

# Granulomatosis with polyangiitis in Poland – epidemiological study

## Ziarniniakowatość z zapaleniem naczyń w Polsce – badanie epidemiologiczne

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**Słowa kluczowe:** ziarniniakowatość z zapaleniem naczyń, zapadalność, Polska.

**Key words:** granulomatosis with polyangiitis, incidence, Poland.

### Summary

**Aim of the study:** Granulomatosis with polyangiitis (GPA) is a disease of unknown aetiology, with a variable course, and with the possibility of exacerbations associated with life-threatening organ damage. Data on the incidence of GPA in Poland are limited. Epidemiological analysis can provide a lot of information that contributes to more accurate knowledge about GPA. The objective of this study was to conduct an analysis of GPA incidence in Poland with comparison of results to selected European countries. An additional analysis was performed according to the distribution of gender, age and hospitalization structure in GPA patients.

**Material and methods:** The estimation of GPA incidence was based on data taken from the Polish hospital morbidity registry of the National Institute of Public Health, in the scope of which data on all inpatients discharged from non-psychiatric hospitals in Poland are collected. Analysed data covered 1112 medical records taken from the first time of hospitalization records with diagnosis of GPA. The observation time ranged from December 2004 to December 2010.

**Results:** The average annual incidence of GPA in Poland was estimated to be 4.9/million in the general population, 5.8/million in the adult population and 1/million in the population of patients below 18 years of age. The annual incidence in Poland was comparable to incidence data from other European countries. The analysis of hospitalizations showed that the GPA patients were most often hospitalized in pulmonary, nephrology and rheumatology departments. During the observation period hospitalizations ended with death in 80 patients and GPA as an underlying cause of death was reported in 60 cases.

### Streszczenie

**Cel pracy:** Ziarniniakowatość z zapaleniem naczyń (*granulomatosis with polyangiitis* – GPA) jest chorobą o nieznannej etiologii, o możliwym zmiennym przebiegu, z możliwością zaostrzeń z towarzyszącymi powikłaniami narządowymi zagrażającymi życiu. Dane na temat zapadalności na GPA w Polsce są ograniczone. Ocena epidemiologiczna może dostarczać wielu informacji przyczyniających się do dokładniejszego poznania tej choroby. Celem tego badania była analiza zapadalności na GPA w Polsce wraz z porównaniem wyników z wybranymi krajami Europy. Dodatkowo dokonano analiz pacjentów z GPA w odniesieniu do opisu rozkładu płci, wieku oraz przyczyn hospitalizacji.

**Materiał i metody:** Oceny zapadalności na GPA dokonano na podstawie danych pochodzących z polskiego programu badania chorobowości szpitalnej realizowanego przez Narodowy Instytut Zdrowia Publicznego, w ramach którego są gromadzone dane dotyczące wszystkich pacjentów hospitalizowanych na oddziałach z wyłączeniem oddziałów psychiatrycznych. Analizie poddano dane pozyskane z dokumentacji medycznej 1112 hospitalizowanych pacjentów, z ustalonym po raz pierwszy rozpoznaniem GPA. Czas obserwacji obejmował okres od grudnia 2004 do grudnia 2010 r.

**Wyniki:** Średnią roczną zapadalność na GPA w Polsce szacuje się na 4,9/mln w populacji ogólnej; 5,8/mln w populacji dorosłych i 1/mln w populacji osób poniżej 18 lat. Analiza hospitalizacji wykazała, że najczęściej pacjenci z GPA byli hospitalizowani na oddziałach pulmonologicznym, nefrologicznym, reumatologicznym. W analizowanym okresie w 80 przypadkach hospitalizacja była zakończona zgonem, a GPA jako przyczyna zgonu była wskazywana w 60 przypadkach.

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**Conclusions:** In this study GPA incidence in Poland was estimated. Analyses of the structure of hospitalizations suggested that symptoms from the respiratory tract, kidneys and joints could be leading symptoms in the early stage of GPA development.

