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ORIGINAL RESEARCH

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Occurrence of alert pathogens in patients hospitalised in the department of lung diseases

Występowanie patogenów alarmowych u chorych hospitalizowanych na oddziale chorób płuc

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Abstract

Introduction: Infections caused by multiple drug-resistant pathogens represent an increasingly often encountered challenge in clinical practice. The problem particularly applies to patients with chronic lung diseases resulting in multiple hospitalisations. The aim of this paper was to analyse the incidence of alert pathogens isolated from patients hospitalised in the department of lung diseases, who were divided into three groups: patients qualified for lung transplantation, patients treated for neoplastic diseases and patients with chronic lung diseases.

Materials and methods: Analysis involved microbiological test results of 3950 samples obtained from 3521 patients divided into: 200 patients being qualified for lung transplantation, 1292 patients treated for neoplastic diseases and 2029 patients with chronic lung diseases.

Results: Infection with alert pathogen was found in 155 of 3521 patients (4.4%). Most often isolated infectious agent was *P. aeruginosa,* which accounted for 27% of infections. Other pathogens were as follows *A. baumanii ESBL(−)* (13%), *S. pneumoniae* (12%), *E. cloacae ESBL(+)* (10%), *K. pneumoniae ESBL(+)* (10%), *S. aureus MRSA* (8%), *E. faecalis* (7%), *E. coli ESBL(+)* (6%), *S. maltophilia ESBL(+)* (5%) and *E. kobei ESBL(+)* (2%). Alert pathogens were found in 31 (15%) of 200 patients being qualified for lung transplantation, 89 (4.4%) of 2029 patients with chronic lung diseases and 35 (2.7%) of 1292 patients treated for neoplastic diseases. Difference between infection frequency in patients being qualified for lung transplantation and the remaining groups was statistically significant ($p < 0.01$). *P. aeruginosa* infection was the most frequent in all groups. It constituted 35% in patients being qualified for lung transplantation, 29% in patients treated for neoplastic diseases and 22% in patients with chronic lung diseases.

Conclusions: Infections caused by alert pathogens were found in more than 4% of patients hospitalised in the department of lung diseases between 2007 and 2011. Their frequency was significantly higher in patients being qualified for lung transplantation than in other analysed groups. In all examined groups the most frequently isolated bacteria was *P. aeruginosa* (27% of all isolates).

Key words: alert pathogens, lung diseases, antibiotic resistance, lung transplantation, lung cancer

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Streszczenie

Wstęp: Zakażenia spowodowane przez patogeny wielolekooporne stają się coraz częściej wyzwaniem terapeutycznym dla klinicystów. Problem ten dotyczy również pacjentów z przewlekłymi chorobami płuc wymagających wielokrotnych hospitalizacji. Celem pracy była analiza częstości występowania patogenów alarmowych wyizolowanych od chorych oddziału chorób płuc, w podziale na trzy grupy: kwalifikowanych do przeszczepienia płuca, leczonych z powodu choroby nowotworowej oraz leczonych z powodu przewlekłych chorób płuc.

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Materiał i metody: Analiza dotyczyła wyników badań mikrobiologicznych 3950 materiałów pochodzących od 3521 chorych: w tym 200 chorych — kwalifikowanych do przeszczepienia płuca, 1292 — leczonych z powodu choroby nowotworowej i 2029 — leczonych z powodu przewlekłej choroby płuc.
Wyniki: Zakażenia patogenem alarmowym stwierdzono u 155 spośród 3521 chorych (4.4%). Najczęściej izolowanym czynnikiem infekcyjnym był *P. aeruginosa*, który stanowił 27% wszystkich zakażeń, kolejno to *A. Baumanii ESBL(−)* (13%), *S. pneumoniae* (12%), *E. cloacae ESBL(+)* (10%), *K. pneumoniae ESBL(+)* (10%), *S. aureus MRSA* (8%), *E. faecalis* (7%), *E. coli ESBL(+)* (6%), *S. maltophilia ESBL(+)* (5%) i *E. kobei ESBL(+)* (2%). Patogeny alarmowe stwierdzono u 31 (15%) spośród 200 chorych kwalifikowanych do przeszczepienia płuc, 89 (4,4%) spośród 2029 chorych na przewlekłe choroby płuc i 35 (2.7%) spośród 1292 chorych leczonych z powodu choroby nowotworowej. Różnica pomiędzy częstością zakażeń w grupie chorych kwalifikowanych do przeszczepienia a pozostałymi grupami chorych była istotna statystycznie ($p < 0.01$). We wszystkich grupach chorych dominowało zakażenia *P. aeruginosa*. Stanowiło ono: w grupie chorych kwalifikowanych do przeszczepienia — 35%, w grupie chorych leczonych z powodu nowotworu — 29%, w grupie chorych z przewlekłą chorobą płuc — 22%.
Wnioski: Zakażenie bakteriami alarmowymi dotyczyło ponad 4% chorych hospitalizowanych na oddziale chorób płuc w latach 2007–2011. Występowało ono istotnie częściej u chorych kwalifikowanych do przeszczepienia płuc niż w pozostałych dwóch grupach analizowanych chorych. We wszystkich grupach najczęściej izolowaną bakterią alarmową była pałeczka ropy błękitnej (27% wszystkich zakażeń).

