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ORIGINAL ARTICLE

Incidence and prevalence of granulomatosis with polyangiitis and microscopic polyangiitis in health management organization in Argentina: a 15-year study

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Abstract

Background/objective Our objective was to estimate incidence and prevalence rates of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) using data from a university hospital-based health management organization (HIMCO) in Latin America.

Methods Multiple methods for case finding were used to ensure complete ascertainment. GPA was diagnosed if fulfilling ACR 1990 criteria or a clinical diagnosis was made by an experienced rheumatologist. For MPA, a clinical diagnosis made by an experienced rheumatologist in concordance with Chapel Hill 2012 consensus. Renal limited vasculitis (RLV) ANCA-P positive was considered along with MPA. Global, age-specific, and sex-specific incidence and prevalence rates were calculated for members of the HIMCO with continuous affiliation ≥ 1 year from January 2000 to January 2015. Each person was followed up until GPA or MPA were diagnosed, voluntarily withdraw of the HIMCO, death, or study finalization. Prevalence was calculated on January 1, 2015.

Results Nineteen incident cases of GPA and 28 of MPA were identified from January 2000 to January 2015. During this period, a total of 349,775 HIMCO persons contributed a total of 2,073,438 person-years. GPA and MPA overall incidence rate per 1,000,000 person-years were 9 (95% CI 5–13) and 14 (95% CI 9–19), respectively. Age-specific incidence rates in both female and male patients peaked in the seventh decade of life in our population. On January 1, 2015, prevalence rates were 7.4 per 100,000 (95% CI 2.8–12) for GPA and 5.2 per 100,000 (95% CI 1.3–9) for MPA. Prevalence rates were higher in ages over 70 for both genders and both diseases.

Conclusion In this first study from Latin America, incidence and prevalence rates were in ranges of previous reports from other sites of the world. In our population, GPA and MPA were more frequent in women and in older ages, and the incidence of MPA was higher than that of GPA.

Key points
- *In Argentina, MPA incidence was higher than GPA, similar to that reported in other parts of the world.*
- *Prevalence and incidence rates were higher in ages over 70 for both sexes and both diseases.*

Keywords Anti-neutrophil cytoplasmic antibody-associated vasculitis (C20.111.193) · Granulomatosis with polyangiitis (C20.111.193.875) · Microscopic lyangiitis (C20.111.193.750) · Statistics (V02.925)

Introduction

Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are two of the main diseases in the spectrum of ANCA-associated vasculitis (AAV). Both can affect almost any organ in the body, mainly through small vessel vasculitis, but medium vessels can be involved as well. In a substantial amount of patient, AAV can be limited to one organ, sometimes only at presentation, and then compromising other tissues over the

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course of the disease, but it can remain limited just to one organ, been renal-limited vasculitis (RLV) one of the main examples [1].

Two of the best-known autoantigen targets of ANCA are myeloperoxidase (MPO) and proteinase-3 (PR3) [2].

AAV are considered rare diseases and epidemiological data on them is limited. Overall, data published from Europe and the USA estimates an incidence ranging from 1.2 to 2.0 cases per 100,000 individuals and a prevalence of 4.6 to 18.4 cases per 100,000 individuals [3]. There are geographical differences that have been observed in the prevalence and incidence of AVV, with data reporting higher incidence of GPA in Northern Europe, Australia, and the USA, and higher incidence of MPA in Southern Europe and Asia [4–7].

To date, precise data on AAV incidence and prevalence are lacking in South America and in Argentina.

The aims of the present study were to estimate the incidence and prevalence rates of GPA and MPA using data from a university hospital-based health management organization in Buenos Aires, Argentina, from 2000 to 2015. Our hypothesis was that the incidence and prevalence in Buenos Aires were similar to the other reported in the world.

Materials and methods

Setting

The population under study was those enrolled in the Hospital Italian health management organization (HIMCO), a prepaid health maintenance organization (HMO) in Buenos Aires City, Argentina. The HIMCO is composed of two central hospitals and 24 peripheral centers where they offer comprehensive health and medical services to approximately 140,000 outpatients.

