# ANTIBIOTIC RESISTANCE DYNAMICS OF ACINETOBACTER SPP. IN ICU

**[1]Ibadov Ravshan Alievich, [2]Shanieva Zulfiya Aymurzaevna, [3]Ibragimov Sardor Khamdamovich**

[1,2,3] State Institution "Republican Specialized Scientific and Practical Medical Center for Surgery named after academician V.Vakhidov", Tashkent, Uzbekistan

***https://doi.org/10.5281/zenodo.10700638***

***Abstract.*** *Objective: to analyze the dynamics of antibiotic resistance of Acinetobacter spp. isolated from patients in ICU. To identify effective antibiotics against isolated strains.*

*Material and methods. We analyzed the isolated strains and analyzed the results of determining the sensitivity of Acinetobacter spp. to antibacterial drugs. The pathogens were isolated from ICU patients in 2008-2019. Clinical material for microbiologic examination included wound secretions, bronchoalveolar lavage, abdominal cavity exudate, abscess contents, bile, urine, and blood. Microbiological studies were carried out in the laboratories of microbiological of the State Institution "RSSPMC for surgery named after V.Vakhidov"*

*Results. Due to the introduction of recommended protocols for antibacterial prophylaxis and treatment, methods of monitoring the effectiveness of antimicrobial therapy, the introduction of forecasting methods (identification of risk groups and more targeted antibiotic prophylaxis of nosocomial infections), effective criteria for ventilator modes, approaches to pathogenetic therapy, nutritional support, etc. since 2012, there is a decrease in the frequency of purulent-septic complications, so that in 2012-2019 in the cardiac block, it was from 1.5-1.3 to 0.3-0.1%, in the abdominal block - from 1.0-1.9 to 0.5-0.2%, in the thoracic block - from 0.7-0.5 to 0.03-0.02%.*

*Conclusion. The increasing antibiotic resistance of Acinetobacter spp. causes the necessity to study antibiotic grams of all strains isolated from patients for adequate choice of means of effective antibiotic therapy. The obtained data were used to optimize empirical antibiotic therapy in patients with purulent-septic complications in ICU.*

***Keywords:*** *antimicrobial therapy, Acinetobacter spp., agents of suppurative and septic complications, resistance, nosocomial infections, intensive care unit.*

## INTRODUCTION

The development of infectious complications in patients with a high risk of sepsis in ICU (severe acute pancreatitis, bleeding, acute respiratory distress syndrome, PON) is the leading cause of mortality. Knowledge of the etiologic structure and antibiotic resistance of the main pathogens is essential for timely adequate antibiotic prophylaxis and empirical antibiotic therapy.

The main problematic pathogens of nosocomial infections in terms of antibiotic resistance are MRSA, MRSE, Ps. aeruginosa, Kl.pneumoniae, E. coli, Acinetobacter spp. etc. The most relevant causative agents of all hospital-acquired infections (except angiogenic infections) and sepsis are microorganisms of the Enterobacteriaceae family and non-fermenting bacteria, which include Ps. aeruginosa and Acinetobacter spp. (Wong D, 2017). Acinetobacter strains prior to 1970 very rarely caused infections in humans, infections were successfully treated with ampicillin, gentamicin, and carbenicillin; in 1975, reports of resistant strains appear; in 1990, Acinetobacter strains resistant to all ABs except carbapenems were isolated in Germany. In Hong Kong, the most frequent pathogens were Acinetobacter *johnsonii* and Acinetobacter *lwoffi*. In most countries of

the world, including Russia, Acinetobacter *baumannii* is becoming the main causative agent. Until 2004, Acinetobacter spp. - was the second most frequent causative agent of nosocomial infections in ICU among NSAIDs in Europe, from 2006 to 2007 it was the first most frequent pathogen in 7 leading ICUs among NSAIDs (Salzer H.J., 2009).

The following risk factors for carbapenem-resistant Acinetobacter infection have been described so far: large size of the hospital (more than 500 beds), prolonged hospitalization in ICU, immunosuppression, ventilator, catheterization, recent surgical intervention, aggravated antibiotic history (recent use of ceftazidime, meropenem, imipenem).

