The Prevalence of Rheumatoid Arthritis in Chile: A Nationwide Study Performed as Part of the National Health Survey

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ABSTRACT. ***Objective.*** Genetic and environmental backgrounds influence the development of rheumatoid arthritis (RA). In Latin America, epidemiologic data are scarce. We aimed to determine the prevalence of RA in Chile in a population-based study.

Methods. The National Health Survey was a cross-sectional household survey with a stratified multistage probability sample of 6233 participants performed between August 2016 and March 2017. A screening instrument for RA was applied to a random sample of 3847 subjects > 30 years old. Positive screening was defined by at least 1 of the following: 2 swollen joints for at least 4 consecutive weeks (past/present), and/or a diagnosis of arthritis in the past. Individuals with positive screening had rheumatoid factor, anticitrullinated protein antibodies, and C-reactive protein measured, as well as clinical examination performed by a rheumatologist. Self-report of doctor-diagnosed RA was also performed.

Results. The screening questionnaire was applied to 2998 subjects. A positive screening was found for 783 (22.1%). Among subjects with positive screening, 493 (66%) had a clinical evaluation performed by a rheumatologist. Using the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria, prevalence was 0.6% (95% CI 0.3–1.2). Prevalence was higher in women, and 3.3% of subjects self-reported having RA.

Conclusion. According to this national population-based study, RA prevalence in Chile is 0.6% (0.3–1.2), a value similar to what has been found in developed countries and slightly lower than some Latin American countries. Self-reporting leads to overestimating RA. (First Release March 15 2020; J Rheumatol 2020;47:951–8; doi:10.3899/jrheum.190396)

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Rheumatoid arthritis (RA) is a chronic systemic disease characterized by joint inflammation that can potentially lead to sequelae and disability[1,2,3,4]. RA reduces quality of life and generates high direct, indirect, and intangible costs[5,6,7,8]. The prevalence of chronic diseases such as RA provides an indication of the burden of disease, which is useful for healthcare planning. Accordingly, given the limited resources available in health expenditure, it is crucial to have data regarding the frequency of chronic diseases to generate rational health policy decisions.

Prevalence studies of RA throughout the world have shown frequencies between 0.3% and 1%[9–18]. Genetic and environmental backgrounds influence RA development and therefore it is important to have local data. In Latin America, nationwide data are scarce; studies have been developed in specific cities or in limited regions within a country and therefore they may not be representative of a nation's prevalence, considering ethnic and cultural differences that exist. In Chile there is only 1 available study, performed in 1993 by Riedemann and Maluje, which reported a prevalence of 0.46% (95 CI 0.24–0.8; unpublished data)[19]. This study did not include any population from the north of the country and evidence exists that genetic background varies in the different regions of Chile[20].

Given the information presented above, we aimed to determine the national frequency of RA in Chile. To achieve this goal, we used the National Health Survey 2016–2017 [Encuesta Nacional de Salud (ENS) 2016-2017] to study RA prevalence in a representative sample of the entire country.

MATERIALS AND METHODS

Sample and measurements. ENS 2016-2017 was a cross-sectional household survey with a sample of 6233 participants over 14 years old. A stratified multistage sampling method was used with 30 strata representing urban and rural areas of the 15 Chilean geographical regions. The multistage sampling included the selection of counties as primary sampling units, household segments within the counties, and 1 participant from selected households. The ENS oversampled people aged 65 years or more to produce reliable estimates among them. Weighting accounted for differences in selection probability and nonresponse rates, along with the poststratification adjustment, which allowed the weights to sum to the estimated Chilean population according to age, sex, and geographical region. ENS 2016–2017 was performed between August 2016 and March 2017. Response rate was 67%, and refusal rate was 9.8%, with no replacements. The study protocol and ethical consent forms were approved by the ethics committee of the Pontificia Universidad Católica de Chile and the Ministry of Health (approval number 16-019). During the first home visit, a trained lay interviewer applied the health questionnaire. In this visit, demographic information was collected as well as musculoskeletal pain screening through the World Health Organization (WHO)–International League of Associations for Rheumatology (ILAR) Community Oriented Programme for Control of Rheumatic Diseases (COPCORD)[21] and RA screening questionnaires. Eighty-nine percent had a second visit with a trained nurse, who administered questionnaires regarding comorbidity and currently used drugs. The nurse also measured blood pressure, recorded anthropometry, and performed biological sampling. The samples were transported at 4°C to regional hospitals where sera and urine were prepared to be shipped to Santiago for centralized analysis. Among subjects who had the nurse visit, 95.9% gave blood samples.

