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RESEARCH ARTICLE

Psoriasis as a Risk Factor for Skin Cancer: An International, Propensity-Matched Retrospective Cohort Study

Hamza Malick, BS[1*]; Seo Won Cho, BS[1]; Kyle C. Lauck, MD[2]; Aaisha Firdaus, MBBS[3]; Dario Kivelevitch[1,2]

[1]Texas A&M College of Medicine, Dallas, Texas
[2]Baylor University Medical Center, Dallas, Texas
[3]Katihar Medical College & Hospital, Katihar, Bihar, India

[*]malick.hamza99@gmail.com

ABSTRACT

Psoriasis, a chronic immune-mediated skin disorder impacting millions globally, is increasingly recognized for its links to various disease processes. As our understanding of immune dysregulation in psoriasis progresses, acknowledging the pivotal role of dysregulated T-cells in the pathogenic development of the persistent inflammatory state becomes crucial. This immune dysregulation and the resulting prevalent inflammatory state have raised concerns about psoriasis potentially serving as a significant comorbidity in cancer development among patients. To contribute to this discussion, we conducted a global retrospective cohort study with propensity score matching (PSM) using the TriNetX Analytics platform. The study aimed to investigate whether patients diagnosed with psoriasis face an elevated risk in the development of cutaneous malignancies, encompassing both melanoma and non-melanoma skin cancers. Our findings confirmed a noteworthy concern, revealing a significantly increased risk of developing cutaneous neoplasms in individuals with psoriasis. In conclusion, our study underscores the importance of heightened awareness and the necessity for routine skin cancer screenings in this unique patient population. The observed association between psoriasis and an increased risk of cutaneous neoplasms highlights the need for proactive medical interventions and emphasizes the potential impact of psoriasis as a comorbidity in the context of cancer development.

Introduction:

Psoriasis is a complex, chronic immune mediated skin disorder affecting 60 million people worldwide.[1] While the pathogenesis of psoriasis is multifaceted involving genetic, immune system, and environmental factors, the primary mechanism involves dysfunctional cytokine production, contributing to the uncontrolled keratinocyte proliferation and development of thickened epidermal plaques.[2] Notably, pro-inflammatory cytokines such as IL-1β, TNF-α, IL-17, and IL-6 have been consistently observed at elevated levels in psoriasis patients.[3] Previous studies underscore IL-6 as one of the most substantial and well-characterized pro-tumorigenic cytokines, establishing an important link between the chronic inflammatory process present in psoriasis and the potential for establishing a pro-oncogenic micronviorment.[4]

Similarly, the chronic inflammation implicated in psoriasis may also aid in the generation of reactive oxygen species (ROS) and similar molecules that are implicated in causing DNA damage and signaling cascades promoting neoplastic growth.[5] Considering these insights, our study aims to investigate the relationship between individuals diagnosed with psoriasis and whether its unique pathophysiology may contribute to an increased risk in the development of cutaneous malignancies.

Methods:

A global retrospective cohort study with propensity score matching (PSM) was conducted utilizing the TriNetX Analytics platform which enabled real-time access to electronic medical record data from 120 million patients and 80 health care organizations globally. Patients were divided into cohorts based on whether they had an occurrence of skin cancer after a diagnosis of psoriasis, and were without comorbid congenital, immunological, or infectious disorders. To balance patient characteristics between cohorts, propensity score matching (PSM) was employed. Analysis of risk and overall survival (OS) between cohorts was undertaken examining risk and impact on survival for malignant melanoma, melanoma in situ, basal cell carcinoma (BCC), and cutaneous squamous cell carcinoma (cSCC). The study measured the likelihood of developing these cutaneous neoplasms. 5-year overall survival (OS) analysis was conducted using Kaplan-Meier method. Statistical significance was defined at two-tailed p-values less than 0.05.

