

Use of hospital morbidity data in an epidemiological analysis of diseases caused by *Legionella pneumophila*

Irena Kosińska¹, Aneta Nitsch-Osuch¹, Krzysztof Kanecki¹, Paweł Goryński², Piotr Zbigniew Tyszko³

¹ Medical University of Warsaw, Poland

² National Institute of Public Health – National Institute of Hygiene, Warsaw, Poland

³ Institute of Rural Health, Lublin, Poland

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Abstract

Introduction. Among infectious diseases in Poland there are two caused by *Legionella pneumophila*: pneumonic legionnaires' disease and non-pneumonic legionnaires' disease (Pontiac fever). The level of prevalence of these diseases in Poland is significantly lower than in other European countries.

Objective. The aim of the study was to assess the suitability of the Polish hospital morbidity database for the purposes of epidemiological analysis of diseases caused by *L. pneumophila*.

Materials and Method. The analysis was based on population-based administrative data, collected between January 2008 – December 2015. The analyzed data covered 84 first time hospitalizations for legionnaires' disease (ICD-10 code: A48.1) and non-pneumonic legionnaires' disease (Pontiac fever) (ICD10 code: A48.2), and other available data included in the infectious disease reporting system.

Results. The obtained data indicated more frequent occurrence of the disease in men than in women and in people living in more urban areas in relation to people living in more rural areas. Patients were mainly hospitalized in internal wards (22,62%), pulmonology wards (19,05%) and infectious diseases wards (11,91%), and less frequently in other hospital wards. On average, hospitalization time amounted to 14,68 days. Legionellosis was the sole reason for hospitalization in 30.95% of patients, whereas in the remaining patients (n=58) comorbidities were observed. Seasonality of hospitalizations was observed in this study with a higher incidence in the summer season.

Conclusions. It was shown that neither hospital morbidity data nor other sources of information on diseases caused by *L. pneumophila* in Poland are sufficient for a full epidemiological analysis. It was concluded that the diagnosis of diseases with symptoms of *L. pneumophila* infection should include an analysis of environmental factors, and in the case of their occurrence, microbiological tests should be performed.

Key words

legionellosis, hospital morbidity data

INTRODUCTION

Among Essential Public Health Operations, the World Health Organization (WHO) has identified health surveillance, including the surveillance of the occurrence of infectious diseases, as one of ten basic public health functions (operations) [1]. Knowledge of the epidemiological situation in the field of infectious diseases facilitates implementation of preventive measures, and influences diagnosis and treatment of diseases. Therefore, the availability and reliability of data on the occurrence of infectious diseases constitutes one of the basic problems of epidemiology.

One source of information on diseases requiring hospitalization is the Polish hospital morbidity database. Every hospital in Poland is obliged to transfer data required within the framework of the implementation of statistical research programmes, which are announced each year on the basis of the Act of 29 June 1995 on public statistics [2].

Among infectious diseases in Poland, there occur pneumonic legionnaires' disease and non-pneumonic legionnaires' disease (Pontiac fever). In the International Statistical Classification of Diseases and Related Health Problems (ICD-10), they have been assigned the following codes: A48.1 and A48.2, respectively [3, 4].

Etiological agent and disease characteristics. The etiological agent of legionnaires' disease is the bacterium *L. pneumophila*, identified in 1976. In 2005, these Gram-negative *Legionellaceae* bacilli were recognized by the Ministry of Health as an alarm pathogen [5, 6, 7, 8]. They exist mainly in an aquatic environment and colonize hot water systems (over 80% of cases), sprinklers, cooling towers, fountains, jacuzzies, pearl pools, showers, and even dental units. The infection is initiated by inhalation of water-air aerosol contaminated with the bacteria [9, 10, 11, 12, 13, 14, 15]. The most pathogenic strains of *L. pneumophila* include Philadelphia and Benidorm strains, medium-pathogenic strains are OLDA and OLDA/Oxford, while the Camperdown strain has low pathogenic potential. In addition, *L. pneumophila* sg1 OLDA ST1 strain possesses a gene coding for RTX toxin, which is present worldwide and

Address for correspondence: Piotr Zbigniew Tyszko, Institute of Rural Health, Lublin, Poland
E-mail: ptyszko@wum.edu.pl

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is considered to be a human factor of infections, including hospital-acquired infections [16, 17, 18, 19].