RA screening. A random sample from the ENS was used for this and other substudies of the survey that included 3847 subjects. Screening for RA was performed among subjects who were over 30 years old using the instrument developed by MacGregor, *et al*, validated and then translated into Spanish by Carmona, *et al* in Spain[12,14]. Modifications were made to this translated version to improve the understanding of the instrument for the Chilean population. These modifications were presented to a group of expert rheumatologists who agreed the new instrument was adequate. This version was back-translated into English by a bilingual individual, whose native language was English. The resulting translation was identical to its original English version. This was administered to 100 patients with diagnosed RA who attend the Red Salud UC-CHRISTUS RA clinic to validate comprehension and sensitivity of the Chilean screening instrument version. None of the evaluated patients reported problems in understanding the questionnaire and the instrument was 100% sensitive.

Positive screening for RA was defined by at least 1 of the following: 2 swollen joints in the past or at the time of interview for at least 4 consecutive weeks, or a diagnosis of arthritis in the past.

All individuals who were considered to have a positive screening were tested for serum rheumatoid factor (RF; Cobas 8000–Modulo c702; Roche) and anticitrullinated protein antibodies (ACPA; ELISA, Triturus; Grifols), as well as for C-reactive protein (CRP; Turbidimetric). In addition, subjects with positive screening were contacted by telephone and scheduled for a clinical visit. After signing informed consent, subjects were evaluated by a rheumatologist to confirm an RA diagnosis supported by established criteria (American College of Rheumatology/European League Against Rheumatism 2010 RA classification criteria; Figure 1)[22].

Finally, once patients had completed the screening questionnaires, all subjects were asked if a physician had diagnosed RA, as a self-report measure.

COPCORD in ENS 2016–2017. The COPCORD musculoskeletal pain questionnaire was part of ENS 2016–2017, to quantify musculoskeletal pain in the population[21]. COPCORD questions inquired about recent (during the last 7 days) musculoskeletal symptoms such as pain, swelling, or stiffness, and further described pain intensity on a scale from 1 to 10. Nontraumatic pain with an intensity > 4 was considered significant musculoskeletal pain. We evaluated the positivity of the COPCORD questionnaire among subjects with RA to determine whether this questionnaire detected all RA cases.

Statistical methods. Prevalence rates and means were calculated using sampling weights that were based on the multistage sampling design and adjusted for poststratification population totals using the Chilean 2017 population.

First, we summarized the sociodemographic profile (sex, age, educational level, working status, marital status, place of residence) of the random subsample of adults aged 31 years and older who answered the screening instrument.

Second, we compared subjects with clinical evaluation to the group without clinical evaluation. To do this, we evaluated the unweighted distribution of sex, educational level, place of residence, self-reported arthritis, and self-reported RA using chi-square test and mean age, ACPA, CRP, RF using t test. We implemented an unweighted logistic regression to calculate the odds of nonparticipation, adjusting simultaneously by significant variables tested above.

Third, we described the demographic characteristics of subjects with confirmed RA. We also calculated the proportion among subjects with RA who were RF+ (RF > 14 IU/ml) and/or cyclic citrullinated peptide–positive (CCP+; CCP > 18 IU/ml).

Fourth, we calculated the prevalence of confirmed RA among the general sample by sex, age, and place of residence. Tables show weighted population prevalence and means, but column totals correspond to the strata sample size. We performed a univariate logistic regression of each of the measured demographic characteristics to estimate the odds of RA. We then performed a multivariate logistic regression including all significant characteristics in univariate analysis. We also used logistic regression to estimate the odds of confirmed RA adjusting for age, sex, and educational level. In the logistic

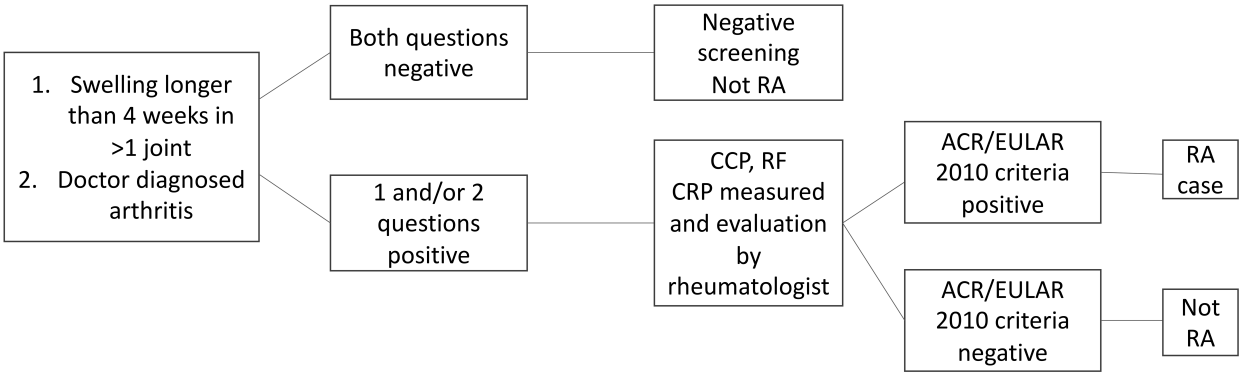

Figure 1. Screening process and RA diagnosis. RA: rheumatoid arthritis; CCP: cyclic citrullinated peptide; RF: rheumatoid factor; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism.

regression, sex and educational level were entered into the models as a 2- and 3-category variable and age as a single continuous variable. Results were summarized using OR with accompanying 95% CI. Pairwise comparisons were used to evaluate differences between sex and educational level, with male and low education as reference categories, respectively.

