Incidence and Prevalence of Rheumatoid Arthritis in a Health Management Organization in Argentina: A 15-year Study

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ABSTRACT. ***Objective.*** To estimate incidence and prevalence rates of rheumatoid arthritis (RA) in the city of Buenos Aires (CABA), Argentina, using data from a university hospital–based health management organization.

Methods. Global, age-specific, and sex-specific incidence and prevalence rates were calculated for members of the Hospital Italiano Medical Care Program (HIMCP), age ≥ 18 years. Incidence study followed members with continuous affiliation ≥ 1 year from January 2000 to January 2015 until he/she voluntarily left the HIMCP, RA was diagnosed, death, or study finalization. Cases from the Rheumatology Section database, electronic medical records, laboratory database, and pharmacy database were filtered with the 2010 American College of Rheumatology/European League Against Rheumatism criteria. Prevalence was calculated on January 1, 2015, and standardized for CABA. Capture-recapture (C-RC) analysis estimated true population sizes.

Results. In the study period, incidence rates (cases per 100,000 person-yrs) were 18.5 (95% CI 16.7–20.4) overall, 25.2 (95% CI 22.4–28.0) for women, and 8.8 (95% CI 6.8–10.8) for men. Prevalence rates (percentage of RA cases in the sample population) were 0.329 (95% CI 0.298–0.359) overall, 0.464 (95% CI 0.417–0.510) for women, and 0.123 (95% CI 0.093–0.152) for men. Standardized CABA prevalence rate was 0.300 (95% CI 0.292–0.307). C-RC adjusted rates were almost the same as unadjusted rates.

Conclusion. This study's incidence and prevalence rates are in the lower range of the rates found around the world. Our female to male prevalence ratio was 4:1. Our peak incidence age was in the sixth and seventh decades for both sexes. (First Release April 15 2016; J Rheumatol 2016;43:1306–11; doi:10.3899/jrheum.151262)

Key Indexing Terms:
RHEUMATOID ARTHRITIS EPIDEMIOLOGY HEALTH SERVICES NEEDS AND DEMAND

Rheumatoid arthritis (RA) is a chronic autoimmune disorder in which the body's immune system attacks joints, leading to their inflammation, erosion, and deformity. RA has incidence and prevalence rates with significant regional variation. Epidemiological data demonstrating regional variation contributes to our understanding of how genetic and environmental factors affect the development of RA in patients.

RA epidemiological data is lacking in Argentina and Latin America. Two previous studies reported only RA prevalence in Argentina: a 1999 study reported a prevalence rate of 0.197% for northwest Argentina[1], and a 2010 study reported a prevalence rate of 0.94% for a pool of patients derived from the RA registry and a telephone survey as a secondary source, in a small city in the Buenos Aires province[2].

To our knowledge, this paper is the first study of RA incidence in Argentina with inclusion of the 2010 American

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College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria. Our aim was to determine the most recent incidence and prevalence of RA in a healthcare organization from the city of Buenos Aires (CABA), the largest populated metropolis in Argentina, using a methodology similar to those used in previous studies for other diseases[3,4,5,6,7].

MATERIALS AND METHODS

Setting. The population studied was the membership of the Hospital Italiano Medical Care Program (HIMCP), a prepaid health maintenance organization (HMO) in CABA, Argentina. The HIMCP provides comprehensive medical and health services through 2 main hospitals and 24 peripheral outpatient centers to around 140,000 members primarily located in the urban areas of CABA. The city covers an area of 202 km^2 and has a subtropical climate. It is located on the western bank of the Rio de la Plata and has a population of 2,890,151 inhabitants (2010 census). In all, 92% of the population is white and of European descent, and the remaining is a mixture of natives and other ethnicities[8].

Argentina has a segmented health system consisting of 3 large sectors: public, private, and social security (the last 2 covering a population of nearly 18.3 million people distributed among close to 300 entities of varying scope and size)[9]. Beneficiaries of the private system can freely choose their HMO.

