Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 16 (65) No. 1 – 2023
https://doi.org/10.31926/but.ms.2023.65.16.1.1

# KLEBSIELLA SPECIES – THE SPECTRUM OF INFECTIONS AND THE PATTERN OF RESISTANCE IN HOSPITALIZED PATIENTS

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**Abstract:** *The study was retrospective-descriptive and consisted of the analysis of the spectrum of infections produced by Klebsiella spp. strains in patients hospitalized in a multidisciplinary hospital as well as the antibiotic resistance pattern of these germs. Klebsiella spp. were identified more frequently in patients hospitalized in ICU (2021: 28,74%; 2022: 40,43%), Internal Diseases (2021: 24,8%; 2022: 15,55%) and General Surgery (2021: 7,87%; 2022: 7,82%) wards being isolated in higher percentages from urine (2021: 44,62%; 2022: 47,21%), respiratory secretions (2021: 25,85%; 2022: 22,71%) and wound secretions (2021: 15,62%%; 2022: 13,28%). Klebsiella species showed higher resistance to the cephalosporins and levofloxacin. Most strains of Klebsiella were sensitive to colistin and carbapenems.*

**Key words:** *Klebsiella species, infections, antimicrobial resistance.*

## 1. Introduction

The Klebsiella genre was taxonomically classified in the family Enterobacteriaceae wich includes species of Gram negative, immobile, aerobic facultatively anaerobic and glucose-fermenting with gas. [1],[2]

Klebsiella species are widespread in nature (in water, in soil, in the digestive tract of the mammals and humans) and can colonize the healthcare facilities, including the medical devices used for diagnostic or for curative purposes. [1],[3]

Currently, the genus Klebsiella includes many species and subspecies, the type species being K. pneumoniae, first described in 1882 by Carl Friedlander, after being isolated from a patient dead due to pneumonia. This species was included in a group named with the acronym ESKAPE (Enterococcus faecium, Staphylococcus aureus, K. pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species) which brings together bacterial species with an increased virulence and a high potential to acquire combined resistance to different classes of antibiotics that could escape from the control of antimicrobials. K. pneumoniae is one of the bacterial species considered by WHO as priority one – critical level for finding

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new therapeutic alternatives due to the multi-resistance to antibiotics. [1],[4],[5],[6]

Klebsiella sp. are opportunistic pathogens, which can be associated with high rates of morbidity and mortality in newborns, elderly and immunocompromised.

The main virulence factors identified are lipopolysaccharide, fimbriae, capsules and siderophores [1],[8].

Risk factor for hospital infections are hydro-electrolyte disorders, cancers, diabetes mellitus, neurological disorders [3], [7].

In the last decade, these germs, involved in nosocomial but also community infections, have produced a growing concern due to the selection and spread of strains with hyper-virulence and multi-resistance to antibiotics (including carbapenems), associated with severe infections, difficult to treat, even in person who are immuno-competent, without comorbidities [4], [8].

K. pneumoniae is isolated most frequently (> 85%), being involved in life-threatening infections as pneumonia, urinary infections, wounds infections, necrotizing fasciitis, liver abscesses, meningitidis, endophthalmitis and sepsis [1], [4], [9].

Other species of Klebsiella genre involved in human pathology are K. ozenae, agent of the atrophic rhinitis called ozene and K. rhinoscleromatis, agent of the rhino-scleroma, chronic granulomatous disease of the nose. K. oxytoca and K. variicola are rarely isolated from human specimens but their pathogenicity are less studied. [1],[4]

Acording to EARS-Net (European Centre for Disease Prevention and Control Anti-microbial resistance), since 2018, more than third of the Klebsiella pneumoniae isolates were resistant to at least 1 antibiotic group and the most frequent identified resistance phenotype was the combined resistance to the third-generation cephalosporins, amino-glycosides and fluoroquinolones. The highest levels of resistance are recorded in southern and eastern Europe, including Romania. The spread of resistance to carbapenems is the most serious threat [1], [10], [11], [12].

The mechanisms of antibiotic resistance found in K. pneumoniae are multiple, being enzymatic inactivation (Extended Spectrum β Lactamase = ESBLs, cephalosporinase = AmpC, carbapenemases), antibiotic targets alteration, porin loss / mutation, increased efflux pump expression (proteins involved in expulsion that reduce drug concentrations in cells) and biofilme formation [13].

