

Prevalence and Clinical Characteristics of Psoriatic Arthritis in Japan

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ABSTRACT. Objective. To investigate the prevalence of psoriatic arthritis (PsA) in Japanese patients with psoriasis.

Methods. A multicenter, noninterventional, retrospective cross-sectional study was conducted at 3 tertiary care centers in Japan. PsA was diagnosed by rheumatologists based on clinical findings. Prevalence of PsA, clinical characteristics, comorbidities, and treatment patterns were examined.

Results. PsA was identified in 431 of 3021 patients with psoriasis, with a mean prevalence of 14.3% (range, 8.8–20.4%). No large differences between these results and previous reports from Western countries were observed in arthritis distribution, skin disease type, or treatment selection.

Conclusion. The prevalence of PsA in patients with psoriasis in Japan approaches 20% in some areas, similar to that observed in Western countries, and is higher than previously reported in Asia. Clinical features including age, sex, age at onset, and manifestation patterns were also similar to those reported in the West. (First Release June 15 2015; J Rheumatol 2015;42:1439–42; doi:10.3899/jrheum.141598)

Key Indexing Terms:

PSORIATIC ARTHRITIS PSORIASIS PREVALENCE ASIA JAPAN

Psoriatic arthritis (PsA) is a complex musculoskeletal disorder that is usually preceded by psoriasis. The cardinal manifestations of PsA include psoriasis, peripheral arthritis, spinal lesions, enthesitis, and dactylitis. New bone formation is characteristic on imaging¹. The prevalence of psoriasis among Asians is reported to be about 0.1%^{2,3}, which is lower than the 2% reported among Westerners⁴. Among Japanese,

the prevalence of psoriasis is also reported to be 0.1%, but may be increasing because of recent Westernization of lifestyle, and other factors⁵. The reported prevalence of PsA among patients with psoriasis ranges from 6% to > 42%^{6,7,8}. Specifically, the prevalence among whites is estimated at 15–30%, whereas many studies indicate the prevalence among Asians to be ≤ 10%^{9,10}; the previously reported prevalence among Japanese patients with psoriasis is 1%¹¹. While these discrepancies are likely due to differences in study populations, they may also be the result of underdiagnosis, owing to an insufficient awareness of PsA in Asia.

We investigated the prevalence of PsA among Japanese psoriatic patients; surveyed the types of psoriasis, varieties of arthritis, and associated comorbidities; and determined whether the Assessment of Spondyloarthritis International Society (ASAS) classification criteria¹² and the CIASsification for Psoriatic ARthritis criteria (CASPAR)¹ were met.

MATERIALS AND METHODS

This was a multicenter, noninterventional, retrospective cross-sectional study. Data from all patients with psoriasis examined between March 2003 and February 2014 at tertiary care centers in 3 major Japanese areas (Tokyo, Osaka, and Chiba) were included. These tertiary care centers represent the flagship psoriasis hospital in each respective area. In the Japanese healthcare system, most patients with skin conditions are able to (and do) access a dermatologist directly without first seeing a primary care physician. The clinical diagnosis of psoriasis was made by dermatologists, distinguishing between psoriasis vulgaris [International Classification of Diseases, 10th edition (ICD-10)-L400], guttate psoriasis (ICD-10-L404), and pustular psoriasis (ICD-10-L401), including palmoplantar pustulosis (ICD-10-L403). Coding, per ICD-10, was done at the time of consultation. Individuals with psoriasis were identified from hospital databases in each tertiary care center. Rheumatologists familiar with the CASPAR made diagnoses of psoriatic

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arthritis (PsA) based on clinical manifestations and individual physician judgment.