In this context, the HIMCP provides a private health system insurance. About 5%–7% of the population in these geographic areas is affiliated with private health system insurance.

Population. For incidence calculation, the population contributing time at risk was all HIMCP members over 18 years old, with continuous affiliation for at least 1 year from January 2000 to January 2015. Each person was followed up until he/she voluntarily left the HIMCP, a diagnosis of RA was established, death, or finalization of the study. For prevalence calculation, the denominator population was the number of active members over 18 years old on January 1, 2015.

Case ascertainment. Multiple methods for case finding were used to ensure complete ascertainment: (1) patients noted in the Rheumatology Section database; (2) patients found to be diagnosed with "arthritis" using searches of the following keywords registered in the list of problems in the electronic medical records: arthritis, rheumatoid arthritis, seronegative arthritis, seropositive arthritis, polyarthritis, seropositive rheumatoid polyarthritis, seronegative rheumatoid polyarthritis, polyarticular rheumatoid arthritis; (3) patients with positive results for rheumatoid factor (RF) and/or cyclic citrullinated peptide (CCP) antibodies in the laboratory database; and (4) patients purchasing medication commonly used in the treatment of RA as noted in the HIMCP pharmacy database: methotrexate, sulfasalazine, leflunomide, or biologic drugs (anti-tumor necrosis factor-α group, rituximab, abatacept, tocilizumab, tofacitinib). Medical records of all patients found were manually reviewed, and only patients older than 18 years and fulfilling the 2010 ACR/EULAR criteria for RA were included. Clinical data for disease description were obtained from this review of the medical records.

Statistical analysis. Global, age-specific, and sex-specific incidence and prevalence rates were calculated with 95% CI. For incidence calculation, the date of diagnosis was considered as that when the diagnosis first appeared in the clinical records, and cases had to have been enrolled with the HIMCP for at least 1 year before this date. Prevalence was estimated on January 1, 2015, and the denominator population was the number of HIMCP active members older than 18 years on that date (n = 135,750).

In addition, we used the direct method to estimate age- and sex-standardized prevalence rates of RA, with the CABA population from the 2010 national census as the reference population.

Capture-recapture (C-RC) methods estimated the completeness of case ascertainment when using multiple information sources. Log-linear models were used to estimate the true RA population size by evaluating the degree of overlap among 3 data sources: the Rheumatology Section database, the database of patients identified by keyword searches in the electronic medical records, and the pharmacy database. Note that all patients in the laboratory database were included in the other databases; therefore, it was excluded for our analysis. Although independence of data sources could not be completely assured, there is no direct relationship among the 3 databases used in our analysis.

Modeling was performed separately for incidence and prevalence data. The log-linear model was used to estimate the number of persons who were missed in the population. Eight hierarchical log-linear models were fit to the data: 1 model assuming independence among the 3 data sources, 3 models of pairwise interaction, 3 models of 2 pairwise interactions, and the so-called saturated model that adjusted for interaction between all 3 pairs of sources. The best-fitting model was determined by the Akaike information criterion and Bayesian information criterion. Based on the estimated undercount, revised C-RC estimates of incidence and prevalence were calculated.

RESULTS

Incidence. In the study period for the HIMCP, 349,775 persons contributed a total of 2,073,438 person-years. A total of 384 patients developed RA between January 2000 and January 2015. The incidence rate was measured as cases per 100,000 person-years. The overall incidence rate was 18.5 (95% CI 16.7–20.4). In more detail, 310 cases of new-onset RA were women (81%), with an incidence rate of 25.2 (95% CI 22.4–28.0). The incidence rate for men was 8.8 (95% CI 6.8–10.8). Age-specific incidence rates in both female and male patients peaked in the sixth and seventh decades of life (Figure 1); however, in the 61–80 age group, the incidence rate for women was almost double that for men. Further, while the incidence rate was 5.4 (95% CI 2.4–8.5) for the female 18–30 age group, no incident cases were found for the male 18–30 age group. Details for demographic and clinical features of incident cases are shown in Table 1.

