

# ANTIMICROBIAL RESISTANCE IN GRAM-NEGATIVE PATHOGENS ISOLATED FROM PATIENTS WITH NOSOCOMIAL LOWER RESPIRATORY TRACT INFECTIONS IN INTENSIVE CARE UNITS

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## Revised abstract

**Objective:** to evaluate antimicrobial resistance in gram-negative pathogens of nosocomial lower respiratory tract infections (LRTIs) in patients from Russian Intensive Care Units (ICUs).

**Methods:** Antimicrobial susceptibility testing of nosocomial gram-negative respiratory pathogens was performed in accordance with NCCLS. To interpret results of cefoperazone/sulbactam testing breakpoints for cefoperazone were used, SFM 2003 breakpoints were applied for polymyxin B.

**Results:** A total of 1555 pathogens isolated from patients with nosocomial LRTIs in 31 Russian ICUs were studied. Most common pathogens were *Pseudomonas aeruginosa* (35.3%), *Klebsiella pneumoniae* (17.2%), *Acinetobacter baumannii* (15.9%), followed by *Escherichia coli* (8%), *Serratia marcescens* (6.2%), *Enterobacter* spp. (5.7%), *Stenotrophomonas maltophilia* (4.1%), *Proteus* spp. (3.4%) and other gram-negative rods (4.2%). Resistance rates (I+R, %) among *Paeruginosa* were: moxifloxacin - 75.4%, gentamicin - 74.9%, cefoperazone - 70.3%, levofloxacin - 63.8%, ciprofloxacin - 62.4%, cefepime - 58.4%, cefoperazone/sulbactam - 58%, ticarcillin/clavulanic acid - 55.3%, ceftazidime - 52.4%, piperacillin - 50.1%, meropenem - 44.1%, amikacin - 42.9%, imipenem - 42.5%, piperacillin/tazobactam - 39.4%, polymyxin B - 5.2%.

Resistance rates (I+R, %) among *K.pneumoniae* were following: piperacillin - 87.7%, ticarcillin/clavulanic acid - 85.8%, cefoperazone - 78%, cefotaxime - 77.6%, ceftriaxone - 77.2%, gentamicin - 76.5%, amoxicillin/clavulanic acid - 74.6%, cefepime - 61.2%, ceftazidime - 55.2%, piperacillin/tazobactam - 39.6%, amikacin - 35.8%, ciprofloxacin - 32.8%, cefoperazone/sulbactam - 30.2%, moxifloxacin - 24.6%, levofloxacin - 23.5%, erapenem - 2.6%. All *K.pneumoniae* strains were susceptible to imipenem and meropenem.

Resistance rates (I+R, %) among *A.baumannii* were: cefoperazone - 98.8%, piperacillin - 91.5%, gentamicin - 86.6%, ceftazidime - 75.3%, piperacillin/tazobactam - 74.9%, ciprofloxacin - 74.1%, levofloxacin - 68%, amikacin - 68%, cefepime - 64%, meropenem - 3.2%, imipenem - 2.4%, cefoperazone/sulbactam - 2%.

**Conclusion:** *Paeruginosa*, *K.pneumoniae*, *A.baumannii* are the most common gram-negative pathogens of nosocomial LRTIs in Russian ICUs patients. Carbapenems studied (imipenem, meropenem) were the most active *in vitro* against *K.pneumoniae*. Cefoperazone/sulbactam showed considerable activity against *A.baumannii*. *Paeruginosa* were highly resistant to all tested antimicrobials except polymyxin B.