## Introduction

Granulomatosis with polyangiitis (GPA) is a relapsing necrotizing, granulomatous vasculitis of unknown origin, which typically involves the upper and lower respiratory tracts and the kidneys, but involvement of the skin, eyes, peripheral and central nervous system, genitourinary system and gastrointestinal tract has also been frequently reported. GPA can occur at all ages, and has been reported from infancy to old age. The disease predominantly affects patients of Caucasian origin [1]. Approximately 15% of patients are less than 19 years at diagnosis [2], but the disease is most common among upper-middle-aged individuals [3, 4]. In some studies GPA was reported to be slightly more common among men than among women [5]. GPA prevalence in Europe differs across countries. In northern Norway the GPA prevalence (per million) increased from 30.4 (95% CI: 16.6–51.0) during 1984–1988 to 95.1 (95% CI: 69.1–129.0) during 1994–1998 [6]. In the United Kingdom the point prevalence of GPA in 1997 was 62.9/million (95% CI: 41.5–91.6) with a 10-year prevalence of 106.4/million (95% CI: 77.3–142.8) [7]. In Sweden GPA point prevalence was 160/million (95% CI 114–206) [8]. In a study from the southern hemisphere region the 5-year period prevalence of GPA was 152/million (95% CI: 117–186) [9]. The observed increase in GPA prevalence may be a result of more effective diagnosis or care. On the other hand, a possible greater physician awareness of GPA with the introduction of antineutrophil cytoplasmic antibodies (ANCA) has been postulated as an explanation for the increased incidence [10]. This study on the incidence of GPA in Poland allows one to better describe the GPA epidemiology in Europe. There are many other reports about the incidence or prevalence of GPA in Norway [11], Spain [12], Germany [13–15] and Sweden [16, 17].

There are few articles about GPA in Poland [18, 19]. These articles describe a small group of patients or are case reports. According to the European Hospital Morbidity Database, the inpatient admission rate for all necrotizing vasculopathies with ICD code-M31 in Poland in 2009 was 50.6/million, in Finland 83/million; in the United Kingdom 37.5/million; and in Norway (2010) 15.4/million [20].

## Objectives

The objectives of this study were to estimate GPA incidence in Poland and compare the results with data from

**Wnioski:** W pracy dokonano oceny zapadalności na GPA w Polsce. Wyniki były porównywalne z danymi z innych krajów europejskich. Analizy struktury hospitalizacji sugerują, że objawy z dróg oddechowych, nerek i stawów mogły być wiodącymi objawami klinicznymi w początkowym okresie rozwoju GPA.

other selected European countries. An additional analysis was focused on gender, age, and hospital morbidity. Analysis of hospitalizations was performed in order to better describe the possible symptoms in the early stage of GPA clinical presentation.

## Material and methods

In this study we analysed data of patients with GPA hospitalized from 2004 to 2010. Data were taken from an inpatients' discharge database. The information was collected by the National Institute of Public Health (NIPH) which in the scope of public health statistics has been carried out for several years in the Polish hospital morbidity study. Data on all inpatients discharged alive or dead from all hospitals, excluding psychiatric and military, are obligatorily sent to the Institute, usually on a monthly basis. All analysed data contained information about hospitalization with many diagnoses but one of them was GPA coded in ICD-10 as M31.3. Demographic data for the general Polish population were obtained from the Central Statistical Office in Poland [21].

In the analysed period from December 2004 to December 2010, there were 1857 cases of hospitalization with diagnosis of GPA and this diagnosis was described with the ICD-10 code of M31.3 in medical documents. The inclusion criteria for this study were the first time hospitalization with diagnosis of GPA in the observed period of time. The registered study data consisted of information about birth date, code of place of residence, gender, age, date of admittance to hospital, date and underlying cause of death, and kind of department in which a patient was hospitalized. These registered data did not include information on patients' names and surnames. These data were sufficient to select a subgroup of hospitalized patients' records with first time diagnosis of GPA. It was assumed that the type of hospital department was associated with first symptoms of GPA. For a better description of the analysed group, in this study the percentage of hospitalizations in departments will be presented. Some information about mortality in the analysed group was also included. The comparative analysis of data from Poland and other European countries is presented in this article. The comparative analysis was conducted using data from the UK, Norway, Germany, Sweden, Finland and Poland. These data were taken for analysis because

