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ANTIMICROBIAL RESISTANCE OF KLEBSIELLA STRAINS ISOLATED FROM HOSPITALIZED PATIENTS

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Abstract: *Klebsiella, a bacterial genre which includes species frequent involved in human pathology, produces a wide range of infections, sometimes severe and difficult to treat. Our retrospective study was made in the Clinical County Emergency Hospital of Braşov and included the Klebsiella strains isolated from various pathological products of the patients hospitalized in 2010. The study shows the wide involvement in the pathology of Klebsiella genre, more frequent in urinary infections (63.6%), wound infections (10.4%) and lower respiratory tract infections (10%). Generally, the non ESBL Klebsiella species have preserved sensitivity to antimicrobials of different classes. The share of Klebsiella ESBL-producing strains was very high in the studied period which represents a reason of serious concern and sustain the importance of optimizing the prescription of antibiotics .Carbapenems remain the first choice for the treatment of severe infections with ESBL-producing strains. Colistin, amikacin and ciprofloxacin can be considered therapeutic solution in some clinical situations.*

Key words: *antibiotic resistance, ESBL, gram negative bacilli, Klebsiella.*

1. Introduction

The Enterobacteriaceae represent a large bacterial family including 44 genres, 25 of them being of medical interest. These germs are important constituents of the intestinal microbiota in humans and mammals, faeces containing over 10^{10}/g. From this primary reservoir, enterobacteria spread widely in the environment. [2], [3], [15]

Klebsiella, genre belonging to the family mentioned above, includes commensal and opportunistic pathogens. From the 7 species identified based on the DNA hybridization, Klebsiella pneumoniae (subsp. pneumoniae, ozaenae, rhinoscleromatis) and K. oxytoca are implicated in human pathology, mostly in nosocomial infections. [2], [3]

The spectrum of infections produced by K. pneumoniae includes pneumonia, urinary infections, cholecystitis, wound infections, bacteraemia or septicemia, meningitis, osteomyelitis, enteritis. Immunocompromised or debilitated patients are receptive to hospital acquired infections, especially after invasive medical procedures. [2], [3], [15]

K. oxytoca was more often associated with neonatal bacteraemia and rarely with other nosocomial infections. [2], [3]

K. rhinoscleromatis and K. ozenae can be involved in rare diseases in the field of oto-rhinolaryngology. [2], [3]

The persistent exposure of bacterial strains to a multitude of antibiotics in the hospital environment has induced the development of resistance mechanisms. [12], [14], [15]

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Acquired-resistance genes can encode the production of enzymes (e.g. lactamases) and can determine the expression of the efflux pumps, the change of the target site or the alteration of a metabolic pathway. [12], [14]

Like other gram negative bacilli, Klebsiella spp. produce extended spectrum β-lactamases (ESBL), an important resistance mechanism to β-lactam antibiotics discovered after the use in clinical practice of extended-spectrum cephalosporins. [4], [6], [11], [12]

Significant percentages of Klebsiella strains producing ESBL were recorded in hospitals worldwide. The infections with these strains evolve isolated or in outbreaks, more often in intensive care units, causing an increase of hospitalization costs. [1], [4], [11], [12], [16]

Several studies showed that the prevalence of ESBL strains vary between hospitals and between departments and can be correlated with the rate of the antimicrobial consumption and other factors. [4], [7], [8], [9], [16]

As an alternative therapy of infections with ESBL-producing Klebsiella strains, aminoglycosides and quinolones can be used. For serious infections, carbapenems are the drugs of choice. The phenomenon of resistance was observed for these classes of antibiotics too, registering alarming levels in many European countries, such a permanent surveillance is an absolute requirement. [5], [10], [13], [17]

2. Material and Methods

The retrospective study was conducted in the Clinical County Emergency Hospital of Braşov and included the Klebsiella strains isolated from various pathological products of the patients hospitalized in 2010.

