Epidemiology of Psoriatic Arthritis in Northwest Greece, 1982–2001

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ABSTRACT. ***Objective.*** To investigate the frequency and distribution of psoriatic arthritis (PsA) in a defined area of Northwest Greece, with a population of about 500,000 inhabitants.

Methods. Cases were recorded from in- and outpatients referred to the Rheumatology Clinics of the Ioannina University Hospital and the Ioannina General Hospital, and from patients referred to private rheumatologists practicing in the study area. All patients recorded between January 1, 1982, and December 31, 2001, resident in the study area, were included. The study area included the Department of Epirus and the northern part of the Department of Ionian Islands. Diagnosis was based on the European Spondylarthropathy Study Group criteria. Incidence and prevalence rates were calculated as number of cases per 100,000 inhabitants. Population data were based on the National Census.

Results. The age-adjusted prevalence of PsA was 56.6 cases per 100,000 adults on December 31, 2001. A total of 221 new cases were diagnosed during the study period, giving an age-adjusted mean incidence rate of 3.02 cases per 100,000 adults. There was no significant difference observed between men and women. The peak of incidence was observed in the age group 45–64 years. Incidence of diagnosed PsA increased during the study period.

Conclusion. The incidence and prevalence of PsA in Northwest Greece was roughly half that reported in studies from the US and Northern Europe. This frequency tended to increase in the last decade. (J Rheumatol 2003;30:2641–4)

Key Indexing Terms:
PSORIATIC ARTHRITIS EPIDEMIOLOGY INCIDENCE FREQUENCY PREVALENCE

Psoriatic arthritis (PsA) was first described as a variant of rheumatoid arthritis. However, over the last 60 years epidemiological studies showed an increased frequency of arthritis among patients with psoriasis. Thus, PsA is an inflammatory arthritis associated with psoriasis. Further, clinical and epidemiological investigations suggest that PsA is a unique arthropathy with distinct clinical and radiological features[1].

There are no validated criteria for the classification of the disease. The absence of a validated or consensual case-definition of PsA places several limitations in the comparison of epidemiological data and the interpretation of epidemiological research[2,3]. However, study of the descriptive epidemiology of the disease and comparisons of its frequency, severity, and distribution among different countries and areas could offer a basis for an approach to the etiology and the natural history of PsA.

There are only a few epidemiological studies assessing the prevalence and incidence of PsA in the general population, carried out in the USA and in Northern European countries. The annual incidence of PsA has been estimated around 6 per 100,000, and the prevalence of the disease has been estimated in the range of 20–100 per 100,000[2].

We investigated the prevalence and incidence of PsA in a defined area of Northwest Greece, within the context of the creation of a systematic recording system for autoimmune rheumatic diseases, using multiple sources of retrieval[4]. The study included a homogeneous Caucasian population leaving in the Mediterranean area, with different nutritional, climatic, and probably other environmental conditions compared to Northern European countries and the USA.

MATERIALS AND METHODS

Study design. The study area represents a population of 488,435 inhabitants according to the National Census of 2001. The characteristics of the area studied and the rheumatology health services implemented have been described[4].

Cases were recorded in the context of a systematic recording system for autoimmune rheumatic diseases, using multiple sources of retrieval, developed in this area of Northwest Greece. The system records cases from the following sources: (1) in- and outpatients referred to the Rheumatology Clinic of the Ioannina University Hospital; (2) in- and outpatients referred

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to the Rheumatology Clinic of the Ioannina General Hospital; and (3) patients referred to the 8 private rheumatologists practicing in the study area. These 3 sources represent all points where patients diagnosed with PsA could be referred in the area studied. The patients directly contacted a rheumatologist, or were referred by the 5 small general hospitals that provide general health services in the region, by the dermatology clinic in the University Hospital, or by private dermatologists practicing in the area. Diagnosis was based on the European Spondylarthropathy Study Group (ESSG) criteria[5]. Specifically, any patient with psoriasis and inflammatory spinal pain or peripheral lower limb synovitis was considered to have PsA. All patients were retrospectively identified using the ESSG criteria.

Analysis. All patients referred between January 1, 1982, and December 31, 2001, resident in the study area, were included in the study. An incidence case was defined as any PsA patient, diagnosed during the study period, resident in the study area for at least one year before the diagnosis. A prevalence case was defined as any PsA patient who was a resident of the study area on December 31, 2001. The prevalence rate on December 31, 2001, represents a cumulative prevalence rate. Incidence and prevalence rates were calculated as the number of cases per 100,000 inhabitants. Confidence intervals (CI) were calculated following the normal distribution. Age-adjusted rates were estimated according to the direct method using the Greek population (2001 National Census). The software used was Microsoft Excel 2000 and Epi Info version 6. Population data were based on the 1981, 1991, and 2001 National Censuses.