Słowa kluczowe: patogeny alarmowe, choroby płuc, antybiotykooporność, przeszczepienie płuca, rak płuca
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Introduction

Infections caused by drug-resistant bacterial strains constitute a significant problem in patients hospitalised in the pulmonology departments. The necessity of frequent use of antibiotics and chemotherapeutic drugs in this group of patients increases resistance of microorganisms to the used drugs and consequently, leads to the appearance of multidrug-resistant strains [1–3]. Furthermore, it should be emphasised that there are more and more people with reduced resistance, who are exposed to infectious complications. It is related to an increased number of older patients with chronic diseases, who undergo lung transplantation and cytostatic treatment [4, 5]. Drug resistance of bacterial strains contributes to limited therapeutic possibilities, prolonged hospitalisations and consequently, a higher probability of failure of the applied treatment [5–8], and a considerable increase in hospitalisation costs [8, 9]. Supervisory programmes that control infections with alert pathogens focus on rapid methods of pathogens identification, implementation of correct procedures for the patient isolation and preparation of specialised therapeutic algorithms [5, 7, 10].

The aim of the study was to analyse the prevalence of alert pathogens isolated from patients of the department of lung diseases divided into three groups: patients qualified for lung transplantation, patients treated for neoplastic diseases and patients treated for chronic lung diseases.

Material and methods

3950 clinical specimens were analysed (85% sputum, 3% urine, 2% blood) from 3521 patients of the pulmonology department, the Third Independent Public Teaching Hospital in Zabrze-Biskupice, hospitalised between 2007–2011.

Basing on clinical characteristics, patients were divided into three groups:

— patients qualified for lung transplantation,
— patients treated for neoplastic lung diseases,
— patients treated for chronic lung diseases.

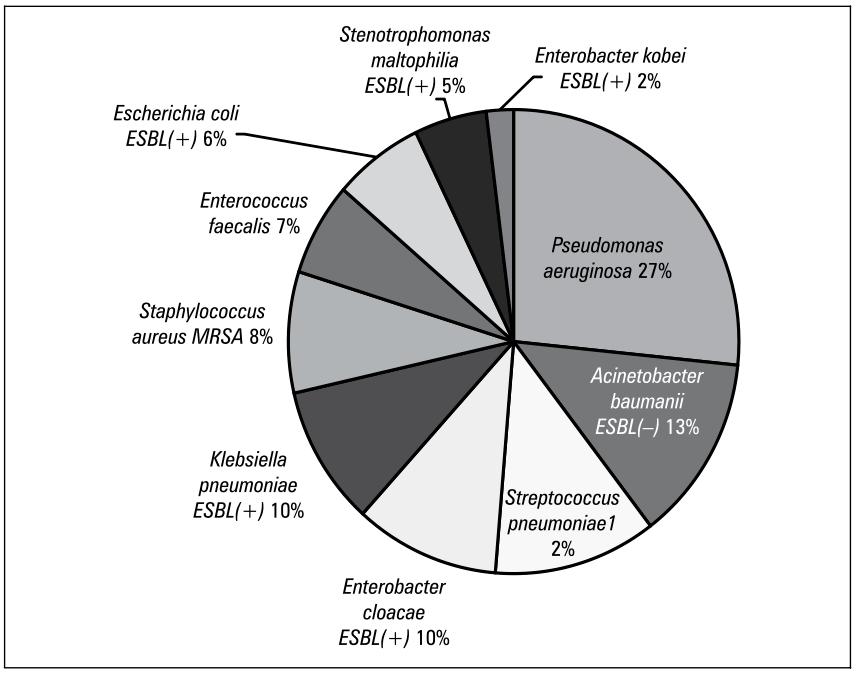
Microbiological diagnosis was conducted basing on applicable standards, collected material was cultured on proper solid or liquid media with their consecutive identification in semi-automatic system manufactured by BioMerieux Polska-Vitek; tests for drug resistance and identification of resistance mechanisms were carried out basing on standards defined in the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

200 specimens from the patients qualified for lung transplantation (5.7% of all specimens), 1292 specimens from patients with neoplasms (36.7% of all specimens) and 2029 from patients with chronic lung diseases (57.6% of all specimens).

