# RESEARCH ON ANTIBIOTIC RESISTANCE OF *KLEBSIELLA PNEUMONIAE* STRAINS ISOLATED IN SEPSIS PATIENTS AT 103 MILITARY HOSPITAL

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## Summary

**Objectives:** To describe the antibiotic resistance in sepsis patients caused by *Klebsiella pneumoniae*. Subjects and methods: a cross - sectional descriptive study of 48 strains of *K. pneumoniae* isolated in septicemia patients at 103 Military Hospital from January 2017 to June 2021.

**Results:** 10.4% were hospital - acquired infections. The rate of ESBL (+) accounted for 25.0%. The MDR and XDR strains were 12.5% and 10.4%, respectively. There was no statistically significant difference between ESBL, MDR, and XDR rates between community and hospital - acquired infections ($p > 0.05$). The *K. pneumoniae* strains had a high rate of resistance to penicillins (50.0 - 100%), followed by quinolones (25.0 - 28.6%), cephalosporins (21.3 - 25.5%), aminoglycosis (6.0 - 19.0%), carbapenems (7.1 - 14.9%), intermediate resistance to colistin (14.3%). *K. pneumoniae* strains originating from hospital-acquired infections had higher rates of resistance to amikacin and gentamicin than strains from community - acquired infections ($p < 0.05$).

**Conclusions:** *K. pneumoniae* strains had a high rate of antibiotic resistance to commonly used antibiotics in clinical practice, and strains with community-acquired infections also had the same antibiotic resistance rates as strains of hospital-acquired infections.


**Key words:** *Sepsis, K. pneumoniae, antibiotic resistance.*

## INTRODUCTION

Sepsis is a severe systemic infection caused by repeated entry into the bloodstream of pathogenic microorganisms and their toxin products[1]. Today, sepsis remains a primary cause of death worldwide[2].

The leading cause of bacteremia is a group of Gram-negative bacteria, especially *K. pneumoniae*[3]. Currently, the overuse of antibiotics has led to the emergence of many antibiotic - resistant strains of bacteria; *K. pneumoniae* is one of the strains with a high rate of resistance to many antibiotics. Antibiotic resistance is an essential cause of treatment failure and increased mortality for patients with sepsis in our country[4].

To assess the drug resistance of *K. pneumoniae* strains in patients with sepsis, thereby contributing to helping clinicians in choosing antibiotics, we conducted a research project: *"Study on antibiotic resistance* of *Klebsiella pneumoniae strains* in sepsis patients at 103 Military Hospital from January 2017 to June 2021*"*.

## SUBJECTS AND METHODS

**Research subjects:** 48 strains of *K. pneumoniae* were isolated from the blood of sepsis patients (according to Sepsis 3) treated at the clinical departments of 103 Military Hospital from January 2017 to June 2021.

Diagnostic criteria: based on recommendations from the consensus conference between the

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European Society of Resuscitation and the Society for Clinical Medicine (ESICM/SCCM) on sepsis (2016)[7]:

– There is an acute change in SOFA score ≥ 2 points due to bacterial infection.

– Results of blood culture isolated *K pneumoniae*.

– Patients ≥ 18 years old.

+ Exclusion criteria: Patients with positive blood culture results for ≥ 2 pathogens.

### Research Methods

– Cross - sectional descriptive study, retrospective, combined with prospective.

– Antibiogram technique: It is performed by determining the minimum inhibitory concentration (MIC) on the Vitek 2 - Compact automatic machine, according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI)[5].

– Content of the study:

+ *Classification of infectious sources*: Based on the classification of CDC/NHSN (2008), patients are divided into two groups: hospital - acquired sepsis and community - acquired sepsis[6].

+ The concept of multi-resistant, extended-resistant, and all-resistant bacteria strains:

– *Multidrug-resistant* (*MDR*): not susceptible to 1 antibiotic in > 3 antibiotics groups.

– *Extensively drug resistance* (*XDR):* not sensitive to ≥ 1 type of antibiotic in all groups except ≤ 2 antibiotics groups.

