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REVIEW ARTICLE

Psoriasis in Taiwan: From epidemiology to new treatments

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ABSTRACT

Psoriasis is a common, chronic immune-mediated disorder that occurs worldwide. The prevalence of psoriasis in Taiwan is lower than that in Caucasian countries. Nevertheless, an increasing trend in the prevalence of psoriasis and psoriatic arthritis has been observed in Taiwan over the past decade. Accumulating studies have also suggested that psoriasis is not a disease limited to the skin and joints but has far-reaching systemic effects, associated with a higher prevalence of comorbid diseases, such as cardiovascular diseases, diabetes mellitus, metabolic syndrome, depression, and chronic kidney disease, than in the normal population. To date, our understanding of the mechanisms linking psoriasis and comorbidities remains far from complete. Psoriasis and its comorbid diseases confer substantial disease and health care burdens and have a significant negative impact on the quality of life of affected patients. The discovery of new, promising drugs has revolutionized psoriasis treatment, but patients still have unmet needs that require further investigation. Studies specifically on the Taiwanese population with psoriasis remain scarce. Herein, we review the medical literature, with a focus on studies examining the Taiwanese population, with regard to epidemiology, comorbidities, and effects of antipsoriatic agents on comorbidities, as well as the efficacy and safety of novel antipsoriatic treatments for patients with psoriasis.

Introduction

Psoriasis is a chronic, immune-mediated, inflammatory condition that is prevalent worldwide.[1,2] However, the prevalence of psoriasis varies among different ethnic groups. The prevalence is 2–11% in Caucasians but is significantly lower in Asians.[3–6] The wide variation seen in prevalence worldwide is likely influenced, at least in part, by genetic factors. The most strongly associated susceptibility gene of psoriasis is the human leukocyte antigen (HLA)-Cw6 locus. However, the prevalence of this allele is actually lower in Taiwanese patients with psoriasis than in Caucasians.[7] The genetic, environmental, and immunological factors specific to ethno-racial groups likely contribute to the observed differences in the prevalence of psoriasis and may potentially predispose psoriasis patients to variations in clinical phenotypes, disease course, associated comorbidities, skin responses when exposed to certain environmental

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insults, and treatment outcomes.[8–13] Although some studies have been published on the clinical variation of psoriasis on the basis of the color of the skin,[9,10] previous data specifically on psoriasis in Taiwanese populations, which may present with a different set of characteristics, are scarce. Until recently, several epidemiological studies using Taiwan's National Health Insurance Research Database (NHIRD), which contains detailed claims records of approximately 23 million beneficiaries (99% of the Taiwanese population) and clinical trials, have been conducted in Taiwan. Thus, we performed a comprehensive review of epidemiological, clinical, and therapeutic data pertaining to psoriasis in Taiwan.

Epidemiology of psoriasis in Taiwan

The prevalence of psoriasis in Taiwan is approximately 0.24%,[14] which is much lower than that in Caucasians (2–11%), African Americans (1.3%), Indians (0.5–1.5%), Malaysians (4–5.5%), Japanese (0.29–1.18%), and Koreans (0.44–0.45%).[3–6,15,16] In Taiwan, 12.7% of psoriasis patients have psoriatic arthritis (PsA),[14] which is also lower than that observed in Caucasians (approximately 30%).[17] The prevalence of psoriasis in male patients is 1.4 times higher than that in female patients, and it increases rapidly in male patients after 30 years of age but has a similar pattern in both sexes for patients younger than 30 years.[18]

In Taiwan, the increment in the prevalence of PsA was higher than that of psoriasis from 2003 to 2013, which may be because of the increased awareness of symptoms of arthritis among patients or by physicians.[14] In addition, the reimbursement for biologics by the Taiwan National Health Insurance since 2009 may have also motivated physicians to diagnosis and treat patients with PsA more aggressively.[14]

Cumulative evidence implicates a substantive role for genetic factors in psoriasis susceptibility. HLA polymorphisms have an impact on the clinical presentation of and a patient's susceptibility to psoriasis.[19] HLA-Cw*06 is a well-known psoriasis-susceptibility gene. However, the allele frequency of HLA-Cw*06 in psoriasis is only 6–17% in Taiwanese patients with psoriasis.[7] Conversely, the frequency of HLA-Cw*06 is 8–26% in Japanese patients with psoriasis, 76.1% in Koreans, 14% in Thais, and 46–67% in Caucasians.[7]

