Psoriatic arthritis in Asia

Lai-Shan Tam¹, Ying-Ying Leung² and Edmund K. Li¹

Geographic or ethnic differences in the occurrence of disease often provide insights into causes of disease and possible opportunities for disease prevention. A wide variation on the incidence and prevalence of PsA was reported in different countries. The prevalence in China was similar to the rest of the world, whereas the incidence and prevalence of PsA was much lower in Japan. Among patients with psoriasis, 6–42% of the Caucasians were reported to have PsA, but figures were lower from Asian countries (1–9%). Divergent distribution of HLA in different ethnic groups and other genetic determinants may account for these differences in prevalence. PsA affects men and women almost equally in Chinese, Japanese and Iranians, which is similar to their Caucasian counterparts. Polyarthritides developing in the fourth decade was the commonest pattern of arthritis among Chinese, Indians, Iranians, Kuwaiti Arabs and Malays. Arthritis mutilans and eye lesions have rarely been reported in Asian countries. Chinese patients with nail disease and DIP joints involvement have a significantly higher risk of developing deformed joints. More data are required on the safety, efficacy and cost effectiveness of TNF blockers for the treatment of PsA in Asia. Premature atherosclerosis has been recognized as an important co-morbidity in Asian patients with PsA. Increased prevalence of traditional cardiovascular risk factors associated with PsA suggested that the two conditions may share the same inflammatory pathway. Carotid intima–media thickness can identify PsA patients with subclinical atherosclerosis who may benefit from early intervention.

KEY WORDS: Psoriatic arthritis, Asia, Epidemiology, Premature atherosclerosis.

Introduction

PsA is an inflammatory arthritis associated with psoriasis. PsA is characterized by the absence of RF and certain clinical features, including asymmetric distribution of arthritis, DIP involvement, enthesitis, dactylitis, spondylitis and the association with HLA-B27. On the basis of these characteristics, PsA has been classified with the HLA-B27-associated SpAs. Researchers have remarked that ethnic and geographic differences exist in the prevalence, clinical manifestations and prognosis of SpA [1]. SpA in the non-white Caucasians, Asians and Africans runs a different course when compared with white Caucasians, and the association between B27 and disease is less strong in some of these populations in whom cross-reacting antigens and other genetic determinants may be more important [1]. None of the studies has ever studied in detail whether there are any ethnic differences in the prevalence, clinical manifestations and prognosis in PsA, but they may possibly provide further insight into the underlying aetiology of this condition. Estimates of prevalence of PsA can also provide information regarding the burden of the disease and would allow provision for health services for patients with PsA. Premature atherosclerosis has been recognized as an important co-morbidity in chronic inflammatory conditions including RA and SLE [2, 3]. Data from Asian countries also support the hypothesis that inflammation associated with PsA contributes to accelerated atherosclerosis. We review recent advances in research on PsA from Asian countries.

Epidemiology

PsA was recognized by the ACR as a distinct clinical entity since 1964 [4]. However, the first study on prevalence and incidence of PsA was published only in 1996 [5]. The results of a recent systematic review suggested a wide variation on the incidence and prevalence of PsA in different countries [5]. On the basis of retrospective and cross-sectional studies, the prevalence of PsA ranged between 20 and 420 per 100 000 population in Europe and USA, respectively. The incidence of PsA was similar between five European studies and one US study that ranged between 3 and 23.1 per 100 000 population, but data from Asia are limited [5]. From population-based surveys in China, the prevalence of PsA appeared to be similar to the rest of the world, ranging from 10 to 100 per 100 000 population [6]. Interestingly, among Japanese, there is a 64- and 180-fold lower incidence with prevalence between 0.1 and 1 per 100 000 population as compared with the median incidence and prevalence of all other studies [7]. A multi-ethnic study reported that PsA was significantly more common among Indians than the ethnic distribution of the Singapore population [8]. Among patients with psoriasis, 6–42% from Europe, USA and South Africa were reported to have PsA [9], but figures were lower from Asian countries. PsA was observed in 9% of the patients with psoriasis in Iran [10], Korea [11] and India [12]; 5% in China [13]; 2% in Turkey [14] and 1% in Japan [15]. A Singaporean study also reported that Indians with psoriasis had twice the risk of developing PsA when compared with Chinese [8], suggesting that different ethnicities may affect the development of PsA.