Unless otherwise stated, analyses were based on complete cases and were weighted accounting for differences in selection probability and nonresponse rates. P values < 0.05 were classed as statistically significant (2-tailed). Analyses were conducted in Stata V14.0 (StataCorp.), adjusting for the complex survey design. Standard error and 95% CI were calculated using a Taylor linear approximation method.

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RESULTS

Study sample. Among a random sample of the national survey of 3847 subjects, 2988 were 31 years old or older and were included in this study. The demographic characteristics of these individuals are described in Table 1.

Screening and prevalence results. A total of 783 (22%, 95% CI 19.6–24.8) subjects had a positive screening for RA, and 752 had RF, ACPA, and CRP measured. Not all subjects had laboratory results available owing to refusal to provide samples and/or problems in processing samples. Of these 752 subjects, 3 subjects died before being evaluated by a rheumatologist and 290 either refused a clinical examination or did not attend the appointment. Therefore, 493 (65.6%) subjects were evaluated by a rheumatologist (Figure 2). It is noteworthy that screening was increasingly positive at an elderly age, with 14% positivity between 31 and 40 years, and 34.8% over 70 years old.

We have characterized subjects who were lost to followup, and according to the unweighted results, significant differences existed in sex, educational level, and urban residence. Age, self-reported arthritis or doctor-diagnosed RA, and ACPA, CRP and RF were not statistically different between participants and nonparticipants. We then performed a logistic regression using nonparticipation as outcome, and sex, education level, and urban residency as explanatory variables. We found that males and low education level and rural residence were associated with higher odds of nonparticipation (Supplementary Tables 1–2, available with the online version of this article).

Table 1. Demographic characteristics of the general sample of the Chilean National Health Survey.

Demographic Characteristics	% (95% CI)	N*
Sex		
Female	52.1 (49.0–55.2)	1931
Male	47.9 (44.8–51.0)	1057
Age, yrs		
Mean	51.8 (50.9–52.7)	2988
31–40	27.2 (24.2–30.4)	521
41–50	22.5 (19.9–25.3)	559
51–60	24.1 (21.6–26.9)	705
61–70	13.8 (12.0–15.8)	607
71+	12.4 (10.7–14.3)	596
Educational level		
Low	22.9 (20.3–25.6)	901
Medium	55.1 (51.5–58.6)	1548
High	21.7 (18.6–25.1)	515
Missing	0.4 (0.2–0.8)	24
Working status		
Paid employment	58.7 (55.5–61.8)	1432
Unemployed	2.6 (1.6–4.0)	66
Housewife	19.9 (17.7–22.4)	615
Retired	15.6 (13.7–17.6)	760
Permanently disabled	1.6 (1.0–2.4)	51
Student	0.6 (0.3–1.3)	15
Other	1.1 (0.7–1.7)	41
Missing	0.1 (0.0–0.3)	8
Marital status		
Married	50.1 (46.8–53.3)	1336
Single	19.1 (16.6–22.0)	556
Stable couple	13.3 (11.2–15.8)	280
Separated/divorced	10.2 (8.6–12.1)	395
Widow	7.2 (6.0–8.5)	415
Missing	0.1 (0.0–0.3)	6
Geographic zone		
Urban	86.9 (85.1–88.5)	2460
Rural	13.1 (11.5–14.9)	528

* N corresponds to the absolute number of subjects without applying sampling weights.

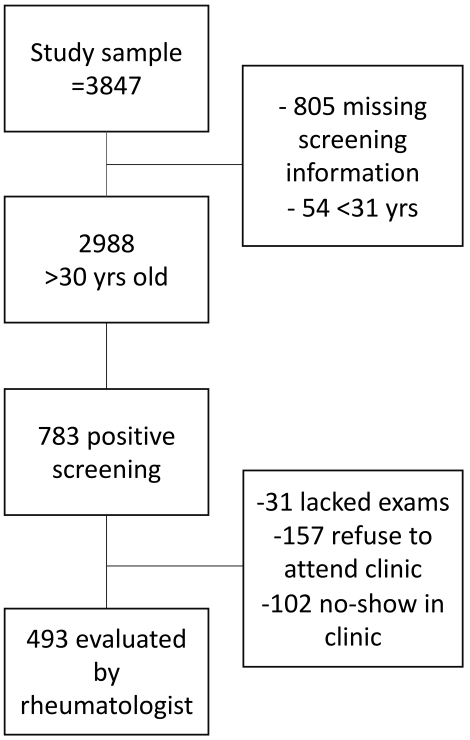

Figure 2. Flow diagram of the study population.

