

CONCISE REPORTS

Prevalence of rheumatoid arthritis in Italy: the Chiavari study

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Abstract

Objective—To ascertain the prevalence of rheumatoid arthritis (RA) in an Italian general population.

Methods—The study was performed in the years 1991–92 in Chiavari, a small town located on the Ligurian coast, and involved 4456 subjects aged 16 years or more from four general practices. The subjects received a postal questionnaire developed to detect patients with current or past inflammatory joint diseases. The age and sex distribution of the sample were similar to those of the Italian population from the 1992 census. Patients reporting a history of joint swelling in at least a pair of symmetrical joints were reviewed by a rheumatologist. The clinical records of non-responders and responders who failed to attend the clinic were also reviewed.

Results—3294 of 4456 (73.9%) subjects answered to the questionnaire. The mean (SD) age of the 3294 responders was 48.3 (19.3) years; 53.7% of them were female. Swelling in at least two symmetrical joints was reported by 230 subjects (7%). Among them, 11 patients fulfilling the 1987 ARA criteria for RA were identified. The prevalence of RA was 0.33% (95% CI 0.13, 0.53) in the general population, 0.13% (95% CI 0, 0.31) in men, and 0.51% (95% CI 0.18, 0.84) in women.

Conclusions—These data are consistent with the results of three earlier studies published in the fifties in the Italian literature and confirm that the prevalence of RA is low in Italy and has remained unchanged in the last 40 years.

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Rheumatoid arthritis (RA) shows a geographical trend with high prevalence in the northern hemisphere and low prevalence in developing countries including the black population of Africa.¹ A geographical trend seems to be present also in Europe, where RA is probably more common in the Anglo-Saxon population than in the Mediterranean basin (fig 1). In addition, RA seems to be less severe,² to have fewer extra-articular manifestations (EAMs),³ and to not be associated with HLA-DR4⁴ in

southern Europe. However, epidemiological studies of RA are rare in southern Europe and, to our knowledge, none has been published in the English language literature.

The putative low prevalence of RA in Mediterranean populations has been ascribed to the low frequency of RA susceptibility genes⁴ or to environmental factors affecting disease incidence and survival. Another possible explanation is a birth cohort related fluctuation of incidence. In fact, RA incidence has been suggested to be decreasing in the UK⁵ and USA.⁶ We studied the prevalence of RA in a north Italian population and compared our result with those observed in the sixties in other Italian areas.

Methods

The study was performed in the years 1991–92 in Chiavari, a small town located on the Ligurian coast, north west Italy. The town has a population of 28 584 and is surrounded by farmland. Nearly one fourth of the inhabitants are farmers.

The study involved 4456 subjects aged 16 years or more from four general practices. In Italy, almost all citizens are registered with a general practitioner (GP) of the National Health System. The choice of the GP is made directly by the patient. The age and sex distribution of the sample were similar to those of the Italian population from the 1992 census.

SCREENING QUESTIONNAIRE

The subjects received a postal questionnaire originally developed by the ARC Epidemiology Unit in Manchester⁷ to detect patients with current or past peripheral joint pain or swelling. Subjects were asked to report (a) any history of joint swelling lasting more than one month and the distribution of the swollen joints on a mannequin; (b) any joint pain lasting more than one month; (c) current joint pain or swelling; (d) morning stiffness lasting more than 30 minutes; (e) a present or previous diagnosis of arthritis; (f) physical activity graded on a three class scale. The questionnaire was translated into Italian and validated in a group of 68 outpatients at their first visit to our rheumatological clinic. In this group, the sensitivity of the single questions ranged from 92% to 98% and their specificity was comprised between 73% and 92%. The perform-

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ance of the complete questionnaire in diagnosing patients with RA varied according to the combinations of questions used. Swelling of two symmetrical joints, showing a sensitivity of 81.8% and a specificity of 86.4%, was chosen as our screening tool. In the general population, sensitivity of the questionnaire to detect both current and previously diagnosed RA, using the "history of joint swelling of two or more joints" criterion, is known to be 100%.⁷ By adopting the same definition in our sample, sensitivity raised to 90.9% but specificity dropped to 47.7%. Non-responders to the first questionnaire received a second mailing. Non-responders were contacted by telephone after the second mailing.