Results:

674,417 patients above the age of 20 were identified to have a diagnosis of Psoriasis. After PSM 106,780 patients were identified. Table 1 illustrates the following findings: Relative Risk (RR) for cutaneous squamous cell carcinoma was 3.113 (95% CI (2.691 – 3.602)). RR for basal cell carcinoma was 2.498 (95% CI (2.261 – 2.76)). RR for malignant melanoma was 1.822 (95% CI (1.56 – 2.127)). RR for melanoma in situ was 1.747 (95% CI (1.44 – 2.119)). All four neoplasms in patients with psoriasis further exhibited statistically significant values when calculating for attributable risk. (Table 1)

Table 1: Risk of Developing Cutaneous Neoplasms in Patients with Psoriasis

Cutaneous Neoplasms	Relative Risk	95% CI	Risk with Psoriasis	Risk without Psoriasis	Risk Difference	95% Confidence Interval (%)	p-value
Malignant Melanoma	1.822	(1.56 – 2.127)	0.42%	0.23%	0.19%	(0.142%, 0.238%)	<0.0001
Melanoma In Situ	1.747	(1.44 – 2.119)	0.27%	0.15%	0.11%	(0.075%, 0.152%)	<0.0001
Cutaneous Squamous Cell Carcinoma	3.113	(2.691 – 3.602)	0.69%	0.22%	0.47%	(0.414%, 0.528%)	<0.0001
Basal Cell Carcinoma	2.498	(2.261 – 2.76)	1.26%	0.50%	0.76%	(0.676%, 0.834%)	<0.0001

Discussion:

Psoriasis is a chronic skin disorder involving dysfunctional cytokine production and persistent inflammatory processes, potentially leading to skin carcinogenesis through two distinct mechanisms.[5] First, reactive oxygen species (ROS) can activate protooncogenes such as BRAF, PTEN, and N-RAS, causing DNA damage in a genotoxic manner. Conversely, the chronic pro-inflammatory state can trigger specific signaling pathways like mitogen-activated protein kinases (MAPK), nuclear factor kappa β (NF-Kβ), and nuclear factor erythroid 2-related factor 2 (Nrf2), leading to the proliferation, angiogenesis, and metastasis of skin cancer cells.[5]

Our study confirms a significant concern regarding the increased risk of cutaneous neoplasms in patients with psoriasis.[6] We found a substantial association with the development of nonmelanoma skin cancers, particularly cutaneous squamous cell carcinoma, with a risk over three times higher. Similarly, the risk of developing basal cell carcinoma more than doubled in patients with psoriasis. The association between psoriasis and non-melanoma skin cancers can be further analyzed through our understanding of tumor-infiltrating lymphocytes (TILs), which play a crucial role in epithelial carcinogenesis.[7] A study by Nardinocchi et al. demonstrated that TILs in BCCs and cSCCs not only expressed high levels of IL-17 and IL-22, but in-vivo experimentation showed a significant enhancement in tumor growth for these neoplasms when placed in IL-17 and IL-22-rich microenvironments.[7] These findings shed light not only on the physiological adaptations occurring in non-melanoma skin cancers but also on how they share a similar cytokine-rich microenvironment nearly identical to that seen in psoriasis.

In contrast to prior literature, our analysis further revealed a relevantly increased risk of developing melanoma—a noteworthy concern that may aid in our understanding of how inflammatory

microenvironments can be intertwined with the development of melanoma skin cancers as well.[8] The use of phototherapy, sun exposure and immune-modulating therapies may serve as confounding variables in our results. Previous studies remain conflicted on the extent biologic treatments have on the development of both melanoma and non-melanoma skin cancers.[8,9]

Conclusion:

Future studies may build on this observed relationship between psoriasis and the development of cutaneous neoplasms to assess for relationships between patients with autoimmune dermatologic conditions, including psoriasis, and the development of skin cancers. Ultimately, our study aims to promote heightened awareness and the necessity for routine skin cancer screenings in this unique patient population.

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Conflict of Interest Disclosure:

The authors have no conflict of interest to declare.

IRB Approval:

Data accessible via TriNetX is presented in aggregate form and only contains anonymized data as per the de-identification standard defined by the US Health Insurance Portability and Accountability Act (HIPAA) in section §164,514(a). Given this study used only de-identified data and did not involve individually identifiable patient data, this study was exempt from Institutional Review Board Approval.

Prior publication:

None of the contents here-in have been presented or published previously nor are under consideration for publication elsewhere.

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