ejpmr, 2024, 11(6), 01-05

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

INVESTIGATING THE LINK BETWEEN SKIN CD103+ MEMORY CELLS AND THE SEVERITY OF PSORIASIS

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Article Received on 31/03/2024 **Article Revised on 21/04/2024** **Article Accepted on 11/05/2024**

ABSTRACT

Background: Tissue-resident memory T cells (TRMs) represent a subpopulation of memory T cells garnering significant attention in contemporary psoriasis research. These cells exhibit the unique capacity to persist within psoriatic skin even during periods of disease remission. This persistence has led researchers to posit a pivotal role for TRMs in the cyclical recurrence of psoriasis. TRMs are hypothesized to contribute to the complex immunopathogenesis of the disease, thereby positioning them as a potential therapeutic target for novel treatment strategies. **Materials and methods:** a prospective observational study conducted at Tishreen University Hospital between December 2021 and December 2023, the severity of psoriasis was assessed using the Psoriasis Area and Severity Index (PASI). Skin biopsies were obtained from previously psoriatic lesions to evaluate the density of CD103+ cells within the epidermis and dermis using immunohistochemistry. Subsequently, correlations between CD103+ cell counts and PASI scores were analyzed. **Results:** Eight participants with healed psoriasis were enrolled in this study, with a median age of 44 years. The gender distribution was balanced, with 50% of participants being male. A significant correlation was observed between PASI scores and epidermal CD103+ cell counts. **Conclusion:** The extent of infiltration with CD103 cells in the epidermis of psoriasis is linked to the severity measured with PASI.

KEYWORDS: Psoriasis – cd103 – memory cells – PASI – severity.

INTRODUCTION

The skin represents a critical interface between the host and the external environment, necessitating a robust and multifaceted immune system for protection against pathogens. T cells serve as a cornerstone of this cutaneous immune response.[1] Following antigen encounter, naive T cells differentiate into effector T cells that orchestrate a potent immune response to eliminate the threat.[2] However, the majority of these effector T cells are short-lived, undergoing apoptosis once the antigenic challenge has subsided.[3] Conversely, a subpopulation differentiates into memory T cells, including tissue-resident memory T cells (TRMs) that strategically localize within peripheral tissues like the skin.[4] TRMs possess a remarkable capacity for prolonged persistence within the tissue microenvironment, even during periods of immunological quiescence. This unique characteristic positions them to mount a rapid and localized immune response upon re-exposure to the same antigen.[5]

In the context of psoriasis, a chronic inflammatory skin disease characterized by the development of red, scaly plaques, TRMs have emerged as critical players in the disease's cyclical nature. These memory T cells are implicated in the phenomenon of immunological memory, manifested by the recurring development of psoriatic plaques in the same anatomical locations.[6] Compelling evidence suggests that TRMs persist within psoriatic lesions even after successful treatment and apparent clinical remission.[7] Furthermore, these resident memory cells are hypothesized to play a pivotal role in initiating the inflammatory cascade that culminates in psoriatic plaque formation upon encountering specific triggers, such as environmental factors or infections.[8] This growing body of research highlights the potential of

TRMs as a therapeutic target to disrupt the immunological memory in psoriasis and potentially achieve long-lasting disease control.[9]

The traditional view of circulating T cells as the primary mediators of psoriatic lesion formation has been challenged by the ineffectiveness of therapies targeting T cell migration from the bloodstream to the skin.[10] This observation underscores the critical role of resident immune cells, particularly TRMs, in the pathogenesis of psoriasis. Early studies from the 1980s provided initial clues regarding the involvement of skin-resident cells in psoriasis.[11] Notably, the development of typical psoriatic lesions in healthy skin grafts from psoriatic patients transplanted onto immunodeficient mice further substantiated the significance of resident immune cells in disease development.[12] Interestingly, a positive correlation has been observed between the expression of TRM markers in patients with plaque psoriasis and the duration of their skin lesions.[13] This finding further strengthens the potential link between TRMs and disease severity. Building upon this existing knowledge, our study aims to investigate the relationship between the number of CD103+ resident T cells in the skin of psoriatic patients and the severity of their disease as assessed by the Psoriasis Area and Severity Index (PASI). By elucidating this potential association, we hope to contribute to the growing body of evidence supporting the role of TRMs in psoriasis and pave the way for the development of novel therapeutic strategies targeting these resident memory T cells.