When we considered patients with available laboratory information, 66% of incident cases were seropositive (when only the patient's level of RF was considered). However, 85% of incident cases were seropositive when we considered patients with either elevated RF or CCP, or both. The majority (44%) of incident cases overall had involvement of 4–10 small joints.

Prevalence. On January 1, 2015, 446 prevalent cases were identified from a denominator population of 135,750 HIMCP members. Prevalence rate was the total number of RA cases observed in the sample population, indicated as a percentage. Our study resulted in a prevalence rate of 0.329 (95% CI 0.298–0.359) overall. The female prevalence rate of 0.464 (95% CI 0.417–0.510) was almost 4 times the male rate of 0.123 (95% CI 0.093–0.152). In terms of age, RA was most prevalent in the 50s for women and the 70s for men (Figure 2). As the population ages, the prevalence rates for both sexes move closer together. Demographic and clinical features of prevalent cases are similar to those of incident cases, as shown in Table 1.

Standardization. Because of differences in sex and age demographics, we standardized our HIMCP results for CABA. For CABA, the overall prevalence rate was 0.300

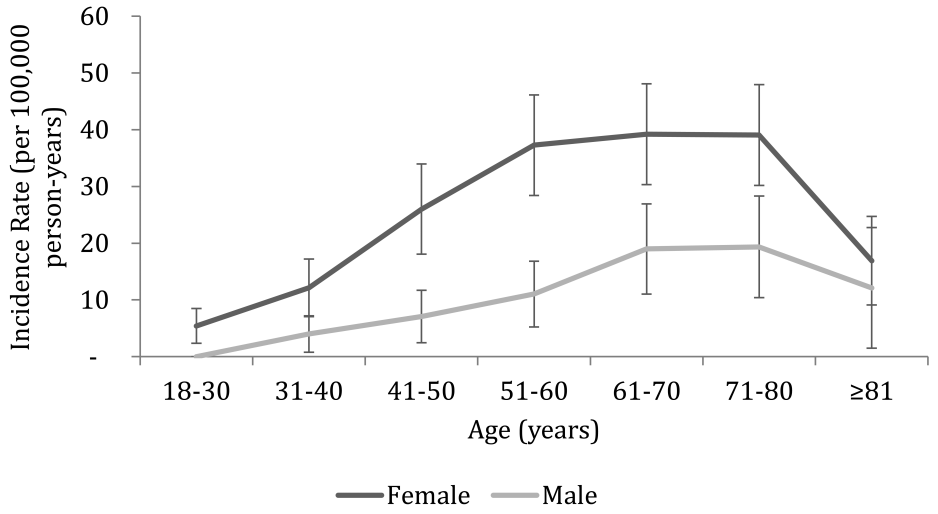

Figure 1. Crude rheumatoid arthritis incidence rate by sex and age group for the Hospital Italiano Medical Care Program, 2000–2015. Error bars represent 95% CI.

Table 1. Demographic and clinical features of rheumatoid arthritis cases at diagnosis in the Hospital Italiano Medical Care Program, Buenos Aires, Argentina, 2000–2015.

