



# Carbapenem-Resistant Bacteria in Oncology Clinic

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## Abstract

The emergence and spread of carbapenem-resistant (*CarR*) bacteria are a global problem for treatment of patients all over the world. This type of antimicrobial resistant is particularly danger by cancer patients. Regular monitoring of carbapenem-resistant microorganisms and the determination of the mechanism of their spread will help keep *CarR* bacteria from spreading This article contains the results of monitoring of carbapenem-resistant strains of microorganisms in the oncological clinic.

**Keywords:** Carbapenemases; Carbapenems; Carbapenem-resistant (*CarR*) bacteria; Cancer patient

## Introduction

The occurrence of carbapenem-resistant (*CarR*) bacteria is a serious problem for the treatment of potentially fatal infections. According to estimates of most authors the mortality rate for infections caused by the *CarR* microorganisms is 24%-70% [1-4]. They are a growing concern in global public-health due to their associative resistance to all or almost all  $\beta$ -lactams and other classes of antibiotics, such as aminoglycosides, fluoroquinolones and cotrimoxazole. Treatment options are limited and there is still no consensus on optimal treatment regimens [5-7]. Therefore, regular monitoring of carbapenem-resistant strains of microorganisms and followed by the determination of the molecular mechanism of resistance is extremely important to prevent the spread of such bacteria and to select the optimal antibiotic therapy in any clinics. The purpose of this study was to determine the species composition of the carbapenem-resistant strains of microorganisms isolated from the biological materials of patients at an oncology clinic, to identify strains producing carbapenemases and to determine the types of carbapenemases.

## Materials and Methods

Studies were conducted in the period 2017-2018. Sources of bacterial isolates were biological materials from patients of the oncological clinic. The study took strains of gram-negative bacteria resistant (R) or intermediate resistant (I) to carbapenems. Microorganisms were identified by the method of matrix-associated laser desorption/ionization-time-of-flight mass

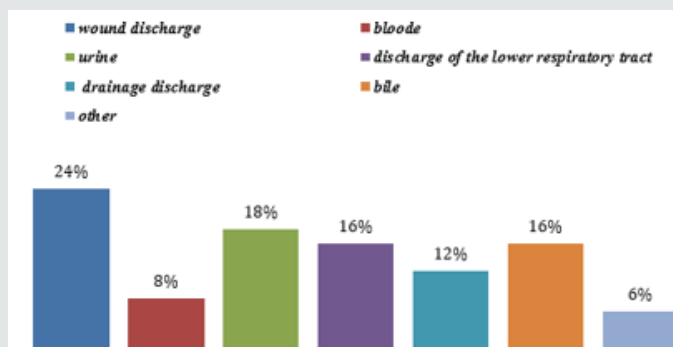
spectrometry (MALDI-TOF) and software MALDI Biotyper v.3.0 (Bruker Daltonics, Germany). Genes encoding carbapenemases of the VIM, OXA-48, OXA-40, OXA-23, NDM groups were detected by real-time polymerase chain reaction using the AmpliSense® MDR MBL-FL and AmpliSense® MDR KPC/OXA-commercial kits 48-FL” (developed by FBUN Central Research Institute of Epidemiology, Russia) and the Rotor-Gene 6000 system (Corbett Research, Australia). The strains of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii* from the RIACH collection (n= 14), producing known carbapenemases of the listed types, were used as positive controls. *Paeruginosa* isolates tested for MBL of the VIM, IMP, NDM and Class A carbapenemases groups (GES-5-like). The strains of *A.baumannii* were tested for the above-mentioned metal beta-lactamase and class A carbapenemases, as well as the presence of OXA-carbapenemases of class D typical of this type (groups OXA-23, -24/40,-51, -58). Bacteria of the *Enterobacteriaceae* family were examined for the presence of MBL and OXA-carbapenemases (group OXA-48).