Evaluation items. The prevalence of PsA among patients with psoriasis was calculated for each institution as well as for pooled data. Dermatologists distinguished psoriasis patterns as described above. Rheumatologists assessed distribution of arthritis, which was further evaluated per Moll and Wright criteria¹³, classifying it as distal interphalangeal arthritis, asymmetrical oligoarthritis, polyarthritis, spondylitis, and arthritis mutilans. The presence of spondylitis, enthesitis, dactylitis, and nail lesions was evaluated per rheumatologist judgment at participating sites. Other variables assessed were obesity, defined per World Health Organization criteria for Asians as a body mass index (BMI) ≥ 25 ; family history of psoriasis within a second degree of relationship; and comorbidities [hypertension (HTN), hyperlipidemia, hyperuricemia, and liver dysfunction] 3 months before or after diagnosis. The prevalence of these comorbidities was assessed in the context of prevalence in the general population as reported in a survey conducted by the Ministry of Health, Labor, and Welfare of Japan. Blood tests were performed to determine the level of rheumatoid factor, anticyclic citrullinated peptide antibodies, matrix metalloproteinase-3, C-reactive protein, and erythrocyte sedimentation rate. Values higher than local reference levels were defined as positive. When arthritis symptoms were present, painful areas were evaluated by radiograph or magnetic resonance imaging at the discretion of the examining physician. The presence of imaging findings typical of PsA was also confirmed (typical peripheral joint new bone formation with or without erosions; sacroiliac joint bone erosions; syndesmophytes on the sacroiliac joint or spine; bamboo spine). Peripheral joint findings conformed to CASPAR criteria, defined as radiological evidence of juxtaarticular new bone formation, i.e., ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of hand or foot¹.

Our study conformed to the principles of the Declaration of Helsinki, and was approved by each hospital's ethics committee or institutional review board.

Statistical analyses. The prevalence of PsA was calculated by dividing the number of patients with PsA by the total number of patients with psoriasis examined as of December 31, 2013. Point estimates and 95% CI were reported. Descriptive statistics of patient characteristics, such as dermatologic and rheumatologic medications, laboratory data, and imaging findings were reported for the overall cohort as well as for each individual institution. For categorical variables, proportions were described as percentages. For imaging findings and diagnostic criteria, proportions were calculated for patients without missing values. For continuous variables, median and interquartile ranges were reported. Associations between comorbidities (obesity, hyperlipidemia, diabetes, hyperuricemia, HTN, and liver dysfunction) were assessed with Fisher's exact test.

RESULTS

From all participating sites, a total of 3021 patients with psoriasis were enrolled. Of these, 431 had PsA (pooled prevalence, 14.3%; range, 8.8–20.4%; Table 1). The prevalence of PsA at each participating hospital was Tokyo, 139/1017 (13.7%; 95% CI, 12%–16%); Osaka, 204/1000 (20.4%; 95% CI, 18%–23%); and Chiba, 88/1004 (8.8%; 95% CI, 7%–11%).

Table 1 gives the median age at psoriasis onset and arthritis onset, median latency time to arthritis onset, distribution of patients with PsA, distribution of skin disease types, types of arthritis, types of skin lesions, timing of onset, laboratory data, imaging results, and comorbidities. Comorbid diseases were more common among patients with psoriasis than among the general population. Hyperlipidemia

Table 1. Overall characteristics of 431 patients with psoriatic arthritis. Data are median [IQR] or n (%).

