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Immuno-Inflammatory and Endocrine Alterations in Psoriasis Patients in Anbar Province

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Abstract

Background: Psoriasis is a chronic immune-mediated inflammatory disease that is now considered a systemic disease with immune and endocrine features.

Methodology: This case-control study was conducted on 80 Iraqi adults; 45 patients and 35 equivalent controls were incorporated. ELISA and an automated analyzer were used to quantify cytokines (IL-10, IL-17A, IFN-γ) and evaluate thyroid function (TSH, T3, T4), and serum calcium concentrations of the Iraqi patients. Statistical analysis: Independent t-tests; age-stratified evaluation ($p<0.05$ significant), between August 2025 and December 2025.

Results: Patients showed a consistent cytokine imbalance: IL-10 decreased (9.78 ± 2.62 vs 12.12 ± 5.67 pg/mL, p=0.016), IFN-γ increased (69.37 ± 4.26 vs 15.70 ± 2.52 pg/mL, p=0.001), and IL-17A increased (10.58 ± 3.65 vs 8.41 ± 4.23 pg/mL, p=0.016). T3 and T4 were within the reference range, while TSH was elevated (4.68 ± 0.7 vs 2.59 ± 0.8 μIU/mL, $p < 0.001$), suggesting possible subclinical thyroid dysfunction. Calcium levels were reduced (8.30 ± 0.7 vs 8.84 ± 0.8 mg/dL, p=0.002). Age-stratified analyses revealed greater alterations with age.

Conclusion: The findings emphasize the systemic inflammatory and endocrine dysregulation throughout psoriasis. To the best of our knowledge, these results demonstrate the interconnectedness of the immunological and endocrine evaluation in psoriasis and stress the importance of this study when managing psoriasis and the utilization of cytokine profiling and thyroid screening to gauge disease severity and systemic complications of psoriasis.

التغيرات المناعية والالتهابية والغدد الصماء لدى مرضى الصدفية في محافظة الأنبار

سفانة سلام دردوح ومحمد عبود محمد و محمد محمود فرحان

الخلاصة

المقدمة: الصدفية هي اضطراب التهابي مزمن مناعي المنشأ، يُنظر إليه بشكل متزايد على أنه حالة جهازية تنطوي على اضطرابات مناعية وغدد صماء.

العينات وطرق العمل: قامت هذه الدراسة التي اتبعت نهج «الحالة والشاهد» بتقييم مستويات IL-10 وIL-17A وIFN-γ ووظائف الغدة الدرقية (TSH، T3، T4) والكالسيوم في مصل الدم لدى مرضى عراقيين. تم تسجيل 45 مريضاً و35 من المجموعة الضابطة المطابقة. تم قياس السيتوكينات باستخدام ELISA؛ وتم تقييم المعلمات الكيميائية الحيوية باستخدام محلل آلي. استخدم التحليل الإحصائي اختبارات t المستقلة والتقييم المصنف حسب العمر، مع دلالة إحصائية عند $p<0.05$.

النتائج: أظهر المرضى خللاً كبيراً في توازن السيتوكينات: انخفض IL-10 (9.78 ± 2.62 مقابل 12.12 ± 5.67 بيكوغرام/مل، $p=0.016$)، وزاد IFN-γ (69.37 ± 4.26 مقابل 15.70 ± 2.52 بيكوغرام/مل، $p=0.001$)، وزيادة IL-17A (10.58 ± 3.65 مقابل 8.41 ± 4.23 بيكوغرام/مل، $p=0.016$). بقيت مستويات T3 وT4 ضمن النطاقات المرجعية، بينما ارتفع مستوى TSH (4.68 ± 0.7 مقابل 2.59 ± 0.8 ميكرو وحدة دولية/مل، $p<0.001$)، مما يشير إلى احتمال وجود خلل وظيفي غير سريري في الغدة الدرقية. وانخفضت مستويات الكالسيوم (8.30 ± 0.7 مقابل 8.84 ± 0.8 ملغ/ديسيلتر، $p=0.002$). أظهر التحليل المصنف حسب العمر تغيرات أكثر وضوحًا مع تقدم العمر.

الاستنتاج: تسلط النتائج الضوء على الاضطراب الالتهابي والغدد الصماء الجهازي في الصدفية. تؤكد هذه النتائج على أهمية التقييم المناعي والغدد الصماء المتكامل في إدارة الصدفية وتشير إلى الأدوار المحتملة لتحديد ملامح السيتوكينات وفحص الغدة الدرقية في فهم شدة المرض والمضاعفات الجهازية لدى المرضى المصابين في النتائج الإجمالية للدراسة.