MATERIALS AND METHODS

This study was an observational comparative study included patients with remissioned psoriasis and healthy individuals. Our study included 8 patients(4 males & 4 females) aged between 12 and 62 years old. The samples were collected from patients at Tishreen University Hospital between December 2021 and December 2023. Inclusion criteria encompassed patients with previous incidents of psoriasis who finished their treatment 4 weeks ago or more, The study was approved by the ethics committee at Tishreen University. Patients were assessed during their first psoriatic flare, and severity was measured using PASI measurement tool and skin biopsies were collected from lesions to and stain for T.cell markers, at the second phase, patients were reassessed after resolution, and immune-staining for Cd103 cells was conducted to measure the count of these cells in both epidermis and dermis in a field under the magnifying of *200 lens.

RESULTS

Eight patients with acute onset psoriasis were enrolled in this study. The median age of participants was 44 years, and the gender distribution was balanced, with 50% being male. We investigated the potential association between psoriasis severity and the abundance of CD103+ resident memory T cells (TRMs) within both the dermal and epidermal layer. Psoriasis severity was assessed using the Psoriasis Area and Severity Index (PASI) during the acute phase, while CD103+ TRM cell counts were enumerated in biopsies obtained from participants during remission. A Pearson correlation coefficient analysis revealed a statistically significant positive correlation (r = 0.841) between PASI scores and epidermal CD103+ TRM cell counts. These findings suggest a potential link between TRMs and disease severity in patients with psoriasis. Appendix 1 provides representative immunohistochemical images that visually depict the distribution of CD103+ cells within psoriatic lesions using PASI- score and cd103 cell count in the epidermis:

1- Correlation between Epidermal CD103 cells and Pasi

Correlation between Epidermal CD103 cells and Pasi	Pearson Correlation	P-value
Pasi- Epidermal CD103	0.841 (very strong)	0.09

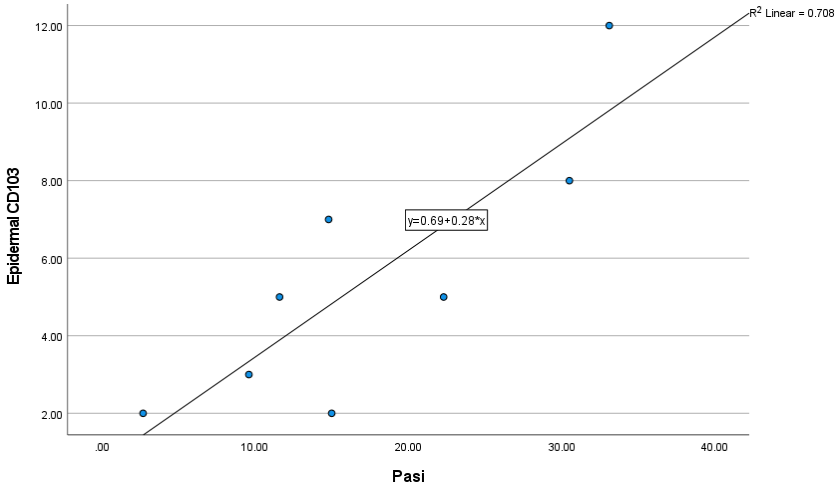

Figure 1: A scatter plot of Epidermal CD103 cells and Pasi (R^2=0.708).

Upon assessing the relationship between the severity of psoriasis, measured with PASI and the count of CD103 cells in the dermis of patients using pearson test, we couldn't find a correlation (0.077). Appendix 2 provides images on the immunohistochemically assessing the correlation between the severity of psoriasis using PASI-score and cd103 cell count in the dermis.

2- Correlation between Dermal CD103 cells and Pasi

Correlation between Dermal CD103 cells and Pasi	Pearson Correlation	P-value
Pasi-dermal CD103	0.077 (very week)	0.857

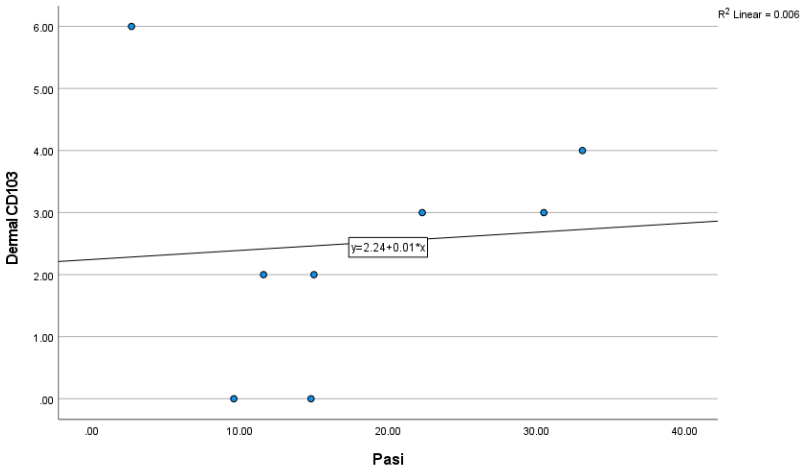

Figure 2: A scatter plot of Dermal CD103 cells and Pasi (R^2=0.006).

