *K. pneumoniae* (cKp)[22-24]. Accordingly, we applied this five-gene definition in the current study. Using this definition, we observed that the proportion of hvKp among K54 isolates was comparable to that among K1 isolates. However, patients in the K1 group had a higher risk of intra-abdominal infection, particularly liver abscess, suggesting that capsular type or other virulence factors may contribute to the observed differences in clinical manifestations between groups. Interestingly, when the K54 cohort was stratified into CA- and HA infections, hvKp was more prevalent in the CA group, although clinical presentations did not differ significantly between the two groups.

In contrast, isolates from the HA group exhibited higher antimicrobial resistance rates. Unlike K1 *K. pneumoniae*, which is predominantly associated with sequence type (ST) 23 and generally remains antimicrobial susceptible, K54 isolates demonstrated greater genetic diversity, including ST29, a representative hypervirulent clone, as well as ST11 and ST15, which are commonly associated with multidrug-resistant clones[30,32]. Our data showing distinct microbiological characteristics of K54 isolates in CA and HA settings suggest that clonal evolution may differ among K54 *K. pneumoniae* strains under different environmental pressures. Further molecular typing studies are underway to validate this inference. Although case reports of carbapenem-resistant K54 hvKp have been described[26], no such isolates were identified in the current study. Nevertheless, continued surveillance is necessary to monitor the potential emergence of these highly resistant and virulent strains.

Several limitations of this study should be acknowledged. First, the retrospective design is subject to potential selection bias. Second, the relatively small number of K54 cases included may have limited statistical power, and certain distinctive clinical or microbiological features of K54 and the corresponding isolates may have been overlooked. Third, only blood isolates were analyzed in this study; therefore, findings derived from isolates obtained from other sources may differ. Finally, as this was a single-center study conducted in an endemic region, the results may not be generalizable to institutions in non-endemic settings.

Conclusion

In conclusion, K54 *K. pneumoniae* bacteremia exhibited distinct clinical characteristics compared with K1 infection, with patients more frequently presenting with underlying hepatobiliary diseases and respiratory tract sources of infection. Notable differences in virulence profiles and antimicrobial resistance were observed between community-acquired and hospital-acquired isolates, suggesting divergent evolutionary pressures under different environmental conditions. Continued surveillance and further molecular characterization are warranted to clarify the evolving clinical significance of K54 *K. pneumoniae*.

Conflicts of Interest

The authors declare no conflict of interest.

Declaration

This research paper has not been published elsewhere.

References

1. Jarvis WR, Munn VP, Highsmith AK, Culver DH, Hughes JM. The epidemiology of nosocomial infections caused by Klebsiella pneumoniae. Infect Control 1985;6(2):68-74.
2. Li B, Zhao Y, Liu C, Chen Z, Zhou D. Molecular pathogenesis of Klebsiella pneumoniae. Future Microbiol 2014;9(9):1071-81.
3. Podschun R, Ullmann U. Klebsiella spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev 1998;11(4):589-603.
4. Hoffman NR, Preston FS, Jr. Friedlander's pneumonia. A report of 11 cases and appraisal of antibiotic therapy. Dis Chest 1968;53(4):481-6.
5. Cheng DL, Liu YC, Yen MY, Liu CY, Wang RS. Septic metastatic lesions of pyogenic liver abscess. Their association with Klebsiella pneumoniae bacteremia in diabetic patients. Arch Intern Med 1991;151(8):1557-9.
6. Liu YC, Cheng DL, Lin CL. Klebsiella pneumoniae liver abscess associated with septic endophthalmitis. Arch Intern Med 1986;146(10):1913-6.
7. Wang JH, Liu YC, Lee SS, et al. Primary liver abscess due to Klebsiella pneumoniae in Taiwan. Clin Infect Dis 1998;26(6):1434-8.
8. Fang CT, Lai SY, Yi WC, Hsueh PR, Liu KL, Chang SC. Klebsiella pneumoniae genotype K1: an emerging pathogen that causes septic ocular or central nervous system complications from pyogenic liver abscess. Clin Infect Dis 2007;45(3):284-93.
9. Fung CP, Chang FY, Lee SC, et al. A global emerging disease of Klebsiella pneumoniae liver abscess: is serotype K1 an important factor for complicated endophthalmitis? Gut 2002;50(3):420-4.
10. Russo TA, Marr CM. Hypervirulent Klebsiella pneumoniae. Clin Microbiol Rev 2019;32(3):e00001-19.
11. Siu LK, Yeh KM, Lin JC, Fung CP, Chang FY. Klebsiella pneumoniae liver abscess: a new invasive syndrome. Lancet

