Prevalence of Ankylosing Spondylitis and Related Spondyloarthritides in an Urban Area of Izmir, Turkey

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ABSTRACT. ***Objective.*** To determine the prevalence of ankylosing spondylitis (AS) and related spondyloarthritides (SpA) in an adult urban population of Izmir, Turkey.

Methods. A survey was conducted of 2887 subjects aged 20 years or over, selected by cluster sampling. Those who responded positively to the screening questions were contacted by 2 rheumatologists and evaluated in detail to establish presence of AS (modified New York criteria) or related SpA (ESSG criteria).

Results. In the initial screening, 2835 subjects participated; 422 were considered screening-positive and a telephone interview was done with 328 (78%). Based on their clinical history, 145 subjects were invited to the hospital and 120 (83%) agreed to do so. After detailed evaluation, 31 subjects were classified as having SpA (including 14 with AS). The age- and sex-adjusted prevalence was estimated to be 0.49% for AS (95% CI 0.26–0.85), and 1.05% for SpA (95% CI 0.70–1.50). The prevalence of AS was 0.54% in men (95% CI 0.19–1.20) and 0.44% in women (95% CI 0.19–0.88), and that of SpA was 0.88% in men (95% CI 0.42–1.59) and 1.22% in women (95% CI 0.73–1.89).

Conclusion. This epidemiological study suggests a high prevalence (0.49%) of AS in an adult urban population from western Turkey, which equals that of rheumatoid arthritis in the same population. The overall prevalence of SpA, including AS, was 1.05%. A minimal male predominance was noted among AS patients, which disappeared among the whole group of patients with SpA. (First Release Dec 15 2007; J Rheumatol 2008;35:305–9)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS
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Epidemiological studies indicate that ankylosing spondylitis (AS) and related spondyloarthritides (SpA) are more prevalent than previously thought, although there are wide variations among different ethnic and racial groups[1]. The prevalence reaches a high of 2.5% among Eskimos, a racial group known to have a 25% to 40% prevalence of HLA-B27 in the general population[2], whereas AS and related SpA are extremely rare in Japan[3], which has only 0.5% prevalence of HLA-B27 in the general population[4]. The reported disease prevalence in different studies also varies according to the study design and the classification criteria employed.

The prevalence of AS and related SpA is not well documented in Turkey. The only previous Turkish study of AS reported a crude prevalence of 0.14% among young army recruits[5]; probably an underestimate due to a considerably younger age group and possible exclusion of some individuals with known AS from army service.

We report the prevalence of AS and related SpA in the general adult population in an urban area of Izmir, a major port city located in western Turkey.

MATERIALS AND METHODS

The survey was conducted among subjects of Balcova and Narlidere districts of Izmir. These 2 urban areas, served by 8 health centers, have an estimated population of 118,368, of whom 84,504 are aged 20 years and over. 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 the survey, the sample size calculation and clustering were performed on the basis of these data.

The total sample size (n = 1494) needed for our study was calculated by assuming a disease 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[6]. Thus a final sample size target was set at a minimum of 2600 subjects. 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 consti-

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tute the study sample. Ethical approval was obtained by the local health authorities.

The questionnaire used for the initial part of the interview process to screen for AS and related SpA consisted of 3 questions (Table 1). The sensitivity of the second question, "low back pain and back stiffness on awakening, which improved by exercise," was 92% when tested on a group of 52 patients with AS.

Nine trained physicians (2 rheumatology fellows and 7 internal medicine residents), using a standard questionnaire, performed a face to face interview with each household member aged 20 and older. These physicians had received specific training regarding the questionnaire before going into the field for interviews. If there was no respondent at home at the time of the visit, an additional visit and/or telephone calls were made. Subjects who could not be contacted and those who refused to be interviewed were recorded as non-responders.