The obtained data were analysed statistically. The significance of proportion differences was examined using z test. Significance of differences between the results was assumed at $p < 0.05$.

Results

During the analysed 5-year period 155 drug-resistant bacterial strains were isolated. In all



Rycina 1. Frequency of the particular bacterial strain isolates in the 5-year period (2007—2012)

groups of patients, most frequently isolated pathogen was *P. aeruginosa,* which accounted for 27% of all infections. Other pathogens in accordance with their prevalence were as follows: *A. baumanii ESBL(−)* (13%), *S. pneumoniae* (12%), *E. cloacae ESBL(+)* (10%), *K. pneumoniae ESBL(+)* (10%), *S. aureus MRSA* (8%), *E. faecalis* (7%), *E. coli ESBL(+)* (6%), *S. maltophilia ESBL(+)* (5%) and *E. kobei ESBL(+)* (2%). The results of analysis of the prevalence of particular strains during a 5-year period were presented in Figure 1.

Patients qualified for lung transplantation

In this group, the results of microbiological tests of 200 patients were analysed. Infection with resistant pathogen was diagnosed in 31 subjects (15.5%). 6 strains were identified: *P. aeruginosa*, *A. baumanii ESBL(−)*, *E. cloacae ESBL*(+), *K. pneumoniae ESBL*(+), *S. aureus MRSA* and *E. kobei ESBL*(+). Among the isolated strains, most frequently were found: *P. aeruginosa* (35.5%), then Gram (−) bacilli: *A. baumanii ESBL(−)* — the strain that does not produce beta lactamases, with a wide substrate spectrum (29% of all isolates), the third pathogen was methicillin-resistant Staphylococcus aureus (MRSA), which made up over 16% of all isolated bacteria in the group (Table 1). The proportion of fermenting bacilli from the *Enterobacteriacae* did not exceed 20%, and most frequently isolated was *K. pneumoniae ESBL(+),* which constituted nearly 10% of all isolates in the group.

Patients treated for lung neoplasms

In the group of 1292 patients treated for lung neoplasms, 35 alert pathogens were isolated (2.7%). Except for bacteria mentioned in the previous group of patients, there were also resistant strains of *E. coli ESBL(+)* and Gram (+) cocci, i.e. *E. faecalis* and *S. pneumoniae* (Table 2). Similarly as in the first analysed group, the most frequent pathogen was *P. aeruginosa*, which was isolated from 28.6% of specimens. The proportion of fermenting bacilli from the *Enterobacteriacae* family was distinctly larger and it exceeded 31%, the most often isolated was *Enterobacter cloacae ESBL(+),* which constituted 14% of all isolates in the group. It should be emphasised that the proportion of Gram (+) cocci, including the proportion of pneumococci — *S. pneumoniae,* which is sensitive to penicillins, was clearly higher, compared to the previous group (1/3 of all isolated bacteria) and accounted for 14%. The proportion of MRSA was lower (8.5%).

Patients treated for chronic diseases of the respiratory system

In the group of patients treated for chronic diseases of the respiratory system, in 89 (4.4%) subjects out of 2029 hospitalised patients, at least one alert pathogen was isolated. In this group of patients, diverse species of isolated pathogens were found, with dominant *P. aeruginosa*, which was an aetiological factor of more than every fifth infection (22.5%), and *S. pneumoniae*, which is sensitive to penicillins (14.6%) (Table 3). The

Table 1. Patients qualified for lung transplantation (n = 200 SPECIMENS)

