The prevalence of rheumatoid arthritis in an urban population of Izmir-Turkey

S. Akar[1], M. Birlik[1], O. Gurler[1], I. Sari[2], F. Onen[1], M. Manisali[3], K. Tirpan[4], T. Demir[2], M. Meral[2], N. Akkoc[1]

Dokuz Eylul University School of Medicine, [2]Department of Internal Medicine, [1]Division of Rheumatology [3]Department of Radiology, [4]Department of Community Medicine, Dokuz Eylul University, Izmir, Turkey.

Abstract

Objective
To estimate the prevalence of rheumatoid arthritis (RA) in an urban area in Izmir, Turkey.

Methods
The study was conducted in the Balcova and Narlidere districts of Izmir and a total of 2,887 people aged 20 years or older were contacted with a 98.2% acceptance rate. Nine medical doctors administered an RA questionnaire by face-to-face interview. Subjects reporting a history of swelling in at least 2 joints lasting more than 4 continuous weeks or a history of a diagnosis of rheumatoid arthritis, inflammatory joint rheumatism or joint rheumatism were considered as screening positive and they were invited to come in for an examination. RA cases were defined by the 1987 American College of Rheumatology (ACR) criteria modified for use in population studies.

Results
A total of 301 subjects (243 women, 58 men), or 10.6% of those who received the questionnaire were screening positive. 240 (79.7%) of these agreed to undergo a clinical examination either in the clinic or at home. Among these, 14 (12 female, 2 male) patients fulfilled the ACR criteria for RA. The prevalence of RA was 0.49% (95% CI 0.27–0.83) in the total population interviewed, 0.77% (95% CI 0.40–1.35) in women and 0.15% (95%CI 0.02–0.60) in men. The age- and sex-adjusted prevalence for the general population was estimated as 0.36%. Five of the 14 RA (36%) cases had not been diagnosed previously.

Conclusion
These data are consistent with the results of other Mediterranean countries. A significant proportion of RA cases remain undiagnosed in the community.

Key words
Arthritis, rheumatoid, prevalence, epidemiology.

Servet Akar, MD; Merih Birlik, MD; Oguz Gurler, MD; Ismail Sari, MD; Fatos Onen, MD, Professor of Medicine; Metin Manisali, MD, Professor of Radiology; Kazim Tirpan, MD; Tevfik Demir, MD; Murat Meral, MD; Nurullah Akkoc, MD, Professor of Medicine.

Please address correspondence to: Servet Akar, MD, Dokuz Eylul Universitesi Tip Fakultesi, Ic Hastaliklari AD, Romatoloji BD, 35340 Inciralti, Izmir/Turkey. E-mail: servet.akar@deu.edu.tr

Introduction

Rheumatoid arthritis (RA) is a chronic, disabling disease which has been described all over the world, with a commonly quoted prevalence rate of 1% (1). Its prevalence varies in different geographic areas and ethnic groups, as well as at different times in the same population (2-18). Comparison of these prevalence rates is difficult mainly owing to methodological differences between the published studies. It is important to ascertain the prevalence of RA in different populations, as this might yield clues to genetic and environmental factors that influence disease risk and provide valuable information for health care providers in targeting the health care systems accurately. The only information specifically pertinent to the prevalence of RA in Turkey comes from a study which was done in a rural area of Istanbul more than 35 years ago (19). The sample population in that study included a high percentage of recent immigrants from the Balkans and cannot be representative of the general Turkish population. We therefore conducted a study aimed at determining the prevalence of RA in an urban area of Izmir, western Turkey, which has a very low rate of migration from surrounding countries.

Subjects and methods

Following approval by the local health authorities, we conducted a two-stage population-based survey. The first stage involved the administration of a screening questionnaire to the sample population aged 20 and older. The second stage included a detailed medical interview and clinical examination of positive responders to the screening questionnaire.