1. Introduction

Psoriasis is a recurrent, non-infectious inflammatory dermatologic disease, derived from the Greek words "psora" (itch) and "iasis" (condition), which together connote the disease's dominant symptom (Dutta, Chawla and Kumar, 2018). It is an immune-mediated disease presenting as episodic inflammatory attacks involving the skin and joints. The multisystem nature of this disease stems from its complex interplay with genetic predisposition and environmental factors, causing the observed diversity in clinical manifestation (Alhetheli *et al.*, 2022). In the general population, the estimated worldwide prevalence of psoriasis is 2 to 3%. In Iraq, it is about 2.3%, a figure equal to the world average (Bader and Al-Abboodi, 2025). Psoriasis results from a multifactorial interplay between several immunogenetic risk factors, particularly both innate and adaptive immune dysregulation. Its disease process is inherently rooted in the abnormal activation of T cells, resulting in a chain of pathogenic mechanisms such as chronic inflammation, angiogenesis, and epidermal hyperplasia (Rendon and Schäkel, 2019). Previously, inflammation in psoriasis was thought to be secondary, manifested by excessive keratinocyte proliferation. But this notion has been revolutionized by significant advances in immune-based research, indicating that cell-mediated adaptive immunity is essential to the pathophysiology of disease. Psoriasis currently appears as a disease of inflammatory immune-mediated immunity caused by the interaction of Th1 and Th17 lymphocyte subclasses (Mahmood, Omran and Abdulla, 2024). Psoriasis presents as clinically discrete plaques of irregular size with silvery scales on the skin, mainly on the scalp, lumbosacral and extensor surfaces (elbows and knees), but may manifest as lesions on any other area of the skin, Acanthosis is present with elongated rete ridges into the dermis, along with a drastically increased keratinocyte turnover rate up to ten times that of normal skin, and while genetic predisposition is a factor in familial aggregation, psoriasis is non-contagious and cannot be spread through interpersonal contact (Rahman[1], Yashika and Anurag[4], 2022). Common symptoms include itching, irritation, stinging, and pain. Very rarely, someone is affected on the whole body surface. Two significant signs are the Koebner phenomenon and Auspitz's sign (Dutta, Chawla, and Kumar, 2018). Psoriasis can be roughly classified into cutaneous and systemic types. Clinical subtypes of cutaneous psoriasis include plaque, inverted, erythrodermic, pustular, and guttate forms (Yan *et al.*, 2021). The largest subtype of these is plaque psoriasis, which accounts for more than 80% of all cases (Armstrong and Read, 2020). Besides skin disease, systemic psoriasis is associated with many comorbidities, indicating that the assessment of the patient should be comprehensive. Taking a comprehensive history and examining the joints and other organ systems is a necessary condition for appropriate disease control as per the specific psoriasis subtype and severity of the disease being studied(Yan *et al.*, 2021). The pathogenesis of psoriasis has been under increasing scrutiny in recent years. Psoriasis is thought to be the result of more complex interactions of extracellular cytokine networks and intracellular signalling molecules (Guo *et al.*, 2023). Cytokines signal to the cell membrane and are intercepted by receptors there, prompting intracellular signalling. It sets off a chain reaction that ultimately worsens inflammation (Vičić *et al.*, 2021). Biomarkers are highly relevant in inflammatory skin diseases, improving the diagnostic, prognostic, and treatment monitoring capabilities of patients, and their possible role in personalized therapy is still elucidated (Corbett *et al.*, 2022). Cytokines regulate several physiological processes, such as the organization of the body's cytoskeleton, differentiation of stem cells, embryonic development, cell proliferation, activation, migration, wound healing, survival, and apoptosis. They are especially important in both innate and adaptive immune modulation by mediating humoral, cytotoxic, and cellular immunity. The cytokines modulate the microenvironment, immune cell migration and tissue architecture, intercellular communication between immune and non-immune cells, and modulate inflammation(Carlini *et al.*, 2023). Th17 cells form the major source of IL-17, a cytokine that consistently correlates with the pathophysiology of inflammatory diseases, including psoriasis. Interferon-γ (IFN-γ) is another cytokine related to psoriasis. Natural killer (NK) cells are the predominant source of this cytokine although Th1

cells can also produce IFN-γ (de Alcantara, Reiche and Simão, 2021). Keratinocytes help regulate the immune response by producing IL-10 that acts to suppress the Th1-mediated inflammatory response(de Alcantara, Reiche and Simão, 2021).The thyroid is frequently affected along with psoriasis. Cira (2023) show that diagnosed patients often have low levels of T3/T4 with normal or high TSH; they are also extremely liable to have hypothyroidism and autoimmune thyroid diseases (Cira *et al.*, 2023). Patra, 2024 say Calcium controls the keratinocyte differentiation and proliferation in psoriasis. Serum calcium levels inversely correlate with affected body surface area during psoriasis flares (Patra and Harrison, 2024). This study aimed to investigate the association between key cytokines involved in the pathogenesis of psoriasis (IFN-γ, IL-10, and IL-17A), metrics of thyroid function (TSH, T3, and T4), and calcium in Iraqi patients with psoriasis

2. Materials and Methods

2.1. Study Subjects

This case-control study was conducted on 80 Iraqi adults, comprising 45 patients with psoriasis and 35 age- and sex-matched healthy controls. Following approval from the Iraqi Ministry of Health, participant recruitment and sample collection were performed at the Dermatology Unit of Al-Fallujah Teaching Hospital, Anbar Province, between August 2025 and December 2025.

2.2. Study Groups and Selection Criteria

The patient group included 45 individuals with a confirmed clinical diagnosis of psoriasis, established by consultant dermatologists based on standard clinical assessment. All patients had not received systemic immunosuppressive therapy before sample collection. The control group consisted of 35 healthy individuals.

2.2.1. Inclusion Criteria

Patient Group: Patients diagnosed with psoriasis aged 15-47years. Clinically confirmed diagnosis of psoriasis established by a consultant dermatologist. No systemic immunosuppressive therapy for psoriasis for the past 4 weeks before sample collection. Control Group: Healthy individuals with no personal history of psoriasis, autoimmune diseases, or chronic inflammatory conditions. Age- and sex-matched to the patient group.

2.2.2. Exclusion Criteria (Both Groups)

Presence of any other autoimmune disease. Current pregnancy. History of chronic systemic illness. Recent infection within the past 4 weeks before sample collection. Current use of vitamin or mineral supplements.

2.3. Sample Collection

Venous blood samples (3 mL) were collected from each participant using disposable syringes. The blood was transferred into a gel tube, then left to coagulate for biochemical and immunological tests at room temperature (20–25°C). Centrifugation at 3000 rpm for five minutes was used to separate the serum, which was then aliquoted into Eppendorf tubes and kept at -20°C until further examination.

2.4. Laboratory Analysis

Serum levels of interferon-gamma (IFN-γ), interleukin-10 (IL-10), and interleukin-17A (IL-17A) were measured utilizing sandwich enzyme-linked immunosorbent assay (ELISA) kits (Shanghai Ideal Medical Technology Co., Ltd., Shanghai, China), in accordance with the manufacturers' instructions. Concentrations were determined by interpolating sample optical density (OD) values from standard curves created after each experiment run. Standard curves were generated by graphing optical density values against known concentrations following the subtraction of the zero standard. Optical density data were collected at 450 nm, and sample concentrations were calculated appropriately. The levels of thyroid hormone (T3,

T4), thyroid-stimulating hormone (TSH), and calcium were assessed using the Cobas Roche c411 automated chemistry analyzer (Roche Diagnostics, Germany). All assays were performed according to the manufacturer's recommendations.

2.5. Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics version 24.0 (IBM Corp., Armonk, NY, USA). Data were expressed as mean ± standard deviation (SD). Two-tailed independent-samples t-tests comparing patients suffering from psoriasis to healthy controls were performed. For age-stratified analysis, independent-samples t-tests for each age group were performed to evaluate differences between patients and controls. Correlations of cytokines, thyroid hormones, and calcium were also assessed with Pearson's correlation coefficient (r). A p-value < 0.05 was considered statistically significant.

