ANTIMICROBIAL RESISTANCE AMONG NOSOCOMIAL *KLEBSIELLA PNEUMONIAE* FROM RUSSIAN INTENSIVE CARE UNITS (ICUs)

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INTRODUCTION

Despite implementation of infection control measures, hospital-acquired or nosocomial infections remain a serious problem for healthcare, especially for ICUs where risk for nosocomial infections is up to 10 times greater than in other wards. Gram-negative pathogens, namely *Enterobacteriaceae* are responsible for a large number of nosocomial infection in ICUs with *K. pneumoniae* being one the most important pathogen accounted for. Since emergence of extended spectrum β-lactamases (ESBL) therapeutic options for this nosocomial disaster became limited. The situation is worsened due to wide spread of co-resistance to other antimicrobial classes (e.g. fluoroquinolones, aminoglycosides) among ESBL-producing *K. pneumoniae*.

Data about current state of antimicrobial resistance in nosocomial *K. pneumoniae* in Russian ICUs are scarce and the objective of our study was to clarify this issue.

METHODS

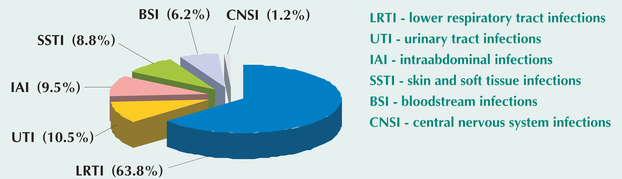
During prospective multicenter microbiology study participating centers collected consecutive *K. pneumoniae* from ICU patients with documented nosocomial infections during 2002-2004. Duplicate isolates were excluded from the study. Strains were transferred to central laboratory in Smolensk. Before antimicrobial susceptibility testing strains were stored at -70^{0}C. In central laboratory minimal inhibitory concentrations (MICs) of amikacin, amoxicillin/clavulanic acid, ampicillin, cefepime, cefoperazone, cefoperazone/sulbactam, cefotaxime, cefotaxime, cefotaxime/clavulanic acid, ceftazidime, ceftazidime/clavulanic acid, ceftriaxone, ciprofloxacin, ertapenem, gentamicin, imipenem, levofloxacin, meropenem, moxifloxacin, piperacillin, piperacillin/tazobactam, 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. Intermediate strains were included into the resistant category. *E. coli* ATCC 25922 and *E. coli* ATCC 35218 were used as quality control strains. Data management and statistical analysis were performed with M-lab software (Institute of Antimicrobial Chemotherapy, Smolensk, Russia).

RESULTS

A total of 420 *K. pneumoniae* were obtained in 29 ICUs from 19 Russian cities. Centers-participants are shown on the picture 1.

Picture 1. Geographical distribution of participating centers.

The majority of strains were collected from patients with nosocomial lower respiratory tract infections. The distribution of infection sites *K. pneumoniae* strains were collected from is presented of picture 2.



Picture 2. Source of nosocomial infections due to *K. pneumoniae*.

Antimicrobial resistance rates, MIC distribution, MIC_{50}, MIC_{90} and MIC range of studied *K. pneumoniae* are shown in tables 1 and 2.

More than 50% of strains were resistant to amoxicillin/clavulanic acid, cefepime, cefoperazone, cefotaxime, ceftazidime, ceftraxone, gentamicin, piperacillin, ticarcillin/clavulanic acid. Cefoperazone/sulbactam, ciprofloxacin, levofloxacin, moxifloxacin, piperacillin/tazobactam possessed better activity. All strains were susceptible to imipenem and meropenem, while 2.6% strains were unsusceptible to ertapenem.

Table 1. Antimicrobial resistance rates of nosocomial *K. pneumoniae*

Antimicrobials	S	I	R	S(%)	I(%)	R(%)	I+R (%)
Amikacin	288	34	98	68.6	8.1	23.3	31.4
Amoxicillin/clavulanic acid	110	145	165	26.2	34.5	39.3	73.8
Ampicillin	0	2	418	0.0	0.5	99.5	100.0
Cefepime	162	59	199	38.6	14.0	47.4	61.4
Cefoperazone	94	8	318	22.4	1.9	75.7	77.6
Cefoperazone/ sulbactam	295	78	47	70.2	18.6	11.2	29.8
Cefotaxime	102	25	293	24.3	6.0	69.8	75.7
Cefoxitin	296	61	63	70.5	14.5	15.0	29.5
Ceftazidime	180	16	224	42.9	3.8	53.3	57.1
Ceftriaxone	103	22	295	24.5	5.2	70.2	75.5
Ciprofloxacin	260	31	129	61.9	7.4	30.7	38.1
Ertapenem	409	4	7	97.4	1.0	1.6	2.6
Gentamicin	104	7	309	24.8	1.6	73.6	75.2
Imipenem	420	0	0	100.0	0.0	0.0	0.0
Levofloxacin	308	23	89	73.3	5.5	21.2	26.7
Meropenem	420	0	0	100.0	0.0	0.0	0.0
Moxifloxacin	301	17	102	71.7	4.0	24.3	28.3
Piperacillin	59	6	355	14.0	1.5	84.5	86.0
Piperacillin/ tazobactam	242	53	125	57.6	12.6	29.8	42.4
Ticarcillin/ clavulanic acid	64	24	332	15.2	5.8	79.0	84.8