According to the last population census (2010), Buenos Aires population is composed of 92% of European descent and white race, the rest being a mixture of natives and other ethnic groups [8].

Study design and case ascertainment

In this cohort study, we retrospectively reviewed electronic medical records of patients seen at the HIMCO, over 18 years old, from January 1, 2000, to January 1, 2015. Members are broadly representative of the Argentine population in terms of age, gender, and ethnicity.

We use multiple methods to ensure complete ascertainment for case finding: (a) patients with diagnosis of vasculitis in the HIMCO electronic medical records, (b) patients with an ANCA, proteinase-3, or myeloperoxidase positive test in the laboratory database, (c) patients who consumed azathioprine, cyclophosphamide, methotrexate, mycophenolate, or rituximab, from the administrative HIMCO drugs database, and (d) patients with a renal biopsy performed from pathology registry.

All individual medical records of the identified patients were reviewed. The following patient data were obtained: demographics, clinical manifestations, radiology findings, laboratory findings, and histopathologic features at baseline.

Patients were diagnosed as GPA if at least one of the following criteria was fulfilled: American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis [9], Chapel Hill Consensus

Table 1 Incident cases of GPA and MPA characteristics

	Granulomatosis with polyangiitis ($n = 19$)	Microscopic polyangiitis ($n = 28$)
Female, *n* (%)	14 (73.7)	21 (75)
Mean age at diagnosis, years (DS)	69.8 (11.3)	73.6 (13.2)
Global incidence per 1,000,000 patient-years (95% CI)	9 (5–13)	14 (9–19)
ANCA-C positive, % (95% CI)	78.9 (52.7–92.7)	14.3 (5.1–33.9)
ANCA-P positive, % (95% CI	15.8 (4.6–42.2)	82.1 (62.1–92.8)
Clinical features, % (95% CI)		
Nasal/sino-nasal involvement	42.1 (21.1–66.5)	14.3 (5.1–34)
Hearing loss	52.6 (29.2–75)	10.7 (3.2–30)
Cartilaginous involvement	10.5 (2.3–37.1)	0
Red eye	15.8 (4.6–42.2)	0
Renal involvement	84.2 (57.8–95.4)	100
Nodules, mass, or cavitation in chest CT	36.8 (17.3–62)	0
Interstitial lung disease	5.3 (0.1–26)	21.4 (8.3–40.9)
Alveolar hemorrhage	15.8 (4.6–42.2)	10.7(3.2–30.1)
Skin vasculitis	15.8 (4.6–42.2)	10.7(3.2–30.1)
Arthritis	31.6 (13.7–57.3)	7.1 (1.6–26.3)
Peripheral neuropathy	15.8 (4.6–42.2)	3.6 (0.4–23.7)
Renal limited vasculitis, % (95% CI)	0	60.7 (40.6–78.5)
Fulfillment of ACR 1990 GPA criteria, % (95% CI)	42.1 (21.1–66.5)	NA
Fulfillment of GPA 2017 provisional criteria, % (95% CI)	89.5 (62.9–97.7)	NA
Follow-up time after diagnosis, years, median (RIC)	4.9 (2.4–7.8)	2.6 (0.7–6.1)

