

Immunohistochemical Expression of Ki-67 and Epidermal Thickness in Psoriasis Vulgaris: A Comparative Study with Healthy Controls

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Abstract: ***Background:** Psoriasis vulgaris is a chronic immune-mediated skin disease marked by keratinocyte hyperproliferation. Ki-67 is a nuclear proliferation marker widely used to quantify this activity. Data on Ki-67 expression and epidermal thickness in Saudi patients are limited. **Objective:** To compare Ki-67 immunohistochemical positivity and epidermal thickness between patients with psoriasis vulgaris and healthy controls. **Methods:** This retrospective comparative cross-sectional study included 50 patients with histologically confirmed psoriasis vulgaris and 50 controls from multiple hospitals in Saudi Arabia, between May 2024 and May 2025. Skin biopsies were stained with hematoxylin and eosin and immunohistochemically for Ki-67. Epidermal thickness was measured in micrometres. Groups were compared using the chi-square test and the independent-samples t-test. **Results:** The groups were comparable in sex distribution (males 66.0% vs. 60.0%; $P = 0.534$). Among patients, disease was mild in 20.0%, moderate in 38.0% and severe in 42.0%. Ki-67 positivity was higher in psoriasis than in controls (60.0% vs. 40.0%; $P = 0.046$). Mean epidermal thickness was $43.1 \pm 32.7 \mu\text{m}$ in psoriasis and $58.3 \pm 27.3 \mu\text{m}$ in controls (mean difference $-15.2 \mu\text{m}$; 95% CI -27.2 to -3.2 ; $P = 0.013$). **Conclusions:** Ki-67 positivity was more frequent in psoriatic skin than in healthy control skin, although statistical significance depended on the test applied. The unexpected lower epidermal thickness in the psoriasis group requires verification of the original measurements and sampling procedures. Further studies using quantitative Ki-67 indices and standardized epidermal measurements are recommended.*

Keywords: psoriasis vulgaris, Ki-67 antigen, immunohistochemistry, epidermal thickness, keratinocyte proliferation, Saudi Arabia

1. Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects millions of people worldwide, with prevalence varying by age, geography and ethnicity [1]. Psoriasis vulgaris (chronic plaque psoriasis) is the most common clinical form [2]. In Saudi Arabia, a hospital-based study in the Eastern Province reported psoriasis in 5.3% of adult dermatology patients, with plaque psoriasis accounting for 87.1% of cases [4].

The disease arises from a dysregulated interaction between immune cells and keratinocytes, driven largely by the interleukin-23/T-helper 17 axis [3]. The histological result is a markedly thickened epidermis (acanthosis), parakeratosis, loss of the granular layer, elongated rete ridges and dilated dermal capillaries [2,3]. Cell-kinetic studies showed that the psoriatic germinative cell cycle is greatly shortened and the proliferating cell population is expanded compared with normal epidermis [5].

Ki-67 is a nuclear protein expressed in all active phases of the cell cycle (G1, S, G2 and mitosis) and absent in resting (G0) cells [6,7]. This makes Ki-67 immunostaining a practical index of the growth fraction of a tissue. In normal epidermis, Ki-67-positive nuclei are confined to scattered basal keratinocytes. In psoriatic lesions, positive nuclei extend into the suprabasal layers, and their number falls after effective treatment [8,9].

Epidermal thickness is the most direct morphological measure of psoriatic hyperplasia and is widely used as a histological endpoint in therapeutic studies. Proliferation (Ki-67) and thickness describe the same process from two angles:

the rate at which keratinocytes are produced and the resulting volume of epidermis.

Few studies have examined these two parameters together in Saudi patients. This study therefore aimed to compare Ki-67 immunohistochemical positivity and epidermal thickness between patients with psoriasis vulgaris and healthy controls in Saudi Arabia.

2. Materials and Methods

Study design and setting

This retrospective comparative cross-sectional study was conducted across multiple hospitals in Saudi Arabia. Cases were collected from May 2024 to May 2025 from departmental pathology archives and electronic medical record systems.

Participants

The psoriasis group comprised 50 patients with clinically diagnosed and histologically confirmed psoriasis vulgaris. The control group comprised 50 individuals with no history of psoriasis or other inflammatory skin disease, whose skin samples were obtained from the excision margins of benign skin lesions.

Inclusion criteria: patients with psoriasis vulgaris who had received no topical therapy, systemic therapy or phototherapy for at least 2 weeks before biopsy.

Exclusion criteria: (1) systemic therapy or phototherapy within the washout period; (2) topical therapy within the washout period; (3) other inflammatory dermatoses; (4) malignancy; and (5) pregnancy.

Disease severity was graded as mild, moderate or severe using the Psoriasis Area and Severity Index (PASI) [10], with mild disease defined as PASI < 10, moderate as PASI 10–20 and severe as PASI > 20.