Variables	Incidence		Prevalence	
	Patients with Data, n	Results, n (%)	Patients with Data, n	Results, n (%)
Sex and age				
Female	384	310 (81)	446	380 (85)
Diagnosis age	384	61 (14)*	446	57 (15)*
Actual age, by Jan. 1, 2015	384	67 (15)*	446	66 (14)*
Yrs from diagnosis	384	6 (4)*	446	9 (7)*
Laboratory				
Positive RF	371	246 (66)	423	273 (65)
Positive CCP	307	244 (79)	352	278 (79)
Elevated ESR	287	225 (78)	232	183 (79)
Elevated CRP	149	99 (66)	136	90 (66)
Joint involvement**				
1 large joint	319	8 (3)	263	5 (2)
2–10 large joints	319	18 (6)	263	15 (6)
1–3 small joints	319	95 (30)	263	84 (32)
4–10 small joints	319	140 (44)	263	113 (43)
> 10 joints, ≥ 1 small joint	319	58 (18)	263	46 (17)
Other clinical presentation				
Symptom duration ≥ 6 weeks	237	219 (92)	194	178 (92)
Morning stiffness ≥ 1 h	151	95 (63)	124	78 (63)
Symmetrical arthritis	285	251 (88)	230	205 (89)
Data source				
Pharmacy	384	335 (87)	446	390 (87)
Electronic medical records***	384	378 (98)	446	429 (96)
Laboratory	384	273 (71)	446	304 (68)
Rheumatology Section	384	152 (40)	446	212 (48)

* Presented as mean (SD). ** With or without involvement of large joints. *** Patients are identified by keyword searches. RF: rheumatoid factor; CCP: cyclic citrullinated peptide; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

(95% CI 0.292–0.307). The female prevalence rate was 0.463 (95% CI 0.451–0.475). The male prevalence rate was 0.099 (95% CI 0.093–0.105).

Capture-recapture. For incidence, C-RC analysis was done for the total population and yielded an estimated 1 missing patient with RA, resulting in an incidence C-RC–adjusted rate of 18.57 cases (95% CI 18.52–18.86) per 100,000 persons-years. For prevalence, C-RC yielded an estimated

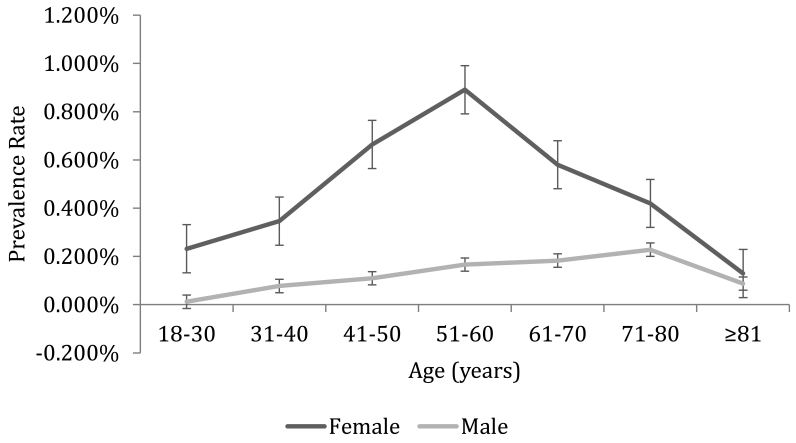

Figure 2. Crude rheumatoid arthritis prevalence rate by sex and age group for the Hospital Italiano Medical Care Program. Error bars represent 95% CI.

1 missing prevalent patient with RA, resulting in a prevalent C-RC–adjusted rate of 0.329 (95% CI 0.3285–0.334). Figure 3 shows the overlaps in the number of cases identified by the different methods of case finding.

DISCUSSION

To our knowledge, ours is the first study of RA incidence in Argentina using the 2010 ACR/EULAR criteria for RA diagnosis by analysis of patient data from the HIMCP, an HMO. Results for the HIMCP are standardized for CABA because of the demographic differences between the 2 populations. The CABA prevalence rate is about 10% lower than that of the HIMCP, probably because of the greater percentage of elderly patients in the HIMCP. Moreover, while the female prevalence rate for both populations is similar, the CABA male prevalence rate is about 20% lower than the HIMCP male prevalence rate. The likely reason is that the ratio of young to elderly men is much greater in the CABA population than in the HIMCP population. However, the results of our study might not be applied to the rest of Argentina because of the demographic differences.

