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Incidence and Prevalence of Polymyalgia Rheumatica and Giant Cell Arteritis in a Healthcare Management Organization in Buenos Aires, Argentina

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ABSTRACT. ***Objective.*** To estimate incidence and prevalence of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) in a university hospital–based health management organization (Hospital Italiano Medical Care Program) in Argentina.

Methods. Overall and sex-specific incidence rates (IRs) and prevalence were calculated (age ≥ 50 yrs). Incidence study followed members with continuous affiliation ≥ 1 year from January 2000 to December 2015. Diagnosis as per the 2012 European Alliance of Associations for Rheumatology/American College of Rheumatology (ACR) criteria for PMR or the ACR 1990 criteria for GCA. Prevalence was calculated on January 1, 2015.

Results. There were 176,558 persons who contributed a total of 1,046,620 person-years (PY). Of these, 825 developed PMR, with an IR (per 100,000 PY) of 78.8 (95% CI 73.4-84.2) overall, 90.1 (95% CI 82.9-97.2) for women, and 58.9 (95% CI 51.1-66.6) for men. Ninety persons developed GCA; the IR was 8.6 (95% CI 6.8-10.4) overall, 11.1 (95% CI 8.5-10.6) for women, and 4.2 (2.2-6.3) for men. There were 205 prevalent PMR cases and 23 prevalent GCA cases identified from a population of 80,335. Prevalence of PMR was 255 per 100,000 (95% CI 220-290) overall, 280 (95% CI 234-325) for women, and 209 (95% CI 150-262) for men; and the prevalence of GCA was 28.6 per 100,000 (95% CI 16.9-40.3) overall, 36.4 (95% CI 20.1-52.8) for women, and 14.2 (95% CI 0.3-28.1) for men.

Conclusion. This is the first study of incidence and prevalence of PMR and GCA in Argentina. There were similarities and differences with cohorts from other parts of the world, but population-based epidemiologic studies in Latin America are needed.

Key Indexing Terms: epidemiology, giant cell arteritis, health services research, polymyalgia rheumatica, systemic vasculitis

Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are inflammatory disorders of unknown etiology that predominantly occur in persons aged 50 years and older.[1] PMR frequency is 3 to 10 times higher than that of GCA; incidence and prevalence are higher in Northern European countries and Nordic countries descendants. Peak of incidence occurs after 60 years of age and the highest peak occurs at 80 years.[2] Both diseases are more common in females and corticosteroids remain the mainstay of treatment.[1-3]

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PMR and GCA epidemiological data are scarce in Latin America and in Argentina, in particular. Therefore, the aim of our study was to determine the incidence and prevalence of PMR and GCA in a population of a healthcare program managed by a university hospital in Ciudad Autónoma de Buenos Aires (CABA), Argentina.

METHODS

The studied population included people affiliated with a prepaid healthcare program provided by a university hospital (Hospital Italiano Medical Care Program [HIMCP]) located in CABA, Argentina. This same population has been studied in epidemiological studies of other diseases; the details of their characteristics and similarities to the CABA general population can be found[4,5] (Supplementary Tables S1-3, available with the online version of this article).

According to the last census, there were 958,343 inhabitants aged ≥ 50 years in CABA in 2010. The great majority of the population are descendants from White European people.[6] Patients with common chronic diseases (eg, type II diabetes, hypertension, dyslipidemia) are admitted to the HIMCP, but patients with acute or complex chronic diseases detected or declared when requiring affiliation are not admitted.

Incidence estimation. Patients were aged ≥ 50 years and were members of the HIMCP, affiliated after the year 2000, for at least 1 year prior to diagnosis. They were followed since affiliation until PMR or GCA diagnosis, voluntary resignation from the HIMCP, death, or termination of the study (January 1, 2015). For incidence calculation, the date of diagnosis was considered as that when the diagnosis first appeared in the electronic medical records (EMRs).

Prevalence estimation. For prevalence estimation, the assigned denominator was the number of active members aged > 50 years of age on January 1, 2015, and the numerator was the number of patients with PMR or GCA receiving treatment (corticosteroids or other treatments) according to EMRs at that timepoint.

Data collection. The data were obtained from the EMRs and the following search criteria were established: (1) rheumatology database: patients included in previous studies; (2) health database: patients with PMR or GCA diagnosis, searched using the following terms: polymyalgia rheumatica, giant cell arteritis, temporal arteritis, arteritis, vasculitis, amaurosis fugax, severe headache, and jaw claudication; (3) pharmacy database: patients who purchased > 3 boxes of meprednisone/prednisone tablets or had purchased them for > 1 year (1 box = 20 8-mg meprednisone pills); and (4) pathology database: temporal arteritis evidenced by temporal artery biopsy (TAB).