Among the 493 positive screening subjects who were evaluated after a clinical examination by a rheumatologist, 31 cases of RA were diagnosed, and after applying the corresponding sampling weights it was determined that the prevalence was 0.6% (95% CI 0.3–1.2). The percentage of RF+, ACPA+, and both RF and/or ACPA positivity was 47.7% (95% CI 20.5-76.2; 9/31), 62.3 (95% CI 28.2-87.5; 10/31), and 72.2% (95% CI 31.2-93.7, 5/31), respectively.

Demographic characteristics of subjects with RA are described in Table 2. The majority of subjects with RA were female (89.4%) and mean age was 53.6 years (95% CI 43.3–64.0). Regarding ethnicity, in the group of RA individuals, 74.9% were nonindigenous, 22.4% were Mapuche, 2% Aymara, and 0.7% Atacameño. These data do not follow the same pattern as the general sample of ENS 2016–2017 in which 91.4% of the subjects included were of nonindigenous origin. Cases were slightly more frequent in high socioeconomic status (SES) subjects, using educational level as an SES proxy (29.8, 23.8, and 46.4% in low, medium, and high SES, respectively). We performed a logistic regression adjusted for sex and age, and the high SES subgroup had an OR of having RA of 5.88 (95% CI 1.3–26.5) versus middle SES and of 2.44 (95% CI 0.6–9.9) versus low SES. In multivariate analysis, sex, being permanently disabled, and being a stable couple (not married but living together for a prolonged time) were associated with RA diagnosis (Supplementary Tables 3–4, available with the online version of this article).

Table 2. Demographic characteristics of subjects with RA identified in the Chilean National Health Survey.

Demographic Characteristics	% or Mean (95% CI)	N
Sex		
Female	89.4 (66.0–97.3)	27
Male	10.6 (2.7–34.0)	4
Age, yrs		
Mean	53.6 (43.3–64.0)	31
31–54	50.4 (21.9–78.7)	8
55+	49.6 (21.3–78.2)	23
Educational level		
Low	27.4 (11.1–53.2)	13
Medium	21.8 (9.0–44.0)	14
High	42.6 (14.6–76.2)	2
Missing	8.3 (1.6–33.3)	2
Working status		
Paid employment	28.1 (6.5–68.9)	4
Unemployed	0.5 (0.1–4.1)	1
Housewife	33.5 (10.6–68.0)	9
Retired	14.3 (5.1–33.9)	10
Permanently disabled	17.4 (6.0–40.7)	6
Other	6.3 (0.8–34.8)	1
Marital status		
Married	69.6 (43.4–87.3)	13
Single	14.5 (5.0–35.1)	7
Stable couple	1.2 (0.2–8.3)	2
Separated/divorced	7.7 (1.8–27.7)	4
Widow	7.0 (1.5–26.5)	5
Geographic zone		
Urban	94.5 (81.6–98.5)	28
Rural	5.5 (1.5–18.4)	3

RA: rheumatoid arthritis.

Prevalence was higher among females, with a frequency of 1% compared to a prevalence of 0.1% among males (Table 3).

Of the 31 identified cases, 7 were not diagnosed and were not receiving any treatment, and there was 1 case that had been diagnosed but was without treatment.

Self-report of doctor-diagnosed RA was positive in 3.3% of subjects. Regarding COPCORD, recent musculoskeletal symptoms questions were positive in 879 subjects, which represents 30% of the sample. All subjects with positive COPCORD screening had a positive result in the RA screening tool, but not all subjects with diagnosed RA had a positive COPCORD screening for recent pain (11 cases of RA did not have a positive result).

DISCUSSION

This is the first nationwide study aimed at determining RA prevalence in Chile, to our knowledge. It was part of the Chilean National Health Survey, which is administered to a representative sample of all geographical areas in the country. We found a prevalence of 0.6% (0.3–1.2), with a higher prevalence among women.

It has to be taken into consideration that we administered the questionnaire to subjects over 30 years old based on

Table 3. Prevalence of RA in the total sample and by subgroups.