– *Pandrug resistance* (*PDR* ): not sensitive to all antibiotics tested. In the absence of antibiograms with all groups of antibiotics recommended for *K. pneumoniae,* it is concluded that the strain may be completely resistant[7].

**Data processing**: The obtained data were processed on SPSS software version 22.0.

## RESULTS

From January 2017 to June 2021, we collected 48 strains of *K. pneumoniae* with 48 antimicrobial susceptibility results from 48 patients with bacteremia due to *K. pneumoniae* that are eligible for the study.

### Characteristics of the source of sepsis caused by Klebsiella pneumoniae

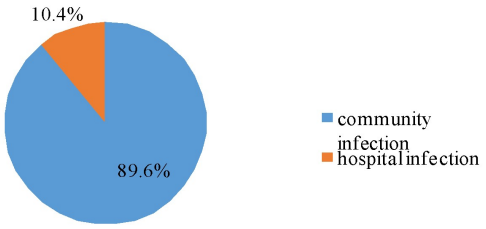


**Chart 1.** Classification of sources of infection

*Comments:* 89.6 % of patients infected from the community and 10.4% infected from hospital.

**Table 1.** Classification of ESBLs by infection source

| Source of infection | Community (n = 43, %) | Hospital (n = 5, %) | Total (n = 48, %) |
|---|---|---|---|
| ESBL (-) | 32 (74.4 ) | 3 (60.0 ) | 36 (75.0 ) |
| ESBL (+) | 10 (25.6 ) | 2 (40.0 ) | 12 (25.0 ) |
| p | 0.42 | | |

*Comments:* Overall rate of ESBL - producing *K. pneumoniae* was 25%. In hospital infection, the rate of ESBL was 40%, which was higher than that in the community- acquired infection group with 25.6 % (p > 0.05).

### Antibiotic resistance of K. pneumoniae isolates

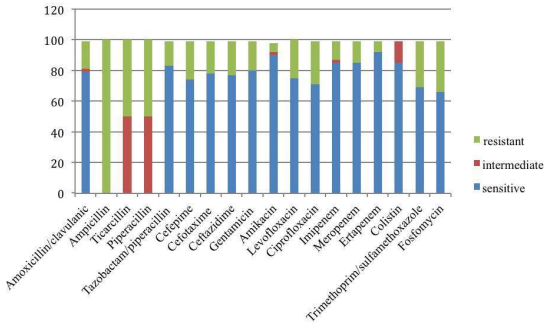


**Chart 2.** Proportion of antibiotic resistant strains of *K. pneumoniae*

*Comments:* Strains of *K. pneumoniae* isolates enough reachable with high resistance rate to penicillin group (50.0 - 100%), followed by quinolon (25.0 - 28.6%), cephalosporin antibiotics (21.3 - 25.5%), aminoglycosisdes (6.0 - 19.0%), carbapenem (7.1 - 14.9%). Recorded 14.3 % cases intermediate resistance to colistin.

**Table 2.** Antibiotic resistance patterns of *K. pneumoniae* strains

| Antibiotic resistance patterns | Number of patients | Ratio % | |
|---|---|---|---|
| Remains sensitive to many antibiotics | 37 | 77.1 | |
| MDR | 6 | 12.5 | 22.9 |
| XDR | 5 | 10.4 | |
| PDR | 0 | | |

*Comments:* The rate of multi - antibiotic and extended - resistant strains was 22.9%. In which, the rate of MDR strains and XDR strains accounted for 12.5% and 10.4%, respectively. There was no record of fully resistant strains.

**Table 3.** Classification of antibiotic resistance patterns by the source of infection

| Source of infection | Community (n = 43,%) | Hospital (n = 5,%) |
|---|---|---|
| MDR | 5 (11.6) | 1 (20.0) |
| XDR | 4 (9.3) | 1 (20.0) |
| p | 0.62 | 0.50 |

*Comments:* The rate of multi - resistant and resistant strains was higher in hospital - acquired sources than in community - acquired sources. However, this difference was not statistically significant, with $p > 0.05$.