Sample selection

The study was conducted between 2001-2002 in the Balcova and Narlidere districts of Izmir, which are located in western Turkey. These two urban areas situated in southeast Izmir were chosen because of their proximity to our university hospital. They are served by 8 health centers. Health aides from these centers update the local population data by door-to-door visits every year and report them to local health authorities. In this study, the sample size calculation and clustering were performed on the basis of these data.

The study area has an estimated population of 118,368 of whom 84,504 are aged 20 years or over according to the local health authorities update in June 2000. The sample size (n = 1494) was calculated based on an estimated RA prevalence of 1%, with a precision limit of 0.5% and a confidence level of 95%. Because cluster sampling was planned, the sample size estimation was multiplied by a constant – design effect (20) – and a final sample size of approximately 2,600 was obtained. The population of the total area was divided into 845 clusters, each consisting of 100 persons aged 20 and older, and 26 clusters were selected randomly by computer to constitute the study sample.

RA screening and data collection

Nine medical doctors trained in the administration of the questionnaire conducted the screening. Two of these doctors were rheumatology fellows and the others were residents in internal medicine. The screening questionnaire was administered to all persons 20 years or older in consecutive households. Each cluster was adjusted for a 10% non-response rate. Interviewers obtained information directly from the respondent whenever possible. If the respondent was not at home at the time of the interview, another visit or telephone call was made.

The following two questions were posed to the study population for screening purposes (3):

(1) Have you ever experienced joint swelling, involving at least 2 peripheral joints for more than 4 continuous weeks?
(2) Has any physician ever told you that you were suffering from rheumatoid arthritis, inflammatory joint rheumatism, or joint rheumatism?

The questionnaire also included questions to elicit the demographic characteristics of the population.

Individuals who gave a positive answer to any of these questions were considered as screening positive. The sensi-

tivity of the criterion "swelling in 2 or more joints lasting more than 4 continuous weeks" as a screening tool to detect both current and past diagnosed RA patients has been reported to be 90.9–100% (3, 6, 9). We found the sensitivity of this criterion to be 97.5% when tested in 40 (33 female, and 7 male) consecutive RA patients being followed at our outpatient clinic.

Screening positive individuals were invited to the rheumatology outpatient clinic, where they were assessed by 2 rheumatologists (S.A, M.B). After a medical interview, a physical examination was performed. Peripheral joints were examined for the presence of tenderness, soft tissue swelling, restricted joint movement, nodules, and deformities. Subjects who were unable to attend the clinic were offered a visit at their home. The medical records of one patient (case number 629), who reported a previous diagnosis of RA but who changed her residence after screening, were obtained from another local hospital and the diagnosis was confirmed.

Case definition
RA cases were defined by the 1987 American College of Rheumatology (ACR, formerly the ARA) criteria (21), modified for use in population studies (22). The modification permits the inclusion of both active and inactive cases, and allows the determination of the lifetime cumulative RA prevalence (22). Rheumatoid factor analysis and direct radiological examination of the hands were performed in those subjects who were classified on the basis of clinical criteria, and in those who were suspected to have RA but did not fulfill the ACR criteria for diagnosis.

Statistical analysis
Sample size calculation was performed using Epi Info 6.04 (Centers for Disease Control & Prevention, Atlanta, GA, USA). The prevalence rate was calculated using the total population interviewed as the denominator, and presented with the 95% confidence interval (CI). The 95% confidence intervals were calculated by using the Poisson distribution.

Results
A total of 2,887 subjects were contacted, of whom only 52 (1.8%) refused to respond. A complete interview was obtained with 2,835 subjects. Among them 1,551 (54.7%) were women and 1,284 (45.3%) were men. The mean age of the total sample population was 43.7 (range 20-97). The mean age of the women and men was 43.8±15.3 and 43.7± 15.5, respectively. A total of 301 subjects (243 women and 58 men), or 10.6% of those who received the screening questionnaire, answered positively to the questions and 229 (76.0%) agreed to come to the outpatient clinic for examination. Those who failed to show up were telephoned. Eleven patients (3.7%) accepted to undergo a detailed clinical examination at home. The rest (20.3%) either refused to be examined or could not be reached after up to 3 repeated telephone calls. There were no differences in age or sex between subjects who agreed to the examination and those refused or who could not be reached (p values 0.71 and 0.35, respectively). The age and sex distribution of the study population is presented in Table I.

