

# Carriage of Multidrug-Resistant Pathogens amongst Patients in a Palliative Care

Bożena Nowaczyk<sup>1,A,B,C,D,E,F</sup>

ORCID: 0000-0002-3493-7884

Monika Lorenz<sup>2,B,E,F</sup>

ORCID: 0000-0002-0572-7167

Danuta Dyk<sup>1,A,D,E,F</sup>

ORCID: 0000-0003-2435-9424

Jerzy T. Marcinkowski<sup>3,A,C,E,F</sup>

ORCID: 0000-0001-6495-8988

<sup>1</sup> Department of Anesthesiology and Intensive Care Nursing,  
Poznan University of Medical Sciences, Poland;

<sup>2</sup> Hospital in Puszczykowo, Poland;

<sup>3</sup> Faculty of Medicine, Lazarski University, Warsaw, Poland

A – research concept and design, B – data collection, C – data analysis and interpretation, D – article writing,  
E – critical review of the article, F – final approval of the article

DOI: 10.26399/rmp.v29.4.2023.21/b.nowaczyk/d.dyk/m.lorenz/j.t.marcinkowski

## ABSTRACT

*Carriage of Multidrug-Resistant Pathogens amongst Patients in a Palliative Care*

Nowaczyk B.<sup>1</sup>, Dyk D.<sup>1</sup>, Lorenz M.<sup>2</sup>, Marcinkowski J.T.<sup>3</sup>

<sup>1</sup> Department of Anesthesiology and Intensive Care Nursing, Poznan University of Medical Sciences, Poland; <sup>2</sup> Hospital in Puszczykowo, Poland; <sup>3</sup> Faculty of Medicine, Lazarski University, Warsaw, Poland

**Objectives of the study.** With the aging population and an increase in cancer incidence, the demand for palliative care is rising both in Poland and worldwide. Experiences and publications on multidrug-resistant organisms (MDRO) and risk factors for healthcare-associated infections (RFHAI) in the Palliative and Hospice Care Department (PHCD), as well as infection diagnosis and treatment, are scarce despite being more common among palliative care patients than in other patient groups. The microorganisms isolated from infections increasingly exhibit resistance to the majority, and sometimes all, available medications. This study aims to estimate the carriage of MDRO and RFHAI among patients in the Palliative-Hospice Care Department.

**Methods.** This prospective study was conducted during the patients' stay at the hospital ward. It involved 799 patients (382 men and 417 women, average age: 73.5 years) hospitalized in PHCD from November 1, 2014, to March 31, 2017. Upon admission, all patients were assessed for 29 predetermined RFHAI and underwent microbiological screening tests (MST) to detect MDRO. Swabs were taken from the nasal vestibule and anus following anti-septic protocols to prevent sample contamination by environmental microorganisms. A statistical analysis of RFHAI and MST results was performed.

**Results.** MDRO carriage was identified in 299 (37.4%) patients admitted to PHCD. The average RFHAI assessment score for patients with MDRO detected in MST was 10.14, higher than in patients without MDRO (8.7). The most common RFHAI in PHCD patients included previous hospitalization within the last six months or transfer from another hospital, eating disorders, antibiotic therapy within three months before hospitalization, and invasive procedures.

## STRESZCZENIE

*Nosicielstwo drobnoustrojów wielolekoopornych wśród pacjentów z oddziału opieki paliatywnej*

Nowaczyk B.<sup>1</sup>, Dyk D.<sup>1</sup>, Lorenz M.<sup>2</sup>, Marcinkowski J.T.<sup>3</sup>

<sup>1</sup> Zakład Pielęgniarstwa Anestezjologicznego i Intensywnej Opieki, Uniwersytet Medyczny w Poznaniu; <sup>2</sup> Szpital w Puszczykowie; <sup>3</sup> Wydział Medyczny, Uczelnia Łazarskiego, Warszawa

**Cele badania.** Ze względu na starzenie się społeczeństwa i wzrost zachorowań na nowotwory wzrasta zapotrzebowanie na opiekę paliatywną zarówno w Polsce, jak i w innych krajach świata. Doświadczenia oraz publikacje dotyczące nosicielstwa drobnoustrojów wielolekoopornych (MDRO) i czynników ryzyka zakażeń szpitalnych (RFHAI) w Oddziale Opieki Paliatywno-Hospicyjnej (OOP-H) oraz rozpoznawania i leczenia zakażeń są niewielkie pomimo tego, że u pacjentów objętych opieką paliatywną występują one częściej niż w pozostałych grupach chorych. Drobnoustroje wyizolowane z infekcji coraz częściej charakteryzują się opornością na większość, a czasem nawet na wszystkie dostępne w terapii leki. Celem badań było oszacowanie nosicielstwa MDRO i RFHAI wśród pacjentów OOP-H.