**MATERIAL AND METHODS.**

We analyzed the isolated strains and analyzed the results of determining the sensitivity of Acinetobacter spp. to antibacterial drugs. The pathogens were isolated from ICU patients in 2008-2019. Clinical material for microbiologic examination included wound secretions, bronchoalveolar lavage, abdominal cavity exudate, abscess contents, bile, urine, and blood. Identification of isolated microorganisms was performed using test kits of "Hi-Media" company, India, Interpretation of results was performed according to NCCLS/CLSI guidelines. Determination of antibiotic sensitivity of strains was performed by disk-diffusion method on Mueller-Hinton medium in accordance with CLSI (formerly NCCLS) standards.

**RESULTS.**

A total of 486 cultures were isolated, of which Acinetobacter spp. - 131 (27%). Acinetobacter spp. strains were isolated mainly from trachea (patients on PIVL) - 77%, drainage secretions - 15%, from blood - 8%. High level of resistance of Acinetobacter spp. to cephalosporins in 2008-2011 amounted to 85%, in 2012-2019 - 100%, to fluoroquinolones - 100%. - 100%, to fluoroquinolones in 2008-2011 amounted to 85%, in 2012-2019 - 100%, to aminoglycosides spp. - 100%, to aminoglycosides in 2008-2011 amounted to 85%, in 2012-2019. - 70%, in 2012-2019. - 100%, to carbapenems in 2008-2011. - 25%, in 2012-2019. - 70%.

***Table 1. Results of biological field samples (%)***

| Biomaterial type | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Surgical wound | 3,7 | 0,6 | 2,6 | - | - | - | - | - | - | - | - | - |
| Blood | 10,4 | 11 | 14 | 5,4 | 3,8 | 2,7 | - | 0,6 | 1,2 | 0,4 | 0,2 | - |
| From abdominal cavity | 1,5 | 0,6 | 2,2 | 1,3 | 0,6 | - | 0,3 | 0,6 | 2,2 | 0,6 | 0,2 | 0,4 |
| From pleural cavity | 0,4 | 0,3 | 0,9 | 2 | - | - | - | 0,3 | - | 0,3 | - | - |
| From drainage | 6,3 | 5,3 | 4,8 | 6,7 | 3,7 | 4,3 | 2,4 | 3,8 | 5,6 | 2,6 | 5,3 | 2,1 |
| From trachea | 10 | 7,3 | 9,6 | 11 | 19 | 17 | 10 | 14 | 19 | 10 | 17 | 19 |
| From bronchi | 4 | 1 | - | 0,6 | - | - | - | 0,6 | 1 | - | 0,6 | 0,2 |
| Urine | 0,4 | - | - | 2 | - | - | - | - | 0,6 | - | 0,2 | - |

These data demonstrate the leading position of respiratory diseases in the structure of severe infections.

*Table 2. Acinetobacter spp. resistance in ICU (%)*

| Antibiotics | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ampicillin /sulbactam | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Amoxicillin | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Piperacillin /Tazobactam | - | - | - | **82** | **76** | **100** | **100** | **100** | **100** | **100** | **100** | **100** |
| Imipenem | **0** | **11,7** | **21** | **11,7** | **13** | **21** | **43** | **85** | **100** | **100** | **100** | **100** |
| Meropenem | **11,7** | **41** | **41** | **60** | **66,6** | **76** | **87** | **100** | **100** | **100** | **100** | **100** |
| Ertapenem | - | - | - | - | - | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Cefazoline | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Cefuroxim | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Cefotaxim | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Ceftazidim | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Ceftriaxone | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Cefaperazone | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Cefaperazone /sulbactam | **66,6** | **66,6** | **84** | **82** | **66,6** | **73** | **85** | **100** | **100** | **100** | **100** | **100** |
| Cefepim | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Gentamicin | 88 | 86 | 78 | 86 | 88 | 90 | 100 | 100 | 100 | 100 | 100 | 100 |
| Amikacin | **86** | **78** | **90** | **90** | **90** | **90** | **100** | **100** | **100** | **100** | **100** | **100** |
| Tetracycline | 66 | 46 | 17,6 | 17,6 | 26 | 68 | 66 | 70 | 100 | 100 | 100 | 100 |
| Doxicycline | **52** | **41** | **16** | **11,7** | **16** | **52** | **50** | **50** | **100** | **100** | **100** | **100** |
| Ofloxacin | 66,6 | 78 | **90** | 76 | 90 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Ciprofloxacin | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Levofloxacin | - | - | 78 | 100 | - | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Gatifloxacin | - | - | - | - | - | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Polymixin | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **4** | **5** | **3** | **4** | **4** |