CLINICAL EVALUATION

Subjects with at least two symmetrical swollen joints were invited to the local clinic for assessment by a rheumatologist (MAC). Anteroposterior radiograms of the hands were arranged and blood was drawn for IgM rheumatoid factor determination by nephelometry. The GP records of the subjects who were invited to the clinic but failed to attend, as well as of those who failed to answer the questionnaire, were

reviewed. In addition, to ascertain all the cases of RA already diagnosed in different settings, we screened the diagnoses of RA made in the local hospital and in the rheumatological outpatient clinic as well as the list of patients who were entitled to obtain free drugs for their RA under the NHS. RA patients can apply for this exemption by providing a rheumatologist's certificate to the local chapter of the NHS.

Disease status was classified using the 1987 ACR criteria⁸ modified for use in population studies. This modification includes evidence of past and inactive disease and is a sensitive measure of RA lifetime cumulative prevalence. Historical data on morning stiffness and previous RF positivity are included. Swelling can be substituted by deformity.⁹

The prevalence of people with RA with 95% confidence intervals was calculated.

Results

The cumulative response rate to the screening questionnaire was 73.9% (3294 of 4456). The response was similar for women (73.2%) and men (74.8%). The mean (SD) age of the 3294 responders was 48.3 (19.3) years and that of non-responders was 50.7 (21) years. The



Figure 1 A rough description of the prevalence of rheumatoid arthritis derived from various studies performed in Europe. Circle size is proportional to the number of people at denominator and the gray tint is proportional to RA prevalence. Note that the results of the different studies are not completely comparable because some methods were different. A list of the relevant references is available on request.

Table 1 Clinical features of patients with rheumatoid arthritis

Patient	Age	Sex	RF	Erosions	Number of criteria fulfilled				EAMs	HAQ disability score
					Modified ARA	'87 ARA	'58 ARA	New York		
A	69	f	+	+	6	6	7	4	+	2.7
B	38	m	+	+	6	3	5	4	-	0
C	67	f	-	-	4	4	5	2	-	1.2
D	68	f	-	-	5	4	6	2	+	0.1
E	62	f	+	-	5	2	3	2	-	0
F	57	f	-	-	4	4	5	2	+	0
G	70	m	+	+	6	6	7	4	-	U
H	91	f	+	+	6	6	7	4	-	2.1
I	89	f	-	+	5*	5*	6*	3	U	U
L	56	f	-	+	5*	5*	6*	3	U	U
M	60	f	+	+	6*	6*	7*	4	U	U

EAMs = extra-articular manifestations; U = unknown; * = without considering nodules.

response varied between practices and was comprised between 68.5% and 77.4%.

Swelling in at least two symmetrical joints was reported by 230 (7%) subjects whose clinical evaluation was deemed necessary. Among them, 11 patients fulfilling the modified 1987 ARA criteria for RA were identified (table 1). Only nine patients fulfilled the traditional 1987 ARA criteria, 10 the 1958 ARA criteria, and seven the New York criteria (with the three out of four format). Seven were identified by visit and four by clinical records of no shows. Two more subjects gave a history of possible rheumatoid polyarthritis in the past but had no convincing clinical records, compatible radiology, or evidence of deformity or clinical synovitis. Of the 11 patients, nine were women and two men. Ten of 11 patients were over 55 years. IgM rheumatoid factor was present in six patients and erosions in seven. EAMs were seen in three of the eight patients who had complete clinical data. Two patients showed Sjögren's syndrome and one had nodules and vasculitis. Two patients were in clinical remission. Disability was absent in four of seven patients (table 1). The prevalence of RA was 0.33% (95% CI 0.13, 0.53) in the general population, 0.13% (95% CI 0, 0.31) in men, and 0.51% (95% CI 0.18, 0.84) in women. To obtain minimum estimates, RA prevalence has been also calculated considering that non-responders had the same prevalence of second time responders and that none of the non-attenders to the visit had RA. The resulting values were 0.26% and 0.21%, respectively. Both values are well within the confidence limits of our original prevalence. Three of 11 cases of RA had not been previously diagnosed by a physician.