Tissue processing and histopathology

Biopsies (3-mm punch) were obtained from the centre of an active psoriatic plaque in patients and from anatomically comparable sites in controls. Specimens were fixed in 10% neutral-buffered formalin, processed routinely and embedded in paraffin. Sections of 4 μ m were stained with hematoxylin and eosin.

Measurement of epidermal thickness

Epidermal thickness was measured in micrometres on hematoxylin and eosin-stained sections for each specimen.

Ki-67 immunohistochemistry

Ki-67 immunohistochemistry was performed on 4- μ m formalin-fixed, paraffin-embedded sections. After deparaffinisation and rehydration, heat-induced epitope retrieval was performed in citrate buffer (pH 6.0) at 120°C for 20 minutes. Endogenous peroxidase was blocked with 3% hydrogen peroxide. The primary antibody was a mouse monoclonal anti-Ki-67 antibody (clone MIB-1; Dako/Agilent, Santa Clara, CA, USA) at 1:100 dilution for 60 minutes at room temperature. Detection used the EnVision FLEX system (Dako) with diaminobenzidine as chromogen, and Mayer's hematoxylin as counterstain. Tonsil tissue served as positive control; omission of the primary antibody served as negative control.

Ki-67 scoring

Only unequivocal brown nuclear staining was considered positive, regardless of intensity. Each specimen was classified as Ki-67 positive or negative according to the proportion of epidermal keratinocytes showing nuclear staining.

Statistical analysis

Data were analysed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as numbers and percentages and were compared with Pearson's chi-square test. Fisher's exact test was used as a sensitivity analysis for 2×2 comparisons. Continuous variables are presented as mean $\pm$ standard deviation and were compared with the independent-samples t-test. A two-sided P value below 0.05 was considered statistically significant.

Ethical approval

The study was approved by the Research Ethics Committee.

3. Results

Baseline characteristics

The study included 100 participants: 50 patients with psoriasis vulgaris and 50 controls. Mean age was 36.8 ± 14.9 years in the psoriasis group and 33.0 ± 13.0 years in the control group ($P = 0.177$), with ranges of 23–72 and 23–71 years, respectively. Males predominated in both groups (66.0% vs. 60.0%), with no significant difference in sex distribution ($\chi^2 = 0.39$, $P = 0.534$). Among patients, disease was severe in 21 (42.0%), moderate in 19 (38.0%) and mild in 10 (20.0%) (Table 1).

Table 1: Baseline characteristics of the study participants

Variable	Psoriasis vulgaris (n = 50)	Control group (n = 50)	P-value
Age, mean $\pm$ SD (years)	36.8 ± 14.9	33.0 ± 13.0	0.177 ^a
Age range (years)	23–72	23–71	—
Male, n (%)	33 (66.0)	30 (60.0)	0.534 ^b
Female, n (%)	17 (34.0)	20 (40.0)	—
Mild disease, n (%)	10 (20.0)	—	—
Moderate disease, n (%)	19 (38.0)	—	—
Severe disease, n (%)	21 (42.0)	—	—

^a Independent-samples t-test. ^b Pearson's chi-square test. SD, standard deviation.

Ki-67 expression and epidermal thickness

Ki-67 positivity was observed in 30 of 50 psoriatic specimens (60.0%) compared with 20 of 50 control specimens (40.0%). This difference was statistically significant by Pearson's chi-square test ($\chi^2 = 4.00$, $P = 0.046$). It did not reach significance with Fisher's exact test ($P = 0.071$) or with Yates' continuity correction ($P = 0.072$). The odds of Ki-67 positivity were 2.25 times higher in psoriasis.

Mean epidermal thickness was 43.1 ± 32.7 μ m in the psoriasis group and 58.3 ± 27.3 μ m in the control group. The mean difference was -15.2 μ m (95% CI -27.2 to -3.2 ; $t(98) = -2.52$; $P = 0.013$), a moderate effect size (Cohen's $d = 0.50$) (Table 2).

Table 2: Ki-67 expression and epidermal thickness in psoriasis vulgaris and controls

Variable	Psoriasis vulgaris (n = 50)	Control group (n = 50)	P-value
Ki-67 positive, n (%)	30 (60.0)	20 (40.0)	0.046 ^b
Ki-67 negative, n (%)	20 (40.0)	30 (60.0)	—
Epidermal thickness, mean $\pm$ SD (μ m)	43.1 ± 32.7	58.3 ± 27.3	0.013 ^a

^a Independent-samples t-test. ^b Pearson's chi-square test; Fisher's exact test $P = 0.071$.