## Background and purpose

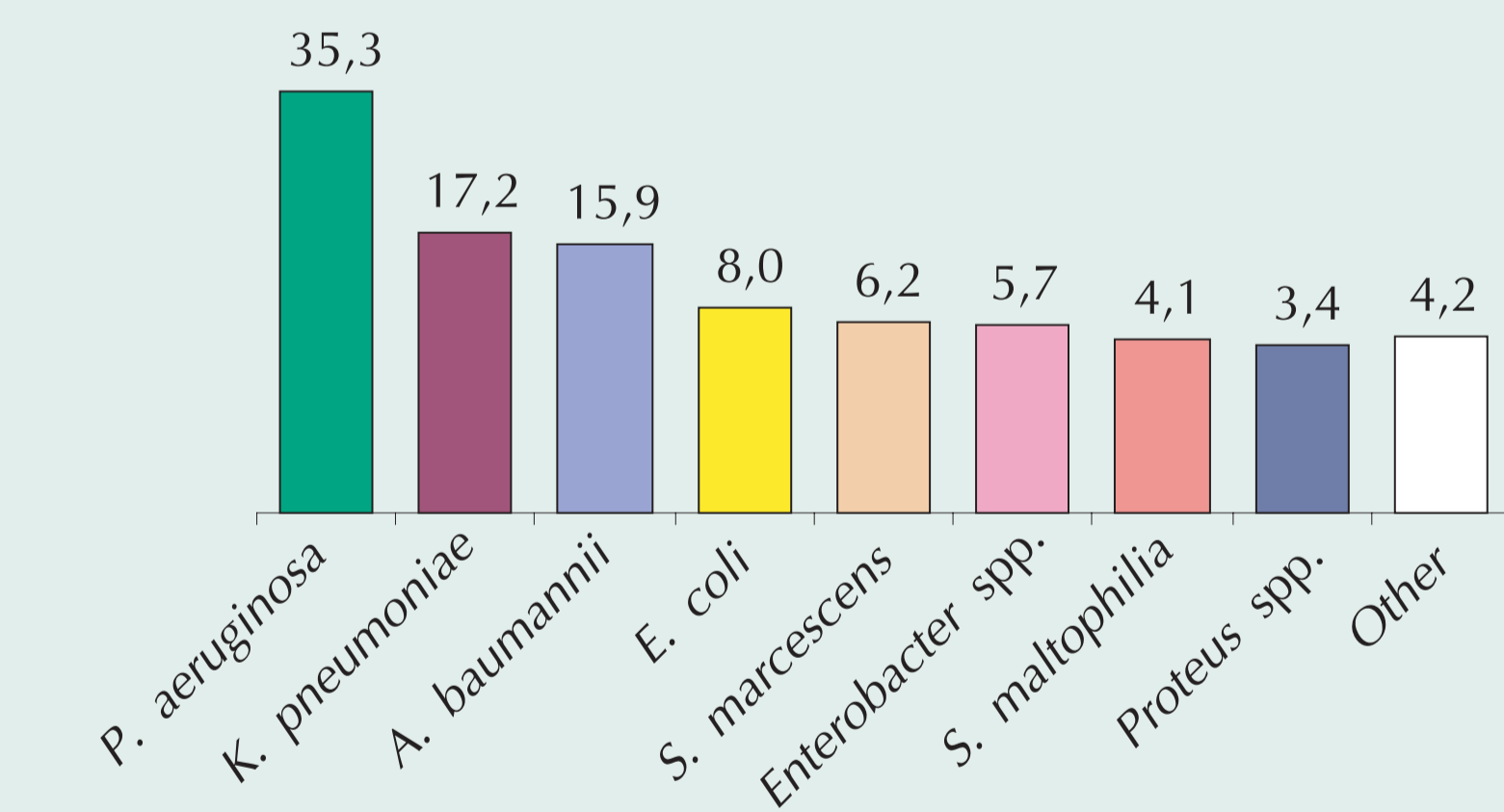
Nosocomial infections remain an important health care problem. Lower-respiratory tract infections (LRTIs) are among the most common types of nosocomial infections. Gram-negative bacteria are the dominant killers among bacterial pathogens in the ICU<sup>1</sup>. Thus the purpose of our study was to evaluate the resistance patterns of nosocomial gram-negative pathogens of lower-respiratory tract infections in Russian intensive care units (ICUs).

## Methods

The study was conducted in 31 ICUs from different parts of Russia. Strains of gram-negative pathogens obtained from patients with nosocomial lower respiratory tract infections were included in analysis. Isolated strains were identified in local laboratories using routine procedures accepted in laboratories. Strains were transferred to central laboratory in Smolensk where reidentification of all bacteria was performed. Before antimicrobial susceptibility testing strains were stored at -70°C. In central laboratory minimal inhibitory concentrations (MICs) of amikacin, amoxicillin/clavulanic acid, ampicillin, cefepime, cefoperazone, cefoperazone/sulbactam, cefotaxime, ceftazidime, ceftriaxone, ciprofloxacin, erapenem, gentamicin, imipenem, levofloxacin, meropenem, moxifloxacin, piperacillin, piperacillin/tazobactam, polymyxin B, ticarcillin/clavulanic acid were determined by agar dilution in accordance with NCCLS guidelines, 2004. To interpret results of cefoperazone/sulbactam testing breakpoints for cefoperazone were used, SFM, 2003 breakpoints were applied for polymyxin B.