2.6. Ethical Approval

Approval to conduct the study and collect clinical samples was obtained from the Research Committee, Anbar Health Directorate, Iraqi Ministry of Health (Decision No. 2025058, dated 12 August 2025), which authorized the implementation of the study in the affiliated healthcare institutions. Subsequently, ethical approval was obtained from the Research Ethics Committee, College of Applied Science, University of Fallujah, Iraq (Reference No. AS-EC/0015, dated 13 January 2026). Written informed consent was obtained from all participants prior to sample collection.

3. Results

3.1. Demographic and Clinical Characteristics of the Study Population

A total of 80 participants participated, including 45 psoriasis patients and 35 age- and sex-matched healthy controls. Psoriasis patients were age-divided into three groups: 44% were 15–25 years, 38% were 26–36 years, and 18% were 37–47 years. Results showed the control group with a comparable distribution with 46% aged 15–25, 40% 26–36, and 14% 37–47 years. The proportions were comparable in that patients and controls were matched by age, limiting the risk of confounding effects in subsequent analyses Table1. No statistically significant changes were detected in age group distribution between psoriasis patients and healthy controls.

Table1: Age Distribution of Patients and Controls.

Age groups (years)	Patients (%)	Controls (%)
15–25	44%	46%
26–36	38%	40%
37–47	18%	14%

3.2. Laboratory Parameter

Among the laboratory measures, IFN-γ, IL-17A, IL-10, TSH, and calcium exhibited statistically significant changes between psoriasis patients and controls. Interferon gamma (IFNγ) was significantly enhanced ($p < 0.001$), interleukin 17A (IL-17A) increased ($p = 0.016$), and interleukin 10 (IL-10) reduced ($p = 0.016$), indicating a cytokine imbalance. TSH levels were markedly elevated in patients ($p < 0.001$), although calcium levels were dramatically decreased ($p = 0.002$), suggesting endocrine and metabolic disturbances. T3 and T4 levels did not exhibit significant differences ($p = 0.504$ and $p = 0.229$, respectively), indicating an absence of substantial thyroid hormone disruption in this group, as illustrated in Table2.

Table2: Comparison of Biochemical and Immunological Parameters Between Patients and Controls.

Parameter	Patients (Mean ± SD)	Controls (Mean ± SD)	p-value
IFN-γ	69.37 ± 4.26	15.70 ± 2.52	0.001
IL-17A	10.58 ± 3.65	8.41 ± 4.23	0.016
IL-10	9.78 ± 2.62	12.12 ± 5.67	0.016
TSH	4.68 ± 0.7	2.59 ± 0.8	0.001
T3	121.88 ± 18	125.42 ± 29	0.504
T4	7.75 ± 0.8	7.43 ± 1.5	0.229
Calcium	8.30 ± 0.7	8.84 ± 0.8	0.002

3.3. Age-stratified Analysis

Age-stratified analysis revealed significant immunological and biochemical differences between psoriasis patients and healthy controls across three age groups. IFN-γ was significantly elevated in all patient groups (Fig.1A, 15–25 years: p = 0.001, 26–36 years: p = 0.001, 37–47 years: p = 0.001). IL-17A showed an increasing trend with age, peaking in the oldest patients, although this did not reach statistical significance in any age group (Fig.1B, 15–25 years: p = 0.9480, 26–36 years: p = 0.494, 37–47 years: p = 0.1510). IL-10 was significantly reduced only in patients aged 37–47 years (Fig.1C, p = 0.0120), while younger groups showed no significant differences (15–25 years: p = 0.1870, 26–36 years: p = 0.293). TSH levels were consistently higher in patients and increased with age (Fig.1D, 15–25 years: p = 0.001, 26–36 years: p = 0.001, 37–47 years: p = 0.0030). Serum calcium was significantly lower in the youngest and oldest patient groups (Fig.1E, 15–25 years: p = 0.0010, 37–47 years: p = 0.0010), with no significant difference in the middle age group (26–36 years: p = 0.071). T3 levels did not differ significantly between patients and controls across any age group (Fig.1F, 15–25 years: p = 0.9540, 26–36 years: p = 0.520, 37–47 years: p = 0.2180). T4 levels were also not significantly different in any age group (Fig.G, 15–25 years: p = 0.1813, 26–36 years: p = 0.476, 37–47 years: p = 0.1950).