Studies to date on incidence and prevalence for PsA have been limited by small cross-sectional studies, selective study populations, limited follow-up and PsA classification criteria lacking diagnostic sensitivity. The Classification of Psoriatic Arthritis (CASPAR) group has developed classification criteria for PsA with a sensitivity of 91.4% and a specificity of 98.7% [16]. Population-based studies using these new criteria reported a point prevalence of 150 per 100 000 persons [17], and an incidence between 6 [17] and 7.2 [18] per 100 000 persons in Denmark and USA, respectively. PsA was clinically recognized in <10% of the psoriasis patients during their lifetime [19]. The CASPAR criteria should help with epidemiological studies of PsA in Asia.

Genetic studies

Reasons for differences in prevalence may be due to genetic differences, environmental exposures or a combination of both.
Cumulated evidence indicates that PsA is a disease caused by the concerted action of multiple disease genes, triggered by environmental factors. Several studies reported linkage between specific HLA and PsA [20–23]. Divergent distribution of HLA was documented in different reports, suggesting that HLA distribution varies with different ethnic groups. HLA-B16, -B17, -B27 and -Cw6 were associated with PsA in Caucasians [20], whereas HLA-A2, -B46, -DR8 and -B27 were associated with PsA in Japanese [21]. A recent study from Taiwan showed that HLA-Cw12 was associated with PsA, whereas HLA-B58 and -DR17 appeared to be protective [22]. In Israeli patients, PsA was associated with HLA-A3, -B13, -B38, -DRB0101 and -DRB0301 [23]. HLA-B27 was not associated with PsA in patients from Israel [23] and Korea [11].

TNF-α gene is also mapped within the HLA region, and its product has been reported as one of the most important cytokines in the pathogenesis of PsA. There are conflicting reports about the association between TNF-α-238G/A polymorphism and PsA [24]; studies from Japan and Taiwan did not find any associations [25, 26]. In Caucasians, TNF-α and β gene polymorphism [26], HLA Cw 0602, Class I MHC chain-related gene A (MICA)-A9 and killer immunoglobulin-like receptor (KIR) 2DS1/S2 [27–30] were associated with PsA, and TNF-α and β gene polymorphisms were significantly associated with presence of joint erosions in PsA and progression of joint erosions in early PsA [26]. Different from the Caucasians, TNF-α and β, HLA Cw 0602, KIR 2DS1/S2, MICA-A9 and other cytokine gene polymorphisms were not associated with PsA in Chinese patients from Taiwan [31]. In addition, PsA patients from Taiwan showed elevated expression of free HLA Class I heavy chains on peripheral blood monocytes compared with psoriasis patients without arthritis [32]. When cytochrome p450 1A1 (CYP 1A1) and manganese superoxide dismutase (MnSOD) gene polymorphisms were assessed in Chinese patients from Taiwan, CYP 1A1 4887A and 4889G were reported to be associated with PsA, but these were not associated with the manifestations and severity of PsA [33]. MnSOD 1183C polymorphisms may be associated with PsA, whereas MnSOD 1183T appeared to be protective from the development of this disease [34]. The role of the I-allele of angiotensin-converting enzyme gene I/D polymorphism was controversial in SpA patients from Kuwait [35, 36].

Clinical features of PsA

Moll and Wright [37] described five clinical patterns among patients with PsA: DIP, asymmetrical oligoarticular, symmetric polyarticular, spondylitis and arthritis mutilans. The exact frequency of the patterns is variable but oligoarthritis was the most commonly reported pattern [37]. The clinical features of PsA patients from Asian countries are summarized in Table 1 together with the largest PsA series from Toronto for comparison [8, 10–12, 23, 36, 38–42]. A number of racial differences in the clinical presentations of PsA were observed. PsA affects men and women almost equally in Caucasians [43]. Studies from Hong Kong, Singapore [8, 40], Japan [39] and Iran [10] also reported the same, whereas others noted a male predominance [11, 12, 23, 38, 41, 44] and one study reported a female predominance from Kuwait [36].

Polyarthritis developing in the fourth decade was the commonest pattern of arthritis in Chinese from Hong Kong [40] and Indians [8]. Koreans [10], Kuwaiti Arabs [36], Malays [8] and Thai patients [44]. On the other hand, oligoarthritis was the predominant pattern in patients from Israel [23], Japan [39] and rural India [12]. Spondylitis was the most common pattern of PsA in Korea [11] and Chinese from Taiwan [41]. Clinically apparent lumbar spondylitis was significantly more common in Indians than Chinese from Singapore. 45% of cases were asymptomatic when present in Chinese and...
the condition was detectable only on radiological examination [8]. Arthritis mutilans was rarely reported in all the studies from Asian regions. The frequency of distribution of the pattern has also varied in previous Caucasian studies [43], and may be explained partly by the different definitions used by individual investigators or the changing patterns over time. Those with longer disease duration tend to develop into the polyarticular pattern [45].