RA, based on the modified 1987 ACR criteria, was diagnosed in 14 (12 female, 2 male) individuals out of the 240 subjects who screened positive and accepted to undergo an examination either in our clinic or at home (79.7%). The mean age (SD) of our RA patients was 53.0 (±12.4). The mean age at symptom onset was 41.6 (± 8.4) (Table II). For one patient (case number 629), diagnosis was achieved via a review of the clinical records. None of the patients was in remission at the time of examination. Five out of the 14 patients had not been previously diagnosed. Rheumatoid factor was positive in 9 patients (64%), and erosions in 10 but none of them had rheumatoid nodules at the time of examination (Table III).

Clinical examination of the positive screened responders revealed that 108 had osteoarthritis, 39 had fibromyalgia, 12 had spondylarthropathy, 4 had benign joint hypermobility syndrome, 2 had gouty arthritis, and 3 had undifferentiated arthritis. No diagnosis could be made for the rest of the subjects.

The lifetime cumulative prevalence of RA was 0.49% (95% CI 0.27–0.83) in our study population, 0.77% (95%CI 0.40–1.35) in women and 0.15% (95% CI 0.02–0.60) in men when the total

Table I. Age and sex distribution of the sample population interviewed, screening positive individuals, examined subjects and RA cases identified.

Age goups (yr)	Sample population interviewed n (%)	Screening positive individuals n (%)	Subjects who agreed to be examined n (%)	RA cases n
Female	1551 (54.7%)	243 (80.7)	191 (79.6%)	
20-24	160 (10.3)	7 (2.3)	4 (1.7)	
25-34	355 (22.9)	18 (6.0)	14 (5.8)	
35-44	319 (20.6)	46 (15.3)	37 (15.4)	3
45-54	331 (21.3)	57 (18.9)	49 (20.4)	4
55-64	213 (13.7)	60 (19.9)	48 (20.0)	4
65-74	127 (8.2)	45 (15.0)	32 (13.3)	1
75	46 (3.0)	10 (3.3)	7 (2.9)	
Male	1284 (45.3%)	58 (19.3)	49 (20.4%)	
20-24	154 (12.0)	5 (1.7)	3 (1.3)	
25-34	264 (20.6)	8 (2.7)	6 (2.5)	
35-44	271 (21.1)	12 (4.0)	10 (4.2)	1
45-54	271 (21.1)	11 (3.7)	11 (4.6)	
55-64	177 (13.8)	12 (4.0)	11 (4.6)	
65-74	109 (8.5)	7 (3.2)	6 (2.5)	
75	38 (3.0)	3 (0.9)	2 (0.8)	1
Total	2835 (100)	301 (100)	240 (100)	14

Table II. Demographic and clinical data for RA (rheumatoid arthritis) patients, aged 20 years or older, in Balcova and Narlidere districts.

	Female (n = 12)	Male (n = 2)	Total (n = 14)
Age (yr)	52.4 ± 9.7	56.5 ± 30.4	53.0 ± 12.4
Age at disease onset (yr)	39.9 ± 17.8	52.0 ± 25.4	41.6 ± 18.4
Disease duration (yr)	12.5 ± 13.0	4.5 ± 4.9	11.36 ± 12.4
Morning stiffness (minutes)	81.2 ± 77.9	120.0 ±169.7	86.8 ± 86.9
Tender joint count	16.3 ± 9.5	17.5 ± 2.1	16.5 ± 8.8
Swollen joint count	9.6 ± 5.2	12.0 ± 2.8	9.9 ± 4.9
HAQ	1.7 ± 0.4	1.3 ± 0.4	1.6 ± 0.4
ESR (mm/h)	30.6 ± 16.0	13.0 ± 9.9	28.0 ± 16.3

HAQ: Modified Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate.