**Metody.** Badania prowadzono metodą prospektywną w trakcie pobytu pacjenta na oddziale. Badaniem objęto 799 pacjentów (382 mężczyzn i 417 kobiet; średni wiek: 73,5 lat) hospitalizowanych na OOP-H w okresie od 01.11.2014 r. do 31.03.2017 r. U wszystkich pacjentów przy przyjęciu na OOP-H wykonano ocenę 29 przyjętych RFHAI oraz mikrobiologiczne badania przesiewowe (MBP) w celu identyfikacji MDRO; w tym celu pobrano wymaz z przedziona nosa oraz odbytu - zgodnie z zasadami antyseptyki, w sposób zapobiegający kontaminacji próbki przez drobnoustroje z otoczenia. Dokonano analizy statystycznej wyników MBP z RFHAI.

**Wyniki.** Nosicielstwo MDRO wykryto u 299 (37,4%) pacjentów przyjmowanych na OOP-H. Średnia punktacja w ocenie RFHAI u pacjentów z wykrytym w MBP MDRO wyniosła 10,14 i była wyższa niż u pacjentów bez MDRO (10,14 vs 8,7). Najczęstsze czynniki ryzyka zakażenia szpitalnego u pacjentów OOP-H to: wcześniejsza hospitalizacja w ostatnich 6 miesiącach lub przeniesienie z innego szpitala, zaburzenia odżywiania, antybiotykoterapia < 3 miesiące przed hospitalizacją oraz sztuczne drogi (cewnik moczowy, cewnik naczyniowy, rurka tracheotomijna).

**Conclusions.** *ESBL-producing Proteus mirabilis, carbapenemase-producing Pseudomonas aeruginosa, Vancomycin-Resistant Enterococcus (VRE), ESBL-producing Escherichia coli, ESBL-producing Enterobacter cloacae, and ESBL-producing Klebsiella pneumoniae detected in MST among patients treated at PHCD were more frequent in patients with certain RFHAI.*

**Key words:** *palliative care, multi-drug resistant bacteria, risk factors for hospital acquired infection, microbiological screening tests.*

**Wnioski.** *Proteus mirabilis ESBL, Pseudomonas aeruginosa szczep wytwarzający karbapenemazy, Enterococcus VRE, Escherichia coli ESBL, Enterobacter cloacae ESBL i Klebsiella pneumoniae ESBL wykryte w MBP u pacjentów przyjmowanych na OOP-H występowały częściej u pacjentów z niektórymi RFHAI.*

**Słowa kluczowe:** *opieka paliatywna, bakterie wielolekooporne, czynniki ryzyka zakażenia szpitalnego, mikrobiologiczne badania przesiewowe*

## Introduction and Objective of the Study

One of the most significant challenges for contemporary medicine and public health is the emergence, selection, and spread of antibiotic-resistant strains of major human pathogenic bacteria, leading to an inability to effectively treat healthcare-acquired infections (HAI). The past year has seen a rapid rise in HAIs caused by multidrug-resistant organisms (MDRO). Contributing factors include the misuse and inappropriate use of antibiotics, a limited pipeline of new effective drugs for treating infections, an increase in patients with infection risk factors, an aging society with more patients in nursing homes and care institutions, lack of, or non-compliance with, infection therapy recommendations in line with the principles of evidence-based medicine, and underutilization of microbiological diagnostics.[1]

The risk of HAI is influenced by the involved microorganism, the patient, and the hospital environment.[1-3]

Over 70% of bacteria responsible for nosocomial infections are resistant to at least one type of antibiotic.[4,5] Multidrug-resistant Gram-negative bacteria account for more than 50% of medical care associated infections.[6,7] Microorganisms of primary concern in the acquisition of resistance to many groups of antibiotics are: *Enterococcus faecium*, *Staphylococcus aureus*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and the *Enterobacteriaceae* family, including *Klebsiella pneumoniae*.