NA not applicable

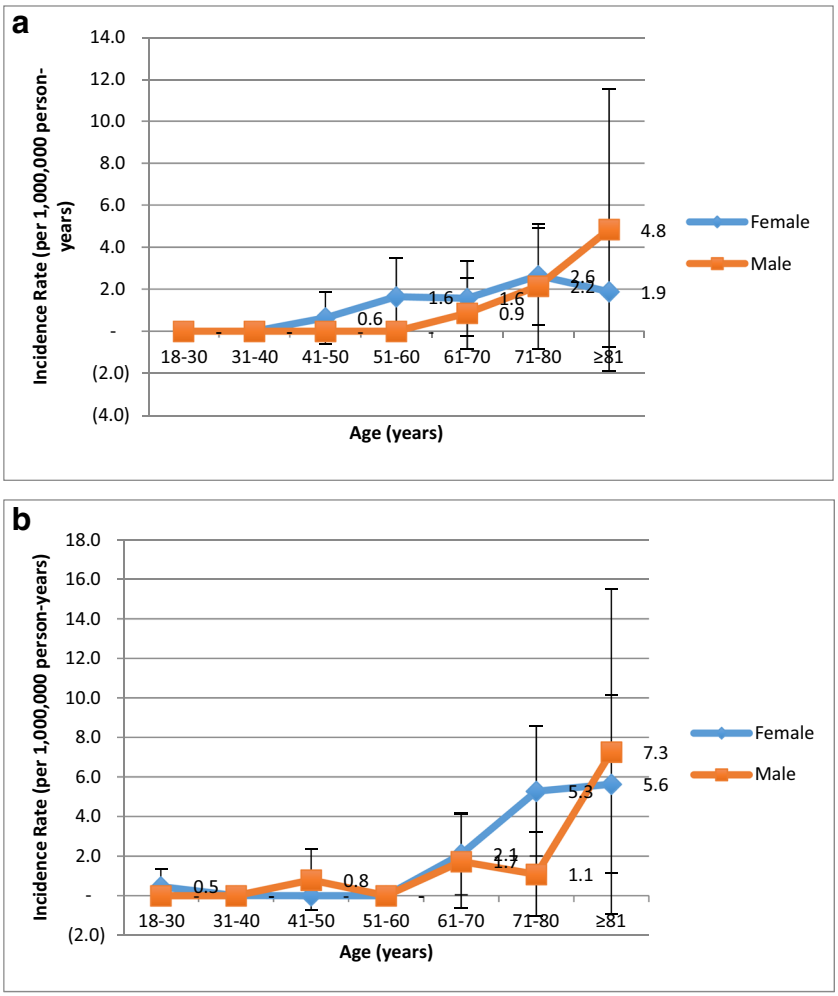

Fig. 1 **a** GPA incidence rates per gender per 1,000,000 person-years. **b** MPA incidence rates per gender per 1,000,000 person-years

Conference (CHCC) definition [10], or if a clinical diagnosis was made by an experienced rheumatologist. For MPA diagnosis, a clinical diagnosis made by an experienced rheumatologist in concordance with Chapel Hill 2012 consensus [10]. Renal limited vasculitis (RLV) ANCA-P positive was considered along with MPA.

Incidence rates were calculated in members with continuous affiliation ≥ 1 year from January 2000 to January 2015. Each person was followed up until voluntarily withdraw of the HIMCO, GPA, or MPA were diagnosed, death, or study finalization. Prevalence was calculated on January 1, 2015, and only patients still on treatment at that time were considered for calculation.

Statistical analysis

Statistical analysis was performed with STATA program 14.1 (StataCorp, USA).

Global and sex- and age-specific annual incidence rates of AAV were calculated with 95% CI. Sex- and age-specific incidence rates of AVV were calculated using the number of incident cases as the numerator and HIMCO adult members as the denominator. AAV prevalence rates were calculated on January 1, 2015 using the number of prevalent cases still on treatment at that time as the numerator and the HIMCO adult members as the denominator.

For descriptive statistics, continuous data are presented as median and interquartile range (IQR) or as mean and standard deviation (SD), according to the variable distribution. Categorical variables are presented as percentage and CI 95%. We used Fisher or chi-square tests to compare categorical variables and Wilcoxon rank-sum test or *T* test to compare continuous ones. A p value ≤ 0.05 was considered statistically significant.

Results

Clinical characteristics, demographics, and laboratory findings at diagnosis in the incident cohort are shown in Table 1. Patients with GPA ad MPA were mostly females (73.7% in GPA and 75% in MPA), and mean age at diagnosis was in the 70th decade of life.