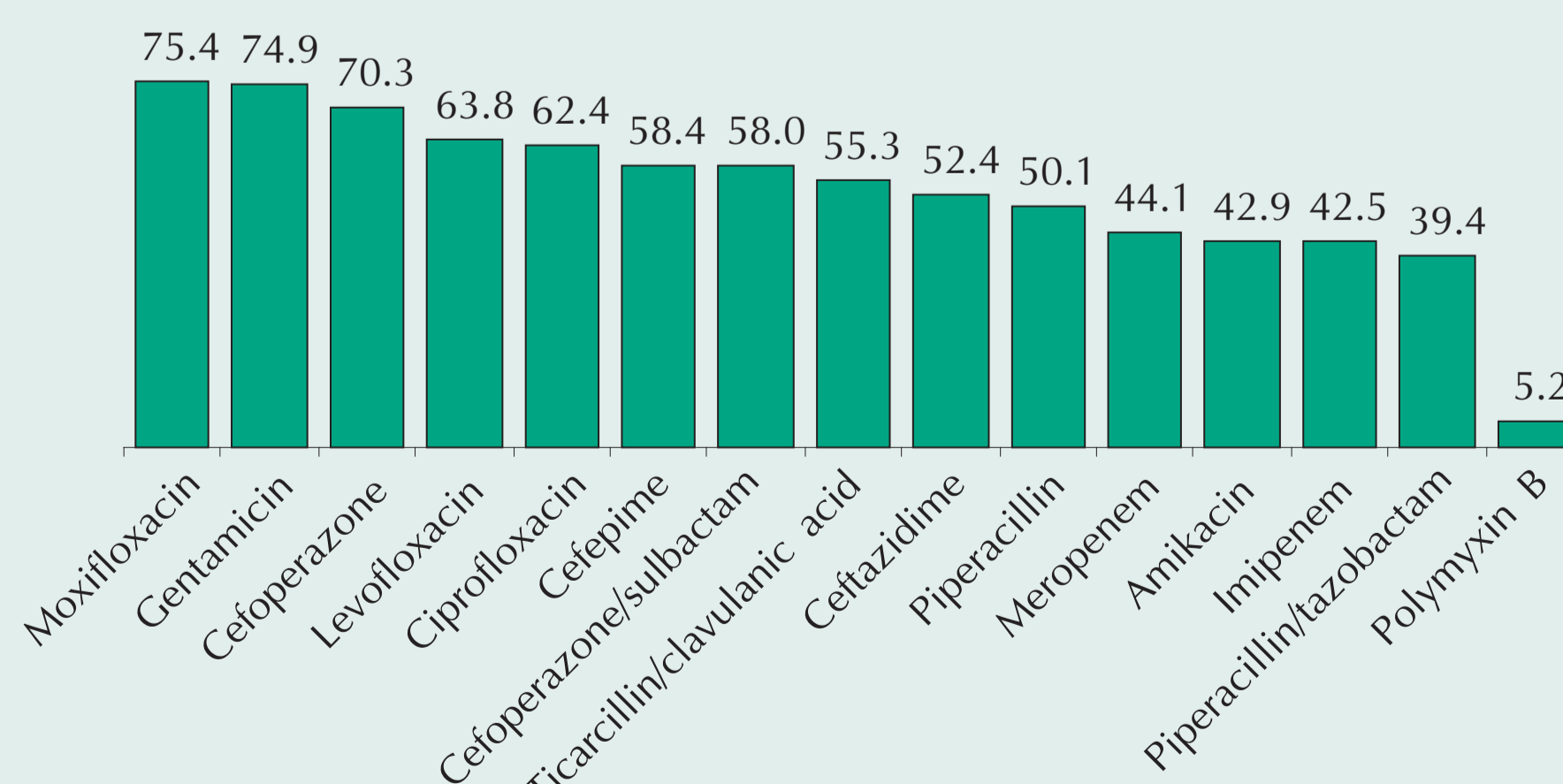
## Results

A total of 1555 pathogens isolated from patients with nosocomial LRTIs were collected in 31 ICUs from 21 Russian towns. Most common pathogens were *Pseudomonas aeruginosa* (35.3%), *Klebsiella pneumoniae* (17.2%), *Acinetobacter baumannii* (15.9%), followed by *Escherichia coli* (8%), *Serratia marcescens* (6.2%), *Enterobacter* spp. (5.7%), *Stenotrophomonas maltophilia* (4.1%), *Proteus* spp. (3.4%) and other gram-negative rods (4.2%).