Erythrocyte sedimentation rate (ESR; automatized method Alifax), high-sensitivity C-reactive protein (immunoturbidimetric method), hemoglobin, and hematocrit were collected from the laboratory database.

GCA diagnosis was made by treating physicians based on clinical symptoms and laboratory data, and the vast majority of them were confirmed by a TAB and/or halo sign detected by temporal Doppler ultrasound (available in our hospital since 2009) performed by an experienced sonographer. PMR diagnosis was made based on clinical symptoms, laboratory data, and confirmed response to low dose of corticosteroids.

All data collected from EMRs were manually reviewed and only patients aged ≥ 50 years and fulfilled the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology 2012 clinical criteria for PMR and ACR 1990 criteria for GCA were included in the incidence and prevalence calculation[7,8] (Supplementary Figure S1, available with the online version of this article). Patients who fulfilled GCA classification criteria[8] and had PMR symptoms were counted as having only GCA.

Statistical analysis. Incidence rate (IR) and prevalence rate (PR) were estimated with their 95% CI and calculated for each age group (per decade), considering age at the time of diagnosis for the identified cases and age at the beginning of the study for the at-risk population.

Ethical approval. This work was approved by the ethics committee of the Hospital Italiano de Buenos Aires (ID: 2752). When becoming a member of the HIMCP, patients give general consent for using their anonymized data for research purposes. In this study, due to its retrospective and anonymized nature, no specific written consent from patients was required by the ethics committee.

RESULTS

From the studied population aged ≥ 50 years, 176,558 people contributed a total of 1,046,620 person-years (PY).

Incidence. There were 825 people diagnosed with PMR in the study period. The IR was estimated per 100,000 PY. The IR in the population was 78.8 (95% CI 73.4-84.2) overall, 90.1 (95% CI 82.9-97.2) for women, and 58.9 (95% CI 51.1-66.6) for men. Ninety people were diagnosed with GCA with an overall IR of 8.6 PY (95% CI 6.8-10.4), 11.1 for women (95% CI 8.5-10.6), and 4.2 for men (95% CI 2.2-6.3).

Prevalence. On January 1, 2015, 205 prevalent PMR cases and 23 GCA prevalent cases were identified from a denominator population of 80,335 members of the HIMCP. PMR prevalence per 100,000 population was 255 (95% CI 220-290) overall, 280 (95% CI 234-325) for women, and 209 (95% CI 150-262) for men. GCA prevalence per 100,000 population was 28.6 (95% CI 16.9-40.3) overall, 36.4 (95% CI 20.1-52.8) for women, and 14.2 (95% CI 0.3-28.1) for men.

Characteristics of the PMR and GCA populations are shown in the Table. Incidence was higher in females, with 73.1% and 82.2% of patients with PMR and GCA, respectively. The mean age at the time of diagnosis was 75.4 (SD 7.9) years for PMR and 75.6 (SD 11.1) years for GCA. The highest incidence was age > 80 years for PMR and age > 70 years for GCA (Figure 1). The peak prevalence for PMR was at age 70 years for females and age > 80 years for males. For GCA, the peak prevalence was at age 70 years for both sexes (Figure 2).

Of the patients with PMR, 96.7% had shoulder girdle involvement, whereas 72.9% had pelvic pain/stiffness. There were 12.9% who had arthritis or peripheral tenosynovitis, predominantly in the hands. Of the patients with GCA, 58.9% showed PMR symptoms. The most frequent GCA symptom was headache in 77.8% of the patients, followed by jaw claudication in 53.3%, and 40% presented some kind of visual alteration (amaurosis fugax and diplopia in 16% and 24%, respectively).

Mean ESR was 56.7 (SD 25.3) mm/h for PMR and 69.8 (SD 25.1) mm/h for GCA at the time of diagnosis. The median initial meprednisone dose was 8.0 (IQR 8.0-8.0) mg/day for PMR and 40.0 (IQR 20.0-40.0) mg/day por GCA, with a median treatment duration of 20.0 (IQR 13.0-31.0) months for PMR 29.0 (IQR 19.0-40.0) months for GCA at the end of the study.

DISCUSSION

To our knowledge, our study is the first to provide PMR and GCA epidemiological data in Argentina and one of the first ones in Latin America. Data published around the world are

Table. Patient characteristics at disease onset (incident cases).