RESULTS

The main characteristics of patients with PsA diagnosed during the period 1982–2001 in Northwest Greece are presented in Table 1. A total of 221 cases were diagnosed among the adult population (age 16 years and over) representing a mean annual incidence of 2.98 cases per 100,000 adult inhabitants (95% CI 1.50–4.46).

Clinical characteristics. Most PsA patients (76.9%) presented with skin involvement before the disease onset; 71.0% presented with asymmetrical polyarthritis, 10.4% of patients with distal interphalangeal joint involvement, and 10.4% with axial involvement. Finally, 8.1% of our patients had symmetrical polyarthritis and none arthritis mutilans[6] (Table 1).

Incidence and prevalence rates. Figure 1 shows the incidence of the disease during the study period (1982–2001). The mean annual incidence rates are higher in the age group 45–64 for both sexes, although men present an increased incidence in the elderly also. The age-adjusted mean annual incidence rate for the adult population was 3.02 (95% CI 1.55–4.49) cases per 100,000 (2.87 for men, 3.14 for women).

Table 1. Demographic and clinical characteristics of all patients with PsA.

Patients, n	221
Women/Men	113/108
Age at diagnosis, yrs (mean ± SD) [range]	47.70 (14.61) [16–82]
Age at disease's onset, yrs (mean ± SD) [range]	41.97 (14.14) [16–78]
Age at psoriasis appearance, yrs (mean ± SD) [range]	32.98 (16.02) [7–77]
Skin involvement before disease onset, %	76.9
Asymmetrical polyarthritis, %	71.0
Classical PsA with DIP involvement, %	10.4
Symmetrical polyarthritis, %	8.1
Axial involvement, %	10.4

DIP: distal interphalangeal joints

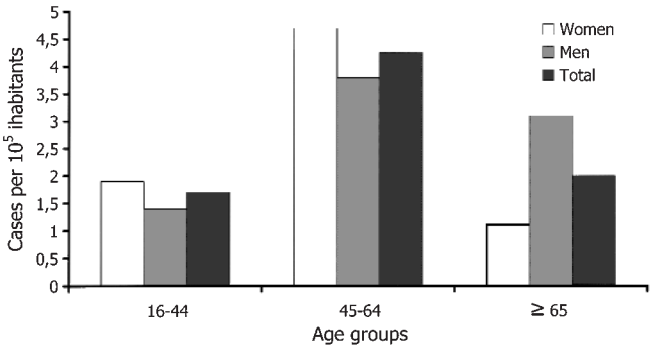

Figure 1. Mean annual incidence rates (cases per 100,000 inhabitants), by sex and age.

Figure 2 shows the prevalence of PsA in the population studied, by December 31, 2001. The age adjusted prevalence rate for the adult population was 56.6 (95% CI 49.9-63.2) cases per 100,000 inhabitants (54.3 for men, and 57.9 for women).

The changes in the incidence of diagnosed PsA are presented in Table 2. There is a significant increase of mean annual incidence rates between 1982–1991 and 1992–2001.

Four deaths were observed in the incidence cohort of 221 PsA patients diagnosed during the study period, while 10 patients were lost to followup; 2 died from cardiovascular diseases, one developed miliary tuberculosis, and one died in a car accident.

DISCUSSION

Descriptive epidemiology of PsA is limited to a few population-based studies from Nordic countries and the study of the Rochester Epidemiology Project[2,7-9]. The annual incidence rate was found to be 6.1/100,000 inhabitants in Finland (95% CI 4.6–7.6)[7]. In Olmsted County (Minnesota, USA), the annual incidence was 6.59/100,000 inhabitants (95% CI 4.99–8.19) and the prevalence 101/100,000 (95%

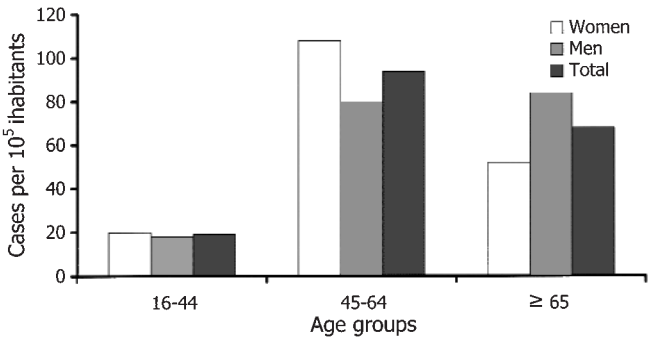

Figure 2. Prevalence of PsA by December 31, 2001. Cases per 100,000 inhabitants, by sex and age.