Extra-articular manifestations
Almost all (51.2–97.5%) patients developed arthritis after the onset of psoriasis, and psoriatic vulgar is was the most common form of psoriasis reported [8, 10–12, 23, 38–41]. Nail lesions were common in PsA, affecting 30.2–97% of the patients, and were significantly more prevalent compared with psoriasis patients without arthritis in one study [10]. The prevalence of dactylitis and enthesitis ranged from 15.4 to 71.4% and from 7.8 to 59.1%, respectively. Eye lesions were rarely reported in PsA patients in Asia (1.7–3.9%) [8, 36, 38, 44].

Aortic incompetence was reported in <4% of the patients with PsA [46]. Other cardiac involvement in PsA included subtle involvement of the atrioventricular node [47] and diastolic dysfunction [48] from Israel and Turkey, respectively. A study from Spain did not find any differences in echocardiographic abnormalities between PsA and healthy controls [49].

Predictors for clinical features and prognosis
The association of HLA antigens with disease expression varies in Caucasian PsA patients [20, 50–52], e.g. HLA-B27 [20, 50–52], -Cw1 [51], -Cw2 [20], -DRw52 [20] and -DQw3 [50] were associated with involvement of the back, whereas HLA-B38 and -B39 were associated with polyarthritus [20]. Studies from Taiwan reported an association between HLA-B27 and the development of sacroilitis [22, 41] and uveitis [22], but not peripheral arthritis [41]. A study from Israel found significant association between DIP involvement and the presence of HLA-A26 and -B38, whereas HLA-DRB301 was related to spinal involvement [23].

Predictors for progression in Caucasian PsA included five or more swollen joints, a high medication level at presentation [53], polyarticular onset [54] and HLA-B27 in the presence of HLA-DR7 and -B39, and HLA-DQw3 in the absence of -DR7 [55]. Similar to Caucasians, Chinese PsA patients with positive HLA-B27 tend to develop deformed joints (P = 0.068) as well as have elevated levels of CRP (P = 0.072), although these results did not attain significance [41]. By contrast, Chinese PsA patients with nail disease and DIP joints involvement had significantly increased risk of developing deformed joints [41].

Quality of life and function in PsA
Instruments validated for the assessment of quality of life and function in PsA included Medical Outcome Survey Short Form 36 (SF-36) [56] and the HAQ [57], respectively. Patients with PsA showed impaired quality of life and reduced function, comparable with those who had RA [57–59]. In a study from Hong Kong, a third reported PsA-related unemployment and change in job nature [60]. Another third experienced a reduction in income due to PsA. Multivariate analysis identified higher damaged joint count, poorer patients’ perception of health, poor socioeconomic factor and higher CRP as factors associated with higher HAQ. This study highlighted a significant socioeconomic effect in Chinese subjects with PsA. Joint damage was found to be associated with functional impairment.

Management of PsA
Diagnosis of PsA
Treatment recommendations for PsA have been recently published by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis [61]. The group recommended that diagnosis of PsA should follow the CASPAR criteria. However, the sensitivity and specificity may vary with different ethnicities. The CASPAR criteria for PsA have recently been validated in Chinese populations [62]. Data were collected prospectively from Han Chinese with PsA and other patients with chronic inflammatory arthritis. Subjects were classified according to Moll and Wright or CASPAR criteria. A total of 108 (53 males and 55 females) subjects with PsA were recruited.

Data were compared with 195 controls with RA (n = 154), AS (n = 41) and undifferentiated arthritis (n = 1). The sensitivity and specificity of Moll and Wright criteria were 85.2 and 100%, respectively, whereas 98.2 and 99.5%, respectively, for the CASPAR criteria, which is similar to the reported values in European populations. The CASPAR criteria performed well in Chinese population, i.e. very different from populations they were developed, and have a higher sensitivity in classifying PsA.

Treatment of PsA
Most rheumatology units in Asia have adopted treatment guidelines from Europe or USA. The therapeutic strategies outlined in the treatment recommendations were based on review of literature and expert consensus mainly from North America and Europe [61]. Although the therapeutic strategy may be appropriate on the whole, there may be subtle differences in the pharmacokinetics, clinical response, as well as side effects of the drugs used. Few therapeutic trials on PsA have been done in Asia, and data for safety and efficacy of DMARDs and biologics in PsA from most of these countries are lacking. A survey from 112 PsA patients from Singapore reported that DMARDs were commonly used (67% on SSZ and 14% on MTX) [63], and case series from Singapore and India suggested that MTX may be safe and effective [64, 65].