Clones of MDR-hv Klebsiella spp. (drug resistance and hypervirulence phenotype) appeares through horizontal gene transfer (the most common mechanism in case of β-lactams, fluoroquinolones) and mutations have access to a mobile pool of virulence and resistance genes with potential for the selection of new clonces that are difficult to combat. These aspects indicate the need for the development of new therapeutic alternatives for ESKAPE infections being widely studied antibiotics combinations (co-administered, conjugated or with adjuvants), bactericidal peptides, bacterio-phages therapy, nanoparticles, photodynamic light therapy. [1],[6],[14],[15].

EARS-net data for 2015-2019 show that K. pneumoniae have recorded higher levels of resistance to 3rd-generation cephalosporins and carbapenems were than E. coli. During the 5 years period, there was a stagnation or an increase in resistance to 3th-generation cephalosporins (2015: 31,1%; 2016: 31,4%; 2017: 31,2%; 2018: 31,7%; 2019: 31,3%) and fluoroquinolones (2015: 30,1%; 2016: 30,3%; 2017: 31,5%; 2018: 31,6%; 2019: 31,2%) in many countries, even of resistance to carbapenems (2015: 6,8%; 2016: 7,4%; 2017: 7,1%; 2018: 7,5%; 2019: 7,9%). The resistance to aminoglycosides (2015: 24,2%; 2016: 24,4%; 2017: 24,1%; 2018: 22,7%;

2019: 22,3%) as well as combined resistance to fluoroquinolones, 3th-generation cephalosporins and amino-glycosides (2015: 19,7%; 2016: 20,6%; 2017: 20,5%; 2018: 19,5%; 2019: 19,3%) decreased during the analyzed period. These trends continued beyond 2020 and 30% of European countries report >25% carbapenem resistance for K. pneumoniae. Romania reported levels of resistance to the 3 classes of antibiotics above 50% and to carbapenems, in range 25-50%. [10],[11],[12]

## 2. Material and Methods

The study group included 1823 Klebsiella strains identified in the biological products of patients admitted to the Clinical County Emergency Hospital Brasov, in the period 1.01.2021-31.12.2022.

The aims of the retrospective-descriptive study ware to analyze the spectrum of the Klebsiella infections in patients admitted to a multidisciplinary hospital and to evaluate the pattern of antibiotic resistance of the germs in order to assess their involvement in the pathology and to optimize the antimicrobial therapy, especially the empirical treatment.

The criteria for including the Klebsiella strains in the study group consisted in the isolation from hospitalized patients during the studied period, the identification of the genre/species level and antibiogram testing.

The processing of samples followed the stages of bacteriological diagnosis. For the preliminary identification, the morphological-tinctorial characters (gram negative bacilli, incapsulated) and inflammatory character of the products on Gram-stained smears were analyzed and the cultural characters on media Columbia Agar Blood (mucous colonies, gray, with a tendency to confluence), Mac Conkey Agar (negative lactose colonies) and Brilliance Urinary Tract Infections (UTI) Agar (mucous blue colonies).

Genre/species identification was based on manual biochemical tests (TSI Agar, Urea Agar, Simmons Citrate Agar) and VITEK 2 analyzer.

Routinely, the antibiogram was performed diffusimetrically and VITEK 2 COMPACT confirming the results. The interpretation of the antibiograms was made by CLSI.

## 3. Results and discussions

The number of Klebsiella species strains from 2021 and 2022 was analyzed, as shows in Table 1.

Table 1

*Number of Klebsiella strains isolated in the studied period*

| Studied period | Nr. strains |
|---|---|
| 2021 | 762 |
| 2022 | 1061 |
| Total | 1823 |

The number of strains of Klebsiella species isolated in 2022 was higher than in 2021, which may be due to the lower number of admissions made in the pandemic year.

During the studied period, Klebsiella spp. were isolated from products collected from patients hospitalized in medical and surgical wards, as show Figure 1-2.

Klebsiella spp. were identified in patients hospitalized in many medical and surgical wards in both years studied.

In both years of the study (2021, 2022), most Klebsiella strains were isolated from patients hospitalized in ICU (2021: 28,74%; 2022: 40,43%), Internal Diseases (2021: 24,8%; 2022: 15,55%) and General Surgery (2021: 7,87%; 2022: 7,82%) departments.

In both studied years, Klebsiella species were involved in infections with various locations in hospitalized patients.

The range of pathological products from which Klebsiella strains were isolated for each year was also analyzed.

In both years, Klebsiella spp. were more frequently isolated from urine (2021: 44,62%;

2022: 47,21%), respiratory secretions (2021: 25,85%; 2022: 22,71%) and infected wound secretions (2021: 15,62%%; 2022: 13,28%), as show Figures 3-4.