Infect Dis 2012;12(11):881-7.
12. Brisse S, Issenhuth-Jeanjean S, Grimont PA. Molecular serotyping of Klebsiella species isolates by restriction of the amplified capsular antigen gene cluster. J Clin Microbiol 2004;42(8):3388-98.
13. Sanikhani R, Moeinirad M, Shahcheraghi F, et al. Molecular epidemiology of hypervirulent *Klebsiella pneumoniae*: a systematic review and meta-analysis. Iran J Microbiol 2021;13(3):257-65.
14. Tsai CC, Lin JC, Chen PC, et al. A 20-Year Study of Capsular Polysaccharide Seroepidemiology, Susceptibility Profiles, and Virulence Determinants of Klebsiella pneumoniae from Bacteremia Patients in Taiwan. Microbiol Spectr 2023;11(3):e0035923.
15. Liao CH, Huang YT, Hsueh PR. Multicenter Surveillance of Capsular Serotypes, Virulence Genes, and Antimicrobial Susceptibilities of *Klebsiella pneumoniae* Causing Bacteremia in Taiwan, 2017-2019. Front Microbiol 2022;13:783523.
16. Tsay RW, Siu LK, Fung CP, Chang FY. Characteristics of bacteremia between community-acquired and nosocomial Klebsiella pneumoniae infection: risk factor for mortality and the impact of capsular serotypes as a herald for community-acquired infection. Arch Intern Med 2002;162(9):1021-7.
17. Enani MA, El-Khizzi NA. Community acquired Klebsiella pneumoniae, K1 serotype. Invasive liver abscess with bacteremia and endophthalmitis. Saudi Med J 2012;33(7):782-6.
18. Friedman ND, Kaye KS, Stout JE, et al. Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137(10):791-7.
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373-83.
20. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315(8):801-10.
21. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36(5):309-32.
22. Russo TA, Alvarado CL, Davies CJ, et al. Differentiation of hypervirulent and classical Klebsiella pneumoniae with acquired drug resistance. mBio 2024;15(2):e0286723.
23. Russo TA, Olson R, Fang CT, et al. Identification of Biomarkers for Differentiation of Hypervirulent Klebsiella pneumoniae from Classical K. pneumoniae. J Clin Microbiol 2018;56(9):e00776-18.
24. Russo TA, Lebreton F, McGann PT. A Step Forward in Hypervirulent Klebsiella pneumoniae Diagnostics. Emerg Infect Dis 2025;31(1):1-3.
25. Iwasaki Y, Inokuchi R, Harada S, et al. Bacterial Meningitis Caused by Hypervirulent Klebsiella pneumoniae Capsular Genotype K54 with Development of Granuloma-like Nodal Enhancement in the Brain during the Subacute Phase. Intern Med 2017;56(3):373-76.
26. Mukherjee S, Bhadury P, Mitra S, et al. Hypervirulent Klebsiella pneumoniae Causing Neonatal Bloodstream Infections: Emergence of NDM-1-Producing Hypervirulent ST11-K2 and ST15-K54 Strains Possessing pLVPK-Associated Markers. Microbiol Spectr 2023;11(2):e0412122.
27. Chuang YC, Lee MF, Yu WL. Mycotic aneurysm caused by hypermucoviscous Klebsiella pneumoniae serotype K54 with sequence type 29: an emerging threat. Infection 2013;41(5):1041-4.
28. Shao C, Xin L, Mi P, Jiang M, Wu H. Phenotypic and Molecular Characterization of K54-ST29 Hypervirulent Klebsiella pneumoniae Causing Multi-System Infection in a Patient With Diabetes. Front Microbiol 2022;13:872140.
29. Hasani A, Soltani E, Ahangarzadeh Rezaee M, et al. Serotyping of Klebsiella pneumoniae and Its Relation with Capsule-Associated Virulence Genes, Antimicrobial Resistance Pattern, and Clinical Infections: A Descriptive Study in Medical Practice. Infect Drug Resist 2020;13:1971-80.
30. Qiu J, Wei D, Ma J, et al. Covert dissemination of pLVPK-like virulence plasmid in ST29-K54 Klebsiella pneumoniae: emergence of low virulence phenotype strains. Front Cell Infect Microbiol 2023;13:1194133.
31. Lee SS, Chen YS, Tsai HC, et al. Predictors of septic metastatic infection and mortality among patients with Klebsiella pneumoniae liver abscess. Clin Infect Dis 2008;47(5):642-50.
32. Turton JF, Payne Z, Micah K, Turton JA. Capsular type K54, clonal group 29 and virulence plasmids: an analysis of K54 and non-K54 closely related isolates of Klebsiella pneumoniae. Epidemiol Infect 2018;146(14):1813-23.

K54 血清型肺炎克雷伯氏菌菌血症之臨床特徵與微生物學特性：台灣單一醫學中心回溯性研究

蔡明航[1] 汪靖勛[2] 張峰義[2] 蕭樑基[3]
林永崇[2] 廖葉媚[2] 邱勝康[4] 陳冠宇[2]

[1] 三軍總醫院松山分院內科部
[2] 三軍總醫院感染及熱帶醫學科
[3] 國家衛生研究院感染症與疫苗研究所
[4] 台北慈濟醫院感染科

摘要

K54 血清型肺炎克雷伯氏肺炎桿菌（*Klebsiella pneumoniae*）為台灣侵襲性社區型菌血症的重要致病血清型之一，惟相關研究仍相對有限。本研究利用本院 9 年期（2014-2022 年）菌血症病人資料庫，分析 K54 型 *K. pneumoniae* 菌血症病人之臨床特徵及其菌株之微生物學特性，並與同期 K1 型 *K. pneumoniae* 感染者進行比較。研究期間共篩檢 772 例 *K. pneumoniae* 菌血症住院病人，其中 33 株（4.2%）為 K54 型，97 株（12.5%）為 K1 型做進一步比較。與 K1 組相比，K54 菌血症病人較常合併肝硬化（$p = 0.013$），且 Charlson 共病指數較高（$p = 0.044$）。K54 組之疾病嚴重度亦較高，顯示出較高之 SOFA 分數（$p = 0.002$），惟其腹腔內感染發生率較 K1 組為低（$p = 0.016$）。兩組之 28 天死亡率並無顯著差異。K54 與 K1 菌株之高毒力菌株盛行率及抗菌藥物抗藥性表現相近。進一步針對 K54 *K. pneumoniae* 菌株依社區感染與院內感染進行次族群分析顯示，社區型感染菌株具有較高比例之高毒力表型，且抗菌藥物抗藥性程度較院內感染菌株為低。總結而言，K54 *K. pneumoniae* 菌血症病人相較於 K1 感染者具有較高之共病負荷與疾病嚴重度；而來自社區與院內感染之 K54 菌株呈現不同之微生物學特性，顯示其在不同環境壓力下可能具有分歧的演化趨勢。