Table III. Selected clinical and laboratory characteristics of the patients with rheumatoid arthritis (RA).

Case no.	Age	Sex	Previous RA diagnosis	Number of criteria fulfilled[1]	Functional class	RF	X-ray[2]
45	64	F	Yes	6	2	pos	pos
180	42	F	Yes	4	3	neg	neg
214	35	M	Yes	6	1	pos	pos
354	58	F	Yes	5	3	neg	pos
557	78	M	Yes	6	2	pos	pos
663	42	F	No	5	2	neg	pos
963	70	F	No	5	2	pos	pos
966	51	F	No	6	3	pos	pos
1424	59	F	No	5	2	neg	pos
1469	47	F	Yes	6	1	pos	pos
2077	47	F	Yes	5[a]	3	pos	neg
2175	62	F	No	6	3	pos	pos
2476	42	F	Yes	4	1	neg	neg
629	45	F	Yes	6	NO	pos	pos

[1]Number of modified 1987 American College of Rheumatology criteria that the patient fulfilled; [2]positive X-ray means fulfilling criterion number 7 of 1987 ARAcriteria for RA; [a]this patient later developed nodules so the number of criteria fulfilled would be 6.
Functional class: Steinbrocker's functional class; RF: rheumatoid factor; NO: not obtained.

sample interviewed was used as the denominator population. When adjustments were made for age and sex according to the general 2000 census, a prevalence of 0.36% was found for the Turkish population.

Among the screening-positive individuals, 29 subjects reported to have been previously diagnosed as having RA. Twenty-eight were able to undergo a clinical assessment, and the diagnosis was confirmed in 9 subjects (32.1%). Fourteen of the remaining 19 individuals had arthritis caused by non-RA diseases; 7 had osteoarthritis, 6 had spondylarthropathy, and 1 had synovitis, acne, pustulosis, hyperostosis and osteitis syndrome (SAPHO). One subject was diagnosed as having benign joint hypermobility syndrome. No rheumatologic diagnosis could be made for the other 4 subjects.

Discussion

This study evaluated the lifetime cumulative prevalence of RA in an urban area in Turkey. We found a crude prevalence of 0.49% in the sample population and an age- and sex-adjusted prevalence of 0.36% in the overall Turkish population.

In an older study investigating the prevalence of RA in the Sagmalcilar district of Istanbul, Turkey, a crude prevalence of 0.22% was found (19). However, this study was carried out in a rural area with recent immigrants from the Balkans composing 70% of the sample population. Thus, that study population cannot represent the entire Turkish population. The present study was conducted in an urban area with a very low concentration of immigrants and thus may be more representative of the general Turkish population (16, 23, 24).

Another difference between the two studies is the set of criteria used for case definition. In the earlier Turkish study, RA was diagnosed according to the 1958 ARA criteria, while in our study, we used 1987 ACR criteria adapted for population studies which have been suggested to be more sensitive than both 1958 and 1987 ACR criteria (22). To be able to compare the prevalence in the Turkish population with that of other countries, we used screening questions originally developed by the Arthritis Research Campaign (ARC) Epidemiology Research Unit (3), which have been recently used in a number of other studies. The usage of similar methods for screening and classification allows us to compare our prevalence figure with data from different geographical areas. The prevalence of RA in the Turkish population is quite comparable to that observed in Chiavari, Italy (0.33%) (6) and in black Caribbeans living in Manchester (0.29%) (3) (UK), but lower than that observed in Sweden (0.51%) (5), Spain (0.5%) (4), Norfolk (0.81%) (9), and the white population in Manchester (0.8%) (3).

The different prevalences found in different studies may be largely attributed to differences in genetic and environmental factors in the study populations. The shared epitope which is the best characterized genetic component for RA (23,24) has been reported in normal Turkish population with a frequency of 32% (25), which is comparable to that of the British (29%) but higher than that of the Spanish population (20%) (24). However, the prevalence of RA found in our study is lower than the reported prevalences in the UK (9) and Spain (4). This suggests that the shared epitope does not entirely explain the genetic predisposition to RA.