The other sources of information were much less sensitive. Of the 11 RA patients identified in this study only five had been visited in the rheumatology outpatient clinic of the local hospital; they were also listed in the exemption group.

The 1162 non-responders included 15 subjects who returned incompletely answered questionnaires, 70 subjects who died, and 166 subjects who moved during the study period. The analysis of their clinical records revealed five additional patients with RA. This raised the total number of RA patients to 16 with a cumulative prevalence that remained nearly unchanged at 0.36%.

Discussion

This is one of the few studies evaluating the lifetime cumulative prevalence of RA in southern Europe and confirms the impression of a low frequency of the disease in this area. It is difficult to compare our figures with those of previous studies for two main reasons. Firstly, the diagnostic definition of RA has changed over time and different methods have been used in the literature to ascertain RA cases. In addition, most studies report point prevalence, not lifetime prevalence. Secondly, comparing studies performed in different years is probably not correct because the incidence of RA may vary with time. The modified version of the 1987 ARA criteria was more sensitive than the traditional one, the 1958 ARA criteria and the New York criteria (3 of 4). Only the latter, when considered positive by satisfying two or more criteria, identified all the patients. The questionnaire developed by the ARC Epidemiology Unit, which has been recently used in a number of studies, permits direct comparison with data from different geographical areas. The prevalence of RA in Italy is higher than that observed in Pakistan (0.14%),¹⁰ similar to that observed in black Caribbeans living in Manchester (0.29%),⁷ and in Hong Kong orientals (0.35%)¹¹ but lower than that observed in a white population from Manchester (0.8%).⁷

The response rate to the questionnaire and to clinical assessment was not high but nevertheless in keeping with the results obtained in most postal surveys from southern Europe. Because of non-responders, ascertainment of RA cases was based in part on the review of clinical records. This fact may have hampered the evaluation of transient or limited disease thus leading to underreporting of RA. However, our data are consistent with the results of three well performed studies published in the fifties in the Italian literature.¹²⁻¹⁴ In 1956, Neri Serneri and Bartoli reported a 0.38% prevalence in Tuscany (0.54% in women and 0.21% in men).¹² In 1963, Einaudi reported a similar value (0.35%) in Piedmont (0.46% for women and 0.24% for men).¹³ Finally, in 1967, Marcolongo *et al* found a prevalence of 0.43% in Tuscany (0.63% in women and 0.25% in men).¹⁴

Most of the studies on RA prevalence in Anglo-Saxon populations show evidence of a secular decline.³⁻⁶ As this trend was not

observed in Italy, we suggest that the putative environmental protective factor was not present in our country. Oral contraceptives, a possible candidate for the decline of RA, are used by a smaller percentage of women in Italy in comparison with those northern Europe and could explain the lack of decrease in RA prevalence. Accordingly, also the finding that most of the patients were older than 55 years may be related to a changing pattern of age distribution as a result of a birth cohort trend with recent generations less likely to develop RA.

As expected from a population survey, several patients had mild disease or were in remission with low disability scores. However, most patients showed positive RF and erosions. EAMs were present in three of eight (37.5%) patients, an observation that is in keeping with those of Salvarani *et al* who showed a 32% frequency of EAMs in Italian outpatients with RA.³ In this study and in Salvarani's, Sjögren's syndrome accounted for most of the EAMs.

In conclusion, our results confirm that the prevalence of RA is low in Italy and similar to that reported over the last 40 years. This finding should encourage further studies to identify the genetic and environmental protective factors that may be at work in our area.

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