For the isolation of the germs from the patient's pathological products blood agar, MacConkey agar and Chromogenic U.T.I. Medium have been used.

For the identification of the Klebsiella spp. classical biochemical tests, API galleries and the automated system VITEK 2 COMPACT were used.

The antibiograms were performed by the difusimetric Kirby-Bauer method or using the automated VITEK 2 COMPACT system.

The detection of ESBL-producing strains was done by double-disk synergy test (DDST) or using the automated VITEK 2 COMPACT system.

The study objectives were to assess the spectrum of infections caused by Klebsiella species, the share of ESBL strains and the level of antibiotic resistance of these germs.

3. Results and discussions

Table 1 illustrates the etiologic spectrum of infections produced by Klebsiella species in patients hospitalized during the study.

Table 1

The spectrum of infections produced by Klebsiella species

Biological products	No.strains	%
Urine	159	63.6
Wound secretions	26	10.4
Sputum	25	10
Varicose ulcers	11	4.4
Pus from abscess	10	4
Genital secretions	9	3.6
Otic secretions	3	1.2
Peritoneal liquid	3	1.2
Pleural liquid	2	0.8
Bile	2	0.8
Total:	250	100 %

The analysis of the previous table shows a more frequent involvement of these germs in urinary infections (63.6%), followed by wound infections (10.4%) and respiratory tract infections (10%).

We can also see the involvement of this bacterial genre, with lower frequencies, in a wide range of infections.

Figure 1 shows the share of ESBL strains in the studied group.

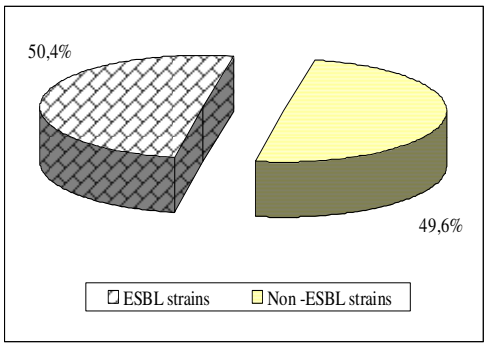

Fig. 1. *The share of Klebsiella ESBl-producing strains*

The share of Klebsiella ESBL-producing strains was very high in the studied period which represents a reason of serious concern and sustains the importance of optimizing the prescription of antibiotics.

We have analyzed the level of antibiotic resistance by analyzing separately the ESBL and non ESBL-producing strains.

Initially, we have analyzed the behavior of non ESBL Klebsiella strains to some β-lactam antibiotics, as indicated in figure 2.

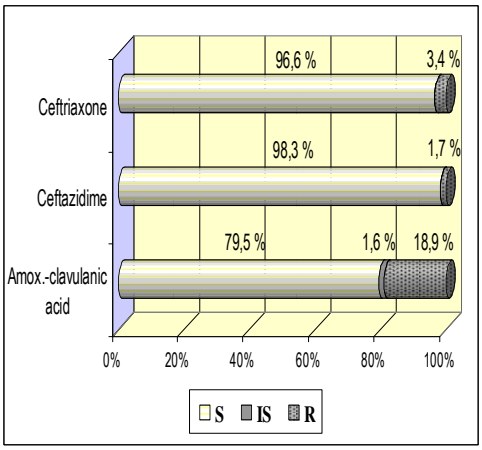

Fig. 2. *The resistance of non ESBL Klebsiella strains to β-lactam antibiotics*

Figure 2 illustrates that the sensitivity of non ESBL-producing Klebsiella strains to the tested cephalosporins was high.

The results show that the antibiotics with beta-lactamase inhibitors may be therapeutic solutions for these infections but under the control of the antibiogram.

Figure 3 illustrates the resistance of non ESBL Klebsiella strains to aminoglycosides.