The RA incidence and prevalence rates found for the HIMCP are in the lower range of the rates found around the world (Table 2[10–19,20,21] and Table 3[1,2,10,12,13,16,18,20,22,23,24,25,26]). Data are insufficient in Latin America to conclusively compare our rates to those of other Latin American countries. However, our RA prevalence of 0.329 is lower than the RA prevalence rate of 0.46 found in Brazil[24], 1.24 in Cuba[27], and 1.6 in Mexico[23]. Regional variability between countries and within Argentina could be because of the differences in genetics, infectious agents, medication, alcohol and tobacco consumption, education, methodology, case ascertainment, and population used for standardization. Further, the results of our study deviated from those of Soriano, *et al*'s study[16], which also took place in the HIMCP. The study reported an RA incidence rate of 0.24/1000 person-years and a preva-

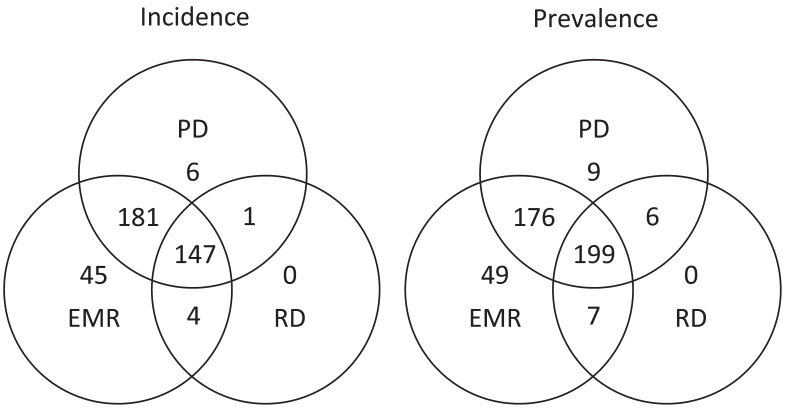

Figure 3. Overlaps of the number of rheumatoid arthritis cases identified by different methods of case finding in the Hospital Italiano Medical Care Program. PD: pharmacy database; EMR: electronic medical records with keyword searches; RD: Rheumatology Section database.

Table 2. Incidence of rheumatoid arthritis around the world.

Study	Region	Study Period, Yrs	Age Range, Yrs	Cases Found, n	Annual Incidence Rate per 100,000 Population			Population used for Standardization
					Overall	Female	Male	
Our study	Buenos Aires, Argentina	2000–2015	≥ 18	384	18.5	25.2	8.8	2010 City of Buenos Aires population
Rossini, *et al*[10]	Various regions in Italy	2011	≥ 18	1648	35	48	20	Not done
Eriksson, *et al*[11]	Sweden	2006–2008	≥ 18	8826	40.6	55.7	25.0	2008 Swedish population
Yu, *et al*[12]	Taiwan, China	2000–2008	All ages	1390	17.3	26.0	8.8	Not done, study performed of whole Taiwan population
Myasoedova, *et al*[13]	Minnesota, USA	1995–2007	≥ 18	466	40.9	53.1	27.7	2000 US population
Carbonell, *et al*[14]	Spain	2004	≥ 16	362	8.3	11.3	5.2	Population of different areas of Spain
Pedersen, *et al*[15]	South Jutland, Denmark	1995–2002	≥ 15	440	30.7	40.4	20.8	2002 Danish population
Soriano, *et al*[16]	Buenos Aires, Argentina	1996–2002	≥ 20	79	24.5	19.8	4.6	Not done
Shichikawa, *et al*[17]	Kamitonda, Japan	1985–1996	All ages	3	8	0	16	1985 Japanese population
Gabriel, *et al*[18]	Minnesota, USA	1955–1985	≥ 35	425	75.3	98.1	49.7	1970 US white population
Uhlig, *et al*[19]	Oslo, Norway	1988–1993	≥ 20	550	25.7	36.7	13.8	Not done
Drosos, *et al*[20]	Northwest Greece	1987–1995	≥ 16	428	24.0	36.0	12.0	1991 Greece population
Symmons, *et al*[21]	Manchester, UK	1990–1991	≥ 16	104	—	35.9	14.3	Not done

Table 3. Prevalence of rheumatoid arthritis around the world.