Subsequently, 2 rheumatologists (FO and SA) conducted a telephone interview with those subjects who, during their first interview, had given a history of "low back pain and back stiffness on awakening, which improved by exercise." Subjects suspected to have a history of inflammatory back pain[7] on the telephone interview were invited to undergo further clinical evaluation at the hospital, along with the 8 subjects who reported having AS or SpA during the first interview, as well as another 8 subjects who had been diagnosed as SpA based on clinical findings during the earlier completed rheumatoid arthritis (RA) arm of this epidemiologic survey[8]. During the evaluation of the subjects at the hospital, 2 rheumatologists (FO and SA) obtained a detailed medical history and performed a complete examination. Standard pelvic radiographs for examination of the sacroiliac joints were performed only when a subject had one or more of the following clinical features: inflammatory back pain, asymmetric oligoarthritis, limited chest expansion, and limited lumbar spinal movements.

The radiographs were read by 2 rheumatologists (FO and SA) "blinded" to the patients' identities. Pelvic radiographs were interpreted according to the established grading system[9]. In subjects whose pelvic radiographs showed suspicion of sacroiliitis but there was no agreement between the readers, we obtained the opinion of an experienced radiologist who was unaware of the clinical findings. All the radiological investigations were also assessed by 2 additional rheumatologists (MAK and NA), who were completely "blinded," to classify the final diagnosis. In cases where there was disagreement with the first evaluation of sacroiliac joints (by FO and SA), a computerized tomography (CT) or magnetic resonance imaging (MRI) scan was ordered to help in reaching a final consensus.

The modified New York criteria[10] were used to classify AS, and the European Spondylarthropathy Study Group (ESSG) criteria[11] for SpA. A diagnosis of reactive arthritis (ReA) was made if the international consensus classification criteria for ReA[12] were met. Undifferentiated SpA (uSpA) was diagnosed if the ESSG criteria were fulfilled in the absence of AS, ReA, psoriatic arthritis, or enteropathic arthritis. HLA-B27 typing by flow cytometry, using a mouse monoclonal anti-B27 antibody (MD Biosciences), was performed in 10 subjects after they had already been classified as having AS.

Statistical analysis. Sample size calculation was performed using Epi Info 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA). Data obtained from the Turkish population census in the year 2000 were used as the reference population for standardization. Stats Direct Statistical software (version 2.4.5, StatsDirect Ltd., Sale, Cheshire, UK) was used for calculating the crude and standardized prevalence, and improved approximate 95% confidence intervals.

Table 1. The questionnaire for identifying potential subjects with AS and related SpA.

1. Have you ever had trouble with your back?
   If yes;
2. Have you ever had back pain and back stiffness on awakening, which improved by exercise?*
3. Has any physician ever told you that you were suffering from ankylosing spondylitis or spondyloarthritis?

* Sensitivity: 92%

RESULTS

The study design and response rate at each stage of our study is shown in Figure 1. Of the 2887 subjects, 2835 (98%) participated in the initial face to face interviews; there were 1551 (54.7%) women and 1284 (45.3%) men. Their mean age was 43.7 years (range 20–97): 43.8 years for women and 43.7 years for men. After the initial interviews, attempts were made by 2 rheumatologists (FO and SA) to telephone a total of 422 subjects. They succeeded in getting further participation from 78%, as some subjects either refused or could not be contacted.

A total of 145 subjects were invited to undergo further clinical evaluation at the hospital, and 120 (83%) agreed to do so. Among these 120 subjects were those 8 who had reported a previous diagnosis of AS or SpA during the first interview and an additional 8 subjects who had been diagnosed as having SpA during the earlier RA prevalence study.

Clinical need for pelvic radiograph was identified in 88 subjects after a complete medical history and a careful clinical examination, and was performed in 86. CT of the sacroiliac joints had to be performed in 8 subjects to better define the status of the sacroiliac joints, and 5 of these subjects demonstrated presence of sacroiliitis. MRI of the sacroiliac joints was performed in only 2 subjects and both of them showed no sign of sacroiliitis.

SpA was diagnosed in 31 subjects on the basis of history, examination, and radiologic findings (Figure 1). Fourteen of these 31 subjects could be classified as having AS (8 women, 6 men), 16 as uSpA, and one as ReA. Although all of these 31 patients, including the 8 patients who were classified as having SpA during the RA arm of this survey, had seen a physician prior to this study for their low back pain or arthritic symptoms, only 8 (26%) of them (6 with AS, 1 ReA, and 1 uSpA) had received a correct diagnosis from their physicians.