Note: "-" - the study was not conducted

***Fig.1. Cultivability of the most important pathogens of purulent-septic complications in ICU***

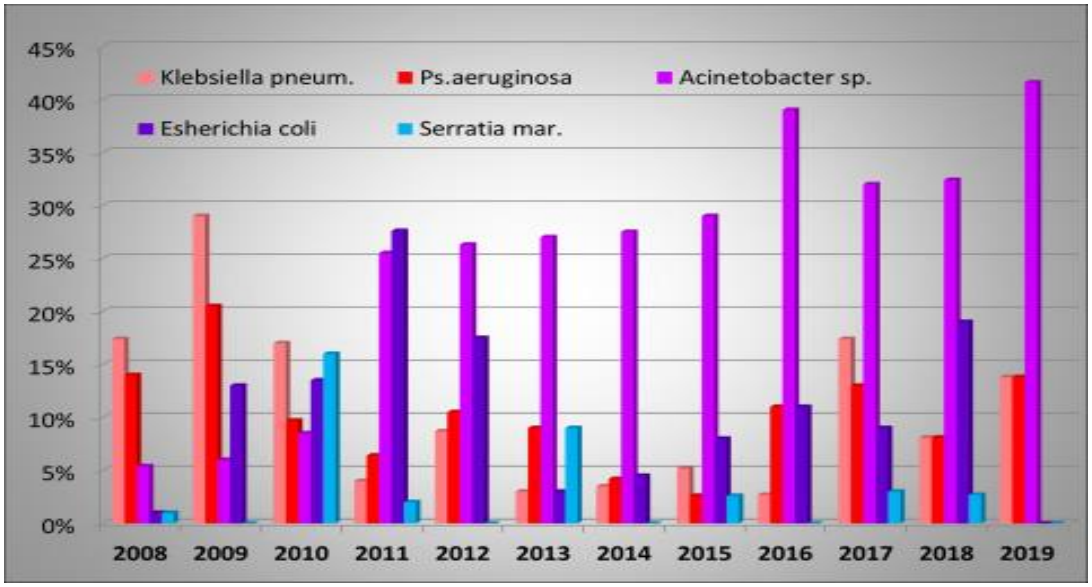
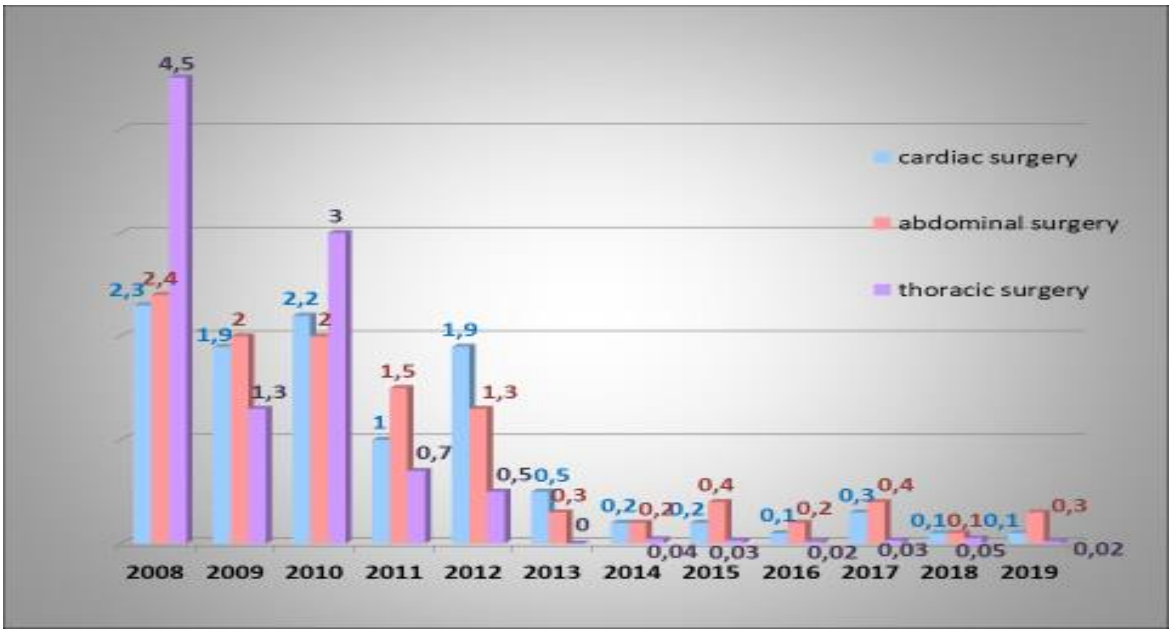