Variables	Estimate	Cases	N*
Total	0.6 (0.3–1.2)	31	2988
Sex			
Male	0.1 (0.0–0.5)	4	1057
Female	1.0 (0.5–2.1)	27	1931
Age, yrs			
31–54	0.5 (0.2–1.6)	8	1349
55+	0.8 (0.5–1.3)	23	1639
Educational level			
Low	0.7 (0.4–1.5)	13	901
Middle	0.2 (0.1–0.5)	14	1548
High	1.2 (0.3–4.7)	2	515
Civil status			
Married	0.8 (0.3–2.0)	13	1336
Single	0.5 (0.2–1.1)	7	556
Stable couple	0.1 (0.0–0.4)	2	280
Separated/divorced	0.5 (0.1–1.8)	4	395
Widow	0.6 (0.1–2.4)	5	415
Work status			
Paid employment	0.3 (0.1–1.4)	4	1432
Unemployed	0.1 (0.0–0.9)	1	66
Housewife	1.0 (0.3–3.4)	9	615
Retired	0.6 (0.2–1.3)	10	760
Permanently disabled	6.6 (2.5–16.3)	6	51
Student	0	0	15
Other	3.4 (0.5–21.1)	1	41
Area of residence			
Urban	0.7 (0.3–1.3)	28	2460
Rural	0.3 (0.1–0.8)	3	528

* N corresponds to the denominator in prevalence calculations. RA: rheumatoid arthritis.

results from the GLADAR Latin American cohort of early arthritis, which showed that the median age of presentation in this region is 42 years, with a 25-75 percentile of 36 and 56 years, respectively[23]. Therefore, it is unlikely that a significant number of cases were missed.

The point estimate of prevalence described in our study is slightly higher than the one reported in Chile in 1993, but not statistically significantly different[19]. However, because there are major methodological differences between these 2 studies, this does not necessarily tell us about changes in prevalence over time. The 1993 study was performed in only 2 cities: the capital, Santiago, with 7 million people, and Temuco, a city with 280,000 people in the south of the country with a large Mapuche population. Therefore, this was not a representative sample of the country because considerable ethnic and genetic variations exist in the north, the central region, and the south[20]. In addition, this study used the WHO-ILAR COPCORD questionnaire as a screening tool to define a positive screening as the presence of nontraumatic pain lasting more than 15 days that generates physical limitation[21]. In contrast, we used a specific RA screening method in which positivity was defined by past or present swelling persistent for more than 4 weeks and/or a previous diagnosis of arthritis.

A rheumatologist confirmed RA diagnosis in subjects with positive screening who attended a clinic[22]. Self-reported doctor-diagnosed RA was considerably higher than the prevalence we found. Self-report has been shown to have low specificity for the diagnosis of arthritis[24]. Given that a difference of more than 2% existed between self-report and confirmed RA, this study reinforces the concept that self-report should not be used to estimate RA prevalence.

COPCORD questions administered in ENS 2016–17, which inquired about recent or current joint symptoms, missed some RA cases. A plausible explanation for this finding is that some subjects with RA under close followup and treatment did not mention current pain and therefore turned out to have a negative screening using this instrument, but would have been identified either by past symptoms or the second question of our screening tool: have you been told you have arthritis? COPCORD is an instrument that evaluates all rheumatologic diseases and has been shown to be an excellent choice in multiple studies; however, to screen for RA positivity, the screening must not only consider questions on recent or current symptoms. Moreno-Montoya, *et al* explored the validity of WHO-ILAR COPCORD for screening of RA and identified 3 factors within the complete questionnaire[25]. Recent symptoms represented only 1 of the 3 factors, while pain in the past and disability were factors that were also key to the validity of the instrument to screen RA. Past pain was not part of the questionnaire used in the ENS 2016–2017 COPCORD section. Therefore, our findings support what was described by Moreno-Montoya, *et al* regarding the validity of WHO-ILAR COPCORD for RA screening[25]. Goycochea-Robles, *et al* also analyzed WHO-ILAR COPCORD validity and concluded that for RA screening, performance of the instrument is optimized incorporating the nonsteroidal antiinflammatory drug use domain[26].

The prevalence we found is similar to the Spanish prevalence found by Carmona, *et al* in 2002 of 0.5 (0.25-0.85)[14]. Chile has a predominantly Spanish ancestry, particularly in the central region, and most of the sample came from there, given the higher population density in this area. However, it is noteworthy that the prevalence found was similar to developed countries given that in Chile, one-third of the country has a low educational level, 30% of the population is obese, 70% is overweight, and there is a higher smoking prevalence (one-third of the population reported in this survey).