The evolving epidemiological situation and increased HAI risk have led to more microbiological screening tests (MST) aimed at detecting MDRO and assessing risk factors for healthcare-associated infections (RFHAI).[8-11] Despite the higher frequency of MDROs in palliative care patients, research and publications on antibiotic-resistant bacteria carriage and RFHAI in PHCD, including diagnosis and treatment of infections, are limited.[12-19] Notwithstanding the advanced palliative care in Poland, there is a noticeable lack of evidence regarding MDRO carriage and RFHAI research in Palliative and Hospice Care Department (PHCD). This study seeks to identify which investigated RFHAI influence MDRO carriage in PHCD patients.

## Materials and Methods

### Place of Study and Patients Involved in the Research

The research was conducted at the PHCD ward at one of the hospitals in Poland. This ward treats patients with chronic, progressive, life-threatening diseases that are deteriorating and require increased medical supervision and intensive symptomatic treatment. The study involved 799 patients (382 men and 417 women, mean age: 73.5 years) hospitalized successively at PHCD from November 1, 2014, to March 31, 2018.

### Bioethics Committee Approval

The study received approval from the Bioethics Committee at Poznań University of Medical Sciences (Resolution no. 748/16).

### Methods and Tools

The study utilized prospective methods during the patients' hospital stay. Upon admission, all patients underwent nasal swabs for MRSA and rectal swabs for MDRO. Within 12 hours of hospital admission, the risk of HAI was evaluated using a form assessing 29 risk factors for infection. This information was recorded in a specially designed observation questionnaire.

### Microbiological Screening Tests

Indications for microbiological screening tests (MST) included: (1) previous hospitalization at other healthcare facilities, (2) long-term stay at care facilities, and (3) experience of health treatment services that are a risk factor for colonization. The indications concerned all patients hospitalized at PHCD. MST was performed for all patients hospitalized at PHCD upon admission to the ward.

MSTs targeted the following MDROs: *Methicillin-Resistant Staphylococcus Aureus* (MRSA), *Vancomycin-Resistant Enterococcus* (VRE), *Enterobacteriaceae* strains producing carbapenemases (CPE), *Enterobacteriaceae* rods, and *Pseudomonas aerugi-*

*nosa* strains producing extended-spectrum beta-lactamases (ESBL); multidrug-resistant *Acinetobacter baumannii* and *P. aeruginosa* strains.

Microbial cultures were conducted under conditions optimal for the growth of the targeted microorganisms. The swabs were inoculated on nutrient and differentiating media for MRSA, VRE, ESBL, and selective chromogenic agars for the detection of carbapenemases - CRE. The antibiotic sensitivities were interpreted according to the European Committee on Antimicrobial Susceptibility Testing – EUCAST and the National Reference Center for Antimicrobial Susceptibility (Krajowy Ośrodek Referencyjny ds. Lekowrażliwości Drobnoustrojów - KORLD) at the National Medicines Institute in Warsaw criteria. MST aimed to identify MDRO-colonized patients and assess the actual carriage among patients in PHCD.

### Statistical Analysis

The authors conducted a statistical analysis of the results from MST, with 29 assumed RFHAI. The statistical analysis included 799 PHCD patients. The following statistical tests were used: (1) the  $\chi^2$  test (chi-square independence test) for comparison of qualitative variables, (2) student's t-test (in cases of heterogeneous variance of variables, a test with independent estimation of variance was used) to compare mean value differences. The statistical analysis of the data was performed using Statistica 12 and MS Excel. In all calculations,  $p < 0.05$  was considered statistically significant.

### Results

Of the 799 patients, MDRO carriage was confirmed in 299 patients (37.4%) (155 men and 144 women). In the remaining 500 patients (62.6%) (227 men and 273 women), no pathogen carriers were identified.