The incubation period of *L. pneumophila* is 2–10 days, but it can be longer (even up to 16 days) [20]. The course of infection can range from mild to life-threatening. Typical symptoms of legionellosis are dyspnoea, high fever, nervous system symptoms (confusion, loss of consciousness), digestive system symptoms (nausea, diarrhea, vomiting), renal failure, and others [21, 22, 23, 24]. The disease can last up to several weeks, and mortality can range from 3% – 50% [21, 22, 23, 24]; however, in the case of immunosuppressive treatment of comorbidities it is estimated at 80% [22, 24]. Death occurs as a result of progressive pneumonia with respiratory failure and/or shock with multiple organ failure [20]. This depends on the disease category, general health condition of the patient and properties of the bacterial strain. [21, 24]

For the purpose of protection against infections, special requirements regarding levels of *Legionella sp* have been introduced, especially in entities offering medical services (stationary and round-the-clock health services), collective housing buildings and public buildings, where a water-air aerosol is produced in the course of their utilization. In medical entities, where immunocompromised patients are staying (including those who are administered immunosuppressive treatment), the limit value <50 CFU/1000 ml of water is allowed [25]. This regulation liberalizes the previous value of 0 CFU/1000 ml, which prevented certain hospital wards from functioning. The current solution is in line with the WHO recommendations [26, 27]. However, identification of all immunocompromised patients in particular wards can pose a certain difficulty. These wards include transplantation wards, oncology wards, wards where immunosuppressive treatment is administered, intensive care units, geriatric, pulmonology, and other hospital wards [28, 29, 30].

Incidence. According to the data of the European Union and the European Environment Agency (EU/EEA), the average incidence in Europe (30 countries) exceeds 1.0/100,000, whereas in Poland it amounts to 0.03–0.23/100,000 [31, 32, 33]. The majority of reported cases (70–80%) are patients over 50 years of age, 60–70% of whom are men [31]. Due to the differences in the disease incidence in Poland and the EU, an up-to-date analysis of the epidemiology of this infectious disease in Poland is becoming an important issue, along with an attempt to explain the observed differences.

OBJECTIVE

The aim of the study is to assess the suitability of the Polish hospital morbidity database for an epidemiological analysis of diseases caused by *L. pneumophila*. In recent years, this type of data has been used to assess the prevalence of several diseases, such as Systemic Sclerosis [34], Behçet's disease [35], Churg and Strauss syndrome [36], Kawasaki disease [37], polyarteritis nodosa [38], granulomatosis with polyangiitis [39], and Paget's disease [40]. Information obtained from the analysis of data on hospital morbidity may be used in clinical practice.

MATERIALS AND METHOD

The analysis was based on population-based administrative data, collected between January 2008 – December 2015. [The analyzed data covered 84 first time hospitalizations for legionnaires' disease (A48.1) and non-pneumonic legionnaires' disease (Pontiac fever) (A48.2). Data were collected by the National Institute of Public Health, as part of the Polish hospital morbidity study. Data on all inpatients discharged alive or dead from all hospitals, excluding psychiatric and military hospitals, are obligatorily sent to the Institute, usually on a monthly basis. The database contains information about each hospitalization, including ICD-10 codes of the admitting diagnosis and comorbidities, dates of admission and discharge, birth date, gender, and place of residence. The database does not contain patients' names. Demographic data for the general Polish population was obtained from the Central Statistical Office in Poland [41]. For the purpose of analysis, the following age categories indicated by the WHO were applied: 0–4, 5–14, 15–24, 25–44, 45–64 and 64+ years of age [31].