Classical comorbidities

Cardiovascular disease

Psoriasis has been linked to metabolic syndrome (MS), including obesity, hypertension, hyperlipidemia, and diabetes, which are associated with an increased risk of cardiovascular death, especially at an early age.[20] A previous study revealed that patients with psoriasis have a significantly increased prevalence ratio (PR) for various clinical cardiovascular disease (CVD) risk factors, including hypertension (PR 1.51; 95% confidence interval (CI) 1.47–1.56), hypertriglyceridemia (PR 1.61; 95% CI 1.54–1.68), and heart disease (PR 1.32; 95% CI 1.26–1.37).[3] Several population-based studies in Taiwan have also provided evidence to support the association between psoriasis and CVD.[3,18,21] Moreover, our study and the study by Ahlehoff et al. showed that patients with psoriasis also face an elevated risk of developing heart arrhythmias, including atrial fibrillation and ventricular arrhythmia.[22,23]

Hypertension is more prevalent among patients with psoriasis. Previous meta-analysis revealed a pooled odds ratio (OR) for the association between psoriasis and hypertension to be 1.58 (95% CI 1.42–1.76).[24] With the increase of disease severity, the odds of developing hypertension increased from 1.30 (95% CI 1.15–1.47) for individuals with mild psoriasis to 1.49 (95% CI 1.20–1.86) for patients with severe psoriasis.[25] As the disease duration of psoriasis is prolonged, the severity of hypertension may proceed from increased systolic and diastolic pressures to left ventricular dysfunction eventually.[26] This result may be also attributed to the inflammatory milieu and cytokine imbalance driven by angiotensin II.[27] In addition, studies have provided evidence of more severe hypertension and poorly controlled blood pressure among patients with psoriasis compared with those without psoriasis.[28] The likelihood of poorly controlled hypertension appears to increase with more severe skin disease, independently of the body mass index and other risk factors.[29] Epidemiologic studies have reached a consensus to suggest psoriasis may be an independent risk factor for myocardial infarction, stroke, and death due to CVD, collectively termed major adverse cardiovascular events (MACE).[28] Two studies specifically examined the risks of MACE according to psoriasis severity and found the greatest risks to be among those with severe disease. Nevertheless, risks among patients with mild disease activity also increased significantly, suggesting that the cardiovascular risk is not only limited to those with severe disease but is also associated with the disease itself.[30,31] Shared pathophysiological pathways, the main hypothesis for the association between psoriasis and cardiovascular disease, involve increased systemic inflammation, including chronic type 1 helper (Th1) T-cell and Th17-mediated inflammation; monocyte and neutrophil modulation; increased oxidative stress as well as angiogenesis; and endothelial cell dysfunction.[28,32] Promoted by high levels of tumor necrosis factor (TNF)-α and interleukin (IL)-6, exacerbation of atherosclerosis was observed and resulted in myocardial infarction or stroke.[27,33] In addition to the traditional risk factors for cardiovascular events, hereditary and genetic backgrounds also play a role in this association. Researchers have examined the possible comanifestation of psoriasis and cardiovascular events as genetic factors via a genome-wide association study, and the data suggested that patients with psoriasis were enriched for genetic variants *HLA*, *FUT2*, *UBE2L3*, *SH2B3*, which predispose to increased risk of dyslipidemia, hypertension, and increased coronary artery disease.[34]

The impact of psoriasis is not only on the vessels of the heart but also on the blood vessels of the brain and peripheral vessels.[35–37] Psoriasis confers an independent risk for cerebrovascular disease (OR 1.70; 95% CI 1.33–2.17),[37] pulmonary arterial hypertension (adjusted hazard ratio (aHR) 1.46; 95% CI 1.09–1.94),[38] peripheral vascular (OR 1.98; 95% CI 1.32–2.82),[37] and aortic aneurysm (aHR1.80; 95% CI 1.25–2.61).[39]

Diabetes mellitus and metabolic syndrome

Epidemiological studies from various countries showed consistent associations between psoriasis and elevated risks of MS and diabetes mellitus (DM),[3,18,21,40–43] and the risks were even higher in more severe psoriasis.[35,44] Insulin resistance has also been demonstrated in non-diabetic psoriasis patients in a case-control study.[45] As the MS is proposed to result from a generalized proinflammatory state,[46] the link between psoriasis and MS is postulated to be a shared systemic inflammatory condition. However, some argue that certain lifestyle choices (such as smoking, alcohol consumption, limited physical activity, etc.), which have been shown to predispose to MS, are found more frequently in psoriasis patients.[42] Chronic inflammation, with elevation in the levels of IL-1β, TNF-α, IL-6, has been demonstrated to be associated with insulin resistance[47] and islet beta cell apoptosis,[48] supposedly leading to type 2 DM eventually. The treatment with anti-TNF-α biologics and alefacept, resulting in improved insulin sensitivity[49] and reducing the risk of DM,[50] further exemplifies the association of the two conditions.

Despite the implications from epidemiological studies, the exact pathophysiological mechanisms underlying the association of

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