Characteristics	
Age, as of December 31, 2013, yrs	53.00 [43.00, 64.00]
Men	258 (59.9)
Age at psoriasis onset, yrs	37.00 [25.00, 51.00]
Age at arthritis onset, yrs	45.00 [36.00, 57.00]
Latency time to onset of arthritis (from psoriasis onset), yrs	5.00 [0.00, 13.00]
Duration of psoriasis, yrs	13.00 [7.00, 22.00]
Duration of psoriatic arthritis, yrs	5.00 [2.00, 10.00]
History of smoking	163 (37.8)
Obesity	112 (26.0)
Family history	42 (9.7)
Arthritis type	
Distal interphalangeal	38 (8.9)
Oligoarthritis	122 (28.6)
Polyarthritis	258 (60.4)
Mutilans	2 (0.5)
No peripheral arthritis	3 (0.7)
Skin lesion	
Psoriasis vulgaris	385 (91.9)
Guttate psoriasis	2 (0.5)
Pustular psoriasis	26 (6.2)
No skin lesions	6 (1.4)
Nail lesions	168 (39.0)
Dactylitis	177 (41.1)
Enthesitis	187 (43.4)
Axial symptoms	149 (34.6)
Timing of onset	
Psoriasis first	312 (72.9)
Simultaneous	69 (16.1)
Arthritis first	47 (11.0)
Imaging findings	
Peripheral arthritis (typical new bone formation with or without erosions)	190/286 (66.4)
Axial joints	164/401 (40.9)
Syndesmophytes in radiograph	165/341 (48.4)
Sacroiliac lesions in radiograph	127/296 (42.9)
Spinal lesions using MRI	54/122 (44.2)
Sacroiliac lesions using MRI	52/151 (34.4)
Blood tests	
Rheumatoid factor-positive	49 (11.9)
Anticyclic citrullinated peptide antibodies	23 (6.1)
Elevated C-reactive protein	195 (45.2)
Elevated matrix metalloproteinase-3	108 (30.5)
Concomitant diseases	
Hyperlipidemia	189 (43.9)
Diabetes	65 (15.1)
Hyperuricemia	90 (20.9)
Hypertension	100 (23.2)
Liver dysfunction	126 (29.2)

IQR: interquartile range; MRI: magnetic resonance imaging.

was numerically more prevalent in the PsA population than in the general population. Additionally, compared to patients without hyperlipidemia, patients with hyperlipidemia had higher BMI ($p = 0.006$) and higher rate of hyperuricemia ($p = 0.004$), HTN ($p = 0.001$), and liver dysfunction ($p = 0.014$). Interestingly, 89.7% of patients fulfilled CASPAR

criteria for PsA, 63% fulfilled ASAS criteria for axial joint spondyloarthritis (SpA), and 98.2% fulfilled ASAS criteria for peripheral SpA. Table 2 shows types of treatments prescribed.

DISCUSSION

In this large-scale, multicenter study, we found a pooled PsA prevalence of 14.3% among patients with psoriasis (range, 8.8–20.4%), similar to that in Western countries.

Psoriasis has been considered relatively rare among Asians, with a reported prevalence of 0.1%^{2,3}, although the rate is reported to be increasing¹⁴. Various reports have estimated the prevalence of PsA among patients with psoriasis in non-Asian populations to be 20–34%^{7,15,16}. In contrast, Fan, *et al* found the prevalence of PsA among a Chinese population to be only 5%, while Yang, *et al*, reported a similar prevalence of 5.8%; several other studies have reported rates of $\leq 10\%$ ^{10,17}. The prevalence of PsA among Japanese populations has been reported to be even lower, at 1%⁵. However, in keeping with our clinical experience that the prevalence of PsA among Japanese patients is actually higher than 1%, we identified prevalence rates of up to 20.4% among Japanese patients with psoriasis.

The comparative prevalence rates found in our study and those reported in Western populations may be related to both environmental factors and improved diagnostic tools. First, the Westernization of the Japanese lifestyle has been associated with the increased prevalence of several risk factors for psoriasis, including family history of psoriasis, obesity, and hyperlipidemia. Additionally, the prevalence of several risk factors for PsA, including obesity, female sex, and presence of severe psoriasis, nail lesions, Koebner's phenomenon, and hyperlipidemia, have also increased^{18,19,20,21}. In our study, a significant correlation was found between PsA and hyperlipidemia. Among the general Japanese population, hyperlipidemia is present in about 9.8% of adult men and 14.7% of adult women; both figures have been rising annually²². Thus, the rising rates of hyperlipidemia in Japan may contribute to the increase in the number of Japanese patients with PsA. Because the PsA prevalence rates differed among the institutions we surveyed, we investigated the relationships

of the above-mentioned risk factors with the patient populations, but did not find any significant correlations. Site-specific differences in PsA prevalence in our study may be secondary to differences in severity of psoriasis among regions. Prevalence of PsA among psoriasis is generally higher among patients with more severe psoriasis, which suggests the need for further investigation¹⁹.