Table I. Patients with GPA in Poland (2004–2010)

	Poland – general population	Poland – adult population	Poland – population under 18
Estimated incidence (patients/million/year)	4.9 F/M – 4.74 vs. 4.98	5.8 F/M – 5.27 vs. 6.35	1.0 F/M – 0.93 vs. 1.04
Gender – F/M (%)	560/552 (50.4% vs. 49.6%)	540/529 (50.5% vs. 49.5%)	20/23 (47% vs. 53%)
Age – median (min.–max., upper quartile, lower quartile)	52 (1–89; 38.5; 61)	53 (18–89; 41; 62)	12.6 (1–17; 10; 16)
patients	1112	1069	43

F/M – female vs. male subpopulation

there are studies about GPA incidence based on relatively large groups of patients.

## Results

Registered data about hospitalized patients with a diagnosis of GPA in Poland were analysed and are presented below. The analysed period of time ranged from December 2004 to December 2010. After selecting data fulfilling the inclusion criteria, we obtained information about 1112 patients. Median time of hospitalization was 8.5 days, min. one day, max. 136 days. Annual incidence distribution, in the analysed group, was not similar to linear: 2005 – 165; 2006 – 168; 2007 – 155; 2008 – 207; 2009 – 238; 2010 – 179. Results on the annual incidence, gender, age and number of patients in the analysed group and subgroups of patients below 18 years and adult are presented in table I. For better description special attention was given to the subgroup of adult patients and below 18 years old. Age distribution in the study group is presented in Figure 1. The highest number of patients was observed between 55 and 60. An increasing trend in number of GPA patients according to age was observed in the range from 1 to 55 years, and a decreasing trend after the age of 60.

Hospitalizations ended with death in 80 patients (47 men and 43 women) during the observation period. The average age in this group of 80 patients was 57 years, min. 19, max. 81 years. GPA, as an underlying cause of death, was reported in 60 from 80 hospitalized patients, pulmonary diseases in 6 patients, renal failure in 3 patients, other vascular diseases in 3 patients, underdetermined in 8 patients. In this group of 80 patients, 27 died in an intensive care unit, 17 in a nephrology department, 12 in an internal medicine department, 9 in a pulmonology department, and other deaths from 1 or 2 cases were reported in other departments.

Seasonal differences in GPA incidence are presented in figure 2. Table II contains data from the UK [22], Norway [6], Germany [23], Sweden [24] and Finland [25].

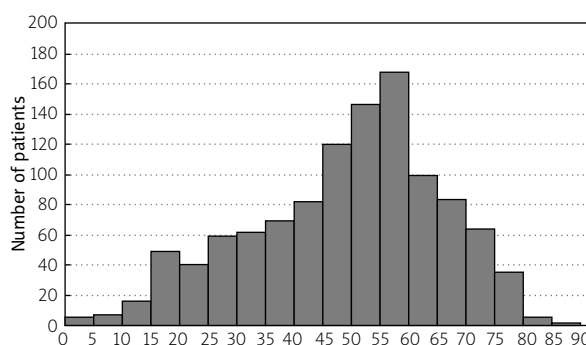


Fig. 1. GPA patients in Poland. Age – distribution

These data describe the annual GPA incidence, gender, age, number of patients in all groups and time of observation. Table III presents the distribution of first time hospitalizations in Poland with GPA diagnosis. Percentage distribution was presented according to the type of departments.

## Discussion

In this article data from government institutions about hospitalization of GPA patients are presented. Extensive information about hospitalizations of GPA patients allows one to present data as an epidemiological report but does not allow one to evaluate in detail the particular medical data of each patient with GPA. The results presented in table I and II describe the incidence of GPA in Poland and other European countries. Incidence of GPA in Poland was slightly lower but comparable to data from other European countries. Annual incidence of GPA in the paediatric population was 1/million in this study. In Canada the annual incidence of GPA in the paediatric population was reported to be between 2.8/million and 6.4/million [26].