*Fig.2. Frequency of purulent-septic complications in ICU (%)*




Analysis of microbiological monitoring data and antibiotic resistance in ICU shows that during the studied period (2008-2019), in patients undergoing PIVL, there is a tendency of prevalence of Gram-negative microflora isolation and expansion of the spectrum of isolated cultures, namely: Klebsiella pneumonia (17.0-29.0%), Ps. aeruginosa (14.0-20.5%) and Candida (4.2-10.0%) were dominant in 2008-2012. The drugs active against them were meropenem (60.0-30.0%S), polymyxin B (100.0-95.0%S), cefoperazone/sulbactam (72.0-58.0%), amikacin (72.0-64.0%), ofloxacin (69.0-56.0%). St.aureus and Enterococcus spp. occurred in 4.0-2.0% of cases.

Subsequent 2012-2019 among the most "topical" pathogens of hospital infections were Acinetobacter spp. (26.0-39.0%), E. coli (27.6-11.0%), gr.r.Candida (11.0-18.5%). The range of perorates active against them was extremely limited: polymyxin B (97.0-95.0%S), imipenem (90.0-30.0%S). Moreover, out of 50 tracheobronchial aspirate samples in 25 cases - were isolated associated. The problem was the development and progression of renal insufficiency when using amikacin in patients with PON.

**RESULTS.**

The effective reduction of purulent-septic complications frequency (despite the annual increase in the number of hospitalized patients) was the isolation of patients with high risk of infection with nosocomial strains, high level of SRB - 70 mg/l and more, protocols of resuscitation in case of purulent-septic complications, timely adequate antibiotic therapy. The achieved results indicate the effectiveness of the applied monitoring system, despite the high resistance of pathogens; the need for continuous control of the microbial landscape.

Due to the introduction of recommended protocols for antibacterial prophylaxis and treatment, methods of monitoring the effectiveness of antimicrobial therapy, the introduction of forecasting methods (identification of risk groups and more targeted antibiotic prophylaxis of nosocomial infections), effective criteria for ventilator modes, approaches to pathogenetic therapy, nutritional support, etc. since 2012, there is a decrease in the frequency of purulent-septic complications, so that in 2012-2019 in the cardiac block, it was from 1.5-1.3 to 0.3-0.1%, in the abdominal block - from 1.0-1.9 to 0.5-0.2%, in the thoracic block - from 0.7-0.5 to 0.03-0.02% (Fig.2).

**CONCLUSION**

In the structure of pathogens of nosocomial infections in ICU - Acinetobacter spp. is the leading one, which has high resistance to all groups of antibacterial drugs. Over the last 12 years, the increase in the isolation rate of this pathogen amounted to: 5.4 - 39%, i.e., an increase of 7 times. Acinetobacter is capable of causing infections of any localization. The increasing antibiotic resistance of Acinetobacter spp. causes the necessity to study antibiotic grams of all strains isolated from patients for adequate choice of means of effective antibiotic therapy. The obtained data were used to optimize empirical antibiotic therapy in patients with purulent-septic complications in ICU.