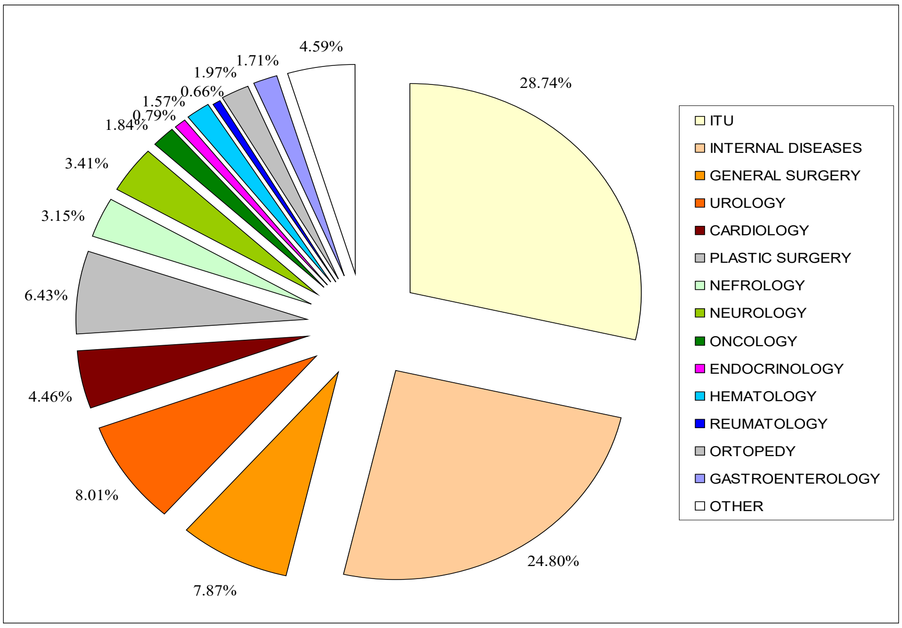


Fig. 1. *Distribution of Klebsiella strains in hospital departments in 2021*

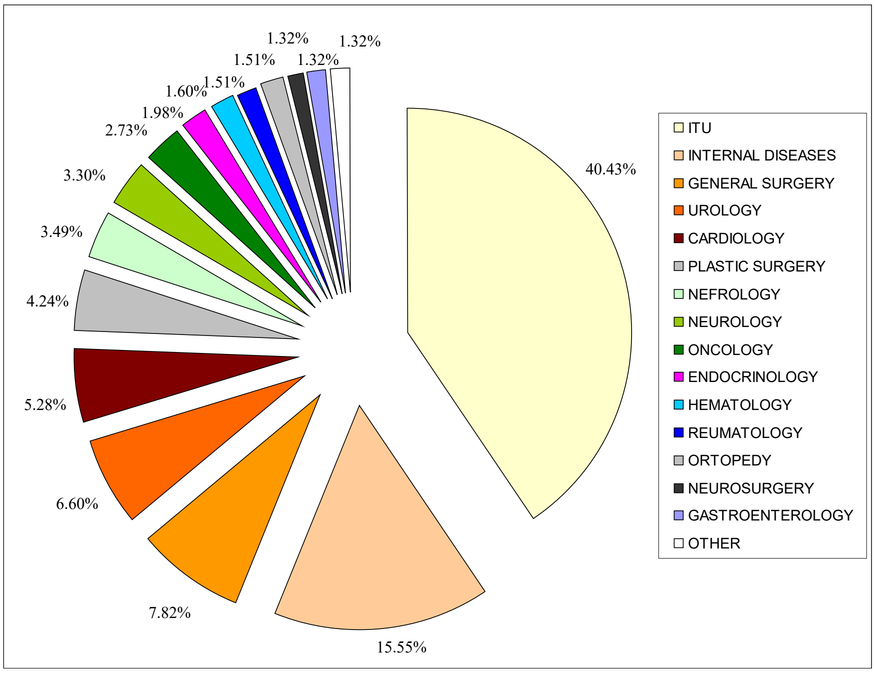


Fig. 2. *Distribution of Klebsiella strains in hospital departments in 2022*

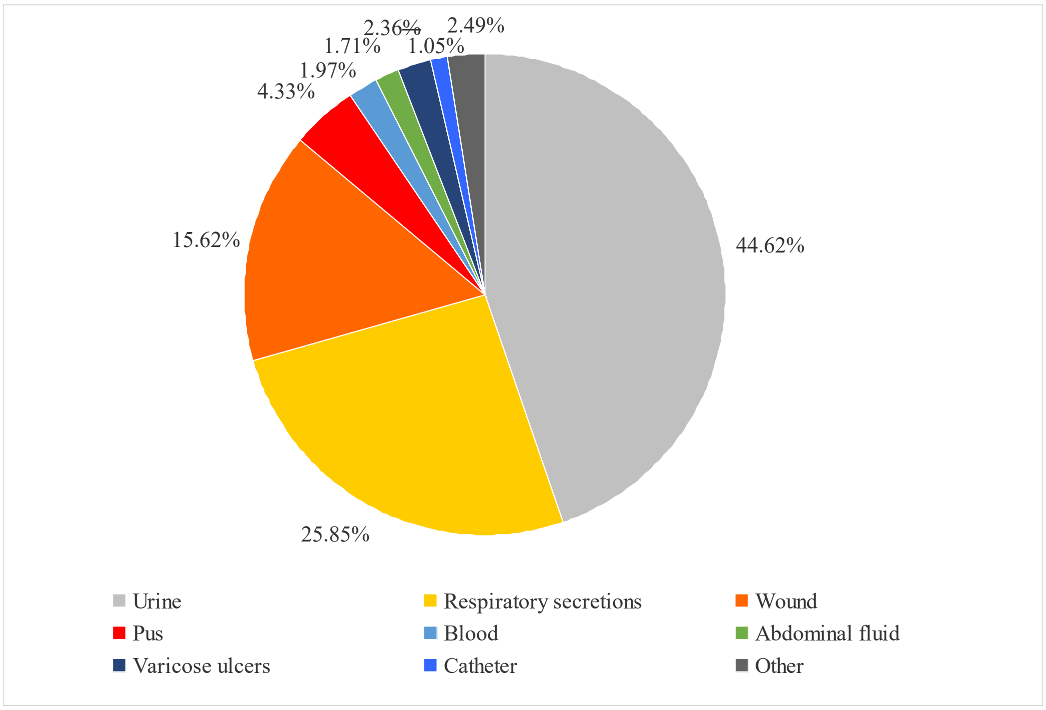


Fig. 3. *Distribution of Klebsiella strains by pathological products in 2021*

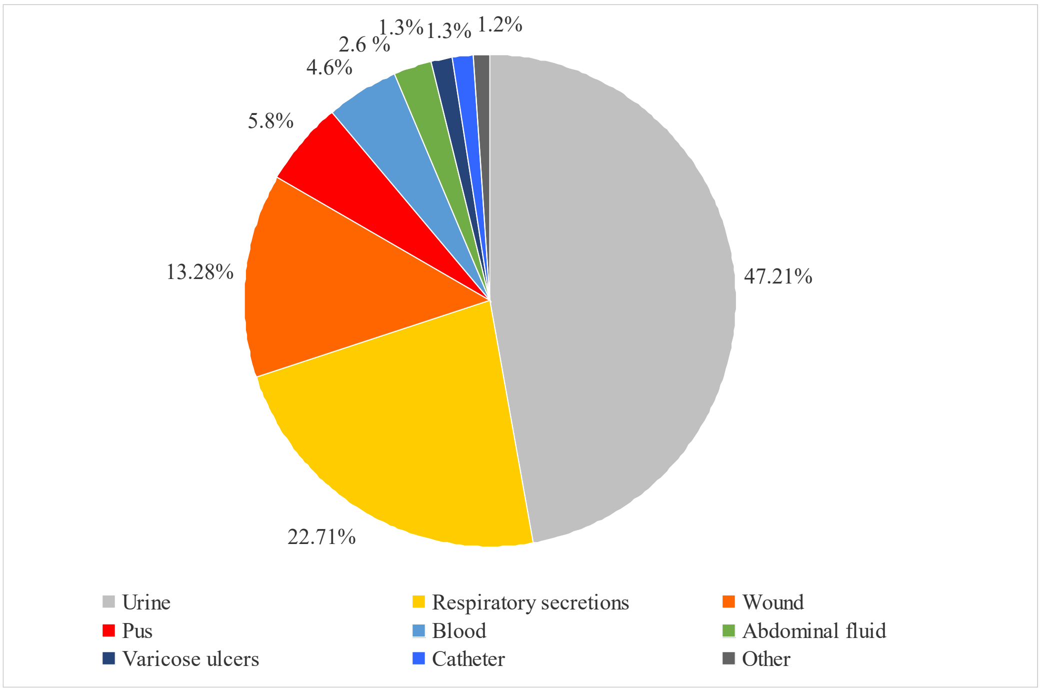


Fig. 4. *Distribution of Klebsiella strains by pathological products in 2022*

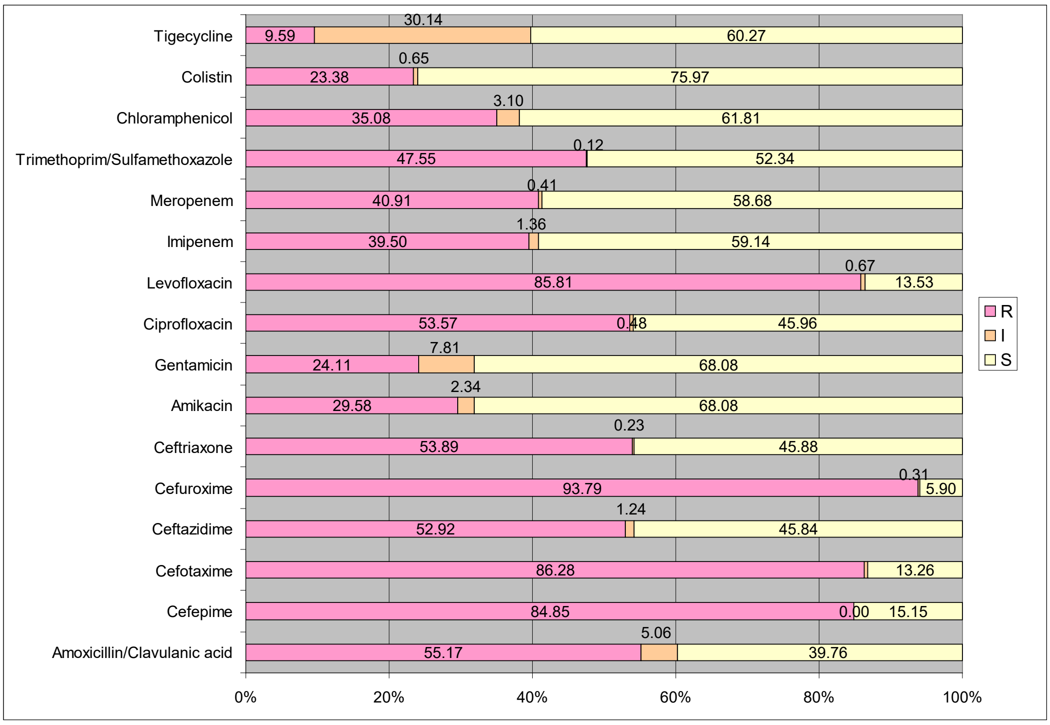


Fig. 5. *Sensitivity to antibiotics of Klebsiella strains in the period 2021-2022*

K. pneumoniae and K. oxytoca have natural resistance to ampicillin and ticarcillin. K. aerogenes has natural resistance to aminopeni-cillin's but also to some cephalosporins [17].

*Klebsiella sp.* had higher levels of resistance to cephalosporins (cefuroxime – 93,79%, cefotaxime – 86,28%, cefepime – 84,85%) and to levofloxacin (85,81%). Sensitivity was higher for colistin (75,97%) and amino glycosides (68,08%). The results are displayed in Figure 5.

