

Epidemiological, genetic, clinical, and treatment differences of palmoplantar pustulosis across ethnicities: a systematic review

INPLASY202530108

doi: 10.37766/inplasy2025.3.0108

Received: 25 March 2025

Published: 25 March 2025

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ADMINISTRATIVE INFORMATION

Support - The authors did not receive support from any organization for the study.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - Francis Li-Tien Hsu has no conflict of interest to disclose. Tsen-Fang Tsai has conducted clinical trials or received honoraria for serving as a consultant for Abbvie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli-Lilly, Galderma, GSK, Janssen-Cilag, Leo Pharma, Merck Sharp & Dohme, Novartis International, Pfizer, PharmaEssentia, Sanofi, and UCB Pharma.

INPLASY registration number: INPLASY202530108

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2025 and was last updated on 25 March 2025.

INTRODUCTION

Review question / Objective Population (P): Patients with palmoplantar pustulosis (PPP), a chronic inflammatory skin disease with sterile pustules on palms and soles. The review focuses on ethnic differences, comparing Asians (e.g., Japanese, Korean, Chinese) and non-Asians (e.g., Europeans, Americans). Included studies report on PPP patients from cohort studies, case series, case-control studies, and RCTs with over five participants. Excluded are studies on quality of life, economics, or paradoxical PPP post-biologics, though case reports with novel findings are discussed.

Intervention (I):

Not applicable as a traditional intervention, since this is an observational systematic review. Treatment-wise, this study compared various

treatment modalities used for PPP across ethnicities, including conventional therapies (e.g., topical corticosteroids, vitamin D analogues, acitretin, colchicine, tonsillectomy), biologics (e.g., guselkumab, brodalumab, TNF- α inhibitors), and novel options (e.g., excimer laser, dupilumab, JAK inhibitors). The focus is on ethnic variations in treatment use and efficacy, not a specific intervention trial.

Comparison (C):

Comparison of PPP characteristics between Asians and non-Asians. Key aspects include epidemiology (incidence/prevalence), genetics (e.g., IL36RN, CARD14 mutations), clinical features (e.g., sex ratio, type A vs. type B PPP, comorbidities), and treatment responses. No direct comparator (e.g., placebo) exists within studies; comparisons are drawn across studies of different

ethnic groups, highlighting regional and ethnic distinctions.

Outcomes (O):

Primary Outcomes:

Epidemiology: PPP prevalence and incidence.

Genetics: Shared and ethnic-specific mutations (e.g., IL36RN, AP1S3).

Clinical Features: Gender predilection, type A/B PPP, comorbidities including psoriasis vulgaris, psoriatic arthritis, smoking, obesity, metal allergy, nail involvement, SAPHO syndrome/PAO.

Treatment: Traditional therapies including acitretin, colchicine, tonsillectomy; biologics; novel therapies.

Measurement: Narrative synthesis due to study heterogeneity, using tables and summaries.

Study Design (S):

Systematic review following PRISMA and SWiM guidelines. Included studies (cohorts, case series, case-control, RCTs, reviews) span the earliest date to February 1, 2025, in English, German, and Chinese, sourced from PubMed, Embase, Cochrane, and Web of Science. Studies with over five patients inform statistics, assessed via JBI checklists and Newcastle-Ottawa Scale. Narrative synthesis to address heterogeneity in design and reporting.

Rationale Palmoplantar pustulosis (PPP) is a chronic, debilitating inflammatory skin condition characterized by sterile pustules on the palms and soles, significantly impairing quality of life due to its recurrent nature and anatomical location. While ethnic differences in immune-mediated dermatoses like atopic dermatitis, psoriasis vulgaris, and generalized pustular psoriasis have been well-documented, PPP remains understudied in this regard. Existing evidence suggests a higher prevalence in Asians, particularly East Asians such as Japanese, yet comprehensive comparisons of epidemiology, genetics, clinical features, and treatment responses across ethnicities are lacking. This gap hinders tailored diagnosis and management in diverse populations.

PPP's pathogenesis involves complex genetic (e.g., IL36RN, CARD14 mutations) and environmental factors (e.g., smoking, metal allergy), which may vary by ethnicity, potentially influencing disease presentation and therapeutic outcomes. For instance, preliminary data indicate distinct clinical subtypes (type A vs. type B PPP) may predominate in specific ethnic groups. Treatment efficacy may also differ, yet no systematic synthesis exists to clarify these patterns.

This systematic review addresses this knowledge gap by consolidating global data to compare PPP across ethnicities, aiming to enhance understanding of its heterogeneous nature. Such insights are critical for improving recognition, refining subclassification, and optimizing management strategies as healthcare serves increasingly diverse populations.

Condition being studied Palmoplantar pustulosis (PPP) is a chronic, relapsing skin disease characterized by clusters of sterile, yellow pustules on the palms of the hands and soles of the feet, often on a red, inflamed base. It typically causes discomfort, itching, or pain, significantly disrupting daily activities and quality of life due to its location and persistence. PPP is considered a rare form of pustular psoriasis. It predominantly affects adults, especially women, and is linked to factors like smoking, metal allergies, and genetic mutations (e.g., IL36RN, CARD14). Associated conditions, such as arthritis or thyroid disease, may also occur.

METHODS

Search strategy The systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify studies on palmoplantar pustulosis (PPP) across ethnicities. A comprehensive literature search was conducted across four bibliographical databases (PubMed, Embase, Web of Science, and Cochrane) from their earliest available records to February 1, 2025. The search strategy combined controlled vocabulary (e.g., MeSH terms in PubMed) and free-text keywords related to PPP ("palmoplantar pustulosis," "pustulosis palmaris et plantaris"), ethnicity ("Asian," "European," "ethnic differences"), epidemiology ("prevalence," "incidence"), genetics ("IL36RN," "CARD14"), clinical features ("comorbidities," "manifestations"), and treatment ("therapy," "biologics"). Boolean operators (AND, OR) were used to refine searches, with terms adjusted for each database's syntax.