Table 2. Age adjusted mean annual incidence rates per 10^5 inhabitants for 10 year periods.

	1982–1991 (95% CI)	1992–2001 (95% CI)
Women	2.18 (0.51–3.85)	3.80 (2.15–5.45)
Men	1.74 (0.1–3.38)	3.73 (2.01–5.45)
Total	1.96 (0.47–3.45)	3.76 (2.32–5.26)

CI 81–121). It is important to state that the Finnish study excluded patients with onset of psoriasis after the development of arthritis, while the US and our study included these patients. Although case identification was based on different criteria and methods for each study, their results suggest similar incidence and prevalence rates, considering the 95% CI presented by the authors.

Our results indicate a lower incidence compared to the incidence rates observed in Finland and in Olmsted County, Minnesota[7,8]. These differences are probably due to the different diagnostic criteria used. We applied the ESSG criteria, while the above studies simply counted patients with arthritis and psoriasis. We believe that the ESSG criteria are more reliable, while counting psoriasis with arthritis may lead to overestimation, since psoriasis may be associated with gout or pseudogout arthritis or even with osteoarthritis (Heberden's or/and Bouchard's nodules). These findings could be explained also by a probable underestimation of PsA cases in the area studied. On the other hand, epidemiological data suggest a relatively low frequency and a milder expression of other autoimmune rheumatic conditions in Northwest Greece, as well as in other southern European countries[4,10,11]. Finally, there are no valid data on the frequency of psoriasis in the study area or in other areas in Greece.

We used several sources for case identification, in the context of a systematic recording system, to reduce a potential underestimation of PsA cases and avoid bias. It has been reported that by using multiple sources of retrieval the completeness of data collection is considerably increased[12]. However, it is possible that a small number of PsA patients could have escaped our recording system. A number of patients could remain undiagnosed, mainly in rural areas, where health services are less developed than in urban centers. This could be true mainly for milder cases of the disease. In addition, milder cases of disease might be diagnosed and treated by other physicians. Misclassification of some cases could also be a source of underestimation, as diagnostic criteria of the disease remain partly uncertain. 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 practicing in 4 of the 6 districts in 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 PsA frequency in the area studied, with the exception of cases presenting a mild expression of the disease, mainly during the first years of the study period.

Genetic, ethnic, environmental, and therapy-related factors have been discussed as factors possibly associated with the occurrence of PsA[1,2,13-16]. A number of reports suggest differences in the manifestations of PsA in different ethnic groups[17,18]. There are no studies comparing the frequency of the disease among different ethnic or racial groups. However, it is reported that oral steroids or pregnancy may influence the development of PsA in patients with psoriasis[16]. The residents of Northwest Greece are a relatively homogeneous Caucasian population. Dietary factors such as olive oil and fish consumption or even the Mediterranean diet could offer a protective effect of disease development. In addition, sun exposure and ultraviolet radiation may have immunosuppressive properties[19,20]. Finally, the milder climate conditions in the Mediterranean area may also contribute to different environmental factors from those of the US and Northern European countries. However, the role of these factors remains uncertain. Further study is needed to investigate the possible role of genetic and environmental factors in the epidemiology of PsA in the area.

It is important that a significant increase of PsA incidence was observed during the study period. This finding could be partly interpreted by an increased recognition of the disease during the last years. This increase of diagnosed cases with time was not observed for other autoimmune rheumatic diseases in the area studied[4,10]. Further observation of disease occurrence in the area for the next years is needed to understand this trend.

Regarding the gender discrepancy, our results are similar to those of the Minnesota study, with a slight preponderance of female cases. The Finnish study found a slight preponderance of male cases. The peak of age-specific incidence rates observed in our study was similar to those found in Finland and in Olmsted County, Minnesota. This suggests a common epidemiological profile of the disease in different populations, studied by different methods of case-definition and different case-recording systems.

The mortality observed among our PsA patients was low, although cases lost from the followup could represent an increased number of deaths. The study from Olmsted County presented a similar picture, although another study, based on patients who were seen in a tertiary referral center, showed a standardized mortality ratio of about 1.6 in comparison to the general population. However, it is normal that community-based studies of PsA present better prognosis compared to studies based on referral centers, because of differences in the severity of cases[8,21].