There were no significant differences in incidence related to season. A slightly marked pattern of fluctuation in the time of study observation could be noted. In the

Table II. Annual incidence (per 1 million) with description of GPA patients in Europe

	Great Britain	Norway	Germany	Sweden	Finland
Incidence	8.4	5.2–12	6–12	7.8	1.9–9.3
Gender – male (%)	51.2	62	63	54	49
Median age (years)	59	50	58–61		
Mean age (years)				60.6	54
Number of GPA patients	295	55	191	1636	492
Time of observation	1990–2005	1988–1998	1998–2005	1975–2001	1981–2000

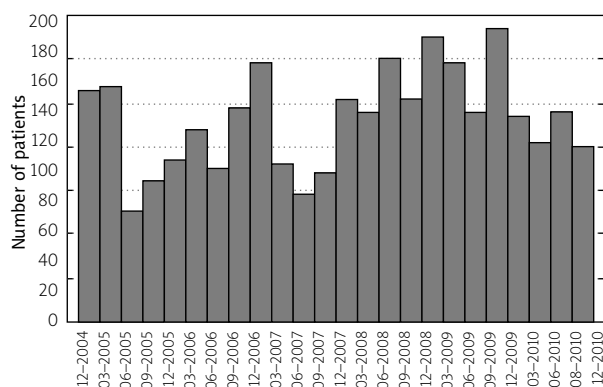


Fig. 2. Seasonal differences in GPA incidence

Table III. Distribution of first time hospitalizations of GPA patients in 2004–2010 (above 1%)

Department	%	Department	%
Pulmonology	29.8	Allergology	2.3
Nephrology	19	Otolaryngology	2.2
Rheumatology	14	Dermatology	1.5
Internal Medicine	12.1	Child Rheumatology	1.3
Clinical Immunology	7.6	Others	10%

literature one study showed higher hospitalization in summer than in other seasons [27]. Seasonal variation in the onset of GPA was reported in studies from Sweden [28]. In a study from the United States the incidence of GPA may increase during winter and spring months [29]. In the literature it was reported that a periodic fluctuation of the frequency with peaks every 3–4 years was noted for patients with GPA [30].

The clinical presentation of GPA is heterogeneous and it may involve many organs. It was reported that the most common disease symptoms were related to involvement of the upper and lower respiratory tract, skin, orbital involvement, peripheral and central nervous system, kidneys, and joints [31]. In one study the clinical

presentation of GPA was related to the upper respiratory tract in more than 50% of patients and other organs in less than 50% of patients [32]. The distribution of hospitalizations to different types of department in this study is presented in table III. It may be supposed that types of department were predicted by the first clinical presentation of GPA. In this study, hospitalizations mainly took place in pulmonology, nephrology or rheumatology departments. Hospitalizations in otolaryngology departments were rare in this study. Patients with first diagnosis of GPA were most often hospitalized in pulmonology departments. Symptoms from the upper and lower respiratory tract seem to be the predominant clinical symptoms of GPA in this study. Renal involvement is probably parallel to respiratory tract involvement but its clinical presentation may not be observed as the first clinical presentation of GPA. Data shown in table III suggest that, in almost 50% of patients, the first symptoms of GPA were probably related to respiratory tract or renal involvement.

There are a few limitations of this study. Hospital discharge diagnoses could not be verified. Many patients are hospitalized with a diagnosis of GPA in the early stages of the disease. However, due to the non-specific symptoms of this disease, in some cases diagnosis of GPA can be established at a later stage of the disease, and this may affect the statistical data on the incidence of GPA. There is a potential problem of left censoring. The fact that a case first appeared in the nationwide morbidity registry with a diagnosis of GPA does not necessarily mean that the diagnosis was newly made. This inaccuracy may result in an overestimation of the number of cases.

## Conclusions

The average incidence of GPA in Poland was estimated to be 4.9/million/year in the general population; 5.8/million/year in the adult population and 1/million/year in the paediatric population (under 18 years). These results showed that the incidence of GPA in Poland is comparable to results observed in other European countries.

Age distribution in Polish GPA patients showed increasing incidence up to 55 years, the maximum incidence at age 55–60, and a gradual decrease of incidence after 60 years of age. There were no significant differences in gender in the analysed groups. The hospitalization analyses suggest that in most cases the first GPA symptoms were related to pulmonary, renal or joint involvement.

*Authors declare no conflicts of interest.*

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