DISCUSSION

Our study identified a significant positive correlation between the abundance of epidermal CD103+ resident memory T cells (TRMs) and Psoriasis Area and Severity Index (PASI) scores in patients with remitted plaque psoriasis. This finding suggests a potential link between TRM levels and disease severity, potentially contradicting prior research by Kasprowicz-Furmańczyk, M and colleagues[13] who reported no such association. Our results underscore the need for further investigation into the multifaceted role of TRMs in psoriasis pathogenesis. The observed discrepancy might be attributed to methodological differences between studies, such as patient population characteristics, disease duration, or specific T cell subset analysis. Interestingly, we did not observe a significant correlation between PASI scores and dermal CD103+ TRM cell counts. This aligns with the findings reported by Kasprowicz-Furmańczyk et al[13] who similarly observed a lack of association between dermal TRMs and disease severity. These combined findings suggest that epidermal TRMs may play a more prominent role in the clinical presentation of psoriasis compared to their dermal counterparts.

A limitation of our study is that we exclusively enrolled patients with newly remitted psoriasis. Therefore, we were unable to analyze potential correlations between CD103+ TRM cell counts and the duration of psoriatic episodes, as investigated by Kasprowicz-Furmańczyk et al.[13] Future studies incorporating patients across various disease stages would provide valuable insights into the dynamic interplay between TRMs and disease course. Furthermore, our findings are consistent with those of Kurihara et al,[14] who reported an association between higher epidermal CD103+ TRM numbers and a more progressive course of psoriasis. These combined observations support the notion that TRMs may contribute to disease severity and potentially influence the clinical course of psoriasis.

CONCLUSION

Our study's observation of a significant positive correlation between epidermal CD103+ resident memory T cell (TRM) counts and Psoriasis Area and Severity Index (PASI) scores in patients with remitted plaque psoriasis raises intriguing possibilities regarding a potential feedback loop between these two elements. This correlation suggests a possible reciprocal relationship, where:

- Severe psoriasis, characterized by heightened inflammation, could directly contribute to an increase in epidermal CD103+ TRMs. These inflammatory conditions might promote the activation, proliferation, and/or preferential localization of TRMs within the psoriatic epidermis.
- Conversely, elevated numbers of epidermal CD103+ TRMs could contribute to a more prompt and robust inflammatory response upon encountering specific triggers. This enhanced immune reactivity could potentially exacerbate psoriatic symptoms and lead to a more severe clinical presentation.

This proposed feedback loop warrants further investigation to elucidate the precise mechanisms underlying this potential bidirectional relationship

between TRMs and disease severity. It is important to note that our findings did not reveal a similar correlation between PASI scores and dermal CD103+ TRM cell counts. This observation suggests that epidermal TRMs might play a more prominent role in the pathogenesis of psoriasis compared to their dermal counterparts.

ETHICS

Assent and informed consent procedures were followed. For participants under the age of 15, written informed consent was obtained from their parents or legal guardians.

LIMITATIONS

The biggest limitation was the small sample size, which was due to two reasons: difficulty collecting untreated psoriasis patients in their first episodes, and the high financial cost of the study, which hindered us from collecting more data.

ACKNOWLEDGMENTS

No acknowledgment.

CONFLICT OF INTEREST

No conflict of interest.

FUNDING

No source of institutional funding.