A second possible reason for the increase in the prevalence of PsA is improved diagnostic methods for and the increased awareness of PsA. Previously, studies in Japanese patients were hindered by small datasets, due in part to poor recognition of the disease and absence of classification criteria prior to 2006. Moreover, diagnoses of PsA were typically made by dermatologists alone. We obtained more definitive PsA diagnoses by recruitment of rheumatologists to collaborate with dermatologists. To ensure appropriate diagnosis of PsA in the future, cooperation among specialists, as well as the introduction of objective PsA screening tools easily applied in daily practice, will be important. While our study did not include a formal screening tool, instruments have become available such as the Psoriatic Arthritis Screening and Evaluation Tool, which facilitates PsA diagnosis using a 1-page questionnaire²³. The use of such tools will likely bring about more rapid identification of PsA and appropriate referral to a rheumatologist.

In past studies from Europe and North America, polyarthritis has been the most common distribution of arthritis, followed by asymmetrical oligoarthritis; relatively few cases demonstrated isolated distal interphalangeal space disease or arthritis mutilans¹⁰. The results of the current study corroborate previous findings. Moreover, the most common skin disease type found in this study was psoriasis vulgaris, similar to previous findings^{7,16}. In addition, treatment choices in our study were consistent with the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis treatment recommendations²⁴.

Our study had several limitations. First, all PsA specialists did not necessarily use the same classification criteria in their respective clinical practices, thus introducing possible misclassification bias in the subject population. Haroon, *et al*, previously reported that up to 30% of patients not known to have PsA did indeed have PsA after a rheumatologic assessment²⁵. Therefore our finding may still be an underestimate. Nonetheless, in our study, concordance with CASPAR and both ASAS peripheral and axial SpA classification criteria was 92.1%, 98.8%, and 54.0%, respectively. Only 1 of 431 cases failed to fulfill the former 2 criteria, indicating that there were no major errors in selecting the subject population. Second, multifactorial diagnostic limitations are possible, including inherent limitations in the cross-sectional study design. For example, as many patients experienced skin symptoms initially, subsequent treatment with antiinflammatory or immunosuppressant therapies could have modified clinical PsA symptoms. Imaging tests, which

Table 2. Treatment (current users) at 3 institutions.

Drug	N (%)
Nonsteroidal antiinflammatory drugs	131 (30.4)
Methotrexate	174 (40.4)
Salazosulfapyridine	71 (16.5)
Cyclosporine	15 (3.5)
Other disease-modifying antirheumatic drugs	11 (2.6)
Infliximab	19 (4.4)
Adalimumab	65 (15.1)
Etanercept	6 (1.4)
Ustekinumab	10 (2.3)
Steroids	24 (5.6)

may have clarified disease activity, were not performed on all patients. Third, patients seen in our tertiary care centers may have higher rates of PsA than patients seen in community dermatology clinics, a potential source of nondifferential bias that may affect the results of our study.

Our study warrants confirmation in other Asian populations to examine whether these prevalence numbers are applicable in other populations. While past epidemiological surveys have typically been single-institution, this study gathered data from 3 relatively large municipal hospitals. Hence, we believe our findings are adequately representative of the status of patients throughout Japan.

The maximum prevalence of PsA in patients with psoriasis in Japan was 20.4% in our study, similar to rates reported in Western countries. It is higher than previously reported prevalence rates in Asia. Clinical features were also similar to those observed in Western countries. Additional studies are required to determine whether these rates are also higher in other Asian countries.

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