Statistical analyses were performed using Statistica Software [42]. Descriptive statistics assessed included means, medians and ranges for continuous variables, and absolute numbers and proportions for categorical data.

RESULTS

Characteristics of the studied group are presented in Table 1.

Table 1. Characteristics of patients hospitalized for diseases caused by *L. pneumophila* in Poland in 2008–2015

No. of hospitalized patients	84	
Gender	Man	Woman
N/%	46 (54.76)	38 (45.24)
Place of residence	Urban area	Rural area
N/%	59 (70.3)	24 (28.57)
Average age of patients	45.6 years (SD±21.32)	
Age range	2 – 84 years	
Average hospitalization time	14.68 days (SD±10.80)	
Deaths	4 (4.76% of hospitalizations)	

The percentage of patients in the youngest age groups, 0–4 years and 15–24 years, ranged from 4.6% – 5.6%. It was higher in older age groups and amounted to 30.6% for the age group 25–44 years, 33.4% for the age group 45–64 years, and 20.1% for the age group 65 years and more. Distribution of legionellosis cases in individual voivodships in Poland in the years 2008–2015 varied greatly. Among 137 reported cases, 25.5% occurred in Silesian Province, 16.6% in the Mazowiecki Province, 9.49% in Kujawski-Pomorski Province and 8.03% in Lubuski Province. The lowest incidence was observed in Zachodni-Pomorski Province (1.46%). In other regions, the incidence ranged between 2–6% [32].

Patients were mainly hospitalized in internal wards (22.62%), pulmonology wards (19.05%) and infectious diseases wards (11.91%), and less frequently in other hospital wards (Tab. 2). The average hospitalization time was 14.68 days (SD ± 10.8).

Table 2. Hospitalization of patients with legionellosis in hospital wards in Poland 2008–2015

Hospital wards	No. of hospitalizations	Percentage [%]
Internal medicine	19	22,62
Pulmonology	16	19,05
Infectious diseases	10	11,91
Observation and infectious diseases	5	5,95
Tuberculosis and lung diseases	4	4,76
Anesthesiology and intensive care	3	3,57
Others (anesthesiology and intensive care, cardiology, urology, gastroenterology, paediatrics, haematology, nephrology, rheumatology, allergology)	30	35,71
Total	84	100,00

Only 23 patients diagnosed with legionnaires' disease (A48.1) and 3 patients with non-pneumonic legionnaires' disease (Pontiac fever) (A48.2) were treated solely for this condition. They constituted 30.95% of all hospitalized patients in the study period. In the remaining patients (n=58), different comorbidities (1–7) were observed (Tab. 3).

Table 3. Number and percentage of comorbidities in patients hospitalized 2008–2015

ICD-10	No. of comorbidities							
	0	1	2	3	4	5	6	7
A48.1	23	23	9	11	6	1	0	1
A48.2	3	5	1	1	0	0	0	0
Percentage [%]	30,95	33,34	11,90	14,29	7,14	1,19	0,00	1,19

In 2008–2015, the highest number of hospitalizations (41.7%) was observed in the summer (3rd quarter) and autumn, and the lowest number was reported in the winter (Fig. 1).

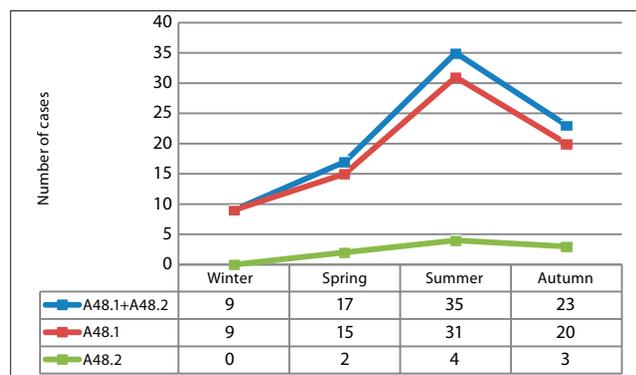


Figure 1. Hospitalization of patients with A48.1 and A48.2 in 2008–2015, in relation to seasons in Poland

In the 2008–2015 period, there were 4 deaths among hospitalized patients, which constituted 4.76% of hospitalizations. The total number of deaths in Poland in the analyzed period of time was 18 (Tab. 4).