**Table 4.** The proportion of antibiotic resistance by sources of infection

| Source of infection / Antibiotic resistance | Community | | Hospital | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Cefepime (n = 47) | 10/42 | 22.8 | 2/5 | 40.0 | 0.689 |
| Ceftazidime (n = 44) | 9/40 | 22.5 | 1/4 | 25.0 | 0.605 |
| Gentamicin (n = 46) | 7/43 | 16.3 | 2/3 | 66.7 | 0.001 |
| Amikacin (n = 44) | 2/42 | 4.8 | 1/2 | 50.0 | 0.002 |
| Levofloxacin (n = 4) | 1/4 | 25.0 | 0 | 0 | 0.776 |
| Ciprofloxacin (n = 42) | 10/37 | 27.0 | 2/5 | 40.0 | 0.547 |
| Imipenem (n = 47) | 5/42 | 11.9 | 1/5 | 20.0 | 0.921 |
| Meropenem (n = 47) | 6/42 | 14.3 | 1/5 | 20.0 | 0.889 |

*Comments*: All the isolated *K. pneumoniae* from hospital - acquired infections in our study have a higher antibiotic resistance rate than community - acquired sources. The difference was statistically significant only in antibiotics amikacin and gentamicin ($p < 0.05$).

## DISCUSSION

### Characteristics of the source of sepsis caused by Klebsiella pneumoniae

According to statistics, *K. pneumoniae* causes about 8% of the total cases of hospital-acquired infections in the United States and Europe[8]. In particular, Vietnam is one of the Asia nations with a high rate of hospital infections caused by *K. pneumoniae*. In our study, 10.4% of patients with sepsis caused by *K. pneumoniae* were derived from the hospital, 89.6% from the community.

### Features of the antibiogram of K. pneumoniae strains

Our study obtained the *antibiogram* results of 48 strains of *K. pneumoniae* isolated from 48 blood samples positive for this etiology from patients with clinical signs of sepsis.

- Ability to produce ESBL

The Antibiotic - resistant caused by *K. pneumoniae* strains is one of the main causes of nosocomial infections and sepsis. The results showed that out of 48 strains of *K. pneumoniae* isolated from the patient's blood samples, 12 strains (25.0%) showed positive ESBL results and 36 strains (75.0%) negative results. According to Nguyen Thi Phuong's research (2016), 12/92 strains gave positive ESBL results[9]. From Trinh Van Son's research (2021), the result of the rate of *K. pneumoniae* strains, which produced ESBL and caused sepsis, was 22.0%[10]. In the study of Almed (2013) in Egypt, the prevalence of ESBL strains in Egypt was 21.0%, and there were signs of an increase in the hospital setting associated with drug resistance[8].

When investigating the relationship between ESBL generation and infectious sources, the group of hospital sepsis had 2/5 ESBL - producing strains, accounting for 40.0%; In the community sepsis group, the ESBL birth rate was 10/43, accounting for 25.6%. However, there was no statistically significant difference between these

two groups. As time went by, K. pneumoniae strains derived from the community were more likely to produce the same ESBL as those derived from the hospital, which raised the risk of antibiotic resistance. We will analyze this problem furthermore in the antibiotic resistance section of isolated strains.

- Rate of antibiotic resistance of isolated strains of K. pneumoniae

Strains of isolated *K. pneumoniae* had high resistance rate to penicillin group (50.0 - 100%), followed by quinolon (25.0 - 28.6%), cephalosporin (21.3 - 25.5%), aminoglycosis (6.0 - 19.0%), carbapenem (7.1 - 14.9%), and 14.3% intermediate resistance to colistin.

From the result of Nguyen Thi Phuong's study (2016), bacteria have high resistance to some antibiotics: ampicillin resistance 88.3%, doxycycline resistance 50.0%; amoxicillin and acid clavulanic resistance 36.4%, cephalosporin resistance ranged from 27.9% to 32.1%, levofloxacine resistance 3/7 (42.9%), nofloxacine resistance 5/13 (38.5%), ciprofloxacine resistance 22/86 (25.6%), ertapenem resistance 8/49 (16.3%), imipenem resistance 7/50 (14.0%), meropenem resistance 1/26 (3.9%). The results from our study were quite similar to Nguyen Thi Phuong's study (2016). There was a slight difference: Nguyen Thi Phuong's study recorded no case of complete resistance to colistin, while our research showed that there were 14.3% cases of intermediate resistance to colistin.