The analysis included RFHAI from 299 patients with MDRO, whose health conditions qualify them for healthcare services in palliative care. The conditions were as follows: cancer in 187 patients (62.5%), pressure ulcers in 70 patients (23.4%), cardiomyopathy in 26 patients (8.7%), and other indications listed in the

current Ordinance of the Minister of Health on guaranteed services in the field of palliative and hospice care of 29<sup>th</sup> October 2013 (*Rozporządzenie Ministra Zdrowia z dnia 29 października 2013 r., w sprawie świadczeń gwarantowanych z zakresu opieki paliatywnej i hospicyjnej*) - 16 (5.4%).[20]

The mean age of patients with carriage of MDRO was 74.5 years (minimum 40 years, maximum 96 years); the mean age of women was 76 years (minimum 40 years, maximum 96 years); the mean age of men was 72 years (minimum 43 years, maximum 94 years). Regarding the state of consciousness, 78 patients were fully conscious, 206 had limited consciousness, and in 15, logical contact was impossible. There were 35 (11.7%) ambulatory patients and 264 (88.3%) bed-bound patients in the study group. Among the 299 patients, 207 were carriers of one pathogen, 87 of two pathogens, and 15 of three pathogens.

**Table 1.** MDRO species detected in the microbiological screening tests

MDRO	N 299 patients	Rectal swab
<i>Klebsiella pneumoniae</i> ESBL	120	109 (90.8%)
<i>Staphylococcus aureus</i> MRSA	33	11 (33.3%)
<i>Escherichia coli</i> ESBL	85	83 (97.6)
<i>Enterococcus</i> spp VRE	136	134 (98.5)
<i>Citrobacter freundii</i> ESBL	11	10 (90.9%)
<i>Proteus mirabilis</i> ESBL	6	6 (100.0%)
<i>Pseudomonas aeruginosa</i> (carbapenemase-producing strain)	7	2 (28.6%)
<i>Enterobacter cloacae</i> ESBL	3	3 (100.0%)
Other: <i>Klebsiella oxytoca</i> ESBL – 3; <i>Morganella morganii</i> – 2.	5	5 (100.0%)

The most common carrier among all surveyed patients was *Enterococcus* VRE. *S. aureus* MRSA was found in 33 patients: in nasal swabs of 16 patients (48.5%) and rectal swabs of 11 patients (33.3%).

The average score from the RFHAI assessment in patients with MDRO detected in MST was 10.14, higher than in patients without MDRO (8.7).

**Table 2.** Assessed risks factors of nosocomial infections

Risk Factor of hospital acquired infection	MDRO yes RF yes	MDRO no RF yes	MDRO yes RF no	MDRO no RF no	Odds ratio for bacteria in RF group	95 % CI	z statistic	Significance level
1. Age over 75 years	20	128	151	480	0.4967	0.2996 to 0.8234	2.713	P = 0.0067
2. Transfer from another hospital / nursing home / hospitalization in the last 6 months	41	222	36	459	<b>2.3547</b>	1.4637 to 3.7883	3.530	P = 0.0004