Table 4. Number of legionellosis cases and deaths in the EU and Poland in 2008–2015

Year	European Union			Poland		
	No. of cases	Deaths	Incidence per 100,000	No. of casus	Deaths	Incidence per 100,000
2008	5014	363	1.16	15	0	0.02
2009	5092	414	1.11	10	0	0.01
2010	5845	440	1.25	36	0	0.02
2011	4451	361	0.98	18	4	0.02
2012	5390	422	1.16	10	2	0.01
2013	5401	462	1.15	11	5	0.02
2014	6374	461	1.34	12	3	0.03
2015	6521	456	1.36	23	4	0.04

Source: Own work based on UE/EEA [31].

DISCUSSION

Analysis of legionellosis cases in Poland in 2005–2009 [33] showed that the highest number of cases occurred in 2006 (89 cases, which corresponds to the incidence of 0.23/100,000 population). As a rule, the number of cases reported in the EPIMELD, an infectious disease register, was higher than the number of hospitalized patients in 2008–2015. In total, in the mentioned period of time, 136 disease cases were reported, compared to 84 hospitalization cases. This comparison shows that in the case of legionellosis, the use of hospital morbidity data results in the underestimation of the disease incidence. The number of cases reported by hospitals seems not to include cases confirmed in epidemiological studies by sanitary and epidemiological stations, which ended after a patient was discharged from hospital.

A comparison of incidence in Poland and the 30 EU/EEA countries shows a significant underestimation of legionellosis incidence in Poland [31,33]. Considering the observed incidence level in Europe, over 380 cases of legionellosis per year should be reported in Poland. For comparison, in the analyzed period there were 475 cases of legionellosis, including 75 deaths (15.8%), reported in the Czech Republic, which is a country with a smaller population than Poland and has similar climate conditions. When comparing data across countries, it should be taken into consideration that the Polish data include the total number of A48.1 and A48.2 diagnoses, whereas the second code is not included in the EU/EEA data [31, 32].

Differences were also observed between Poland and the EU/EEU with regard to the disease incidence in men and women. In the analyzed period (2008–2015), the incidence rate per 100,000 people in Europe was much higher for men than for women, and amounted to 1.41–1.94/100,000 and 0.55–0.77/100,000, respectively. In Poland, the incidence rate for men reached 0.03–0.12/100,000, average 0.06/100,000, whereas the rate for women amounted to 0.01–0.07/100,000, average 0.03/100,000 (EU/EEA) [31].

The situation presented above seems surprising in the light of the fact that research on *Legionella sp.* and Legionella-like amoebal pathogens (LLAP) was carried out in Poland as early as in the 1980s. This research focused on the occurrence of *Legionella sp.* and LLAP bacteria in water and their interaction with amoebae. The study conducted involved

members of selected risk groups (gardeners, workers of drilling platforms) who were exposed to water-air aerosol contaminated with these bacteria. The study was limited to infections caused by *L. pneumophila* bacteria classified as serogroup 1 (*L. pneumophila* sg1) [7]. A breakthrough occurred in 1997, when official cooperation between Poland and the European Working Group on Legionella Infections (EWGLI) was initiated. EWGLI was a group of experts whose task was to conduct epidemiological investigations for suspected cases of legionellosis pneumonia. At that time, the Polish Institute of Hygiene (currently, National Institute of Public Health – National Institute of Hygiene) appointed a team of researchers, nominated by the Ministry of Health, who participated in epidemiological investigations and studies conducted by an international group of experts [33].

