Epidemiology of ankylosing spondylitis in Northwest Greece, 1983–2002

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Objective. To investigate the incidence and the prevalence of ankylosing spondylitis (AS) in a defined area of northwest Greece with a total population of about 500 000 inhabitants.

Methods. AS cases were recorded from (i) in- and out-patients referred to the rheumatology clinics of the Ioannina university hospital and the Ioannina general hospital, and (ii) patients referred to private rheumatologists practising in the study area. An incident case was defined as any patient with AS, diagnosed during the period between 1 January 1983 and 31 December 2002 who was resident in the study area for at least 1 yr before the diagnosis. A prevalent case was defined as any patient with AS who was a resident of the study area on 31 December 2002. Diagnosis was based on the modified New York criteria for AS. Population data were based on the 1981, 1991 and 2001 National Censuses.

Results. A total of 113 cases were diagnosed among the population of the area studied during the period 1983–2002. Men constituted a 4.65-fold higher number of patients than women, and had a significantly higher mean age at diagnosis. All patients presented bilateral sacroiliitis, 40 patients (35.9%) had peripheral joint involvement and 15 patients presented extra-articular manifestations (13.27%). HLA-B27 antigen was found in 80.5% of our patients. The age-adjusted mean annual incidence rate for the population aged ≥16 yr was 1.5 cases per 10⁵ inhabitants [95% confidence interval (CI) 0.4–2.5], and the age-adjusted prevalence rate on 31 December 2002 was 29.5 cases per 10⁵ inhabitants (95% CI 25.9–33.1). The incidence rates were higher in the age group 35–44 yr for men and in the age group 25–34 yr for women.

Conclusion. The incidence and prevalence of AS in the area studied were significantly lower than in other white populations and higher than in the Japanese population.

Key words: Ankylosing spondylitis, Epidemiology, Incidence, Prevalence.

Ankylosing spondylitis (AS) is an inflammatory rheumatic disease affecting the axial skeleton, often associated with involvement of peripheral joints and the presence of extra-articular manifestations. It is strongly associated with the HLA-B27 antigen, as are other spondyloarthropathies. The clinical expression of the disease is likely to vary widely [1–3].

Although there is little information on the incidence and prevalence of AS, the occurrence of the disease seems to present significant variation among populations. Ethnic, racial and geographical factors have been associated with the occurrence and expression of the disease. However, the role of environmental and genetic factors that may be related to the occurrence and expression of the disease are not well understood [4]. The generally reported prevalence of 0.1–0.2% for AS in Caucasian populations is probably too low, because it is based mainly on hospital records. Studies using community data are needed in order to have a more complete picture of the occurrence of the disease in the general population [5]. There are no studies published on the epidemiology of AS in southern European countries. Investigation of the epidemiological profile of AS and other spondyloarthropathies in southern Europe and the Mediterranean countries would be of interest because of the possible effects of environmental and lifestyle factors on the occurrence and expression of the disease.

In this study we investigated the incidence and the prevalence of AS in a defined area of northwest Greece with a total population of about 500 000 inhabitants. The study was based on a systematic recording system for autoimmune rheumatic diseases implemented in this area, using several sources of retrieval.

Materials and methods

The area studied had a total population of 488 435 inhabitants at the National Census of 2001. It is a defined area of northwest Greece including six districts, four on the mainland and two on islands. Urban residents represented 36.5% of the total population, living in the capitals of the districts. There are two rheumatology clinics in the area, both in Ioannina, the largest city of the study area, which has a medical school and a university hospital. Eight private rheumatologists are practising in the area, in four of the six district capitals.