Picture 1. Most common gram-negative pathogens of nosocomial lower respiratory tract infections (n=1555).

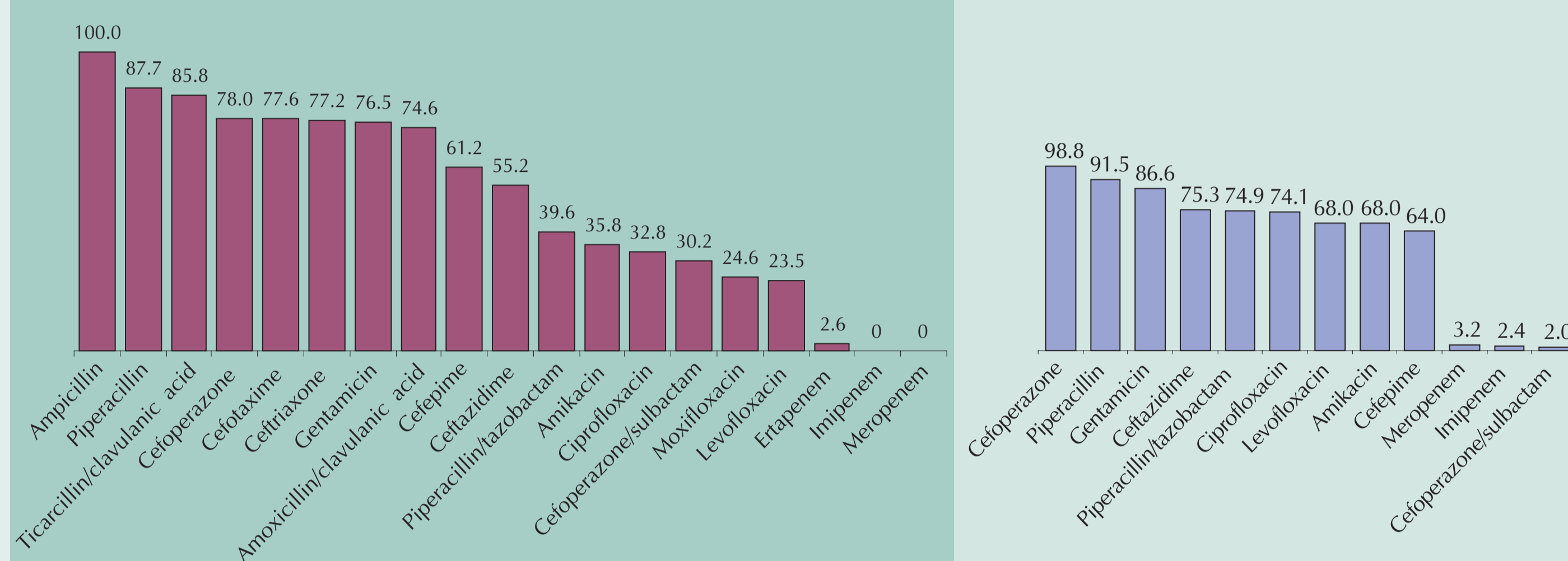
Resistance patterns of *P. aeruginosa*, *K. pneumoniae*, *A. baumannii* are presented on tables and pictures below. As in previous study of the same design conducted in 1997-992, *P. aeruginosa* and *K. pneumoniae* were among the most common pathogens. These data were comparable to results of ICARE (CDC-NNIS) program, there *P. aeruginosa* and *K. pneumoniae* were the most frequently isolated gram-negative bacteria for pneumonias in the ICU<sup>3</sup>. At the same time we would like to note the increase of *A. baumannii* role in these infections: during previous study *A. baumannii* was isolated only in 6.4% cases versus 15.9% found in current one<sup>2</sup>. Among strains collected in 1997-99 amikacin was highly active against *P. aeruginosa* and *K. pneumoniae* with resistance rates 11% and 10.9% respectively. Results of current study showed the