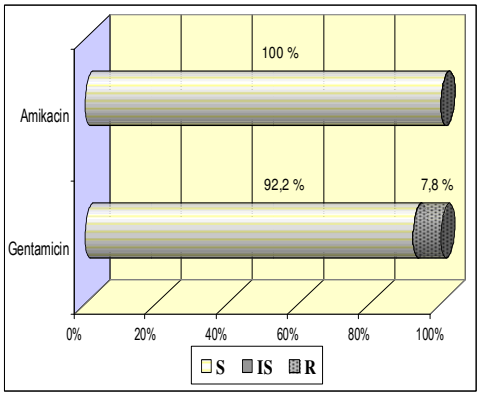

Fig. 3. *The resistance of non ESBL Klebsiella strains to aminoglycosides*

The sensitivity to aminoglycosides of non ESBL Klebsiella strains was high. A similar result was obtained for the quinolones.

Figure 4 illustrates the resistance of non ESBL Klebsiella strains to quinolones.

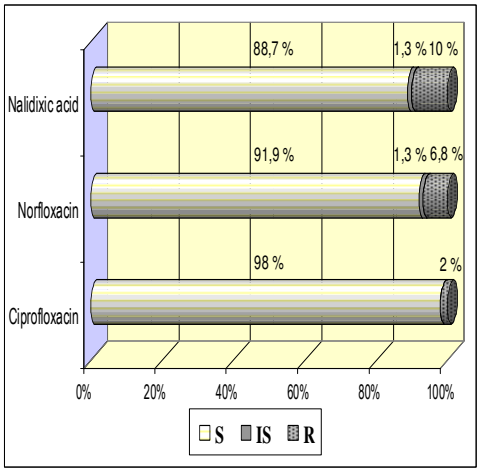

Fig. 4. *The resistance of non ESBL Klebsiella strains to quinolones*

During the study we have also analyzed the level of resistance to carbapenems registered for non ESBL Klebsiella strains, as shown in figure 5.

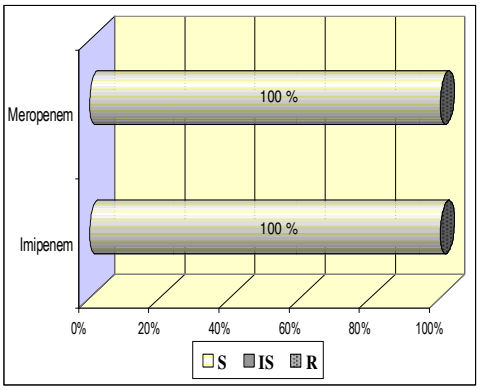

Fig. 5. *The resistance of non ESBL Klebsiella strains to carbapenems*

All non ESBL strains were susceptible to both tested carbapenems.

Figure 6 illustrates the resistance of non ESBL Klebsiella strains to antibiotics of other antimicrobial classes.

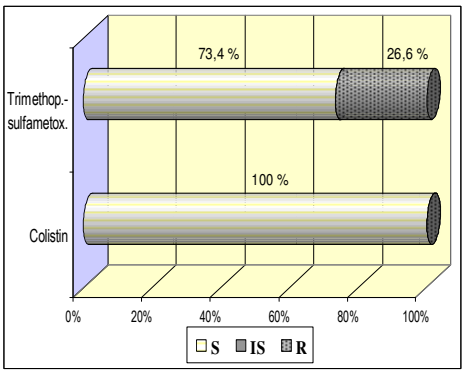

Fig. 6. *The resistance of non ESBL Klebsiella strains to other antibiotics*

All tested non ESBL Klebsiella strains were susceptible to colistin, while for trimethoprim-sulfamethoxazole the percentage of resistance was relatively high.

We have also analyzed the resistance to antibiotics of ESBL-producing Klebsiella spp.