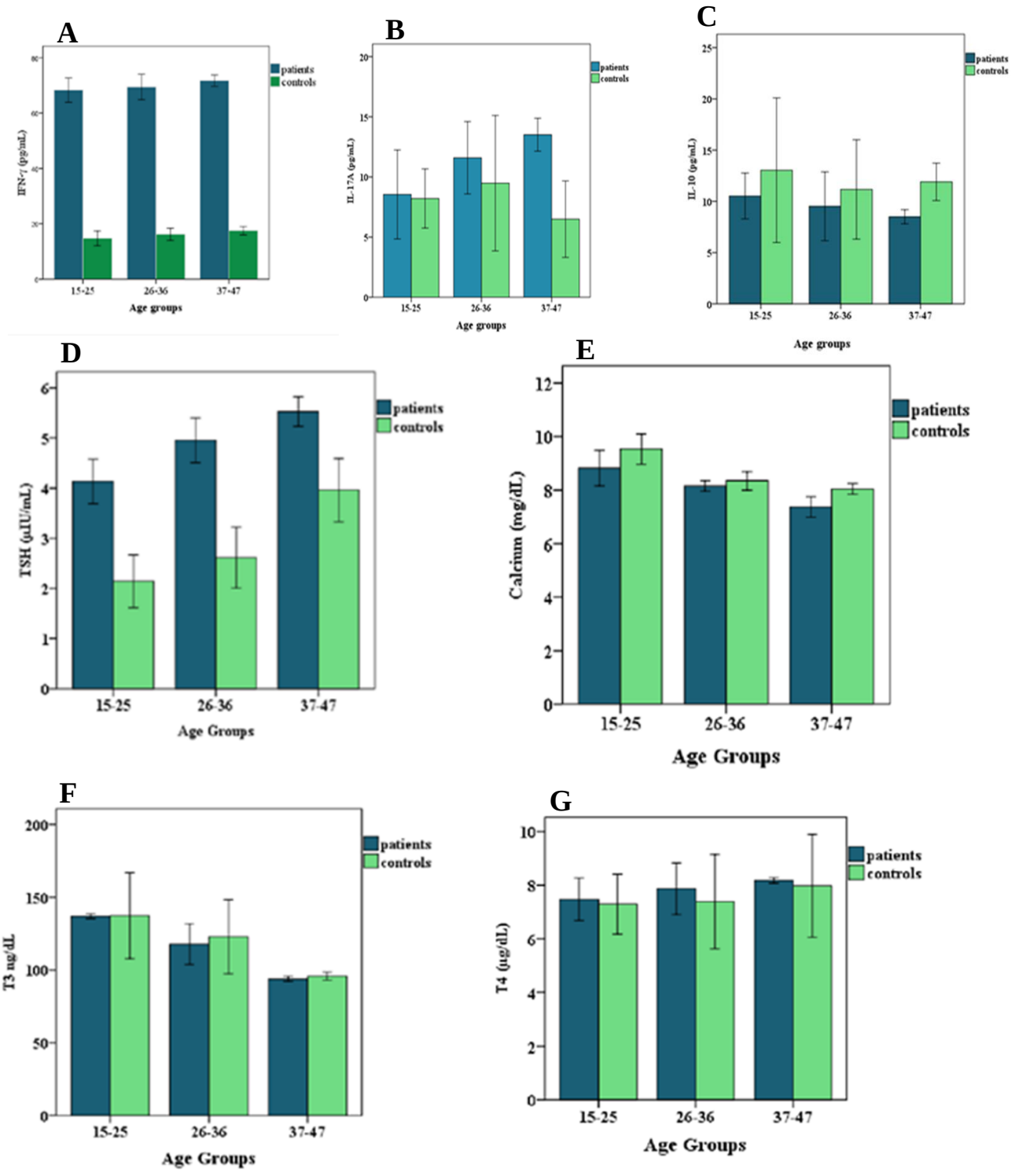

Figure1: Comparison of Inflammatory Cytokines, Thyroid Hormones, And Calcium Levels Between Patients and Healthy Controls Stratified by Age Group. Bar graphs represent the mean ± standard deviation (SD) values of **(A)** interferon-γ (IFN-γ), **(B)** interleukin-17A (IL-17A), **(C)** interleukin-10 (IL-10), **(D)** thyroid-stimulating hormone (TSH), **(E)** serum calcium, **(F)** triiodothyronine (T3), and **(G)** thyroxine (T4) among patients and healthy controls across three age groups (15–25, 26–36, and 37–47 years). Blue bars represent patients, whereas green bars represent healthy controls. Error bars indicate the standard deviation (SD).

3.4. Correlation Analysis of Cytokines, Thyroid Hormones, and Calcium in Psoriasis Patients

Pearson correlation analysis was performed to examine the interrelationships between cytokines (IFN-γ, IL-10, IL-17A), thyroid hormones (T3, T4, TSH), and calcium in the psoriasis patient group, as presented in Fig.2.

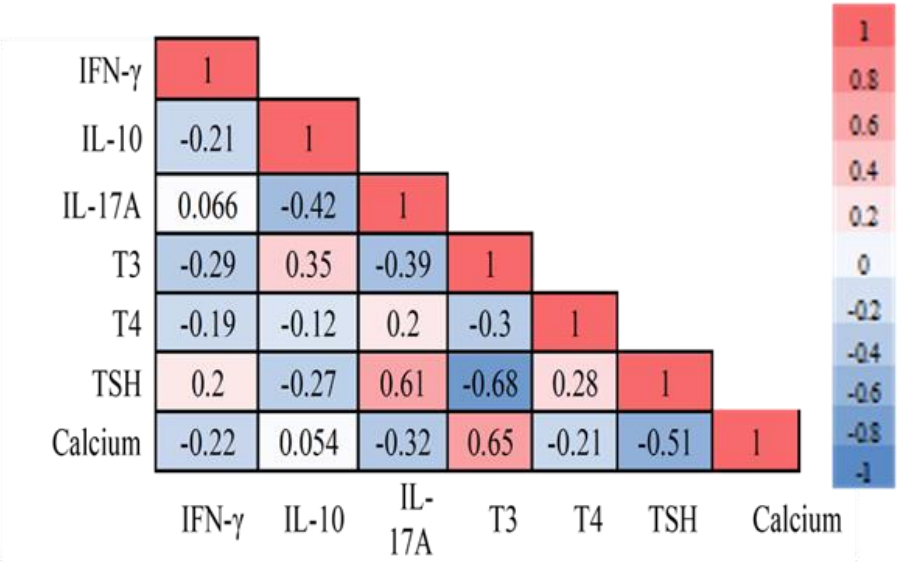

Figure2: The correlation matrix illustrates the correlations between the examined parameters, with coefficients varying from −1 to +1. Positive values signify direct correlations, whereas negative values denote inverse correlations. The majority of correlations were either weak or non-significant, with statistical significance defined as $P \leq 0.05$.

4. Discussion

4.1. Immunological and Biochemical Alterations in Psoriasis Patients

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by complex interactions between environmental triggers, genetic susceptibility, and dysregulation of innate and adaptive immunity. The present study investigated the pro-inflammatory cytokine imbalance in Iraqi psoriasis, which was characterized by an overproduction of IFN-γ and of IL-17A, with decreased IL-10 as the anti-inflammatory cytokine. The result may reflect the established Th1/Th17 paradigm in psoriasis—IL-10 exerts counter-regulatory effects while IFN-γ (Th1) and IL-17A (Th17) facilitate keratinocyte hyperproliferation and sustain chronic inflammation (Armstrong and Read, 2020; Donniacuo *et al.*, 2025; Ma and Ma, 2026). Donniacuo et al. carried out a detailed study on the relationship between autoimmune diseases and pro-inflammatory cytokines, including major cytokines, for example, IL-17 and IFN-γ, which are significantly involved in the development and course of autoimmune diseases. Such findings may be relevant to psoriasis, as IFN-γ and IL-17 promote keratinocyte hyperproliferation and chronic inflammation, and IL-10 is a critical anti-inflammatory cytokine involved in modulating immune tolerance and resolution (Donniacuo *et al.*, 2025). Similarly, Li et al. (2025) emphasized that the IL-23/Th17 axis is central to psoriasis pathogenesis, with IL-17A upregulating pro-inflammatory mediators and fostering proliferation of keratinocytes (Li *et al.*, 2025). A balance between pro-inflammatory and anti-inflammatory cytokines is essential for immune homeostasis (Li *et al.*, 2025). Its work is one of a growing number of recent papers on cytokine imbalance; in fact, it is widely accepted that psoriasis is produced or spread among many ethnic groups. The high TSH levels in patients with psoriasis were significantly higher than in the controls. But levels of T3 and T4 did not change. The presence of such a pattern in which there's high TSH but normal amounts of thyroid hormone suggests the possibility of subclinical hypothyroidism, a condition that has been recognized more frequently in the context of psoriasis(Cira *et al.*,