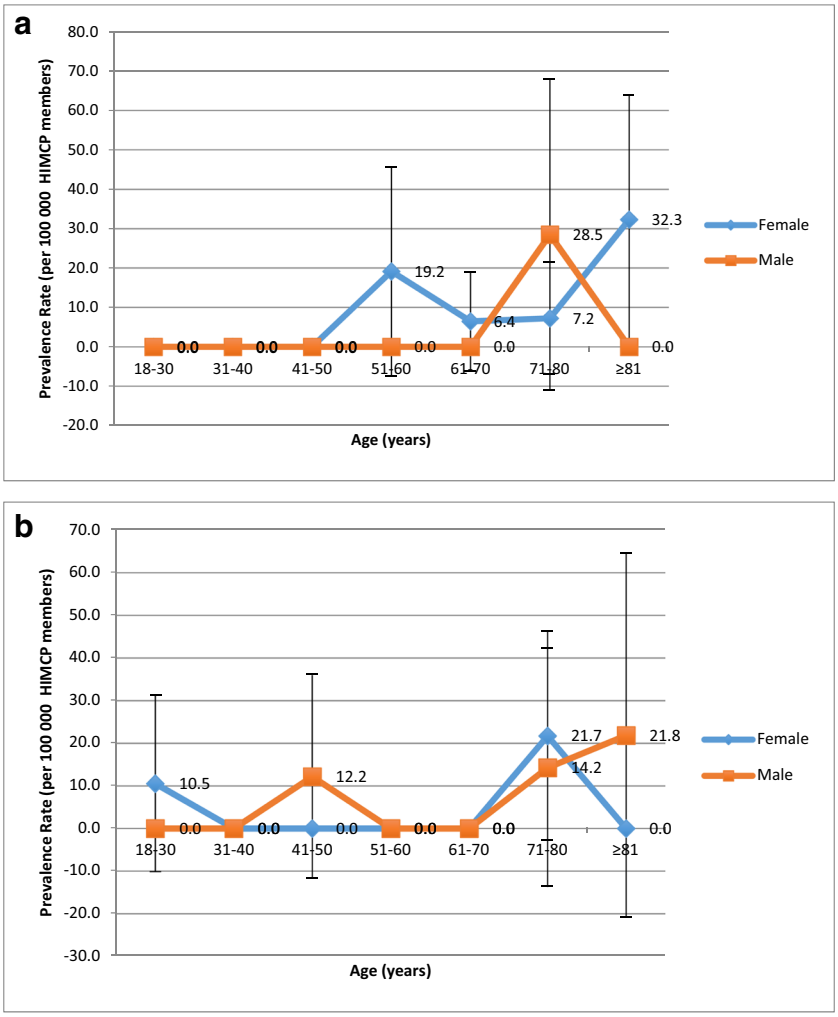

Fig. 2 **a** GPA prevalence rates per 100,000 persons **b** MPA prevalence rates per 100,000 persons

42.1% fulfilled ACR 1990 criteria for GPA. We also evaluated the performance of the 2017 provisional criteria for GPA with 89.5% fulfillment [11]. The most common clinical characteristic at diagnosis in GPA and MPA was renal involvement

Table 2 Data on GPA and MPA incidence and prevalence around the world

Area	Authors	Study period	Incidence (cases per million person-years)		Prevalence (cases per 100,000 habitants)	
			GPA	MPA	GPA	MPA
Buenos Aires, Argentina (our study)	Pierini et al.	2000–2015	9	14	7.4	5.2
Italy	Catanoso et al. [5]	1988–1998	1.7		34.3	
France	Mahr et al. [12]	2000			2.37	2.51
Lugo, Spain	González-Gay et al. [13]	1988–2001	2.95	7.9		
Southern Sweden	Mohammad et al. [6]	1997–2002			160	94
Norwich, UK	Watts et al. [14]	1990–2005	8.4		64.8	
Southern Sweden	Mohammad et al. [15]	1997–2006	9.8	10.1		
Japan	Fujimoto et al. [7]	2005–2009	2.1	18.2		
UK	Pearce et al. [16]	1997–2013	14		134.9	
Turkey	Pamuk et al. [17]	2004–2014	4.8	2.4	4.19	1.93
Minnesota, EEUU	Berti et al. [18]	1996–2015	13	16	21.8	18.4

(84.2% and 100%, respectively), followed by hearing loss in GPA (52.6%), and interstitial lung disease in MPA (24.1%). RLV represented 60% of MPA patients. In both diseases, ANCA (by immunofluorescence) was positive in the majority of patients (≈ 80%) (Table 1).