Treatment guideline for the use of TNF-α blockers in Asian patients with rheumatic diseases including PsA has been published from Lebanon, whereas the guideline from Japan targeted RA patients only [66, 67]. The guideline for the prevention of latent tuberculosis reactivation in rheumatic disease patients given TNF-α blockers was published from Israel [68]. Reports from Israel [69] and Taiwan [70] suggested that TNF-α blockers were effective and well tolerated in PsA. A post-marketing surveillance study of 5000 Japanese RA patients treated with infliximab showed that infliximab in combination with low-dose MTX was well tolerated [71]. Nonetheless, a study from Korea reported an increased risk of TB reactivation in RA patients treated with TNF blockers [72], and another report from Japan noticed a higher risk of pneumocystis pneumonia [73]. Etanercept was found to be cost effective in Japanese patients with RA [74]. More data are required on the safety, efficacy and cost effectiveness of TNF blockers for the treatment of PsA in Asia.

Co-morbidity of premature atherosclerosis in PsA
Patients with PsA may experience substantial morbidity and unfavourable outcomes at referral centres [75, 76], although investigators from other centre did not report a significant increase in mortality in unselected patients [77]. Mortality data of Asian PsA patients were lacking; nonetheless, investigators from Hong Kong and Israel have ascertained the prevalence and risk factors for premature atherosclerosis in PsA patients.

In a study by Kimhi et al. [78] from Israel, the prevalence of traditional cardiovascular diseases (CVD) risk factors including smoking, altered lipid profile, hypertension and diabetes mellitus (DM) was similar between 50 PsA patients and age-matched
controls, although the BMI was significantly increased in the patient group. On the contrary, Han et al. [79] from the USA reported a higher prevalence ratio of type II DM, hyperlipidaemia and hypertension in PsA patients compared with controls. To address the central question that if individuals with PsA have an increased prevalence of CVD risk factors, a study from Hong Kong compared CVD risk factors between 102 consecutive PsA patients and 82 controls [40]. The BMI of the PsA patients was significantly higher than healthy controls. PsA patients had a higher prevalence of DM and hypertension, but a lower prevalence of low density lipoprotein cholesterol after adjusting for the BMI. Further adjustment for high sensitive C-reactive protein level rendered the differences in the prevalence of hypertension and DM non-significant between the PsA and controls. These data support the hypothesis that PsA may be associated with obesity, hypertension and insulin resistance because of the shared inflammatory pathway.

Early diagnosis of atherosclerosis in PsA might trigger more aggressive prophylaxis. Increased intima–media thickness (IMT) of the carotid artery, a sign of early atherosclerosis [80], has been reported in PsA patients from Spain and Israel [78, 81–83]. Increased IMT significantly correlated with traditional risk factors including age [78, 82], BMI [78], uric acid [83], triglycerides [82], total cholesterol and low density lipoprotein cholesterol levels [81]; and disease-related parameters including age at the time of PsA diagnosis [81], disease duration [78, 81], spine involvement [78], ESR [78] and fibrinogen [78] levels. A study from Hong Kong reported an increased prevalence of subclinical atherosclerosis in Chinese, defined as the average of IMT measures above the 95th percentile of healthy controls [84]. Using logistic regression analysis, independent explanatory variables associated with subclinical atherosclerosis in PsA including increased sugar and total cholesterol were BMI, hypertension, and insulin resistance because of the shared inflammatory pathway.

Conclusions
A wide variation on the incidence and prevalence of PsA has been reported in different countries, ranging from 1 to 100 per 100,000 population in China to 1 per 100,000 population in Japan. Amongst Asian patients with psoriasis, 1–9% were reported to have PsA. Divergent distribution of HLA in different ethnic groups and other genetic determinants may account for these prevalence differences. Polyarthritis developing in the fourth decade was the commonest pattern of arthritis among Asian PsA patients, whereas arthritis mutilans and eye lesions were rarely reported. More data are required on the safety, efficacy and cost-effectiveness of TNF blockers for the treatment of PsA in Asia. An increased prevalence of traditional cardiovascular system risk factors and subclinical atherosclerosis has been reported in patients with PsA, including Asian patients. Such risk factors should be routinely monitored and treated aggressively in high-risk patients.

Disclosure statement: The authors have declared no conflicts of interest.


Tam LS, Tomlinson B, Chu TT et al. Cardiovascular risk profile of patients with psoriatic arthritis compared to controls—the role of inflammation. Rheumatology 2008;47:718–23.