Regarding Latin America, prevalence studies performed in the region have found values ranging from 0.3% to almost 2%. In Mexico the prevalence was found to be 1.6% (95% CI 1.43–1.78), but with values ranging from 0.9 to 2.8 in different regions within the country[16]. In Argentina, one study in the northwest found a prevalence of 1.9% (95% CI 1.8–2.0), and in 2 studies including the central region of Argentina, the prevalence was found to be 0.94%

(95% CI 0.82–1.02) and 0.33 (95% CI 0.30–0.36)[19,27,28]. A study of 5 cities in Colombia also found a prevalence greater than 1%[29]. In Cuenca in Ecuador, Tambo Viejo in Perú, and Monagas in Venezuela, RA prevalence was similar to the values found in our study with an estimate of 0.8% (95% CI 0.5–1.2), 0.5% (95% CI 0.19–0.82), and 0.4% (95% CI 0.2–0.6), respectively[17,30,31]. Although these studies are not general population studies, it seems that RA prevalence is not uniform in Latin America and this is probably related to genetic background being variable according to local indigenous populations and European ancestry, which varies in different areas of America. In addition, differences in methodology and RA definitions exist in these studies.

Among RA cases in Chile, there was a high frequency of Mapuche ethnicity (22%), which represents more than the usual proportion of this ethnicity in the country (9.9%)[32], suggesting RA may be more frequent in Mapuche people. A higher prevalence of RA has been found in other indigenous populations[33]. However, these findings are tentative because the total number of RA cases was low and this result could be a random finding.

There was a high female predominance. In Latin America the GLADAR cohort of early arthritis showed that it affects women 6 times more than men[23]. Our results support that in this region there is an important female predominance in RA. It must be taken into consideration that we found males were more likely to be lost to followup, and this might bias our results. Given that 614 of 783 positive screening results were among females, it is likely that female predominance in RA diagnosis is still very large.

Our study is suggestive of a higher risk of RA in subjects with high SES. Findings regarding the risk of developing RA in relation to SES have not been uniform in the past[33,34,35,36]. There are some characteristics in this population that may be related to our findings. In ENS 2016–2017, subjects with a higher SES were more frequently smokers (38.9% vs 18% in higher and lower SES, respectively), and smoking is a known risk factor for the development of RA. Alcohol intake, on the other hand, was higher in lower SES, and some studies point to an inverse association between alcohol intake and RA[37,38]. Still, this association could be due to selection bias because we found that low SES subjects were more likely to be lost to followup. Also, response bias may exist, given that subjects with a lower educational level may not have reported previously diagnosed RA as accurately.

It is noteworthy that 7 out of 32 RA cases had not been previously diagnosed. There is a lack of rheumatologists in Chile, particularly outside the central region[39]. A delay of many months and sometimes more than a year may pass from the moment the general medicine physician refers a patient to the rheumatologist and the patient is actually seen; in some regions there are no rheumatologists and the process may take longer. This is detrimental given the importance of the initiation of treatment early in disease[40]. Similar barriers of access to optimal RA care have been seen in the Latin America region[41]. Only 1 diagnosed subject was not receiving disease-modifying antirheumatic drugs (DMARD). A national program guarantees that all subjects with RA will have access to DMARD[42].

Regarding limitations of our study, there was a large dropout among positive screening subjects. If not attending clinic is associated with already having a diagnosis of RA, this could lead to an underestimation of RA prevalence. However, having positive RF and/or ACPA, high CRP, and self-report of RA was not different in subjects who were lost to followup, making this possibility less likely.

We identified differences in sex, educational level, and rural residence among subjects lost to followup compared to the subjects who completed the study. Given that males were more likely to discontinue the study and RA is more frequent in women, this could have led to overestimating prevalence. On the other hand, subjects with lower SES were also more likely to be lost to followup and this might have biased results in the opposite direction (if we assume low SES is associated with RA as some studies have shown).

We performed the first nationwide RA prevalence study in Chile, to our knowledge. This study has important implications for our region given the effect of this disease on quality of life, functional impairment, and the high direct and indirect costs it generates. Surprisingly, the prevalence we found is very similar to the one found in previous studies in developed countries, despite the genetic and socio-demographical differences that exist in our population. Findings in Latin American countries, on the other hand, have not been uniform.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Allaire S, Wolfe F, Niu J, LaValley MP. Contemporary prevalence and incidence of work disability associated with rheumatoid arthritis in the US. Arthritis Rheum 2008;59:474–80.
2. Chorus AM, Miedema HS, Boonen A, Van Der Linden S. Quality of life and work in patients with rheumatoid arthritis and ankylosing spondylitis of working age. Ann Rheum Dis 2003;62:1178–84.
3. Strand V, Khanna D. The impact of rheumatoid arthritis and treatment on patients' lives. Clin Exp Rheumatol 2010;3 Suppl 59:S32-40.
4. Verstappen SM, Bijlsma JW, Verkleij H, Buskens E, Blaauw AA, ter Borg EJ, et al. Overview of work disability in rheumatoid arthritis patients as observed in cross-sectional and longitudinal surveys. Arthritis Care Res 2004;51;488–97.
5. Minnock P, Fitzgerald O, Bresnihan B. Quality of life, social support, and knowledge of disease in women with rheumatoid arthritis. Arthritis Rheum 2003;49:221-7.
6. Clarke AE, Zowall H, Levinton C, Assimakopoulos H, Sibley JT, Haga M, et al. Direct and indirect medical costs incurred by Canadian patients with rheumatoid arthritis: a 12 year study. J Rheumatol 1997;24:1051–60.
7. Michaud K, Messer J, Choi HK, Wolfe F. Direct medical costs and their predictors in patients with rheumatoid arthritis: a three-year study of 7,527 patients. Arthritis Rheum 2003;48:2750–62.