The name of the strain	2007 n = 55		2008 n = 49		2009 n = 37		2010 n = 30		2011 n = 29		Total (percentage)	
	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%
Pseudomonas aeruginosa	1	4.30%	3	12.50	3	7.14	2	5.40	2	6.89	11	35.48
Acinetobacter baumanii ESBL(–)	4	17.40%	2	8.30	1	2.38	1	2.7	1	3.44	9	29
Streptococcus pneumoniae	–	–	–	–	–	–	–	–	–	–	–	–
Enterobacter cloacae ESBL(+)	–	–	1	4.20	–	–	1	2.70	–	–	2	6.45
Klebsiella pneumoniae ESBL(+)	–	–	1	4.20	2	4.76	–	–	–	–	3	9.68
Staphylococcus aureus MRSA	–	–	1	4.20	1	2.38	2	5.40	1	3.44	5	16.13
Enterococcus faecalis	–	–	–	–	–	–	–	–	–	–	–	–
Escherichia coli ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–
Stenotrophomonas maltophilia ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–
Enterobacter kobei ESBL(+)	–	–	–	–	–	–	–	–	1	3.44	1	3.23
Entrobacter aerogenes ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–

Table 2. Patients treated for lung neoplasm (n = 1292 SPECIMENS)

The name of the strain	2007 n = 225		2008 n = 267		2009 n = 288		2010 n = 253		2011 n = 259		Total (percentage)	
	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%
Pseudomonas aeruginosa	2	8.70	4	16.60	2	4.76	2	5.40	–	–	10	28.6
Acinetobacter baumanii ESBL(–)	2	8.70	1	4.20	–	–	–	–	–	–	3	8.57
Streptococcus pneumoniae	1	4.30	1	4.20	1	2.38	1	2.70	1	3.44	5	14.29
Enterobacter cloacae ESBL(+)	–	–	1	4.20	1	2.38	3	8.10	–	–	5	14.29
Klebsiella pneumoniae ESBL(+)	–	–	2	8.30	1	2.38	–	–	1	3.44	4	11.43
Staphylococcus aureus MRSA	1	4.30	–	–	–	–	1	2.70	1	3.44	3	8.57
Enterococcus faecalis	1	4.30	–	–	–	–	1	2.70	1	3.44	3	8.57
Escherichia coli ESBL(+)	1	4.30	–	–	1	2.38	–	–	–	–	2	5.71
Stenotrophomonas maltophilia ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–
Enterobacter kobei ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–
Entrobacter aerogenes ESBL(+)	–	–	–	–	–	–	–	–	–	–	–	–

Table 3. Patients treated for chronic lung diseases (n = 2029 SPECIMENS)

The name of the strain	2007 n = 403		2008 n = 369		2009 n = 410		2010 n = 428		2011 n = 419		Total (percentage)	
	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%	No of infected patients	%
Pseudomonas aeruginosa	3	13.04	1	4.20	9	21.42	6	16.21	1	3.44	20	22.5
Acinetobacter baumanii ESBL(−)	3	13.04	3	12.50	1	2.38	–	–	1	3.44	8	8.99
Streptococcus pneumoniae	–	–	–	–	5	11.90	5	13.50	3	10.39	13	14.61
Enterobacter cloacae ESBL(+)	2	8.70	1	4.20	3	7.14	3	8.10	–	–	9	10.11
Klebsiella pneumoniae ESBL(+)	2	8.70	–	–	2	4.76	1	2.70	3	10.39	8	8.99
Staphylococcus aureus MRSA	–	–	–	–	1	2.38	2	5.40	2	6.89	5	5.62
Enterococcus faecalis	–	–	–	–	2	4.76	2	5.40	3	10.39	7	7.87
Escherichia coli ESBL(+)	–	–	1	4.20	3	7.14	3	8.10	1	3.44	8	8.99
Stenotrophomonas maltophilia ESBL(+)	–	–	–	–	3	7.14	1	2.70	4	13.79	8	8.99
Enterobacter kobei ESBL(+)	–	–	–	–	–	–	–	–	2	6.89	2	2.25
Entrobacter aerogenes ESBL(+)	–	–	1	4.20	–	–	–	–	–	–	1	1.12

prevalence of the remaining pathogens in the group was well-balanced. A lower proportion of MRSA (5.6%), compared to the two previous groups was observed.

In the analysed groups, resistant strains were isolated significantly more often in patients qualified for transplantation ($p < 0.01$), compared to the remaining subjects. The group of patients with neoplasms and the group with chronic diseases of the respiratory system did not differ significantly in respect of proportions of patients infected with alert microorganisms.