In addition, the resistance of K. pneumo*niae* strains is also influenced by the source of infection. The strains isolated from patients with nosocomial infections in our study had a higher rate of antibiotic resistance than the community - acquired sepsis group.

Currently, scientists have provided over 200 biomarkers for diagnosis, treatment monitoring, and prognosis of patients with sepsis. However, it does not reduce microbiological tests' important role, including blood culture tests and antibiograms. When the whole world faces a higher antibiotic resistance rate, the role of microbiological tests becomes more critical.

In summary, the results from our research are basically similar to the previous study of sepsis by *K. pneumoniae*. Strains of *K. pneumoniae* are increasingly resistant to multiple antibiotics. The fact that the strain *K. pneumoniae* infected from the community and hospital has become more similar is a matter of concern. It creates a challenge for clinicians in choosing the right antibiotic for treatment. Especially when the overuse of antibiotics is an alarming problem in our country.

## CONCLUSIONS

Through the study of 48 strains of *K. pneumoniae* isolated from blood samples of patients with sepsis caused by *K. pneumoniae* treated at Military Hospital 103, we draw some conclusions:

- 10.4 % of patients with sepsis have the source of infection from the hospital.

- Overall rate of ESBL (+) 25.0%. The rate of ESBL in nosocomial infections (40.0%) was higher than the community infection (25.6%), ($p > 0.05$).

- The percentage of MDR strains was 12.5%, and XDR strains accounted for 10.4 %; no resistant strains were recorded. There was no difference in the rates of MDR and XDR strains between the strains originating from the hospital and the community.

- The strains of isolated *K. pneumoniae* had high resistance rate to penicillin group (50.0 - 100.0%), followed by quinolon (25.0 - 28.6%), cephalosporin (21.3 - 25.5%), aminoglycosis (6.0 - 19.0 %), carbapenem (7.1 - 14.9%), and 14.3% intermediate resistance to colistin.

- *K. pneumoniae* strains infected from the hospital have a higher rate of antibiotic resistance than those from the community. The only statistically significant difference was in amikacin and gentamicin antibiotics ($p < 0.05$).

## REFERENCES


1. Department of Infectious Diseases - Military Medical Academy (2008). Sepsis, Medical Publishing House.
2. Salomao R (2019). Sepsis Eveloping concepts and challenges.
3. Gustinetti G., Mikulska M. (2016). Bloodstream infections in neutropenic cancer patients: a practical update. Virulence, 7 (3), 280-297.
4. Dat VQ, Vu HN, Nguyen HT, et al. (2017). Bacterial blood infection in a tertiary infectious diseases hospital in Northern Vietnam: etiology, drug resistance, and treatment outcome. BMC infectious diseases, 17 (1), 1-11.
5. Livermore D., Struelens M., Amorim J., et al. (2002). Multi- centre evaluation of the VITEK 2 Advanced Expert System for interpretive reading of antimicrobial resistance tests. Journal of Antimicrobial Chemotherapy, 49 (2), 289-300.
6. Horan TC, Andrus M., Dudeck MA (2008). CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. American journal of infection control, 36 (5), 309-332.
7. Exner M., Bhattacharya S., Christiansen B., et al. (2017). Antibiotic resistance: What is so special about multidrug-resistant Gram-negative bacteria? GMS hygiene and infection control, 12,
8. Ahmed OI, El - Hady SA, Ahmed TM, et al. (two thousand and thirteen). Detection of bla SHV and bla CTX-M genes in ESBL producing Klebsiella pneumoniae isolated from Egyptian patients with suspect nosocomial infections. Egyptian Journal of Medical Human Genetics, 14 (3), 277-283-277-283.
9. Nguyen Thi Phuong (2016). Study on clinical, subclinical characteristics and severe prognostic factors in patients with sepsis caused by Klebsiella, Master of Medicine Thesis, Military Medical Academy.
10. Trinh Van Son (2021). Research on antibiotic resistance of Klebsiella and E. coli, Doctor of Medicine Thesis, Clinical Research Institute 108.