Study	Region	Study Period, Yr	Age Range, Yrs	Cases Found, n	Prevalence, %			Population used for Standardization
					Overall	Female	Male	
Our study	Buenos Aires, Argentina	2015	≥ 18	446	0.329	0.46	0.12	2010 City of Buenos Aires population
Quintana, *et al*[22]	Rosario, Argentina	2012	≥ 18	40	2.4	3.4	0.7	Not done
Rossini, *et al*[10]	Various regions in Italy	2011	≥ 18	19,226	0.41	0.57	0.23	Not done
Yu, *et al*[12]	Taiwan, China	2000	All ages	505	0.05	0.09	0.02	Not done, study performed in whole Taiwan population
Peláez-Ballestas, *et al*[23]	5 regions Mexico	2009	≥ 18	110	1.49	2.09	0.85	2005 Mexican Population
Scublinsky, *et al*[2]	Lujan, Argentina	2008	≥ 16	203	0.94	1.54	0.40	Not done
Myasoedova, *et al*[13]	Minnesota, USA	2005	≥ 18	—	0.72	0.98	0.41	2000 US population
Senna, *et al*[24]	Montes Claros, Brazil	2003	≥ 16	14	0.46	0.68	0.09	Not done
Soriano, *et al*[16]	Buenos Aires, Argentina	2002	≥ 20	158	0.236	0.33	0.09	Not done
Carmona, *et al*[25]	Spain	1998	≥ 20	11	0.5	0.8	0.2	Not done
Spindler, *et al*[1]	Tucumán, Argentina	1998	≥ 16	695	0.197	0.32	0.06	City of San Miguel de Tucumán population
Gabriel, *et al*[18]	Minnesota, USA	1985	≥ 35	—	1.07	1.36	0.74	1970 US white population
Cimmino, *et al*[26]	Chiavari, Italy	1992	≥ 16	11	0.33	0.51	0.13	Not done
Drosos, *et al*[20]	Northwest Greece	—	≥ 16	428	0.24	0.48	0.20	1991 Greece population

lence rate of 0.24%. This deviation could be because (1) the 2003 study analyzed a denominator patient population that was half the size of our study, (2) electronic medical records at the HIMCP and its associated databases were not established until 2001, and (3) the 2010 ACR/EULAR criteria were not used in that study period.

Peak incidence for the HIMCP population was in the 61–70 and 71–80 age groups for both sexes. These data are important because they confirm information from previous studies that show RA to be a disease frequently occurring in the elderly, therefore challenging the concept that "elderly RA" is a different disease[18,21].

Our study has some strengths. It was based on a large population that was followed for a long period of time. Multiple sources were used to assure complete case ascertainment. In fact, C-RC methods showed very similar results, suggesting that few cases were missed. Finally, our results were standardized for CABA using census data.

As in many other epidemiologic studies, our study has some limitations. It was an analysis based on clinical encounters with the medical system, so unless patients sought care, they would not be identified. The HIMCP data, however, showed that almost 90% of patients enrolled have at least 1 medical encounter per year (data not published). In addition, because of the fact that HIMCP is a healthcare plan in which "ill" patients are not incorporated, our prevalent cases may be reduced because patients with existing disease would not be allowed to enter. However, this limitation would not affect the incident cases because these would be defined by patients developing disease during the observation period. Another limitation for incidence estimation: the 2010 ACR/EULAR criteria include anti-CCP antibodies that were

not commonly used for diagnosis in the earlier years of our study. This could result in an underestimation of global incidence.

We showed that RA incidence and prevalence rates in CABA, one of the largest populated cities in Latin America, are in the lower range of the rates found around the world. Our female to male prevalence ratio was 4:1. Our peak incidence age was in the sixth and seventh decades for both sexes. RA epidemiological data are much needed in Latin America for global comparison and study.

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