Methodological differences in the study design may also complicate the comparison between studies. Common dif-

ficulties include those relative to the criteria used, the sample size, and the age and sex distribution of the denominator population (26). For instance, hospital-based prevalence studies may miss undiagnosed cases in the community, depending upon the availability of and access to rheumatology care. In our study 5 of 14 (36%) RA patients who had had symptoms for a mean of 3 years were only diagnosed during the study. This figure is slightly higher than the 27% reported for Spain and Italy (4, 6).

Although the non-responder rate was very low during the screening phase of our study, 20% of the responders did not accept our invitation to undergo a clinical examination. We used the total interviewed population as the denominator when calculating the prevalence of RA, assuming that those who refused to cooperate were more likely to be free of any rheumatic disease (27). However, it is possible that some patients who were in remission may have not attended the examination. Even if the same rate of RA was assumed for attenders and non-attenders, the crude prevalence would be 0.59%, still within the confidence limits of our original prevalence estimate.

It is controversial whether self-reporting is a reliable way to estimate the prevalence of RA (5,10,28). In our study, the self-reported RA diagnosis was confirmed in only 32.1% of the patients. The rest had other musculoskeletal disorders, as reported previously (28). We had no opportunity to review the clinical records of these patients, nor those of non-attendee individuals, as there is no systematic patient recording system for the primary care practices in our country.

A total of 64% of our RA patients were RF positive, and 71.4% had erosions, which is consistent with previous reports (3, 4, 6, 8, 13). No rheumatoid nodules were seen at the time of examination. This finding was also reported in Indonesian and Oman population surveys (14, 18). However, one patient (case number 2077) has since developed nodules which were observed during the follow-up.

Our results suggest that the prevalence of RA in Turkey is low and seems to be in the range of other Mediterranean countries (4,6,13). Further studies of RA epidemiology in Turkey are necessary to confirm these results.