EWGLI/ELDSNet data show a certain seasonality of the disease in Europe, which is associated with the summer period (August-September), when there are the most favourable thermal conditions in Europe for the growth of *L. pneumophila* bacteria in water installations in hotels, cruise ships, water parks or fountains [42, 43]. Data from 2008–2015 reveal seasonality of disease cases, with the highest intensification in the third quarter, which could confirm the tendency observed in the European data (Fig. 1). There is only one study [21] which shows no seasonality of legionellosis cases in Poland.

It is difficult to attribute the differences in the occurrence of the disease across provinces to environmental factors or differences in the health care system. The reason behind these differences, as well as the low level of disease reporting in Poland in general, should be sought in the procedures of pneumonia diagnostics. Diagnostics of diseases with symptoms of dyspnoea, high fever, nervous system symptoms (confusion, loss of consciousness), digestive system symptoms (nausea, diarrhea, vomiting) and renal failure, as well as diagnostics of suspected pneumonia, give particular consideration to data on risk factors obtained in the interviews.

The key risk factors for legionnaires' disease are as follows: environmental factors – occurrence of *L. pneumophila* strains in water systems and installations in a number that can pose a threat, properties of the strains and time of exposure to contaminated water-air aerosol [9]. Human risk factors are: immunosuppressive treatment, recurrent and chronic respiratory diseases, metabolic diseases (diabetes), smoking, alcohol abuse, international travels to places with an increased risk of exposure to water-air aerosol [42, 43], hospitalizations, spending free time in aquaparks, jacuzzi and shopping malls, [29, 30, 44], sanatorium treatment, work places, such as: car washes, plantations, cooling towers and sanatoriums) [14, 29]. Legionellosis cases can therefore be divided into out-of-hospital cases (acquired in the social environment), hospital cases and travel-related cases. [27]. According to ECDC, the following legionellosis sources can be distinguished: community, travel abroad, domestic travel, healthcare associated sources and others.

The above-mentioned risk factors should be determined in the physical examination, for the purpose of further diagnostic proceedings aimed at the microbiological confirmation or exclusion of *L. pneumophila* as the etiological factor of the disease.

Following the ECDC guidelines, the causes of legionellosis in Poland can be referred to as mostly indefinite – 25.0%

– 75.0% of cases. In the EU/EEA countries, an indefinite cause was found in 6.9–13.8% of cases. The dominant source of legionellosis in the EU/EEA was community – 60.04–69.0% of cases in the period 2008–2015, with the average of 63.5%. Travel abroad were another source of the disease in the EU/EEA and remained at a steady level (8.2–11.4%, average 9.0%). They were followed by domestic travels – 6.6–9.5%, with an average of 8.1%. Healthcare associated sources of disease also remained at a steady level in the EU – 6.0–8.3% (average 7.6%). In Poland, foreign travel accounted for 19.6% of cases, on average, and their distribution differed (0,0–50,0%). National travels were reported as a source of legionellosis in Poland only in 2008 and 2009 (8.3% and 20.0%, respectively) [31].

Comparison of data on infection sources indicates huge differences between Poland and the EU/EEA region. In the European countries, the source of most legionellosis cases is community (e.g. France, Germany), whereas in Poland the cause of disease is most frequently described as 'unknown'. These differences can be due to the small number of cases registered in Poland.

It is worth noting that diagnosis and treatment of diseases caused by *L. pneumophila* takes place in various hospital wards. This shows that physicians referring patients for hospital treatment most probably do not formulate the suspicion of *L. pneumophila* etiology. However, an accurate environmental interview should be carried out at the beginning of the diagnosis process.

An important element in the study on epidemiology of infectious diseases is a joint assessment of both clinical condition and results of laboratory tests, in particular microbiological and immunological tests. An analysis of disease cases caused by *L. pneumophila* based only on the results of laboratory tests may give a false picture of the actual prevalence of the disease. On the other hand, infections caused by *L. pneumophila* can be treated without identifying the infectious agent, which is often the case in outpatient care. In this case, the actual incidence of diseases caused by *L. pneumophila* may be higher than the incidence determined on the basis of hospital data. A proper solution to this problem requires organizational changes in the functioning of outpatient healthcare or implementation of procedures for identification of infectious agents at the beginning of treatment.