The crude prevalence of AS was estimated as 0.49% (95% CI 0.22–0.77), while that of SpA was 1.09% (95% CI 0.66–1.42). Direct standardization adjusting for age and sex was made using the population of Turkey, which yielded very similar estimates: 0.49% for AS (95% CI 0.26–0.85) and 1.05% for SpA (95% CI 0.70–1.50) (Table 2).

The age- and sex-adjusted prevalence of AS in male and female subjects was 0.54% (95% CI 0.19–1.20) and 0.44% (95% CI 0.19–0.88), respectively. The age- and-sex adjusted prevalence of SpA in male and female subjects was 0.88% (95% CI 0.42–1.59) and 1.22% (95% CI 0.73–1.89), respectively (Table 2).

Among the subjects classified as having AS, 10 were subsequently tested for HLA-B27 to further validate our diagnostic classification, and 8 of them (80%) were positive.

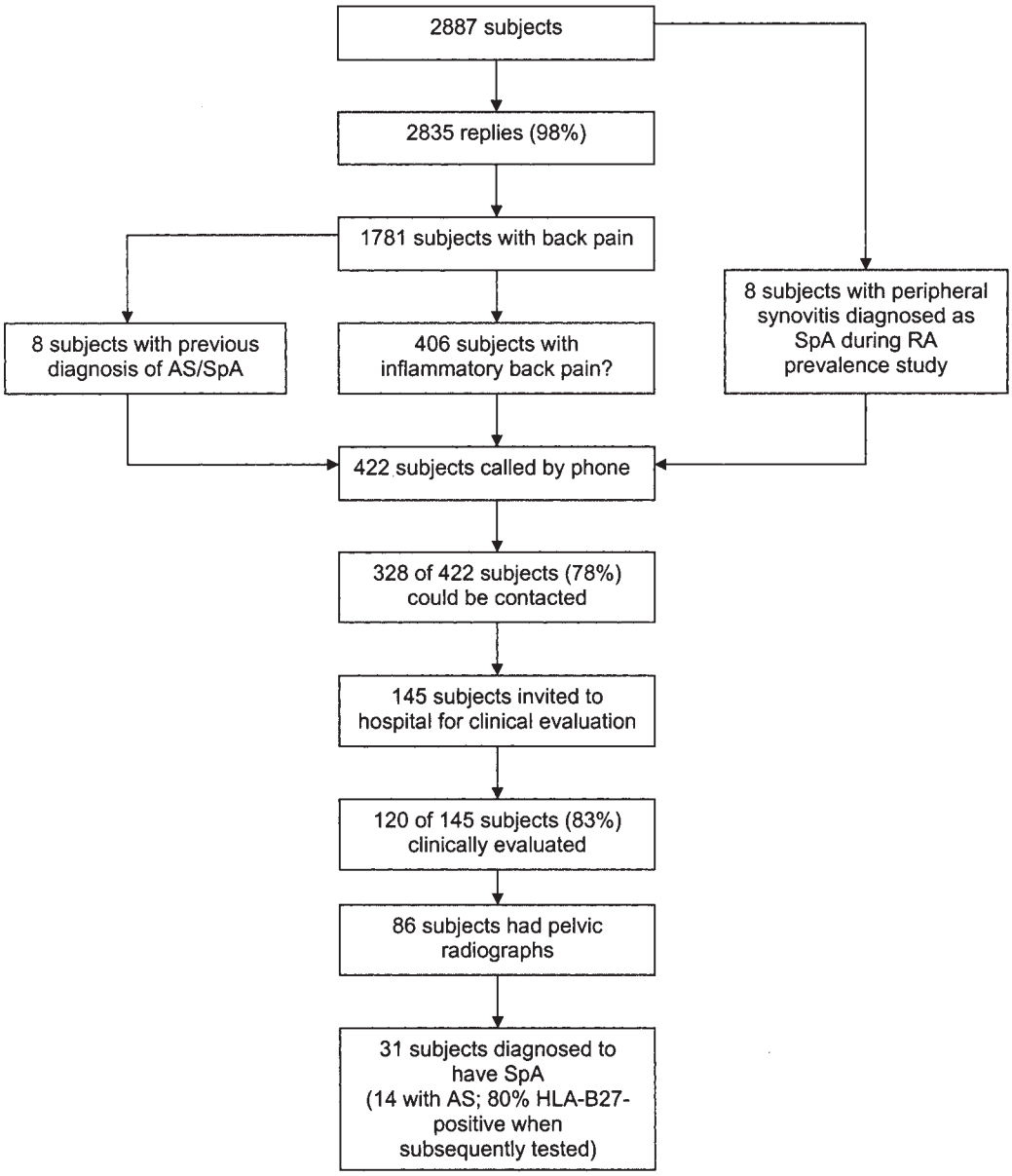

Figure 1. Study design and response rates in each stage of the study.

Table 2. Standardized prevalences of SpA and AS in the adult population (over age 20) of Turkey.

	Total (%)	95% CI	Female (%)	95% CI	Male (%)	95% CI
SpA	1.05	0.70–1.50	1.22	0.73–1.89	0.88	0.42–1.59
AS	0.49	0.26–0.85	0.44	0.19–0.88	0.54	0.19–1.20

SpA: spondyloarthritides; AS: ankylosing spondylitis.

DISCUSSION

Our population based epidemiological study suggests a relatively high prevalence of 0.49% for AS and 1.05% for the whole group of SpA. These figures are within the upper range of other such studies in European populations[1]. The difference between the various studies may be due to genetic (such as HLA-B27) and environmental differences, as well as methodological factors. The reported prevalence of HLA-B27 in Turkey varies between 6.8% and 8%[13-15].

A German study of HLA-B27-positive adult blood donors

estimated a 0.55% prevalence of AS in Berlin[16], very similar to what we found in Izmir. The overall prevalence of SpA, including AS, was estimated to be 1.72%[16]. Lower prevalence of AS and related SpA has been reported from Greece[17] and France[18], possibly related to methodological differences (screening and case ascertainment) and the age and sex distributions of the study populations. The study from Greece was based on ascertainment of diagnosed cases in hospitals and at private rheumatologists' offices[17]. The French study was a telephone survey to determine only subjects with previous diagnosis of SpA[18].