Table 2. MIC distribution, MIC_{50}, MIC_{90} and MIC range of antimicrobials for nosocomial *K. pneumoniae* isolated in Russian ICUs in 2002-2004.

Antimicrobials	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	MIC_{50}	MIC_{90}	MIC range
Amikacin				2	18	95	33	47	28	65	34	4	4	13	77	8	512	0.25-512
Amoxicillin/clavulanic acid						2	30	34	44	145	125	39	1			16	32	1-128
Ampicillin										2	14	33	11	360		256	256	16-256
Cefepime		61	6	9	6	17	13	21	29	59	57	45	47	50		16	256	0.06-256
Cefoperazone			3	24	24	8	2	10	12	11	8	7	26	285		256	256	0.125- 256
Cefoperazone/s ulbactam		1	6	33	17	22	12	19	49	136	78	40	7			16	64	0.06-128
Cefotaxime		50	17	5	5	1	3	8	13	15	10	28	78	187		128	256	0.06-256
Cefoxitin							5	172	119	61	33	15	11	4		8	32	2-256
Ceftazidime			17	40	10	11	25	43	34	16	28	43	79	74		32	256	0.125- 256
Ceftriaxone		58	9	9	3	1	2	6	15	12	10	9	26	260		256	256	0.06-256
Ciprofloxacin	89	71	22	19	23	36	31	22	13	8	48	9	29			0.5	32	0.03-128
Ertapenem		244	69	50	31	11	4	4	5	2						0.06	0.5	0.06-16
Gentamicin				5	67	27	4	1	7	24	51	29	66	139		64	256	0.25-256
Imipenem		3	108	201	86	17	4	1								0.25	0.5	0.06-4
Levofloxacin	7	128	51	18	41	46	17	23	32	45	11	1				0.5	16	0.03-64
Meropenem		365	34	9	1	8	3									0.06	0.125	0.06-2
Moxifloxacin		39	108	47	43	33	31	17	25	38	31	8				0.5	16	0.06-64
Piperacillin							7	17	35	4	2	7	348			256	256	4-256
Piperacillin/tazobactam						1	21	108	44	68	36	17	8	117		16	256	1-256
Ticarcillin/clavulanic acid						1	4	39	12	8	11	13	38	294		256	256	1-256
Cefotaxime/ clavulanic acid		120	111	86	45	15	7	5	9	8	2	5	1	6		0.125	2	0.06-256
Ceftazidime/ clavulanic acid		2	32	85	110	132	35	10	1	3		4	6			0.5	2	0.06-128

Among evaluated strains ≥3 twofold concentration decrease in an MIC for cefotaxime/clavulanic acid vs MIC of cefotaxime was observed in 323 strains (76.9%) and in 310 strains (73.8%) ≥3 twofold concentration decrease in an MIC for ceftazidime/clavulanic acid vs MIC of ceftazidime was found.

More or equal 3 twofold concentration decrease in an MIC for cefotaxime/clavulanic acid or ceftazidime/clavulanic acid vs MIC of cefotaxime or ceftazidime was observed in 293 strains (69.7%).

CONCLUSIONS

1. In Russian ICUs studied *K. pneumoniae* most commonly were isolated from patients with nosocomial lower respiratory tract infections (63.8%).

2. Russian *K. pneumoniae* characterized with high level resistance to cephalosporins III-IV, aminoglicosides, fluoroquinolones, inhibitor-protected β-lactams.

3. More or equal 3 twofold concentration decrease in an MIC for cefotaxime/clavulanic acid or ceftazidime/clavulanic acid vs MIC of cefotaxime or ceftazidime was observed in 69.7% strains.

4. Only imipenem and meropenem remain universally active against nosocomial *K. pneumoniae* collected in Russian ICUs in 2002-2004.

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