Incidence

Nineteen incident cases of GPA and 28 of MPA were identified from January 2000 to January 2015. During this period, for the HIMCO, a total of 349,775 people contributed a total of 2,073,438 person-years. Incidence rates were calculated as cases per 1,000,000 person-years. GPA and MPA overall incidence rates were 9 (95% CI 5–13) and 14 (95% CI 9–19), respectively. Incidence rates were greater in women (GPA 11 (95% CI 5–17) and MPA 17 (95% CI 10–24)) than in men (GPA 6 (95%CI 1–11) and MPA 8 (95% CI 2–14)). Age-specific incidence rates in both female and male patients peaked in the seventh decades of life in our population (Fig. 1a, b).

Prevalence

On January 1, 2015, 10 GPA and 7 MPA prevalent cases were identified from a denominator population of 135,750 HIMCP members. Prevalence rates were 7.4 per 100,000 (95% CI 2.8–12) for GPA and 5.2 per 100,000 (95% CI 1.3–9) for MPA. Prevalence rates were higher in ages over 70 for both sexes and both diseases (Fig. 2a, b).

Discussion

To our knowledge, this is the first study regarding GPA and MPA epidemiology in South America. Although this is the first report, it may not be representative of all Latin American countries because of the different ethnicities. As it has been shown, there are ethnic differences in many rheumatic diseases and the development of local data is important for public health. Here, we present the incidence and prevalence of GPA and MPA in a health plan of a University Hospital in Buenos Aires, Argentina, during a 15-year follow-up period. Data published around the world is shown in Table 2 [12–18]. Rates are variable with lower incidence in some European countries and the USA. We could not find Latin America data to which we can compare with.

In our study, MPA incidence was higher than GPA, similar to data reported by Berti et al. in Minnesota, USA, Watts et al. in Lugo, Spain, Fujimoto et al. in Japan, and Mohammad et al. in southern Sweden.

Interestingly, even when the incidence of MPA was higher than that of GPA, GPA was more prevalent. This could be explained because GPA has a higher relapse rate than MPA, and for prevalence analysis, we only considered patients that were still on treatment by January 1, 2015. This is different from other epidemiological GPA and MPA studies, in which for prevalence rates, all patients alive with an AAV diagnosis were considered for calculation. Our study has some strengths. It is a study based on a population with a long follow-up period. We used multiple methods to capture patients to assure complete ascertainment. For this study, we included patients with renal-limited vasculitis along with MPA, since we considered them to be part of the same disease.

Our study has also some limitations. Identification of cases relied on patients contacting the medical system. These could underestimate incidence of mild forms of AAV not requiring a patient consultation. Unpublished data from our HIMCO indicated that almost 90% of members contact the system every year.

The HIMCO does not allow "sick" patients to be incorporated "de novo" as new members of the HIMCO, so this could decrease our number of prevalent cases. This limitation would not influence the number of incident cases.

We only considered renal histology as a part of the case search, so any other tissue biopsy was not included and can be considered as a limitation.

In summary, in this first study from Argentina, incidence and prevalence rates of GPA and MPA were estimated for the first time in a Latin American country, with higher incidence of MPA over GPA. Our figures were similar to those found in Europe and the USA. In our population, GPA and MPA were more frequent in women and in older ages (70th decade).

Compliance with ethical standards

Disclosures None.

Ethical approval This study was approved by the Clinical Research Ethics Committee of Hospital Italiano de Buenos Aires (protocol number 3089). Since this is a retrospective study, formal consent is not required.

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