**REFERENCES**

1. Antunes LC, Visca P, Towner KJ. Acinetobacter baumannii: evolution of a global pathogen. Pathog Dis. 2014; 71 (3): 292301. doi: 10.1111/2049-632X.12125.
2. Al Atrouni A, Joly-Guillou ML, Hamze M, Kempf M. Reservoirs of Non-baumannii Acinetobacter Species. Front Microbiol. 2016; 7: 49. doi: 10.3389/fmicb.2016.00049.
3. Ershova K, Savin I, Kurdyumova N, Wong D, Danilov G, Shifrin M, et al. Implementing an infection control and prevention program decreases the incidence of healthcareassociated infections and antibiotic resistance in a Russian neuro-ICU. Antimicrob Resist Infect Control. 2018; 7: 94. doi: 10.1186/s13756-018-0383-4.
4. Briko NI, Brusina EB, Zueva LP, Kovalishena OV, Ryapis L, StasenkoVL, et al. Hospital Strain – Mysterious Reality. Epidemiology and Vaccinal Prevention. 2013; № 1 (68): 30-35. Russian (Брико Н.И., Брусина Е.Б., Зуева Л.П., Ковалишена О.В., Ряпис Л.А., Стасенко В.Л. и др. Госпитальный штамм – непознанная реальность // Эпидемиология и вакцинопрофилактика. 2013. № 1 (68). С. 30-35).
5. Brusina EB, Barbarash OL. Risk management of infections connected with providing medical aid (risk management). Medical Almanac. 2015; 5 (40): 22-25. Russian (Брусина Е.Б., Барбараш О.Л. Управление риском инфекций, связанных с оказанием медицинской помощи (риск-менеджмент) // Медицинский альманах. 2015. № 5 (40). С. 22-25).
6. Cray JA, Bell AN, Bhaganna P, Mswaka AY, Timson DJ, Hallsworth JE. The biology of habitat dominance; can microbes behave as weeds? Microb Biotechnol. 2013; 6 (5): 453-492. doi: 10.1111/1751-7915.12027.
7. Doughari HJ, Ndakidemi PA, Human IS, Benade S. The ecology, biology and pathogenesis of Acinetobacter spp.: an overview. Microbes Environ. 2011; 26 (2): 101-112. doi: 10.1264/jsme2.ME10179.
8. Ershova K, Savin I, Kurdyumova N, Wong D, Danilov G, Shifrin M, et al. Implementing an infection control and prevention program decreases the incidence of healthcareassociated infections and antibiotic resistance in a Russian neuro-ICU. Antimicrob Resist Infect Control. 2018; 7: 94. doi: 10.1186/s13756-018-0383-4.
9. Eze EC, Chenia HY, El Zowalaty ME. Acinetobacter baumannii biofilms: effects of physicochemical factors, virulence, antibiotic resistance determinants, gene regulation, and future antimicrobial treatments. Infect Drug Resist. 2018; 11: 22772299. doi: 10.2147/IDR.S169894.
10. Kenyon JJ, Hall RM. Variation in the complex carbohydrate biosynthesis loci of Acinetobacter baumannii genomes. PLoS One. 2013; 8 (4): e62160. doi: 10.1371/journal.pone.0062160.

11. Salzer HJ, Rolling T, Schmiedel S, Klupp EM, Lange C, Seifert H. Severe community-acquired bloodstream infection with Acinetobacter ursingii in person who injects drugs. Emerg Infect Dis. 2016; 22 (1): 134-137. doi: 10.3201/eid2201.151298.
12. Towner A, Park AN, Gander R, Orr K, Arocha D, Zhang S, et al. Acinetobacter infections and outcomes at an academic medical center: a disease of long term care. Open Forum Infectious Diseases. 2015; 2 (1): ofv023. doi: 10.1093/ofid/ofv023.
13. Wong D, Nielsen TB, Bonomo RA, Pantapalangkoor P, Luna B, Spellberg B. Clinical and Pathophysiological Overview of Acinetobacter Infections: a Century of Challenges. Clin Microbiol Rev. 2017; 30 (1): 409-447. doi: 10.1128/ CMR.00058-16.
14. WHO priority pathogens list for R&D of new antibiotics. Acinetobacter: Microbiological, Pathogenetic and Resistant Properties [Electronic resource]. Available at: https: //www. who.int/ru/news-room/detail/27-02-2017-who-publishes-listof-bacteria-for-which-new-antibiotics-are-urgently-needed (accessed 15.02.2019).