Cases were recorded from the following sources: (i) in- and out-patients referred to the rheumatology clinics of the Ioannina university hospital and the Ioannina general hospital; and (ii) patients referred to the private rheumatologists practising in the study area. These sources represent all points at which patients diagnosed with an autoimmune rheumatic disease could be referred in the area. Patients were identified retrospectively through medical records from the two hospitals and the private practices. They were selected on the basis of clinical diagnosis.
Diagnosis was confirmed by our study group on the basis of the modified New York criteria for AS [8]. Criteria were satisfied when a patient presented bilateral sacroiliitis grade ≥2 or unilateral sacroiliitis grade ≥3, and one of the following: (i) low back pain of at least 3 months’ duration; (ii) limited lumbar spinal motion; and (iii) a decrease in chest expansion. The patients contacted a rheumatologist directly or were referred by the five small general hospitals that provide general health services in the region, by the orthopaedic clinics at the university and general hospitals, or by the private orthopaedic doctors practising in the area. An incident case was defined as any patient with AS, aged 16 yr or over, diagnosed during the period between 1 January 1983 and 31 December 2002, and resident in the study area for at least 1 yr before the diagnosis. A prevalent case was defined as any patient with AS, aged 16 yr or over, who was a resident of the study area on 31 December 2002 (point prevalence). Individuals diagnosed before 1983 who were still alive and resident in the study area on this date were included in the prevalence estimate.

### Results

The main characteristics of AS patients diagnosed during the period 1983–2002 in northwest Greece are presented in Table 1. A total of 113 cases were diagnosed among the population of the area studied. Men accounted for a 4.65-fold higher number of patients than women and had a significantly higher mean age at diagnosis. All patients presented bilateral sacroiliitis, 40 patients (35.9%) had peripheral joint involvement and 15 patients (13.3%) presented extra-articular manifestations, mainly uveitis. HLA-B27 antigen was found in 80.5% of our patients.

![Figure 1](https://academic.oup.com/rheumatology/article-abstract/43/5/615/1788604/1)

**Fig. 1.** (A) Incidence of AS during the period 1983–2002 by sex and age. (B) Prevalence of AS at 31 December 2002 by sex and age.

The peak of prevalence was in the age group 35–44 yr among women and in the age group 45–54 yr among men (Fig. 1B). The age-adjusted prevalence rate for the population aged ≥16 yr was 29.5 (95% CI 25.9–33.1) cases per 105 inhabitants (48.8 for men and 10.1 for women).

Two patients died during the study period, one because of coronary disease and the other because of neoplasia. Five other patients were lost from the follow-up.

### Discussion

There are few epidemiological studies on the incidence of AS. Studies from Finland, the USA and Japan suggest significant geographical variations in the occurrence of AS [6–8]. According to the results of the present study, the incidence and prevalence rates of AS in the area studied are significantly lower than in North American and North European populations, but higher than in the Japanese population. There have been several studies of the prevalence of the disease in different areas of the world, and these also suggest wide variation [9–12].

Genetic, ethnic, racial and environmental factors are likely to influence the occurrence and clinical expression of AS. The disease is less common among black Americans than in whites, and seems to be extremely rare among black African populations. The disease is considered to be closely associated with the HLA-B27 molecule. The prevalence of HLA-B27 presents significant variation among populations, although ethnic and racial differences of AS seem also to be related to other factors [13–15]. HLA-B27 has a prevalence of about 7% in Caucasians and 14% in the Finnish population, while it is reported in less than 1% of the Japanese population [7, 16]. The use of different case identification criteria could affect the AS rates observed in various studies. However, it is unlikely that the use of different diagnostic criteria could explain the wide variation observed among several populations because the diagnostic criteria for AS are quite similar [16].

The study area has a relatively homogeneous Caucasian population. The following factors may partly explain the lower incidence and prevalence in our study. The prevalence of HLA-B27 in Greece has been estimated to be about 6% [17]. On the other

### Statistical analysis

Incidence and prevalence rates were calculated as the number of cases per 100,000 inhabitants. Age-adjusted rates were calculated by the direct method using the Greek population (National Census 2001). Population data were based on the 1991 and 2001 National Censuses. More specifically, the calculation of the mean annual incidence rates for the period 1983–2002 was based on the demographic data of the 1991 census. The calculation of prevalence rates for 31 December 2002 was based on demographic data of the 2001 census. All rates were calculated considering the population 16 yr and over in the denominator.