8. McBride S, Sarsour K, White LA, Nelson DR, Chawla AJ, Johnston JA. Biologic disease-modifying drug treatment patterns and associated costs for patients with rheumatoid arthritis. J Rheumatol 2011;38:2141-9.
9. Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. Semin Arthritis Rheum 2006;36:182-8.
10. Simonsson M, Bergman S, Jacobsson LT, Petersson IF, Svensson B. The prevalence of rheumatoid arthritis in Sweden. Scand J Rheumatol 1999;28:340-3.
11. Guillemin F, Saraux A, Guggenbuhl P, Roux CH, Fardellone P, Le Bihan E, et al. Prevalence of rheumatoid arthritis in France: 2001. Ann Rheum Dis 2005;64:1427–30.
12. MacGregor AJ, Riste LK, Hazes JM, Silman AJ. Low prevalence of rheumatoid arthritis in black-Caribbeans compared with whites in inner city Manchester. Ann Rheum Dis 1994;53:293–7.
13. Rasch EK, Hirsch R, Paulose-Ram R, Hochberg MC. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: effect of different methods of case classification. Arthritis Rheum 2003;48:917–26.
14. Carmona L, Villaverde C, Hernandez-García C, Ballina J, Gabriel R, Laffon A; EPISER Study Group. The prevalence of rheumatoid arthritis in the general population of Spain. Rheumatology 2002;41:88-95.
15. Peláez-Ballestas I, Sanin LH, Moreno-Montoya J, Alvarez-Nemegyei J, Burgos-Vargas R, Garza-Elizondo M, et al; Grupo de Estudio Epidemiológico de Enfermedades Músculo Articulares (GEEMA). Epidemiology of the rheumatic diseases in Mexico. A study of 5 regions based on the COPCORD methodology. J Rheumatol Suppl. 2011 Jan;86:3-8.
16. Guevara-Pacheco S, Feicán-Alvarado A, Sanín LH, Vintimilla-Ugalde J, Vintimilla-Moscoso F, Delgado-Pauta J, et al. Prevalence of musculoskeletal disorders and rheumatic diseases in Cuenca, Ecuador: a WHO-ILAR COPCORD study. Rheumatol Int 2016;36:1195-204.
17. Senna ER, De Barros AL, Silva EO, Costa IF, Pereira LV, Ciconelli RM, et al. Prevalence of rheumatic diseases in Brazil: a study using the COPCORD approach. J Rheumatol 2004;31:594-7.
18. Spindler A, Bellomio V, Berman A, Lucero E, Baigorria M, Paz S, et al. Prevalence of rheumatoid arthritis in Tucumán, Argentina. J Rheumatol 2002;29:1166-70.
19. Riedemann JP, Maluje V. [Epidemiology of rheumatic diseases in Chile]. [Article in Spanish] Proyecto Fondecyt 1930390, 1993 [Chilean National Archives].
20. Eyheramendy S, Martinez FI, Manevy F, Vial C, Repetto GM. Genetic structure characterization of Chileans reflects historical immigration patterns. Nat Commun 2015;6:6472.
21. Bennett K, Cardiel MH, Ferraz MB, Riedemann P, Goldsmith CH, Tugwell P. Community screening for rheumatic disorder: cross cultural adaptation and screening characteristics of the COPCORD Core Questionnaire in Brazil, Chile, and Mexico. The PANLAR-COPCORD Working Group. Pan American League of Associations for Rheumatology. Community Oriented Programme for the Control of Rheumatic Disease. J Rheumatol 1997;24:160-8.
22. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010; 69:1580-8.
23. Massardo L, Pons-Estel BA, Wojdyla D, Cardiel MH, Galarza-Maldonado CM, Sacnun MP, et al. Early rheumatoid arthritis in Latin America: low socioeconomic status related to high disease activity at baseline. Arthritis Care Res 2012;64:1135–43.
24. Sacks JJ, Harrold LR, Helmick CG, Gurwitz JH, Emani S, Yood RA. Validation of a surveillance case definition for arthritis. J Rheumatol 2005;32:340-7.
25. Moreno-Montoya J, Alvarez-Nemegyei J, Trejo-Valdivia B, Peláez-Ballestas I; GEEMA (Grupo de Estudio Epidemiológico de Enfermedades Musculo Articulares). Assessment of the dimensions, construct validity, and utility for rheumatoid arthritis screening of the COPCORD instrument. Clin Rheumatol 2014;33:631–6.