No language filters initially restricted the search, but only articles in English, German, and Chinese were included during screening. Reference lists of included studies were manually searched for additional relevant publications. Duplicate removal was facilitated by Covidence software. The two authors independently screened titles and abstracts, followed by full-text assessments, resolving discrepancies through discussion. Studies were selected based on their focus on PPP epidemiology, genetics, clinical presentation, or treatment, with a minimum cohort size of five

patients for statistical inclusion, though case reports with novel findings were also considered.

Participant or population The systematic review includes participants diagnosed with palmoplantar pustulosis (PPP), a chronic inflammatory skin condition marked by sterile pustules on the palms and soles. Participants are drawn from studies worldwide, with a focus on comparing individuals across ethnic groups, primarily Asians (e.g., Japanese, Korean, Chinese) and non-Asians (e.g., Europeans, Americans). Studies encompass adults of all ages. Participants are sourced from cohort studies, case series, case-control studies, and randomized controlled trials (RCTs), with a minimum cohort size of five patients for statistical descriptions. Case reports with fewer participants are included only for novel insights. Studies focusing exclusively on paradoxical PPP (post-biologic onset) or quality-of-life/economic outcomes are excluded.

Intervention This systematic review does not involve a specific interventional trial but examines a range of treatments used for palmoplantar pustulosis (PPP) across ethnic groups, as reported in included studies. The interventions assessed are grouped into three categories: conventional therapies, biologics, and novel treatments. A part of this review compares treatment patterns and efficacy across ethnicities (Asians vs. non-Asians) and highlighting the ethnic differences. No uniform intervention is applied; instead, the focus is on synthesizing real-world treatment data from observational and trial-based studies.

Comparator This systematic review does not apply a specific comparative intervention in the traditional sense (e.g., placebo vs. treatment), as it is an observational synthesis. Instead, the comparison focuses on differences in treatment approaches and outcomes for palmoplantar pustulosis (PPP) across ethnic groups. No standardized comparator is applied across all participants; rather, this review seeks to evaluate how each interventions' usage and efficacy differ between ethnicities.

Study designs to be included Cohort studies, case series, case-control studies, randomized controlled trials (RCTs), review articles.

Eligibility criteria Studies were included if they reported on palmoplantar pustulosis (PPP) in any setting, regardless of healthcare context, provided they addressed epidemiology, genetics, clinical presentation, or treatment. Articles in English, German, and Chinese were eligible. Only studies

with a cohort size greater than five patients were included in statistical descriptions and tables, though case reports with fewer participants were retained for novel or unique findings.

Exclusion criteria included studies focusing solely on quality of life or economic aspects of PPP, as these were outside this review's scope. Additionally, articles specifically addressing paradoxical PPP (arising post-biologic use) were excluded due to potential differences in pathogenesis and treatment responses.

Information sources This systematic review utilized four key bibliographical databases (PubMed, Embase, Web of Science, and Cochrane) to gather data on PPP from their inception to February 1, 2025. To enhance completeness, reference lists of included studies were manually reviewed for additional relevant publications.

Main outcome(s) The systematic review evaluated four primary outcomes for palmoplantar pustulosis (PPP) across ethnicities: Epidemiology, Genetic background, Clinical manifestations, Treatment response. Outcomes were narratively described due to heterogeneity, without statistical effect measures like odds ratios, as meta-analysis was unfeasible.

Quality assessment / Risk of bias analysis The quality of primary studies in this systematic review was assessed using standardized tools to ensure reliability of findings. For cohort studies reporting epidemiological data, the Joanna Briggs Institute (JBI) prevalence checklist was applied. Case series were assessed with the JBI case series checklist. The Newcastle-Ottawa Scale (NOS) was used for cohort studies and case-control studies reporting on clinical characteristics. Potential sources of bias, including selection bias and information bias, were narratively addressed.

Strategy of data synthesis A narrative synthesis strategy was employed to integrate findings on PPP across ethnicities, guided by the Synthesis Without Meta-Analysis (SWiM) guidelines. A standardized extraction template was used to document key variables for comparison of clinical characteristics between Asians and non-Asians. Heterogeneity was explored by tabulating differences in study characteristics and outcomes. The two authors independently extracted and synthesized data using Covidence software, resolving discrepancies through discussion.

Subgroup analysis This systematic review does not perform formal statistical subgroup analysis

due to its narrative synthesis approach and the heterogeneity precluding meta-analysis. However, it inherently focuses on subgroup comparisons by stratifying data on PPP across ethnic groups, primarily Asians (e.g., Japanese, Korean, Chinese) versus non-Asians (e.g., Europeans, Americans).

Sensitivity analysis This systematic review does not conduct a formal statistical sensitivity analysis, as it employs a narrative synthesis rather than a meta-analysis due to substantial heterogeneity in study designs, outcome definitions, and reporting methods.

Language restriction No initial language restriction, but only articles in English, German, and Chinese were included during screening.

Country(ies) involved Taiwan.

Keywords Palmoplantar pustulosis; ethnicity; pustular psoriasis.

Contributions of each author

Author 1 - Tsen-Fang Tsai - Tsen-Fang Tsai is responsible for study conception, supervision and critical revision.

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Author 2 - Francis Li-Tien Hsu - Material preparation, data collection and analysis were performed by Francis Li-Tien Hsu. The first draft of the manuscript was written by Francis Li-Tien Hsu.

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