	PMR, n = 825	GCA, n = 90
Female sex	603 (73.1)	74 (82.2)
Age at diagnosis, yrs, mean (SD)	75.4 (7.9)	75.6 (11.1)
Bilateral shoulder pain	798 (96.7)	–
Bilateral pelvic girdle (hip) pain	602 (72.9)	–
Peripheral synovitis[a]	107 (12.9)	–
PMR symptoms	825 (100)	53 (58.9)
Elevated ESR	700 (84.8)	87 (96.7)
Mean ESR (SD)	56.7 (25.3)	69.8 (25.1)
Initial meprednisone dose, mg, median (IQR)	8.0 (8.0-8.0)	40.0 (20.0-40.0)
Duration of steroid treatment, months, median (IQR)	20.0 (13.0-31.0)	29.0 (19.0-40.0)
Jaw claudication	–	48 (53.3)
Headache	–	70 (77.8)
Visual impairment	–	36 (40)

Values are expressed as n (%) unless indicated otherwise. [a] Peripheral synovitis: distal swelling, tenosynovitis, or arthritis. ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; PMR: polymyalgia rheumatica.

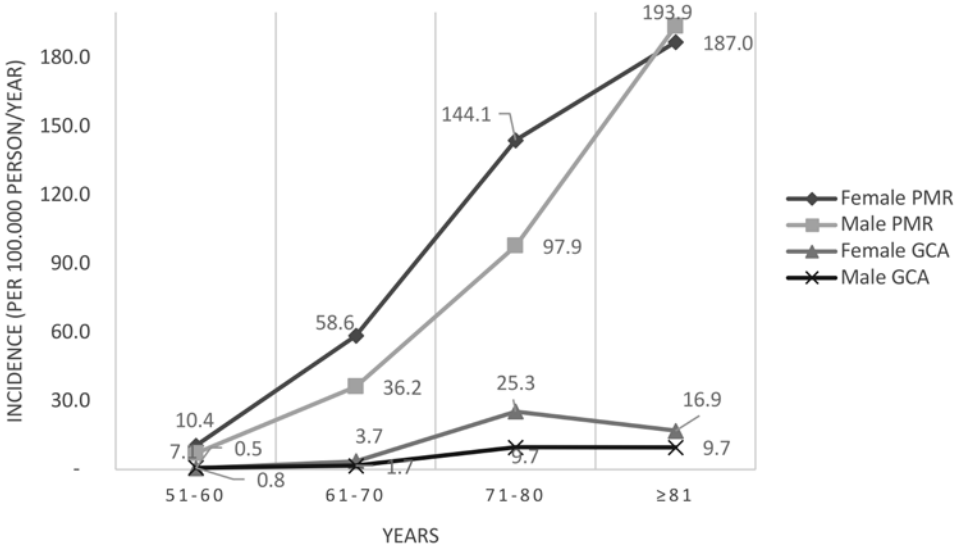

Figure 1. PMR and GCA incidence rates, by sex and age. GCA: giant cell arteritis; PMR: polymyalgia rheumatica.

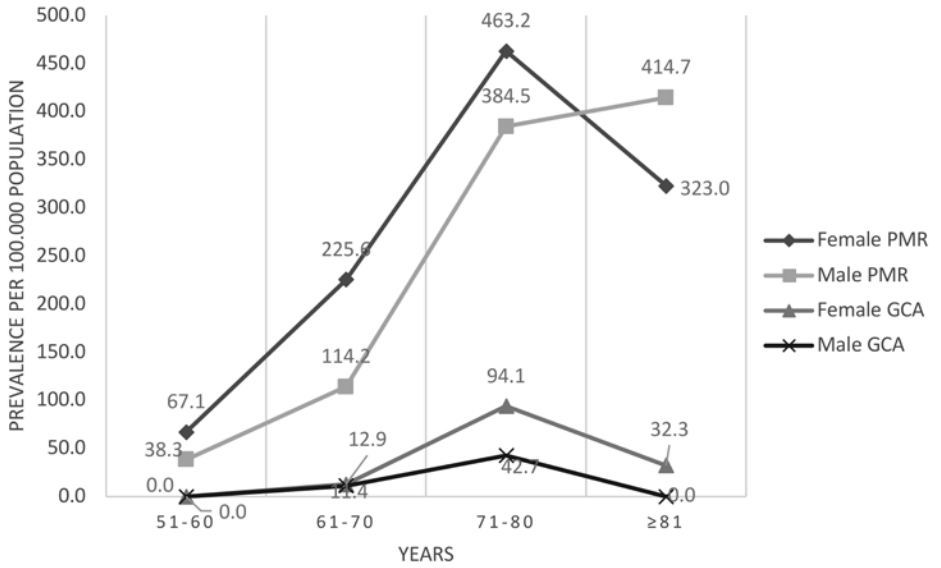

Figure 2. PMR and GCA prevalence, by sex and age. GCA: giant cell arteritis; PMR: polymyalgia rheumatica.

variable. PMR incidence is high in Nordic countries,[9-11] as well as in Olmsted County in the United States,[12] where most of the population descends from Northern Europe. One of the highest IRs is the one published in the United Kingdom, which was 84.2/100,000 PY in the period between 1990 and 2001.[13] In contrast, in Southern European countries, IRs are low, at approximately 22/100,000 PY.[14] In a previous review of the epidemiology of PMR in Italy, an incidence between 12 and 23 cases per 100,000 inhabitants was reported.[15]

The IR in our population was higher at 78.8/100,000 PY (95% CI 73.4-84.2), but it was within the range of rates reported in a recent systematic review and close to those reported in the UK and US.[16] Regarding Latin America, in Colombia, a PMR prevalence was reported of 200 per 100,000 inhabitants aged > 50 years[17]; these results are very similar to our data (255/100,000).