2023; Ruiz-Villaverde *et al.*, 2025). There are several studies of psoriasis and its association with autoimmune thyroid disease, which reveal inconsistent findings. Ruffilli et al. (2017) recently conducted a systematic review of the literature on thyroid disease. Most studies in adults with psoriasis and psoriatic arthritis showed a greater incidence of thyroid autoimmunity and subclinical (Ruffilli *et al.*, 2017). This discrepancy underscores the need for population-specific investigations. There are those, particularly in our patients, with an average TSH of 4.68 μIU/mL above the relatively standard upper range of normal (ca 4.2 to 4.5 μIU/mL), Our findings may indicate possible subclinical thyroid dysfunction in a proportion of patients and warrant further clinical evaluation. Ruiz-Villaverde et al. recently conducted a cross-sectional study (2025) in 401 moderately severe psoriasis patients and found thyroid dysfunction in 4.2% of those being assigned hypothyroidism, with a largely subclinical phenotype. While their results suggest that hypothyroidism may be a potential comorbidity of psoriasis, rather than the direct cause of the disorder, with overlapping inflammatory pathways and a lack of association leading to separate paths (Ruiz-Villaverde *et al.*, 2025). Patients in their cohort had a higher mean age of onset (mean age 57.4 years), whereas their affected patients had a lower age than our patients (mean age 15 to 47 years), despite a significant increase in the TSH. These differences may be related to population-specific genetic and environmental factors, as well as autoimmune susceptibility and chronic inflammation (Ruiz-Villaverde *et al.*, 2025). Recently, Mendelian randomization tests have helped to define the genetic basis of the relationship between psoriasis and thyroid dysfunction. Cong et al. (2025) provided the genetic information indicating a suggestive association between hypothyroidism and risk of developing psoriasis (OR = 1.059, p = 0.038), and there is a robust association with psoriatic arthritis (OR = 1.184, $p = 2.40 \times 10^{-5}$)(Cong *et al.*, 2025). In the inverse MR analyses, psoriasis vulgaris also indicated a significantly higher risk of Graves' disease (OR = 1.113, p = 0.002) and hyperthyroidism (OR = 1.053, p = 0.040), but a suggestive inverse association was found with a decreased risk of hypothyroidism (OR = 0.977, p = 0.025) (Cong *et al.*, 2025). These bidirectional causative associations highlight the complex dynamics of the relationship between thyroid autoimmunity and psoriatic disease and also underscore the association between common inflammatory pathways, including cytokines such as IL-17 and IL-23, which are associated with both disorders (Cira *et al.*, 2023; Prema and Shanmugamprema, 2025). Cira et al. (2023) conducted a thorough study and reported that psoriatic patients commonly have hormonal aberration with low T3/T4 while their TSH level is at a normal or greater level, which confirmed that the presence of multiple thyroid involvements is common in individuals with psoriasis. Risks are considerably elevated for hypothyroidism (OR =1.34–1.38), hyperthyroidism (OR =1.17–1.32), autoimmune thyroid disease (OR =1.42–2.05), Hashimoto's thyroiditis (OR = 1.47–2.09), and Graves' disease (OR = 1.26–1.38), indicating that they are intertwined (Cira *et al.*, 2023). Our results may reflect and extend previous findings by suggesting that elevated TSH, in the absence of significant changes in T3 and T4, may represent a pattern compatible with possible subclinical thyroid dysfunction in Iraqi patients with psoriasis. This finding may reflect chronic low-grade inflammatory effects on the hypothalamic–pituitary–thyroid axis(Ruffilli *et al.*, 2017). In this study, it was shown that serum calcium levels of psoriasis patients were drastically reduced compared to those of controls. This result may reflect the well-established role of calcium in keratinocyte development and the function of the epidermal barrier. Shao et al.'s recent meta-analysis and comprehensive review (2025) comprising 113 studies of 7,014 patients revealed that serum levels of calcium decrease significantly in patients with immune-mediated inflammatory skin diseases, including psoriasis (Shao *et al.*, 2025). Recent works have elucidated the mechanistic association between hypocalcemia and exacerbation of psoriasis. Normal keratinocyte differentiation demands calcium and the final differentiation is determined by an epidermal calcium gradient; disturbance of this gradient is pathological in psoriatic lesions, Uchida et al. (2025) investigated the key role played by ion channels, particularly calcium channels, in the pathophysiology of psoriasis and pointed out that when calcium channels become dysregulated, inflammation, failure of the epidermal barrier, and malfunction of keratinocytes are possible. High calcium levels in

suprabasal layers activate the calcium-sensing receptor (CaSR) and transient receptor potential canonical (TRPC) channels, increasing intracellular calcium and driving terminal differentiation. However, low concentrations in the basal layer of normal epidermis encourage proliferation. Psoriasis results from the decrease of capacitive calcium inflow and TRPC channel down-regulation resulting from this gradient breaking down, especially at the level of keratinocytes (Uchida *et al.*, 2026). Patra et al(2024) performed a systematic review of data showing that serum calcium levels are inversely associated with the body surface area affected during plaque psoriasis exacerbations, which investigated trace elements and minerals in psoriasis and found calcium regulation for differentiation and proliferation of cells associated with psoriasis pathogenesis (Patra and Harrison, 2024). The last investigations have repeatedly shown a negative correlation between serum calcium and psoriasis severity, where lower calcium concentrations correlate with more pronounced disease activity. Hashem et al. (2025) recently described a case of a 52-year-old patient with persistent hypoparathyroidism who had episodes of severe psoriatic plaques after instances of significant hypocalcaemia (7.2 mg/dL). After extensive calcium repletion, the dermal lesions exhibited remarkable improvement. The authors emphasized that aberrant inflammatory processes and impaired skin homeostasis arise from hypocalcaemia's disruption of calcium-dependent keratinocyte differentiation pathways(Hashem *et al.*, 2025). Although the decreases in our cohort were slight (around 0.5 mg/dL), they might be the result of long-term, low-grade disruptions in calcium regulation that eventually lead to compromised epidermal differentiation and persistent inflammation(Patra and Harrison, 2024; Uchida *et al.*, 2026).