It is important to point out that the few epidemiological studies of PsA were based on different methods and sources of retrieval. The Olmsted County study (carried out during

2000) was based on medical records of people with arthritis among those with psoriasis. The study from Finland (1996) identified people with inflammatory arthritis, using certified drug treatment for arthritis, and then selected patients with psoriasis among them. Other studies carried out between 1963 and 1984 used different methods of recording. However, the most recent of those studies tended to use similar criteria of case-identification, producing similar results[2,7,9,22,23].

The incidence and prevalence of PsA in the study area was roughly half that in other recent studies from Finland and the US, although the age and sex distributions were similar. There was a trend toward an increasing frequency of the disease.

REFERENCES

1. O'Neill T, Silman AJ. Psoriatic arthritis. Historical background and epidemiology. Bailleres Clin Rheumatol 1994;8:245-61.
2. Taylor WJ. Epidemiology of psoriatic arthritis. Curr Opin Rheumatol 2002;14:98-103.
3. Taylor WJ, Fellow DE, Helliwell PS. Case definition of psoriatic arthritis [letter]. Lancet 2000;356:2095; author reply 2096.
4. Alamanos Y, Voulgari PV, Siozos C, et al. Epidemiology of systemic lupus erythematosus in a defined area of Northwest Greece, 1982-2001. J Rheumatol 2003;30:731-5.
5. Dougados M, van der Linden S, Juhlin R, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum 1991;34:1218-27.
6. Moll JMH, Wright V. Psoriatic arthritis. Semin Arthritis Rheum 1973;3:55-78.
7. Kaipiainen-Seppanen O. Incidence of psoriatic arthritis in Finland. Br J Rheumatol 1996;35:1289-91.
8. Shbeeb M, Uramoto KM, Gibson LE, O'Fallon WM, Gabriel SE. The epidemiology of psoriatic arthritis in Olmsted County, Minnesota, USA, 1982-1991. J Rheumatol 2000;27:1247-50.
9. Van Romunde LK, Valkenburg HA, Swart-Bruinsma W, Cats A, Hermans J. Psoriasis and arthritis. I. A population study. Rheumatol Int 1984;4:55-60.
10. Drosos AA, Alamanos I, Voulgari PV, et al. Epidemiology of adult rheumatoid arthritis in northwest Greece 1987-1995. J Rheumatol 1997;24:2129-33.
11. 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.
12. Jonsson H, Nived O, Sturfelt G, Silman A. Estimating the incidence of systemic lupus erythematosus in a defined population using multiple sources of retrieval. Br J Rheumatol 1990;29:185-8.
13. Hohler T, Kruger A, Schneider PM, et al. A TNF-alpha promoter polymorphism is associated with juvenile onset psoriasis and psoriatic arthritis. J Invest Dermatol 1997;109:562-5.
14. Hamamoto Y, Tateno H, Ishida T, Muto M. Lack of association between promoter polymorphism of the tumour necrosis factor-alpha gene and psoriatic arthritis in Japanese patients. J Invest Dermatol 2000;115:1162-4.
15. Barton AC, Bruce IN, Silman AJ. Genetic studies of psoriatic arthritis: dissecting joints and skin. J Rheumatol 2001;28:3-5.
16. Thumboo J, Uramoto K, Shbeeb MI, et al. Risk factors for the development of psoriatic arthritis: a population based nested case control study. J Rheumatol 2002;29:757-62.
17. Thumboo J, Tham SN, Tay YK, et al. Patterns of psoriatic arthritis in Orientals. J Rheumatol 1997;24:1949-53.
18. Marchesoni A, Helliwell P, Gallazzi M, Gibertini P, Rossetti A, Galli L. Psoriatic arthritis in British and Italian patients: a comparative clinical, radiologic, and scintigraphic study. J Rheumatol 1999;26:2619-21.
19. Skoldstam L, Hagfors L, Johansson G. An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. Ann Rheum Dis 2003;3:208-14.
20. Ponsonby AL, McMichael A, van der Mei I. Ultraviolet radiation and autoimmune disease: insights from epidemiological research. Toxicology 2002;181-182:71-8.
21. Wong K, Gladman DD, Husted J, Long JA, Farewell VT. Mortality studies in psoriatic arthritis: results from a single outpatient clinic. I. Causes and risk of death. Arthritis Rheum 1997;40:1868-72.
22. Hellgren L. Association between rheumatoid arthritis and psoriasis in total populations. Acta Rheumatol Scand 1969;15:316-26.
23. Lombolt G. Psoriasis: prevalence, spontaneous course and genetics: a census study on the prevalence of skin diseases on the Faroe Islands. Copenhagen: GEC Gad; 1963.