There are several differences between the reported studies that might explain varying results, such as the criteria used for diagnosis (some studies used Bird or Healey criteria, others the ACR criteria, and others physician diagnosis), the use of normal ESR as an exclusion criterion (as in one of the Italian studies),[15] different cut-off values for ESR as inclusion criteria, and different populations included (such as patients diagnosed by general practitioners, those referred to rheumatology centers, population-based studies). With all these differences among studies, it is difficult to draw a conclusion on which data are more accurate. We took a population-based approach, although our population might have some special characteristics that are not necessarily generalizable, as discussed below.

In a recently published metanalysis that included 107 studies, the pooled incidence (95% CI) of GCA was 10.00 (9.22-10.78) cases per 100,000 people aged > 50 years.[18] The incidence was

highest in Scandinavia at 21.57 (18.90-24.23), followed by North and South America at 10.89 (8.78-13.00), Europe at 7.26 (6.05-8.47), and Oceania at 7.85 (−1.48 to 17.19). These figures are similar to what we found in our study. Pooled prevalence in that metanalysis was 51.74 (42.04-61.43) cases per 100,000 people aged > 50 years.[18] Our prevalence was within that range, lower than the ones reported in Denmark, Italy, the US, and Germany, and higher than those reported in Tunisia, Japan, Turkey, and Spain.[18] As in PMR, several factors might explain the differences. First, there is the lack of a standardized definition for GCA, in particular when administrative databases are used, as there are no specific billing codes for GCA. Second, there is inconsistency in the inclusion criteria used, wherein the majority of hospital-based studies included only biopsy-proven cases, whereas most population or community-based studies (such as ours) also included clinical diagnoses. Last, most studies on prevalence included cases with GCA or PMR with a past diagnosis who were alive and living in the study area at the time of the study.[16] Because as we consider that a patient who has stopped all treatment and has no symptoms does not have prevalent disease, we did not include those patients; this exclusion might explain our lower prevalence.

This work has several limitations. One is that the HIMCP is a medical care plan that does not incorporate "sick" patients. Therefore, our prevalent cases could be reduced because people with either disease would not have been allowed into the plan. Although this limitation would affect prevalence and would not affect incidence, it is possible that PMR or GCA is more often diagnosed in healthy people rather than in patients with multiple comorbidities. It is also possible that healthier patients receive corticosteroids for extended periods of time (usually, we are more concerned about steroid use in patients with multiple comorbidities), and that bias could affect prevalence.

Another limitation is the generalizability. Although the population of the HIMCP is similar in age and economic distribution to the overall CABA population (Supplementary Tables S1-3, available with the online version of this article), we have to be cautious in considering this valid for the whole city and even more so to the rest of the country. However, ours are the first results published in Argentina, to our knowledge, and may be useful for future comparisons.

Another difficulty is GCA definition. As we currently know, GCA is a more complex disease affecting not only cranial arteries but also large vessels, mainly thoracic. In this study and almost every study published around the world, GCA epidemiology takes into account mainly cranial disease, since large vessel involvement is not easily recognized nor properly registered in databases and EMRs. Therefore, the true incidence and prevalence of the disease may have been underestimated.

We did not investigate whether patients with both GCA and PMR symptoms fulfilled PMR classification criteria also; we classified them as GCA only. In our cohort, there were 53 patients with incident GCA and PMR symptoms (Table 1). In the case that these patients would have fulfilled PMR classification criteria and we counted them as having incident PMR, the PMR IR would have been 83.9/100,000 PY, a little bit higher than the one we are reporting but within the 95% CI. In cases where both entities coexist, GCA diagnosis is the one that will lead treatment decisions; that is the reason why we have classified it as such, but we do recognize that it can be another study limitation.

Differences and similarities in incidence and prevalence with cohorts from other parts of the world are difficult to explain. True genetic and environmental differences may be, in part, confounded by referrals bias and case definitions, particularly for GCA.

To our knowledge, this is the first GCA epidemiological study published from Latin America and one of the first ones showing epidemiological PMR data of this region. We know that the Latin American population is different from those in other sites in the world, and having appropriate data may allow us to have a better understanding of diseases and to plan for proper medical care of these patients. Clearly, population-based epidemiology studies are needed in Latin America.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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