Discussion

Alert pathogens made up a significant proportion of bacteria isolated from biological material of patients of the department of lung diseases. Among the isolated pathogens, *P. aeruginosa* prevailed. Currently, this pathogen is becoming the most frequent cause of infections worldwide, it is also changing into more and more resistant to the drugs such as quinolones, carbapenems and aminiglycosides [1]. *P. aeruginosa* is an aetiological factor of exacerbations of chronic lung diseases causing progressive impairment of functioning of the respiratory system expressed in lowered forced expiratory volume in 1 second (FEV_1) [11, 12]. Among patients with lowered immunity after lung transplantation, this pathogen is an aetiological factor of pneumonia, contributing to higher mortality in the early post-transplant period and at long-term follow-up. According to the authors who conducted the studies in Spain, approximately 24% of pneumonia cases after lung transplantation is caused by this pathogen [13–16]. Moreover, *P. aeruginosa* is frequently isolated in patients with neutropenic fever in the course of lung cancer chemotherapy [17, 18].

The consecutive, in respect of frequency, pathogen isolated among patients qualified for lung transplantation was *A. baumanii,* which occurred comparably as often as *P. aeruginosa* (29% and 35% of infections respectively). The results of the published studies have shown that the colonisation of the airways with *A. baumanii*, and infection with this pathogen in the post-transplant period, constitute a risk factor of prolonged pneumonia in the group of patients after lung transplantation, and consequently, lead to pulmonary fibrosis with compensatory hyperinflation of a native lung [19, 20]. The recent studies have clearly shown that *A. baumanii* play a crucial role in the increase in mortality among patients infected with this pathogen [4].

In the presented material, in the group of patients with chronic diseases of the respiratory system and patients with neoplasms, infection with *A. baumanii* occurred more rarely than infection with *S. pneumoniae*: 8.57% and 14.29%, and 8.99% and 14.61% respectively. These results correspond with the researches carried out by other authors [11, 18, 21].

Infection with *S. pneumoniae* was not found in the group of patients qualified for lung transplantation. Presumably, it is related to relatively lower resistance of the species to antibiotics [5, 10]. Gram (+) cocci — *E. faecalis* were not found in this group of patients either [18].

Among the analysed pathogens, the *Enterobacteriaceae* were represented by: *E. cloacae ESBL(+), K. pneumoniae ESBL(+), E. kobei ESBL(+)* and *E. coli ESBL(+)* present in the material in the largest numbers in the group of patients with lung neoplastic diseases and in patients with chronic pulmonary pathology (31% and 30% respectively). Resistance of *Enterobacteriaceae* to antibiotics is a significant risk factor of prolonged hospitalisation [22]. In the analysed material, in patients qualified for lung transplantation, infections with pathogens from the *Enterobacteriaceae* family constituted 19%. According to the literature, *K. pneumoniae* is a pathogen that frequently constitutes an infectious agent in the early post-transplant period [23].

According to the agency of the federal government of the United States — Centers for Disease Control and Prevention — methicillin-resistant *S. aureus* is becoming more and more frequently recognised infectious agent and the cause of deaths. In the United States, infections with MRSA cause more deaths than tuberculosis and AIDS combined [1]. Next to *P. aeruginosa*, MRSA is the most frequent factor of pneumonia and bronchitis among patients who underwent immunosuppression due to lung transplantation [16, 24], which is in accordance with the results of the present study.

The last analysed pathogen was *S. maltophilia ESBL(+).* This non-fermenting Gram-negative bacillus is phylogenetically close to *P. aeruginosa* and it often colonises the airways of the patients with chronic lung diseases, in immunosuppression or treated for neoplasms. COPD patients and the persons who repeatedly undergo therapy with antibiotics, are at risk of colonisation with this bacterium. Its presence is associated with prolonged hospitalisation and increased patients' mortality and longer time of mechanical ventilation [6, 25].

To sum up, alert pathogens constitute a vital problem in the group of patients of the department of lung diseases. According to our data, the group most exposed to infections with these bacteria are patients qualified for lung transplantation. For infections influence long-term prognosis, their efficient therapy is crucial in all groups of patients. It should be emphasised that in the analysed material, there were no pathogens of most dangerous resistance mechanisms, i.e. *K. pneumoniae* KPC (+) producing beta lactamases active to carbapenems, *Pseudomonas* and *Acinetobacter MBL(+)* strains producing metallo beta lactamases or OXA-48 (+) producing oxacillinases that hydrolise carbapenems or vancomycin-resistant *Enterococcus* strains (VRE) or penicillin-resistant pneumococci.

Conclusions

Infection with alert pathogens affected 4% of patients hospitalised in the department of lung diseases. It occurred significantly more often in patients qualified for lung transplantation, compared to the remaining subjects. The pathogen that occurred in all study groups was *P. aeruginosa* (27% of all infections).

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Conflict of interest

The authors declare no conflict of interest.

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