## Results

The Gram-negative bacteria resistant to carbapenems were studied in the laboratory of microbiological diagnostics and treatment of infections in oncology N.N. Blokhin National Medical Research Cancer Center, Russia in conjunction with the Microbiology Laboratory of the Research Institute of Antimicrobial Chemotherapy, Russia, in 2017-2018. A total of 123 strains of the most frequently isolated microorganisms were studied (A.

*baumannii*-35 (28.5%), *P. aeruginosa*-26 (21.1%), *E. coli*-11 (8.9%), *K.pneumoniae*-37 (30.1%). Also, the study took strains of such microorganisms as: *Enterobacter cloacae*, *Serratia marcescens*, *Enterobacter asburiae*, *Burkholderia cepacia* the relative amount of

which was 10.6%. All test isolates were obtained from biological materials of oncological clinic patients. The ratio of carbapenem-resistant microorganisms from different biological materials of cancer patients is presented in Figure 1.



**Figure 1:** The ratio of carbapenem-resistant microorganisms from various biological materials of cancer patients.

**Table 1:** Types of carbapenemases CarR strains of microorganisms circulating in the oncological clinic.

No	Name of microorganisms (n=123)	Types of carbapenemases					
		VIM	NDM	OXA-23	OXA-40	OXA-48	GES-5-like*
1	<i>A.baumannii</i> (n=35)			34 (97,1%)	1 (2,8%)		
2	<i>Paeruginosa</i> (n=26)	12 (46,1%)					3 (11,5%)
3	<i>K.pneumoniae</i> (n=37)		1 (2,7%)			32 (86,5%)	
4	<i>E.coli</i> (n=11)					1 (9,1%)	
5	<i>Enterobacter asburiae</i> (n=1)					1 (100,0%)	
6	<i>Enterobacter cloacae</i> (n=5)		2 (40,0%)				
7	<i>Serratia marcescens</i> (n=2)					1 (50,0%)	

\* VIM, NDM, GES, OXA-48, OXA-40, OXA-23 - name types of carbapenemases

The most frequently carbapenem-resistant strains of microorganisms were isolated from wound discharge (24%), from urine (18%), in equal amounts from the discharge of the lower respiratory tract and from bile (16%). In the discharge drainage and in the blood, *CarR* strains were found in 12% and 8% respectively. When conducting research, the types of carbapenemases produced by microorganism strains isolated from biological materials of cancer patients were determined. Types of carbapenemases *CarR* strains of microorganisms circulating in the oncological clinic are presented in Table 1. As a result of the research, it was revealed that out of 123 strains of microorganisms resistant to carbapenems, 88(71.5%) strains of bacteria were producers of carbapenemases. The carbapenemase-producing of type OXA-48 were: *K.pneumoniae* (86.5%), *E.coli* (9.1%), *Enterobacter asburiae* (100%) and *Serratia marcescens* (50.0%). The producers of NDM-type carbapenemases were also identified - this is *Enterobacter cloacae* (40.0%) and *K.pneumoniae* (2.7%). *A. baumannii* produced carbapenemases OXA-23 (97.1%) and OXA-40 (2.8%). Among the *Paeruginosa* strains studied 46.1% produced VIM-type carbapenemases and 11.5% GES-5-like.

## Conclusion

The species composition of gram-negative carbapenem-resistant microorganisms isolated from the biological materials of cancer patients is presented as the most frequently isolated hospitals pathogens (*A. baumannii*, *P. aeruginosa*, *E. coli*, *K.pneumoniae*) and microorganisms, the relative amount of which as infectious complications pathogens not large (*Enterobacter cloacae*, *Enterobacter asburiae*, *Serratia marcescens*, etc.). Endemic strains of bacteria producers of globally common carbapenemases: OXA-48, OXA-23, NDM, VIM - types are circulate in the oncological clinic. Obviously, regular monitoring of *CarR* strains of microorganisms, determination of resistance genes by molecular-genetic methods, well thought-out antimicrobial therapy and effective infection control strategy are necessary to effectively inhibit the spread of carbapenem-resistant bacteria.

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