26. Goycochea-Robles MV, Sanin LH, Moreno-Montoya J, Alvarez-Nemegyei J, Burgos-Vargas R, Garza-Elizondo M, et al; Grupo de Estudio Epidemiológico de Enfermedades Músculo Articulares (GEEMA). Validity of the COPCORD core questionnaire as a classification tool for rheumatic diseases. J Rheumatol 2011;86:31-5.
27. Scublinsky D, Venarotti H, Citera G, Messina OD, Scheines E, Rillo O, et al. The prevalence of rheumatoid arthritis in Argentina. A capture-recapture study in a city of Buenos Aires province. J Clin Rheumatol 2010;16:317-21.
28. Di WT, Vergara F, Bertiller E, Gallardo Mde L, Gandino I, Scolnik M, et al. Incidence and prevalence of rheumatoid arthritis in a health management organization in Argentina: a 15-year study. J Rheumatol 2016;43:1306-11.
29. Cuervo F, Santos A, Saldarriaga E, Angarita I, Peláez-Ballestas I, Rueda J, et al. [Prevalence of rheumatic diseases in Colombia]. [Article in Spanish] Medicina 2018;40:94-5.
30. Granados Y, Cedeño L, Rosillo C, Berbin S, Azocar M, Molina ME, et al. Prevalence of musculoskeletal disorders and rheumatic diseases in an urban community in Monagas State, Venezuela: a COPCORD study. Clin Rheumatol 2015;34:871–7.
31. Gamboa R, Medina M, Acevedo E, Pastor C, Cucho J, Gutiérrez C, et al. [Prevalence of rheumatic diseases and disability in a marginal urban community: results of the first COPCORD study in Peru]. [Article in Spanish] Rev Peru Reumatol 2009;15:40-6.
32. Instituto Nacional de Estadisticas Chile. [Synthesis from results. Census 2017 Chile]. [Article in Spanish] [Internet. Accessed January 16, 2020.] Available from: www.censo2017.cl/descargas/home/sintesis-de-resultados-censo2017.pdf
33. Peláez-Ballestas I, Granados Y, Quintana R, Loyola-Sánchez A, Julián-Santiago F, Rosillo C, et al; Latin American Study Group of Rheumatic Diseases in Indigenous Peoples (GLADERPO). Epidemiology and socioeconomic impact of the rheumatic diseases on indigenous people: an invisible syndemic public health problem. Ann Rheum Dis 2018;77:1397-404.
34. Bengtsson C, Nordmark B, Klareskog L, Lundberg I, Alfredsson L; EIRA Study Group. Socioeconomic status and the risk of developing rheumatoid arthritis: results from the Swedish EIRA study. Ann Rheum Dis 2005;64:1588–94.
35. Verstappen SM. The impact of socio-economic status in rheumatoid arthritis. Rheumatology 2017,56:1051–2.
36. Mackie SL, Taylor JC, Twigg S, Martin SG, Steer S, Worthington J, et al. Relationship between area-level socio-economic deprivation and autoantibody status in patients with rheumatoid arthritis: multicentre cross-sectional study. Ann Rheum Dis 2012;71:1640–5.
37. Di Giuseppe D, Discacciati A, Orsini N, Wolk A. Cigarette smoking and risk of rheumatoid arthritis: a dose-response meta-analysis. Arthritis Res Ther 2014;1:R61.
38. Källberg H, Jacobsen S, Bengtsson C, Pedersen M, Padyukov L, Garred P, et al. Alcohol consumption is associated with decreased risk of rheumatoid arthritis: results from two Scandinavian case-control studies. Ann Rheum Dis 2008;68:222-7.
39. Torres-Quevedo R. [Deficit specialists in regions and public system]. [Article in Spanish] Rev Chil Cir 2016;68:279-80.
40. Nell VP, Machold KP, Eberl G, Stamm TA, Uffmann M, Smolen JS, et al. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology 2004;43:906–14.

41. Miltenburger C, Munkombwe M, Lekander I. A survey of barriers to treatment access in rheumatoid arthritis in major Latin American countries – Argentina, Brazil and Mexico. [Internet. Accessed January 16, 2020.] Available from: www.comparatorreports.se/LA%20RA%20barrier%20report_FINAL.pdf
42. Ministry of Health. [List of GES (Explicit Health Guarantees) benefits]. [Article in Spanish] [Internet. Accessed January 16, 2020.] Available from: diprece.minsal.cl/wrdprss_minsal/wp-content/uploads/2018/03/Lep_incluye-Decreto-8-de-2018.pdf

APPENDIX 1.

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