Acknowledgements

References

1. ALARCON GS: Epidemiology of rheumatoid arthritis. *Rheum Dis Clin North Am* 1995; 21: 589-604.
2. SILMAN AJ, HOCHBERG MC: *Epidemiology of the Rheumatic Diseases*. Oxford, Oxford Medical Publications; 1993.
3. 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.
4. CARMONA L, VILLAVERDE V, HERNANDEZ-GARCIA C, BALLINA J, GABRIEL R, LAFFON A: The prevalence of rheumatoid arthritis in the general population of Spain. *Rheumatology (Oxford)* 2002; 41: 88-95.
5. SIMONSSON M, BERGMAN S, JACOBSSON LT, PETERSSON IF, SVENSSON B: The prevalence of rheumatoid arthritis in Sweden. *Scand J Rheumatol* 1999; 28: 340-3.
6. CIMMINO MA, PARISI M, MOGGIANA G, MELA GS, ACCARDO S: Prevalence of rheumatoid arthritis in Italy: the Chiavari Study. *Ann Rheum Dis* 1998; 57: 315-8.
7. STOJANOVIC R, VLAJINAC H, PALIC-OBRADOVIC D, JANOSEVIC S, ADANJA B: Prevalence of rheumatoid arthritis in Belgrade, Yugoslavia. *Br J Rheumatol* 1998; 37: 729-32.
8. RIISE T, JACOBSEN BK, GRAN JT: Incidence and prevalence of rheumatoid arthritis in the county of Troms, northern Norway. *J Rheumatol* 2000; 27: 1386-9.
9. SYMMONS D, TURNER G, WEBB R *et al*.: The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century. *Rheumatology (Oxford)* 2002; 41: 793-800.
10. SARAUX A, GUEDES C, ALLAIN J *et al*.: Prevalence of rheumatoid arthritis and spondyloarthropathy in Brittany, France. Societe de Rhumatologie de l'Ouest. *J Rheumatol* 1999; 26: 2622-7.
11. SHICHIKAWA K, INOUE K, HIROTA S *et al*.: Changes in the incidence and prevalence of rheumatoid arthritis in Kamitonda, Wakayama, Japan, 1965-1996. *Ann Rheum Dis* 1999; 58: 751-6.
12. GABRIEL SE, CROWSON CS, O'FALLON WM: The epidemiology of rheumatoid arthritis in Rochester, Minnesota, 1955-1985. *Arthritis Rheum* 1999; 42: 415-20.
13. DROSOS AA, ALAMANOS I, VOULGARI PV *et al*.: Epidemiology of adult rheumatoid arthritis in northwest Greece 1987-1995. *J Rheumatol* 1997; 24: 2129-33.
14. DARMAWAN J, MUIRDEN KD, VALKENBURG HA, WIGLEY RD: The epidemiology of rheumatoid arthritis in Indonesia. *Br J Rheumatol* 1993; 32: 537-40.
15. SPECTOR TD, HART DJ, POWELL RJ: Prevalence of rheumatoid arthritis and rheumatoid factor in women: evidence for a secular decline. *Ann Rheum Dis* 1993; 52: 254-7.
16. HAMEED K, GIBSON T, KADIR M, SULTANA S, FATIMA Z, SYED A: The prevalence of rheumatoid arthritis in affluent and poor urban communities of Pakistan. *Br J Rheumatol* 1995; 34: 252-6.
17. HAMEED K, GIBSON T: A comparison of the prevalence of rheumatoid arthritis and other rheumatic diseases amongst Pakistanis living in England and Pakistan. *Br J Rheumatol* 1997; 36: 781-5.
18. POUNTAIN G: The prevalence of rheumatoid arthritis in the Sultanate of Oman. *Br J Rheumatol* 1991; 30: 24-8.
19. YENAL O, LAV I, BILECEN L: [Epidemiological study on the infectious rheumatic syndrome in Turkey. II. Occurrence of rheumatoid arthritis in the Sagmalcilar district of Istanbul. Influencing of various factors and tuberculosis]. *Z Rheumaforsch* 1968; 27: 215-23.
20. ULUSOY M: Sampling errors for selected variables from the 1988 Turkish Population and Health Survey. *Nufusbil Derg* 1991;13:33-55.
21. ARNETT FC, EDWORTHY SM, BLOCH DA *et al*.: The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31: 315-24.
22. MACGREGOR AJ, BAMBER S, SILMAN AJ: A comparison of the performance of different methods of disease classification for rheumatoid arthritis. Results of an analysis from a nationwide twin study. *J Rheumatol* 1994; 21: 1420-6.
23. GONZALEZ-GAY MA, GARCIA-PORRUA C, HAJEER AH: Influence of human leukocyte antigen-DRB1 on the susceptibility and severity of rheumatoid arthritis. *Semin Arthritis Rheum* 2002; 31: 355-60.
24. BALSA A, MINAUR NJ, PASCUAL-SALCEDO D *et al*.: Class II MHC antigens in early rheumatoid arthritis in Bath (UK) and Madrid (Spain). *Rheumatology (Oxford)* 2000; 39: 844-9.
25. SARUHAN-DIRESKENELI G: Shared epitope homozygosity' is strongly associated with rheumatoid arthritis in Turkey. Istanbul Rheumatology Study Group. *Br J Rheumatol* 1998; 37: 1126-8.
26. ABDEL-NASSER AM, RASKER JJ, VALKENBURG HA: Epidemiological and clinical aspects relating to the variability of rheumatoid arthritis. *Semin Arthritis Rheum* 1997; 27: 123-40.
27. LAWRENCE JS: Prevalence of rheumatoid arthritis. *Ann Rheum Dis* 1961; 20: 11-7.
28. KVIEN TE, GLENNAS A, KNUDSROD OG, SMEDSTAD OLM: The validity of self-reported diagnosis of rheumatoid arthritis: Results from a population survey followed by clinical examinations. *J Rheumatol* 1996; 23: 1866-71.