4.2. Age-stratified Analysis

Psoriasis commonly presents between the ages of 15 and 25 years, with a reported mean age of onset of 33 years; approximately 75% of cases develop before the age of 46 years (Yamamoto and Kawada, 2018; AL-Sariay *et al.*, 2021). A bimodal age distribution has also been described, with peak incidences observed during adolescence and late adulthood (Iskandar *et al.*, 2021). Epidemiological evidence indicates that psoriasis prevalence increases with advancing age, with the highest burden reported in individuals aged 50–69 years (Maksymowych *et al.*, 2018), (Hasan and Alajeel, 2021). There is no gender difference with the disease, and the disease presents equally in males and females (Scotti *et al.*, 2018; Kizilyel, Akdeniz and Metin, 2019). Aging has a critical factor called inflame-maging, which denotes a chronic, diffuse but low-grade inflammatory state caused by dysregulation of the cytokine network and reduced immunity(Rea *et al.*, 2018).

An age-stratified analysis elucidated age-linked variations in immunological and endocrine phenotypes evidenced in Figure1A–1G, of the current investigation. IFN-γ and IL-17A were higher among 15–25-year-olds, as shown for Th1/Th17 immune activation in acute and early psoriasis. Total IL-10 declined significantly in older subjects (37–47 years of age), whereas IL-17A showed an age-related increasing trend without reaching statistical significance (Figure 1A–1C). These results parallel immunosenescence and old age effects in immune modulation. Liu et al. (2025) have presented BACH2 as a gene candidate for immunosenescence and exerting control over T cell activation and the development of psoriasis as a consequence(Liu *et al.*, 2025). Besides, the acceleration of phenotypic age is linked with the increased risk of psoriasis and elevated all-cause mortality(Zhao *et al.*, 2025). A systematic review by Dulai et al. (2025) reported that individuals with psoriatic arthritis—but not those with psoriasis alone—exhibited accelerated epigenetic aging compared to healthy controls (Dulai *et al.*, 2026) Our evidence on age-associated immune and endocrine alterations in case of psoriasis–in particular the increase in TSH and IL-17A with age–hints that age-modifying chronic inflammation, which is independent of joint involvement, could be a factor in premature biological aging (psoriatic arthritis was not investigated in this article). These observations are evidence for the continued need of studies with psoriatic arthritis patients to establish the specific effects of cutaneous inflammation versus articular inflammation on trajectories of aging. There was also an age-dependent difference in thyroid function found. As shown in Figure 1D. TSH levels increased progressively across age groups in the

patients with psoriasis. Such patterns have been consistent with results by Ruiz-Villaverde et al. (2025) that psoriatic patients with thyroid dysfunction were predominantly older and showed subclinical hypothyroidism(Ruiz-Villaverde *et al.*, 2025). There was a bimodal distribution of calcium concentration, with a significant reduction in both the youngest and oldest patient groups, with no significant change in the middle-aged group (Figure 1E). This finding emphasizes the critical aspect of keratinocyte differentiation and the epidermal barrier in which calcium is necessary, as reported by Hashem et al. (2025) with noticeable psoriasis exacerbation induced by hypocalcemia and relief of clinical symptoms after calcium restoration(Hashem *et al.*, 2025). Based on our findings, a case-control study conducted by Robati et al. (2013) with 30 psoriasis patients and 30 healthy controls showed that no statistically significant differences were found for serum concentrations of T3 or T4 between both groups(Robati *et al.*, 2013), as shown in Figure 1F and 1G. Together, our data emphasize the fact that age is a defining factor as it relates to immune-endocrine profile in psoriasis and call for adopting age-selective strategies for optimal clinical evaluation and disease management.

4.3. Correlation Analysis

As per established Th17 activity in psoriasis, IL-10 and IL-17A were significantly correlated negatively ($r = -0.416$, $p = 0.0045$). This supports the prior studies of elevated IL-17A and lowered IL-10 levels in psoriatic patients, which highlighted the role of cytokine dysregulation in disease activity(Kutwin *et al.*, 2021). The current work provides population-specific reference values for Iraqi patients and integrates the international literature around cytokine alterations, bolstering the support that cytokine dysregulation is more directly related to the etiology of psoriasis in different ethnic populations.

IL-17A was also positively related to thyroid-stimulating hormone (TSH) levels ($r = 0.61$, $p < 0.001$), indicating a significant relationship between Th17-mediated inflammation and activation of the thyroid axis. This is consistent with recent clinical data reported from Ruiz-Villaverde et al. (2025) that showed a remarkable prevalence of subclinical hypothyroidism in psoriatic patients and may be mediated by common inflammatory pathways with Th17 cytokines (Ruiz-Villaverde *et al.*, 2025). A negative correlation between T3 and IL-17A was strongly reported in the psoriasis case population ($r = -0.39$, $p = 0.0074$). This may indicate the well-studied association between psoriasis and autoimmune thyroid diseases in terms of immunopathological pathways, especially the IL-23/Th17 axis(Hansen *et al.*, 2019; Panopio and Loconico-Tumalad, 2024). Hansen et al. (2019) suggested that interleukin-17-mediated mechanisms and common loci of genetic vulnerability are implicated in these diseases (Hansen *et al.*, 2019). The negative correlation that was found in this investigation implies a complex relationship between thyroid hormone signaling and Th17-mediated inflammation in psoriasis. Regarding thyroid function, the typical negative feedback loop of T3 and TSH ($r = -0.68$, $p < 0.001$) persisted, thus stressing that a central regulation of the hypothalamic-pituitary-thyroid axis did not break down even after elevation in TSH levels. The current findings are in agreement with previous reports from individuals with psoriasis, a condition that has become more accepted in the psoriatic community (Ruiz-Villaverde et al. (2025) (Ruiz-Villaverde *et al.*, 2025). IFN-γ was unrelated to IL-10 ($r = -0.21$, $p = 0.1653$), IL-17A, thyroid hormones or calcium levels. This finding may reflect the predominantly local role of IFN-γ within psoriatic lesions, where its role is primarily found in lesions as opposed to in the systemic domain. de Alcantara et al. (2021) have observed that chronic psoriasis can overburden the anti-inflammatory feedback mechanism, and a disjunction is documented between Th1 and regulatory cytokine networks(de Alcantara, Reiche and Simão, 2021). A significant positive association was found between T3 and calcium ($r = 0.65$, $p < 0.001$). Thyroid hormones have a physiological role in calcium metabolism, according to recent studies. These findings support the physiological role of thyroid hormones in calcium metabolism by balancing minerals and bone remodeling (Stanley and Martin, 2023). Grabarek et al. (2025) demonstrated that successful treatment in psoriasis restores calcium homeostasis, supporting the concept that inflammation-associated disturbances in calcium homeostasis may improve following