Picture 2. Resistance pattern (I+R, %) of nosocomial *P. aeruginosa* isolated from patients with nosocomial LRTIs (n=553).

decreased activity of amikacin against these pathogens. Imipenem and meropenem were active against all *K. pneumoniae* tested, while 2.6% *K. pneumoniae* were unsusceptible to erapenem. Among *A. baumannii* strains 2.4% and 3.2% were found to be unsusceptible to imipenem and meropenem, respectively, and this fact was a new phenomenon for this pathogen in Russia according to our data, as far as all *A. baumannii* isolates collected in 1997-99 were susceptible to imipenem<sup>2,4</sup>.

Picture 3. Resistance pattern (I+R, %) of nosocomial *K. pneumoniae* isolated from patients with nosocomial LRTIs (n=268).



Picture 4. Resistance pattern (I+R, %) of nosocomial *A. baumannii* isolated from patients with nosocomial LRTIs (n=247).

Table 1. Resistance pattern (n, %), MIC<sub>50</sub>, MIC<sub>90</sub>, MIC range of nosocomial *P. aeruginosa* isolated from patients with nosocomial LRTIs (n=553).

Antimicrobial	S (n)	I (n)	R (n)	S (%)	I (%)	R (%)	I+R (%)	MIC <sub>50</sub> , mg/l	MIC <sub>90</sub> , mg/l	MIC range, mg/l
Amikacin	316	33	204	57.1	6.0	36.9	42.9	16	128	0.5-512
Cefepime	230	197	126	41.6	35.6	22.8	58.4	16	32	1-256
Cefoperazone	164	63	326	29.7	11.4	59.0	70.3	64	256	1-256
Cefoperazone/sulbactam	232	181	140	42.0	32.7	25.3	58.0	32	64	0.5-256
Ceftazidime	263	81	209	47.6	14.6	37.8	52.4	16	64	0.5-256
Ciprofloxacin	208	17	328	37.6	3.1	59.3	62.4	8	64	0.06-128
Gentamicin	139	57	357	25.1	10.3	64.6	74.9	256	256	0.25-256
Imipenem	318	40	195	57.5	7.2	35.3	42.5	4	32	0.5-128
Levofloxacin	200	29	324	36.2	5.2	58.6	63.8	8	64	0.25-128
Meropenem	309	77	167	55.9	13.9	30.2	44.1	4	32	0.06-128
Moxifloxacin	136	59	358	24.6	10.7	64.7	75.4	32	128	0.5-128
Piperacillin	276	0	277	49.9	0.0	50.1	50.1	128	256	1-256
Piperacillin/tazobactam	335	0	218	60.6	0.0	39.4	39.4	64	256	1-256
Polymyxin B	524	0	29	94.8	0.0	5.2	5.2	1	2	0.25-8
Ticarcillin/clavulanic acid	247	0	306	44.7	0.0	55.3	55.3	128	256	1-256

Table 2. Resistance pattern (n, %), MIC<sub>50</sub>, MIC<sub>90</sub>, MIC range of nosocomial *K. pneumoniae* isolated from patients with nosocomial LRTIs (n=268).

Antimicrobial	S (n)	I (n)	R (n)	S (%)	I (%)	R (%)	I+R (%)	MIC <sub>50</sub> , mg/l	MIC <sub>90</sub> , mg/l	MIC range, mg/l
Amikacin	172	24	72	64.2	9.0	26.9	35.8	16	512	0.5-512
Amoxicillin/clavulanic acid	68	99	101	25.4	36.9	37.7	74.6	16	64	1-128
Ampicillin	0	1	267	0.0	0.4	99.6	100.0	256	256	1-256
Cefepime	104	45	119	38.8	16.8	44.4	61.2	16	256	0.06-256
Cefoperazone	59	7	202	22.0	2.6	75.4	78.0	256	256	0.125-256
Cefoperazone/sulbactam	187	51	30	69.8	19.0	11.2	30.2	16	64	0.06-128
Cefotaxime	60	21	187	22.4	7.8	69.8	77.6	128	256	0.06-256
Ceftazidime	120	9	139	44.8	3.4	51.9	55.2	32	256	0.125-256
Ceftriaxone	61	19	188	22.8	7.1	70.1	77.2	256	256	0.06-256
Ciprofloxacin	180	16	72	67.2	6.0	26.9	32.8	0.25	32	0.03-128
Erapenem	261	3	4	97.4	1.1	1.5	2.6	0.06	0.5	0.06-16
Gentamicin	63	4	201	23.5	1.5	75.0	76.5	128	256	0.5-256
Imipenem	268	0	0	100.0	0.0	0.0	0.0	0.25	0.5	0.125-2
Levofloxacin	205	16	47	76.5	6.0	17.5	23.5	0.25	16	0.03-64
Meropenem	268	0	0	100.0	0.0	0.0	0.0	0.06	0.125	0.06-2
Moxifloxacin	202	11	55	75.4	4.1	20.5	24.6	0.25	16	0.06-64
Piperacillin	33	4	231	12.3	1.5	86.2	87.7	256	256	4-256
Piperacillin/tazobactam	162	28	78	60.4	10.4	29.1	39.6	16	256	1-256
Ticarcillin/clavulanic acid	38	16	214	14.2	6.0	79.9	85.8	256	256	1-256