4. Discussion

This study found that Ki-67 positivity was more frequent in psoriatic skin than in control skin (60.0% vs. 40.0%). This direction agrees with the established view of psoriasis as a hyperproliferative disorder [2,3,5]. Earlier immunohistochemical studies reported markedly higher Ki-67 expression in psoriatic lesions than in normal epidermis, with positive nuclei extending into the suprabasal layers [8,9]. Kim et al. also showed that Ki-67 expression in treated lesions fell to levels similar to normal skin [9], which supports Ki-67 as a marker of disease activity.

The size of the difference in our cohort was smaller than in some previous reports, and its statistical significance depended on the test used. It was significant with Pearson's chi-square test ($P = 0.046$) but not with Fisher's exact test ($P = 0.071$). Two features of the design may explain this. First, a binary positive/negative classification discards information compared with a continuous Ki-67 index. Second, normal epidermis contains proliferating basal keratinocytes [6,7], so a low positivity threshold can classify many control specimens as positive. Reporting the Ki-67 labelling index as

a continuous percentage would give a more sensitive comparison.

The epidermal thickness finding was unexpected. Acanthosis is a defining histological feature of psoriasis vulgaris [2,3], and psoriatic lesions are typically several times thicker than normal skin. In our data, mean thickness was lower in the psoriasis group (43.1 vs. 58.3 μm). Several technical factors could produce this result: biopsy of non-lesional or partially treated skin, inconsistent measurement landmarks between groups, tangential sectioning, differences in anatomical sites between patients and controls, or an error in group labelling during data entry. The wide standard deviation in the psoriasis group (32.7 μm) also points to heterogeneity in sampling or measurement.

This study does not assess the relationship between Ki-67 expression and epidermal thickness within individual patients. Group-level comparisons show whether each parameter differs between psoriasis and controls, but they cannot show whether patients with higher Ki-67 expression have thicker epidermis. That question requires paired patient-level data and a correlation analysis.

The sex distribution of our cohort, with a male predominance, is similar to that reported in an earlier Saudi series [4]. A high proportion of our patients had moderate or severe disease (80.0%), which may reflect referral of more extensive cases to hospital dermatology and pathology services.

This study has several limitations. The sample size was modest (50 per group), which limits statistical power, particularly for categorical comparisons. Ki-67 was analysed only as a binary variable, and a continuous labelling index was not reported. Paired patient-level data were not available, so the correlation between Ki-67 expression and epidermal thickness could not be assessed. Ki-67 expression and epidermal thickness were also not compared across severity categories, and disease duration was not available for the psoriasis group. Finally, the epidermal thickness results run counter to the expected acanthosis and require verification.

5. Conclusion

This study observed a higher frequency of Ki-67 positivity in psoriasis vulgaris than in healthy control skin, supporting the role of keratinocyte proliferation in psoriasis. However, the statistical evidence was sensitive to the test applied. The unexpectedly lower epidermal thickness in psoriatic specimens requires verification of the measurements and sampling procedures. Future studies using quantitative Ki-67 assessment, standardized epidermal thickness measurements and paired patient-level analyses may provide further insight into the relationship between cellular proliferation and epidermal changes.

References

- [1] Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. *BMJ*. 2020;369:m1590.
- [2] Griffiths CEM, Barker JNWN. Pathogenesis and clinical features of psoriasis. *Lancet*. 2007;370(9583):263–271.
- [3] Boehncke WH, Schön MP. Psoriasis. *Lancet*. 2015;386(9997):983–994.
- [4] Fatani MI, Abdulghani MH, Al-Afif KA. Psoriasis in the eastern Saudi Arabia. *Saudi Med J*. 2002;23(2):213–217.
- [5] Weinstein GD, McCullough JL, Ross PA. Cell kinetic basis for pathophysiology of psoriasis. *J Invest Dermatol*. 1985;85(6):579–583.
- [6] Gerdes J, Lemke H, Baisch H, Wacker HH, Schwab U, Stein H. Cell cycle analysis of a cell proliferation-associated human nuclear antigen defined by the monoclonal antibody Ki-67. *J Immunol*. 1984;133(4):1710–1715.
- [7] Scholzen T, Gerdes J. The Ki-67 protein: from the known and the unknown. *J Cell Physiol*. 2000;182(3):311–322.
- [8] Jesionek-Kupnicka D, Chomiczewska-Skóra D, Rotsztejn H. Influence of phototherapy in psoriasis on Ki-67 antigen expression: a preliminary study. *Pol J Pathol*. 2013;64(2):96–103.
- [9] Kim SA, Ryu YW, Kwon JI, Choe MS, Jung JW, Cho JW. Differential expression of cyclin D1, Ki-67, pRb, and p53 in psoriatic skin lesions and normal skin. *Mol Med Rep*. 2018;17(1):735–742. doi:10.3892/mmr.2017.8015.
- [10] Fredriksson T, Pettersson U. Severe psoriasis — oral therapy with a new retinoid. *Dermatologica*. 1978;157(4):238–244.