3. Surgical procedures / invasive tests performed less than 6 months before hospitalization	25	142	132	475	0.6335	0.3972 to 1.0104	1.916	P = 0.0553
4. Carrying alert pathogens	4	34	261	496	0.2236	0.0785 to 0.6369	2.805	P = 0.0050
5. Hygienic negligence / incontinence / fecal incontinence	22	154	123	478	0.5552	0.3406 to 0.9050	2.360	P = 0.0183
6. Previous infections associated with a hospital stay <12 months	21	107	171	479	0.5498	0.3337 to 0.9058	2.348	P = 0.0189
7. Invasive procedures (catheter, stoma, vascular catheter, tracheotomy tube)	33	196	70	467	1.1233	0.7189 to 1.7550	0.511	P = 0.6097
8. Open injury / internal injury / multi-organ injury / victim of physical violence	2	8	289	498	0.4308	0.0909 to 2.0425	1.061	P = 0.2889
9. Damaged skin / tattoos / large scars / piercing	8	51	240	492	0.3216	0.1502 to 0.6884	2.922	P = 0.0035
10. Unconscious / after ingestion / after sudden cardiac arrest / immobilization	6	36	257	494	0.3204	0.1332 to 0.7703	2.543	P = 0.0110
11. Recurrent inflammatory processes	4	18	277	496	0.3979	0.1333 to 1.1875	1.652	P = 0.0985
12. Chronic infection	0	2	297	500	0.3365	0.0161 to 7.0326	0.702	P = 0.4825
13. Acute active infection	5	43	251	495	0.2293	0.0897 to 0.5861	3.076	P = 0.0021
14. Pressure ulcers / skin changes	28	135	136	472	0.7198	0.4592 to 1.1283	1.433	P = 0.1517
15. Antibiotic therapy <3 months before hospitalization	35	198	66	465	1.2454	0.8002 to 1.9382	0.973	P = 0.3308
16. Current radiotherapy / chemotherapy / steroid therapy	7	52	240	493	0.2765	0.1237 to 0.6179	3.134	P = 0.0017
17. Blood coagulation disorders / transfusions of blood preparations <6 months	8	72	219	492	0.2496	0.1182 to 0.5272	3.638	P = 0.0003
18. Metabolic disease	17	79	203	483	0.5120	0.2957 to 0.8866	2.390	P = 0.0169
19. Active cancer	23	155	121	477	0.5850	0.3615 to 0.9465	2.184	P = 0.0290
20. Eating disorders / malnutrition / dysphagia	46	196	57	454	<b>1.8693</b>	1.2245 to 2.8537	2.898	P = 0.0038
21. Decompensated autoimmune disease / allergy in the period of worsening symptoms	0	1	298	500	0.5589	0.0227 to 13.7646	0.356	P = 0.7219
22. Alcoholism / other addictions to narcotic substances, drugs	4	25	270	496	0.2939	0.1012 to 0.8534	2.252	P = 0.0243
23. Smoking >10 cigarettes a day	1	26	272	499	0.0706	0.0095 to 0.5228	2.595	P = 0.0095
24. Ischemic heart disease / decompensated / circulatory insufficiency	24	115	160	476	0.6209	0.3861 to 0.9983	1.967	P = 0.0492
25. Ischemic limb disease / thromboembolic syndrome	3	25	271	497	0.2201	0.0658 to 0.7356	2.459	P = 0.0139
26. Chronic renal failure / dialysis	3	46	250	497	0.1297	0.0399 to 0.4210	3.400	P = 0.0007
27. Chronic hypertrophy of the prostate / impaired urine outflow / urinary incontinence	7	47	245	493	0.2997	0.1335 to 0.6728	2.920	P = 0.0035
28. COPD / asthma / respiratory failure	9	34	256	491	0.5077	0.2398 to 1.0749	1.771	P = 0.0765
29. Risky behaviors / psychiatric disorders / dementia / confusion	25	150	124	475	0.6384	0.4001 to 1.0187	1.882	P = 0.0598





A statistically significant relationship was observed between the occurrence of the risk factor “carrying an alarm pathogen” and the occurrence of *P. mirabilis* ESBL; “previous infections associated with a hospital stay within 12 months” and *P. aeruginosa* strain producing carbapenems; “damaged skin, tattoos ,large scars, piercing” and occurrence of *E. coli* ESBL; “unconsciousness, after ingestion, after cardiac arrest, immobilization” and occurrence of *Pseudomonas aeruginosa* strain producing carbapenems:  $p = 0,00090$ ; “recurrent inflammatory” and *E.coli* ESBL:  $p = 0.00984$  and  $p = 0.02135$ ; “current radiotherapy, chemotherapy and steroid therapy” and the occurrence of *E. cloacae* ESBL:  $p = 0.04336$ ; “active cancer” and *Proteus mirabilis* ESBL:  $p = 0.03070$ ; “alcoholism and other addictions to narcotic substances, drugs” and *Enterococcus* spp. VRE:  $p = 0.04165$ ; “ischemic heart disease, decompensated, circulatory insufficiency” and *Enterococcus* spp. VRE:  $p = 0.01210$  and  $p = 0.03557$ ; “ischemic limb disease , thromboembolic syndrome” and the occurrence of *P. mirabilis* ESBL:  $p = 0.04177$ .