REFERENCES

1. Kasprowicz-Furmańczyk, M., Czerwińska, J., Placek, W., & Owczarczyk-Saczonek, A. Assessment of the tissue resident memory cells in lesional skin of patients with psoriasis and in healthy skin of healthy volunteers. *International Journal of Environmental Research and Public Health*, 2021; *18*(21): 11251. https://doi.org/10.3390/ijerph182111251
2. Shin, H., & Iwasaki, A. Tissue-resident memory T cells. *Immunological Reviews*, 2013; *255*(1): 165–181. https://doi.org/10.1111/imr.12087
3. Khalil, S., Bardawil, T., Kurban, M., & Abbas, O. Tissue-resident memory T cells in the skin. *Et al [Inflammation Research]*, 2020; *69*(3): 245–254. https://doi.org/10.1007/s00011-020-01320-6
4. Gallais Sérézal, I., Classon, C., Cheuk, S., Barrientos-Somarribas, M., Wadman, E., Martini, E., Chang, D., Xu Landén, N., Ehrström, M., Nylén, S., & Eidsmo, L. Resident T cells in resolved psoriasis steer tissue responses that stratify clinical outcome. *The Journal of Investigative Dermatology*, 2018; *138*(8): 1754–1763. https://doi.org/10.1016/j.jid.2018.02.030
5. Owczarczyk-Saczonek, A., Krajewska-Włodarczyk, M., Kasprowicz-Furmańczyk, M., & Placek, W. Immunological memory of psoriatic lesions. *International Journal of Molecular Sciences*, 2020; *21*(2): 625. https://doi.org/10.3390/ijms21020625
6. Lande, R., Botti, E., Jandus, C., Dojcinovic, D., Fanelli, G., Conrad, C., Chamilos, G., Feldmeyer, L., Marinari, B., Chon, S., Vence, L., Riccieri, V., Guillaume, P., Navarini, A. A., Romero, P., Costanzo, A., Piccolella, E., Gilliet, M., & Frasca, L. The antimicrobial peptide LL37 is a T-cell autoantigen in psoriasis. *Nature Communications*, 2014; *5*(1). https://doi.org/10.1038/ncomms6621
7. Bhushan, M., Bleiker, T. O., Ballsdon, A. E., Allen, M. H., Sopwith, M., Robinson, M. K., Clarke, C., Weller, R. P. J. B., Graham-Brown, R. A. C., Keefe, M., Barker, J. N. W. N., & Griffiths, C. E. M. Anti-E-selectin is ineffective in the treatment of psoriasis: a randomized trial. *The British Journal of Dermatology*, 2002; *146*(5): 824–831. https://doi.org/10.1046/j.1365-2133.2002.04743.x
8. Vu, T. T., Koguchi-Yoshioka, H., & Watanabe, R. Skin-resident memory T cells: Pathogenesis and implication for the treatment of psoriasis. *Journal of Clinical Medicine*, 2021; *10*(17): 3822. https://doi.org/10.3390/jcm10173822
9. Conrad, C., Boyman, O., Tonel, G., Tun-Kyi, A., Laggner, U., de Fougerolles, A., Kotelianski, V., Gardner, H., & Nestle, F. O. α1β1 integrin is crucial for accumulation of epidermal T cells and the development of psoriasis. *Nature Medicine*, 2007; *13*(7): 836–842. https://doi.org/10.1038/nm1605
10. Boyman, O., Hefti, H. P., Conrad, C., Nickoloff, B. J., Suter, M., & Nestle, F. O. Spontaneous development of psoriasis in a new animal model shows an essential role for resident T cells and tumor necrosis factor-α. *The Journal of Experimental Medicine*, 2004; *199*(5): 731–736. https://doi.org/10.1084/jem.20031482
11. Tokura, Y., Phadungsaksawasdi, P., Kurihara, K., Fujiyama, T., & Honda, T. (2021). Pathophysiology of skin resident memory T cells. *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.618897
12. Kasprowicz-Furmańczyk, M., Czerwińska, J., Placek, W., & Owczarczyk-Saczonek, A. Assessment of the tissue resident memory cells in lesional skin of patients with psoriasis and in healthy skin of healthy volunteers. *International Journal of Environmental Research and Public Health*, 2021; *18*(21): 11251. https://doi.org/10.3390/ijerph182111251
13. Kasprowicz-Furmańczyk, M., Czerwińska, J., Placek, W., & Owczarczyk-Saczonek, A. Assessment of the tissue resident memory cells in lesional skin of patients with psoriasis and in healthy skin of healthy volunteers. *International Journal of Environmental Research and Public Health*, 2021; *18*(21): 11251. https://doi.org/10.3390/ijerph182111251
14. Kurihara, K., Fujiyama, T., Phadungsaksawasdi, P., Ito, T., & Tokura, Y. Significance of IL-17A-producing CD8+CD103+ skin resident memory T cells in psoriasis lesion and their possible

relationship to clinical course. *Journal of Dermatological Science*, 2019; *95*(1): 21–27. https://doi.org/10.1016/j.jdermsci.2019.06.002