treatment (Grabarek *et al.*, 2025). The strong negative correlation of TSH with calcium ($r = –0.51$, $p < 0.001$) also supports the connection of endocrine and metabolic dysregulation in psoriasis. This relationship may be related to the well-established effects of thyroid hormones on calcium homeostasis since thyroid hormones cause bone remodelling through their direct action on osteoblasts and osteoclasts, and consequently in calcium metabolism (Cira *et al.*, 2023; Patra and Harrison, 2024). The fact that low calcium levels are observed independent of substantial thyroid hormone changes in the present cohort suggests a variety of mechanisms underlying calcium disturbances in psoriasis: chronic inflammation, impaired keratinocyte differentiation, and endocrine dysregulation (Prema and Shanmugamprema, 2025; Uchida *et al.*, 2026). A negative connection exists between IL-17A and calcium ($r = –0.32$, $p = 0.0319$), indicating that Th17-mediated inflammation may disrupt calcium homeostasis. Calcium signaling via the calcineurin-NFAT pathway is crucial for IL-17 synthesis and T cell activation (Vaeth, Kahlfuss and Feske, 2020). Uchida et al. (2025) noted that dysregulation of calcium channels in psoriasis bypasses normal homeostatic controls, contributing to both keratinocyte dysfunction and sustained inflammation (Uchida *et al.*, 2026). This work supports that psoriasis is not only a skin-limited disorder, but a systemic disease with widespread health-related risks, in which immune cells, cytokines, and multiple organ system involvement are a dynamic process(Prema and Shanmugamprema, 2025; Ma and Ma, 2026). Dysregulation of calcium channels may play a key role in driving inflammation, skin barrier dysfunction, and keratinocyte malfunction, respectively, and the thyroid dysfunction reported may be another systemic manifestation of the chronic inflammatory state (Prema and Shanmugamprema, 2025; Uchida *et al.*, 2026). Th17-activated inflammatory pathways may also function without reference to the mechanisms that control thyroid function and calcium homeostasis during disease, because there was no association with other markers in the patient population for IL-17A. Uchida et al. (2025) conclude that the abnormal functioning of inflammatory pathways and calcium channels may also escape traditional homeostatic machinery, adding to the multifactorial pathophysiology of psoriasis(Uchida *et al.*, 2026). Similarly, while measurements of T4 showed no significant correlations with other measures, this is consistent with normal thyroid hormone levels remaining unchanged despite high TSH, a pattern established earlier on by Cira et al. (2023) in psoriatic populations(Cira *et al.*, 2023).

Conclusion

In this study, we aimed to investigate the cytokine profiles, thyroid function, and calcium homeostasis of Iraqi patients with psoriasis. The core findings indicated severe pro-inflammatory cytokine imbalance (IFN-γ, IL-17A increased, IL-10 decreased) and a high level of TSH, with stable T3 and T4 in agreement with subclinical hypothyroidism, and lower serum calcium levels. Older individuals showed more severe immunological and endocrine derangements in age-stratified studies. These findings offer insights into immunology, endocrinology, and mineral metabolism, conceptualizing psoriasis as a systemic inflammatory disorder with multidisciplinary implications, and they support the idea that routine evaluation of thyroid function and calcium levels, especially in the elderly, may have clinical significance.