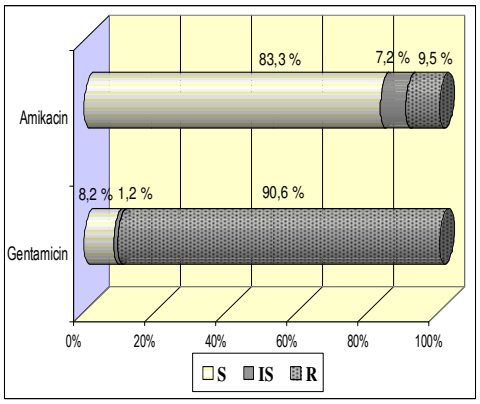

Fig. 7. *The resistance of ESBL-producing Klebsiella strains to aminoglycosides*

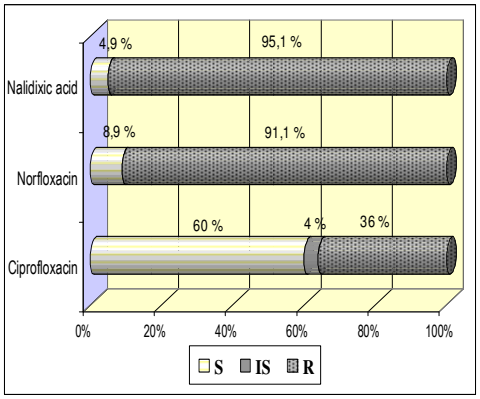

Fig. 8. *The resistance of ESBL-producing Klebsiella strains to fluoroquinolones*

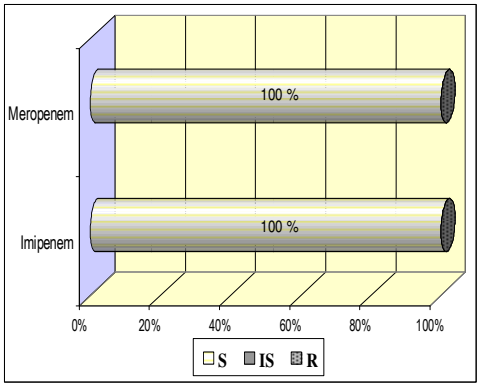

Fig. 9. *The resistance of ESBL-producing Klebsiella strains to carbapenems*

For the ESBL-producing Klebsiella strains, the therapeutic possibilities are limited, so we have evaluated the sensitivity to amino-glycosides, quinolones and carbapenems, antibiotics that could be used to treat these infections, according to C.L.S.I. (Clinical and Laboratory Standards Institute). The results are illustrated in figure 8, 9 and 10.

It can be seen that resistance to gentamicin has recorded a high level (90.6%), probably due to the extensive use of this antibiotic in the treatment of various infections. Instead, according to the antibiogram, amikacin may be used with success in the therapy of these infections.

The quinolones used to treat urinary tract infections (nalidixic acid and norfloxacin), in our study, were ineffective to ESBL - producing strains. Instead, ciprofloxacin can be used under antibiogram control, although the level of resistance is relatively high (40%) for ESBL strains.

All ESBL-producing Klebsiella strains were susceptible to both tested carbapenems.

All ESBL-producing Klebsiella strains were also sensitive in vitro to colistin.

4. Conclusions

1. The study shows the wide involvement in the pathology of Klebsiella genre.
2. Klebsiella species were more frequent involved in urinary infections (63.6%), wound infections (10.4%) and lower respiratory tract infections (10%).
3. With lower frequencies, Klebsiella spp. were etiologic implicated in infected varicose ulcers, abscess, vaginitis and urethritis, otitis, peritonitis, empyema and colecistitis.
4. The non ESBL Klebsiella species have preserved sensitivity to antibiotics from different classes.
5. The share of Klebsiella ESBL strains was very high in the studied period which represents a reason of concern.
6. Carbapenems remain the first choice for the treatment of severe infections with ESBL-producing strains.
7. Colistin, amikacin and ciprofloxacin can be considered therapeutic solution in some clinical situations.

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