Alarming is the presence, with high rates, of strains resistant to carbapenems (59,14% to imipenem, 58,68% to meropenem) and even to colistin (75,97%), which makes the therapeutic options very limited in the case of infections with these germs [8].

Compared to the results of other studies carried out previously in the same medical unit, the rate of the carbapenems resistant Klebsiella strains have increased (2019 – 48,48%), aspect revealed by other studies too. These studies are relevant to the fact that these strains are more frequent, consistently, in the ITU ward (23,69%). [18], [19]

The study shows that Klebsiella species have being involved in various infections, most frequently in urinary, respiratory and wounds infections, results which are in according with other studies [7], [8].

The analysis of the results of the antibio-grams showed that the antibiotic resistance rates are like those reported in other studies carried out in hospitals [20].

## Conclusions

1. The number of *Klebsiella* strains isolated in 2022 was higher than in 2021, which may be due to a lower number of admissions made in the pandemic year.
2. In both years, *Klebsiella* spp. were detected in pathological products of patients hospitalized in various medical and surgical wards having a relatively widespread in the hospital.
3. In both years, most *Klebsiella* strains were detected in patients hospitalized in Intensive Care Unit ICU, Internal Diseases and General Surgery wards.
4. *Klebsiella* species had higher levels of resistance to some cephalosporins (cefuroxime – 93,79%, cefotaxime – 86,28%, cefepime – 84,85%) and levofloxacin (85,81%). Sensitivity was higher for colistin (75,97%) and aminoglycosides (68,08%).
5. The high resistance to antibiotics of *Klebsiella* sp., including to reserve drugs, sustains the importance of the monitoring of multi-resistance in the case of these infections, as well as the selective, sequential reporting of the antibiogram to optimize the use of antibiotics.

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