A striking finding in our study is that the prevalence of AS among women was close to that in men (female to male ratio = 0.82:1) and the prevalence of SpA was slightly higher in women (female to male ratio = 1.39:1). The older studies of hospitalized patients have documented a clear male predominance in AS. However, many of the earlier reports were based on records from military or veteran administration hospitals in which the overwhelming majority of patients were male. In subsequent studies, AS was found to be only 2 to 3 times more frequent in men than in women[19]. But these studies relied partially on diagnoses made in previous decades without the possibility of using CT or MRI. As shown by Feldtkeller, *et al*[20] the female percentage within a large group of patients with AS increased from 10% among patients diagnosed in the 1960s to almost 50% among patients diagnosed in the 1990s. There are many factors that may contribute to underdiagnosis of AS and related SpA in women. For example, women manifest more gradual worsening of low back pain and stiffness than men[19], and their spinal involvement with resultant ankylosis evolves more slowly[20]. Women tend to have more pronounced appendicular skeletal symptoms that may lead to their misdiagnosis as RA[21], and the disease may stay limited to cervical and thoracic spine for longer periods before the occurrence of typical low back symptoms.

SpA has been reported to be as prevalent as RA in France[18,22]. Our study indicates that in Izmir, Turkey, the prevalence of SpA is higher than that of RA, and that AS itself is as common as RA[8]. Detailed investigation of inflammatory back pain in all subjects in our study and the ability to diagnose AS in subjects with mild symptoms may have resulted in better disease detection, especially in women. Most of the patients had not been diagnosed prior to the study, although they had previously consulted physicians for their low back pain and stiffness. This is not surprising, since the delay in diagnosis of AS may range from 5 to 10 years after the onset of symptoms[23-25].

Our epidemiological study of adults aged 20 and above in an urban area of Izmir, a major city in Turkey, suggests a high prevalence of AS (0.49%) that equals that of RA in our population[8]. The overall prevalence of SpA, including AS, was found to be 1.05%. Men show only a minimal predominance among patients with AS, and it disappears among the whole group of patients with SpA.

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