The presented study used data from the Polish hospital morbidity database. It should be assumed that the doctor's indication of the disease code results from the diagnosis of clinical symptoms of the infection, which has been confirmed in additional laboratory tests. The statutory obligation to provide data on recognized disease entities guarantees a high level of data completeness.

A certain limitation of this study is the inability to directly verify the diagnosis of an individual patient. However, a significant benefit of the study is assessment of the disease incidence based on data covering almost the whole population of Poland.

One solution that could increase data credibility would be the possibility of correcting earlier data on the basis of the results of laboratory tests, which the doctor receives after hospitalization is completed and patient care is no longer required. In the future, the proposed solution can reduce the differences between the data on the prevalence of legionellosis in Poland and in other European countries.

CONCLUSIONS

Neither the analyzed data on hospital morbidity nor other information on the occurrence of diseases caused by *L. pneumophila* infections that is available in Poland are sufficient for a full epidemiological analysis.

1. Low incidence rates for diseases caused by *L. pneumophila* are most likely the result of poor recognition of these diseases, which might result from inadequate consideration of environmental factors in physical examination.
2. In order to improve the diagnosis of diseases caused by *L. pneumophila*, it is of crucial importance to carefully consider environmental factors in the physical examination, especially in the case of a patient with symptoms of pneumonia.
3. If environmental risk factors for a *L. pneumophila* infection are identified, microbiological testing should be a standard procedure.
4. The pre-graduate and postgraduate training of physicians should provide better knowledge and skills related to the environmental determinants of health.

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Wykorzystanie danych na temat chorobowości szpitalnej do celów analizy epidemiologicznej chorób spowodowanych *Legionella pneumophila*

Wprowadzenie

Cel pracy. Celem pracy jest ocena przydatności ogólnopolskiego rejestru chorobowości szpitalnej do celów analizy epidemiologicznej chorób wywoływanych przez *L. pneumophila*.

Materiał i metody. Analiza została oparta na danych administracyjnych dotyczących populacji, zebranych w okresie od stycznia 2008 r. do grudnia 2015 r. Przeanalizowano dane dotyczące 84 pierwszorazowych hospitalizacji z powodu choroby legionistów z zapaleniem płuc (A48.1) i choroby legionistów bez zapalenia płuc (A48.2). Wykorzystano także dane z systemu zgłaszania chorób zakaźnych.

Wyniki. Uzyskane dane wykazały większą częstość zachorowań wśród mężczyzn niż wśród kobiet oraz wśród mieszkańców obszarów wiejskich niż miejskich. Chorzy byli najczęściej hospitalizowani w oddziałach wewnętrznych – (22,62%), a rzadziej – na oddziale pulmonologii – 16 (19,05%) i w oddziale chorób zakaźnych – 10 (11,91%). Ponad 1/3 chorych było hospitalizowanych w innych oddziałach. Czas hospitalizacji wynosił średnio 14,68 dnia. Legioneloza była wyłączną przyczyną hospitalizacji w przypadku 30,95% chorych, a u pozostałych pacjentów (n = 58) zgłaszano występowanie chorób współistniejących. Stwierdzono sezonowość hospitalizacji z dominacją w okresie letnim.

Wnioski. Wykazano, że dane dotyczące chorobowości szpitalnej, jak również inne źródła polskie na temat chorób spowodowanych *L. pneumophila* nie pozwalają przeprowadzić pełnej analizy epidemiologicznej. W rozpoznawaniu chorób z objawami charakterystycznymi dla zakażeń *L. pneumophila* w większym stopniu powinny być uwzględniane czynniki środowiskowe, a w przypadku ich obecności – badania mikrobiologiczne.

Słowa kluczowe

legioneloza, dane o chorobowości szpitalnej