### Table 1. Characteristics of AS patients diagnosed during the period 1983–2002 in northwest Greece

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total number of patients</th>
<th>Men/women</th>
<th>Age at diagnosis (yr): mean (s.d.) [range]</th>
<th>Age at disease onset (yr): mean (s.d.) [range]</th>
<th>HLA-B27-positive</th>
<th>Axial involvement</th>
<th>Peripheral joints</th>
<th>Extra-articular manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>113</td>
<td>93/20</td>
<td>39.8 (11.5) [16–76]</td>
<td>30.5 (10.7) [16–69]</td>
<td>91 (80.5)</td>
<td>113 (100%)</td>
<td>40 (35.4%)</td>
<td>15 (13.3%)</td>
</tr>
</tbody>
</table>

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*Table 1.* Characteristics of AS patients diagnosed during the period 1983–2002 in northwest Greece.
hand, dietary factors such as olive oil and fish consumption or even the Mediterranean diet could protect against disease development. In addition, sun exposure and ultraviolet radiation may have immunosuppressive properties [18, 19]. Finally, the milder climatic conditions in the Mediterranean area may also contribute to environmental factors that are different from those of the USA and northern European countries. However, the role of the above factors remains uncertain. Further study is needed to investigate the possible role of genetic and environmental factors in the epidemiology of AS in this area.

The sex ratio of incident cases was about 4.7:1. This ratio varies significantly among other population-based studies, from 5.4:1 in the Japanese study to 2.3:1 in the Finnish study. Studies based on patient series also suggest a male predominance, with sex ratios varying widely among racial and ethnic groups. A reason for the lower occurrence of AS among females could be that females may require a higher genetic susceptibility load before they present with disease [6–8, 20–22].

The peak of incidence and prevalence of the disease and the mean age at diagnosis were higher in men than in women in the present study. This difference between the sexes was not found in the studies in Rochester and Finland. In the Japanese study, the mean age at diagnosis was significantly higher among women. The mean age at diagnosis was generally close to that found in Finland and Japan, as well as that found in a British study. In Rochester the mean age at diagnosis was several years lower [6–8, 23].

There was a decline in the prevalence of AS in those aged more than 35–44 yr. This could be related to a cohort effect such that subjects born in earlier time periods present a lower incidence of the disease. Another possible explanation of this finding could be related to the underdiagnosis of AS cases before 1980, as the rheumatology clinics were established in the area during the first years of the 1980s.

The study was based on several sources of case ascertainment in the frame of a systematic recording system, in order to reduce the likelihood of underestimation of AS cases and to avoid bias. The system records all potential cases of autoimune rheumatic diseases presented in the rheumatology clinics and private rheumatology practices of a defined area. Diagnosis was confirmed retrospectively, using medical records, by our study group. We did not evaluate all patients with a history of inflammatory low back pain in order to identify AS cases. However, it is possible that a number of AS patients could have escaped the recording system. In addition, a number of patients could have remained undiagnosed, mainly in rural areas, where health services are less developed than in urban areas. This may be true mainly for milder cases of the disease. Some milder cases of the disease might have been diagnosed and treated by other physicians. Thus, systematic selection of the more severe cases, referred to rheumatologists, could be a partial explanation of the relative low rates observed in this study. Misclassification of some cases could also be a source of underestimation. On the other hand, it is important to note that access to the rheumatology clinics of Ioannina is relatively easy for all inhabitants of the area studied, and private rheumatologists are practising in four of the six districts of the area. Patients initially diagnosed by other physicians are usually also referred to a rheumatologist. As a consequence, we do not expect any significant underestimation of AS cases in the area studied, which could modify the total picture obtained in the frame of this study. In addition previous studies by our group suggest a relatively low incidence and prevalence of other autoimmune rheumatic diseases in this area [24–26].

The epidemiological profile of AS observed in the population of northwest Greece seems to present some particularities compared with other populations studied. The incidence and prevalence of the disease are significantly lower than in other white populations, and higher than in the Japanese population.

The authors have declared no conflicts of interest.

References