Table 3. Resistance pattern (n, %), MIC<sub>50</sub>, MIC<sub>90</sub>, MIC range of nosocomial *A. baumannii* isolated from patients with nosocomial LRTIs (n=247).

Antimicrobial	S (n)	I (n)	R (n)	S (%)	I (%)	R (%)	I+R (%)	MIC <sub>50</sub> , mg/l	MIC <sub>90</sub> , mg/l	MIC range, mg/l
Amikacin	79	12	156	32.0	4.9	63.2	68.0	128	256	0.5-512
Cefepime	89	109	49	36.0	44.1	19.8	64.0	16	32	1-256
Cefoperazone	3	12	232	1.2	4.9	93.9	98.8	256	256	8-256
Cefoperazone/sulbactam	242	4	1	98.0	1.6	0.4	2.0	2	16	0.5-256
Ceftazidime	61	61	125	24.7	24.7	50.6	75.3	32	64	1-256
Ciprofloxacin	64	2	181	25.9	0.8	73.3	74.1	64	128	0.06-128
Gentamicin	33	12	202	13.4	4.9	81.8	86.6	128	256	1-256
Imipenem	241	1	5	97.6	0.4	2.0	2.4	1	2	0.125-32
Levofloxacin	79	28	140	32.0	11.3	56.7	68.0	8	16	0.06-32
Meropenem	239	4	4	96.8	1.6	1.6	3.2	1	2	0.125-32
Piperacillin	21	12	214	8.5	4.9	86.6	91.5	256	256	8-256
Piperacillin/tazobactam	62	84	101	25.1	34.0	40.9	74.9	64	256	1-256

## Conclusions

- P. aeruginosa*, *K. pneumoniae*, *A. baumannii* were the most common gram-negative pathogens of nosocomial lower respiratory tract infections in Russian ICU patients.
- P. aeruginosa* were highly resistant to all tested antimicrobials except polymyxin B.
- Erapenem, imipenem, meropenem were the most active *in vitro* against *K. pneumoniae*.
- Inspite that emergence of carbapenem-resistant *A. baumannii* was found, carbapenems (imipenem, meropenem) and cefoperazone/sulbactam showed the highest *in vitro* activity against this pathogen.

## References

- M.V. Villegas, J.P. Quinn. Infect Med 2004; 21: 595-99.
- L. Strachounski, G. Reshedko, E. Ryabkova, O. Stetsiouk, O. Kretchikova et al. Clin Microbiol Antimicrob Chemother 2002; 4: 379-90 [http://www.antibiotic.ru/cmact/pdf/4\\_4\\_379.pdf](http://www.antibiotic.ru/cmact/pdf/4_4_379.pdf) (Russian).
- CDC NNIS System. National Nosocomial Infections Surveillance (NNIS) system report, data summary from January 1990-May 1999. Am J Infect Control 1999; 27: 520-32
- L. Strachounski, G. Reshedko, O. Stetsiouk, O. Kretchikova, E. Ryabkova. Proceedings of 41th Interscience Conference on Antimicrobial Agents and Chemotherapy; 2001; Chicago, USA, p. 113, abstr. #67. (for detailed poster presentation please refer to <http://www.antibiotic.ru/en/pdfs/007-67.pdf>).