## Discussion

The progress of medicine has prolonged the lives of patients with chronic diseases, but the quality of life, especially at the end of life, often remains a challenge. The basis for undertaking this research was the lack of national information on MDRO and RFHAI carriage status at PHCD, according to the available literature data. Knowledge of RFHAI has had an impact on minimizing the undesirable effects of therapeutic devices used in patients. The assessment of the risk of infection carried out during hospital admission allows for the assessment of patients' initial condition and is an extension of the patients' subjective and objective examination conducted to assess the risks associated with the planned range of activities during hospitalization. The literature increasingly emphasizes that the number of patients with a high number of RFHAI at the time of admission to hospitals is constantly growing. Therefore, it is important to assess the risk of HAI immediately at the point of hospital admission. An analysis of infection risk assessment cards at hospital admission by Skibińska revealed that the most important RFHAI in the Sosnowiec Municipal Hospital are bedsores, the presence of urinary and vascular catheters, and an active, acute inflammatory process.[3] According to Skibińska, an increase in the number of RFs increases the probability of HAI.

In the study by Grądalski and Burczyk-Fitowska, the most common RF were chronic steroid therapy, previously used antibiotic therapy, and catheterization of the urinary bladder.[13]

Our own research indicates the most important RF-HAIs are previous hospitalization in the last 6 months or transfer from another hospital, eating disorders, antibiotic therapy within 3 months before hospitalization, and so-called artificial pathways (urinary catheter, vascular catheter, tracheotomy tube). Given that eating disorders and artificial pathways are frequent risk factors for infections in patients hospitalized at the PHCD, care procedures should be observed for venepuncture, bladder catheterization, and the care of patients with artificial pathways. Care should also be taken to ensure shorter days of exposure to modifiable risk factors (vascular catheters, urinary catheters) and better provision of nutritional treatment.

The urinary catheter should only be inserted into the urinary bladder if there is an indication or at the explicit request of the patient to improve comfort during the end of life. The assessment of the risk of infection at the moment of patients' admission to the hospital has a practical application in directing active supervision of high-risk patients, conducted by an epidemiology specialist, from the moment of admitting the patient to the hospital.

In this paper, we present for the first time the results of MDRO carriage among palliative care patients. Our studies have shown that some RFHAI correlate with the occurrence of MDRO carriage. It was observed that the occurrence of MDRO in patients who had the RF of “previous hospitalization in the last 6 months or transfer from another hospital” was more than twice as frequent as in the case of other RF (OR = 2.3547), and for the RF “eating disorder” occurrence of MDRO was almost twice as frequent as in the case of other RFs (OR = 1.8693).

*P. mirabilis* ESBL is much more common in patients with the following risk factors: “carriage of an alert-pathogen”, “active cancer disease” and “ischemic limb disease / thromboembolic syndrome”. *P. aeruginosa*, the carbapenemase-producing strain, is more common in patients with the following risk factors: “previous experience of infection associated with hospital stay within last 12 months”, “unconscious / after aspiration /after cardiac arrest / immobilization”. *Enterococcus* VRE is more common in patients with the following risk factors: “alcoholism / other addictions to intoxicating substances, drugs” and “ischemic heart disease / decompensated / circulatory insufficiency”. *E. coli* ESBL is more common in patients with the following risk factors: “damaged skin / tattoos / large scars / piercing” and “chronic infection”. *E. cloacae* ESBL is more common in patients currently undergoing radiotherapy / chemotherapy / steroid therapy, and *K. pneumoniae* ESBL in patients with active cancer.

The results obtained in this study support the need for continued research on the correlation between

RFHAI and the occurrence of MDRO in other patient groups.

Research limitations: Despite an advanced level of palliative care in Poland, the literature reveals a lack of evidence concerning MDRO carriage and research concerning RFHAI at PHCD. Research was conducted in one PHCD. In Poland, monitoring HAI in PHCD is not a standard conduct.

## Conclusions

1. Carriage of MDRO among patients admitted to PHCD is high.
2. Most common RFHAI by patients in PHCD are: earlier hospitalization during the last 6 months or transfer from another hospital, eating disorders, antibiotic therapy < 3 months before hospitalization, and artificial routes (urinary catheter, vascular catheter, tracheostomy tube).
3. MST and knowledge of RFHAI can restrain HAI among patients admitted to PHCD.

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No potential conflict of interest was reported by the authors.

### Address for correspondence:

Bożena Nowaczyk  
e-mail: [bnowaczyk@ump.edu.pl](mailto:bnowaczyk@ump.edu.pl)  
Zakład Pielęgniarstwa Anestezjologicznego  
i Intensywnej Opieki,  
Uniwersytet Medyczny w Poznaniu, Polska  
ul. Rokietnicka 2a  
60-806 Poznań