Conflicts of Interest

The authors declare no conflict of interests

References

AL-Sariay, A.H. *et al.* (2021) "Genetic study of psoriasis disease: a review," *Plant Archives*, 21(1), pp. 2046–2048.
de Alcantara, C.C., Reiche, E.M.V. and Simão, A.N.C. (2021) "Cytokines in psoriasis," *Advances in clinical chemistry*, 100, pp. 171–204.
Alhetheli, G. *et al.* (2022) "Vitamin D receptor gene polymorphism ApaI as a predisposing factor for psoriasis and its relation with serum vitamin D levels and psoriasis severity," *Cureus*, 14(12).
Armstrong, A.W. and Read, C. (2020) "Pathophysiology, clinical presentation, and treatment of psoriasis: a review," *Jama*, 323(19), pp. 1945–1960.
Bader, R.M. and Al-Abboodi, S.M.H. (2025) "Serum Level of High Mobility Group Box1 Protein Among Iraqi Psoriatic Patients and its Relationship with Disease Severity and Comorbidities," *Al-Rafidain Journal of Medical Sciences (ISSN 2789-3219)*, 8(2), pp. 176–181.
Carlini, V. *et al.* (2023) "The multifaceted nature of IL-10: regulation, role in immunological homeostasis and its relevance to cancer, COVID-19 and post-COVID conditions," *Frontiers in immunology*, 14, p. 1161067.
Cira, C.-I. *et al.* (2023) "Conundrum for psoriasis and thyroid involvement," *International Journal of Molecular Sciences*, 24(5), p. 4894.
Cong, X. *et al.* (2025) "Causality between thyroid disease and psoriasis: Bidirectional Mendelian randomization analysis.," *Medicine*, 104(36), p. e43426. Available at: https://doi.org/10.1097/MD.0000000000043426.
Corbett, M. *et al.* (2022) "Biomarkers of systemic treatment response in people with psoriasis: a scoping review.," *The British journal of dermatology*, 187(4), pp. 494–506. Available at: https://doi.org/10.1111/bjd.21677.
Donniacuo, A. *et al.* (2025) "Comprehensive profiling of cytokines and growth factors: pathogenic roles and clinical applications in autoimmune diseases," *International Journal of Molecular Sciences*, 26(18), p. 8921.
Dulai, A.S. *et al.* (2026) "Systematic Review of Accelerated Epigenetic Aging in Chronic Inflammatory Dermatology Conditions," *International Journal of Dermatology*, 65(2), pp. 273–280.
Dutta, S., Chawla, S. and Kumar, S. (2018) "Psoriasis: A review of existing therapies and recent advances in treatment," *differentiation*, 4(1), pp. 12–23.
Grabarek, B.O. *et al.* (2025) "Monitoring Minerals and Redox Balance During Cyclosporine A Therapy in Psoriasis," *Journal of Clinical Medicine*, 14(22), p. 7908.
Guo, J. *et al.* (2023) "Signaling pathways and targeted therapies for psoriasis.," *Signal transduction and targeted therapy*, 8(1), p. 437. Available at: https://doi.org/10.1038/s41392-023-01655-6.
Hansen, P.R. *et al.* (2019) "Thyroid function in psoriasis," *British Journal of Dermatology*, 181(1), pp. 206–207.
Hasan, A.S. and Alajeel, A.I. (2021) "Psoriasis in Al-Anbar Government clinical and epidemiological study," *Periodicals of Engineering and Natural Sciences*, 9(3), pp. 393–399.
Hashem, W. *et al.* (2025) "Severe Hypocalcemia as an Unexpected Trigger for Psoriasis Exacerbation in Chronic Hypoparathyroidism: A Case Report.," *Clinical medicine insights. Case reports*, 18, p. 11795476251404256. Available at: https://doi.org/10.1177/11795476251404256.
Iskandar, I.Y.K. *et al.* (2021) "Systematic review examining changes over time and variation in the incidence and prevalence of psoriasis by age and gender," *British Journal of Dermatology*, 184(2), pp. 243–258.
Kizilyel, O., Akdeniz, N. and Metin, M.S. (2019) "Investigation of oxidant and antioxidant levels in patients with psoriasis," *Turkish journal of medical sciences*, 49(4), pp. 1085–1088.
Kutwin, M. *et al.* (2021) "An analysis of IL-10, IL-17A, IL-17RA, IL-23A and IL-23R expression and their correlation with clinical course in patients with psoriasis," *Journal of clinical medicine*, 10(24), p. 5834.
Li, L. *et al.* (2025) "Interventions in cytokine signaling: novel horizons for psoriasis treatment," *Frontiers in Immunology*, 16, p. 1573905.
Liu, Y. *et al.* (2025) "Identification of a novel immunosenescence-related genes and integrative analyses in patients with psoriasis," *Human Immunology*, 86(1), p. 111218.
Ma, R. and Ma, W. (2026) "The Common Immune Pathological Mechanism and Therapeutic Challenges of Chronic Skin Diseases: Psoriasis, Atopic Dermatitis and Vitiligo," *Frontiers in Bioscience-Landmark*, 31(1).
Mahmood, N.S., Omran, R. and Abdulla, A.A. (2024) "A brief epidemiologic review of psoriasis," *Medical Journal of Babylon*, 21(4), pp. 757–765.
Maksymowych, W. *et al.* (2018) "Construct Validation of The Screening for Inflammatory Pain in the Lower Back Questionnaire: Data from the Screening in Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Cohort," *2018 ACR/ARHP Annual Meeting*. ACR.
Panopio, A.-C.G. and Loconico-Tumalad, L.-L. (2024) "A case of concomitant psoriasis vulgaris and Graves' Disease in a 27-year-old Filipino female," *Journal of the Philippine Dermatological Society*, p. 18.
Patra, P. and Harrison, T. (2024) "Trace elements in psoriasis presentation and treatment.," *Archives of dermatological research*, 316(10), p. 728. Available at: https://doi.org/10.1007/s00403-024-03468-1.
Prema, S.S. and Shanmugamprema, D. (2025) "Systemic Psoriasis: from molecular mechanisms to global management strategies," *Clinical Reviews in Allergy & Immunology*, 68(1), p. 79.
Rahman[1], M., Yashika, M.K. and Anurag[4], O.S. (2022) "A Review on Psoriasis," *NeuroQuantology*, 20(16), pp. 5786–5793.
Rea, I.M. *et al.* (2018) "Age and age-related diseases: role of inflammation triggers and cytokines," *Frontiers in*

immunology, 9, p. 586.
Rendon, A. and Schäkel, K. (2019) "Psoriasis pathogenesis and treatment," *International journal of molecular sciences*, 20(6), p. 1475.
Robati, R.M. *et al.* (2013) "Association of psoriasis severity with serum prolactin, thyroid hormones, and cortisol before and after treatment," *The scientific world journal*, 2013(1), p. 921819.
Ruffilli, I. *et al.* (2017) "Psoriasis, Psoriatic Arthritis, and Thyroid Autoimmunity.," *Frontiers in endocrinology*, 8, p. 139. Available at: https://doi.org/10.3389/fendo.2017.00139.
Ruiz-Villaverde, R. *et al.* (2025) "Subclinical Hypothyroidism in Moderate-to-Severe Psoriasis: A Cross-Sectional Study of Prevalence and Clinical Implications," *Diseases*, 13(8), p. 237.
Scotti, L. *et al.* (2018) "Prevalence and incidence of psoriatic arthritis: a systematic review and meta-analysis," *Seminars in arthritis and rheumatism*. Elsevier, pp. 28–34.
Shao, X. *et al.* (2025) "Trace Elements and Risk of Immune-Mediated Skin Disease: A Systematic Review and Meta-analysis," *Nutrition Reviews*, 83(8), pp. 1462–1474.
Stanley, S. and Martin, A. (2023) "Thyroid, parathyroid hormones and calcium homeostasis," *Anaesthesia & Intensive Care Medicine*, 24(10), pp. 639–643.
Uchida, H. *et al.* (2026) "Role of ion channels in immune regulation of psoriasis.," *Current opinion in immunology*, 98, p. 102688. Available at: https://doi.org/10.1016/j.coi.2025.102688.
Vaeth, M., Kahlfuss, S. and Feske, S. (2020) "CRAC channels and calcium signaling in T cell-mediated immunity," *Trends in immunology*, 41(10), pp. 878–901.
Vičić, M. *et al.* (2021) "Current concepts of psoriasis immunopathogenesis," *International journal of molecular sciences*, 22(21), p. 11574.
Yamamoto, T. and Kawada, A. (2018) "Clinical characteristics of Japanese patients with psoriatic arthritis: comparison with East Asian countries," *The Journal of Dermatology*, 45(3), pp. 273–278.
Yan, B.-X. *et al.* (2021) "Cutaneous and systemic psoriasis: classifications and classification for the distinction," *Frontiers in medicine*, 8, p. 649408.
Zhao, W.-Q. *et al.* (2025) "Psoriasis and phenotypic age acceleration in relation to all-cause and cardiovascular disease mortality risks in US adults," *European Journal of Medical Research*, 30(1), p. 894.