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Research Article

A COMPARATIVE STUDY OF CLINICOHISTOPATHOLOGICAL CORRELATION IN PATIENTS OF PSORIASIS AND PSORIASIFORM LESIONS WITH KI67 AND CD34 IMMUNOHISTOCHEMICAL EXPRESSION

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ABSTRACT

Objectives: Psoriasis, characterized by chronic inflammation of the skin, stands as a notable example of a psoriasiform tissue pattern. In dermatology, the term "psoriasiform dermatitis" frequently appears across various inflammatory skin conditions, presenting challenges for dermatologists and pathologists alike in accurate differentiation. Relying solely on clinical features may prove insufficient in distinguishing between psoriasis and other psoriasiform dermatoses. Therefore, comprehensive differentiation requires consideration of clinical, histopathological, and immunohistochemical factors. Our study is to compare the clinicohistopathological features of psoriasis and psoriasiform dermatitis and to evaluate the immunohistochemical expression of CD34 and Ki67 in psoriasis and psoriasiform dermatitis.

Methods: This retrospective study was conducted at the Department of Pathology, Mediciti Institute of Medical Sciences, Ghanpur, focusing on cases between January 1, 2020, and December 31, 2022. Clinical histories were extracted from requisition forms submitted by the Department of Dermatology. The study analyzed paraffin blocks from 50 patients each diagnosed with psoriasis and psoriasiform dermatitis. Formalin-fixed paraffin-embedded tissue samples were processed into 4-micron sections and initially stained with hematoxylin and eosin. The immunohistochemical analysis included primary antibodies against Ki-67 and CD34, with positive controls sourced from strongly positive samples of squamous cell carcinoma and capillary hemangioma, respectively. Appropriate negative controls were employed to ensure the accuracy of our findings.

Results: In our study, we analyzed a total of 100 cases, comprising 50 cases each of psoriasis and psoriasiform dermatitis. Among the psoriasis cases, there was a male predominance with 29 males and 21 females, while psoriasiform dermatitis also showed male predominance with 32 males. The mean age was 33.8 years for psoriasis and 34.8 years for psoriasiform dermatitis. The majority of psoriasis cases fell in the 21–30 years age range, whereas for psoriasiform dermatitis, it was between 31 and 40 years. Significantly, our immunohistochemical analysis revealed that the mean staining intensity of the two markers was notably higher in psoriasis compared to psoriasiform dermatitis.

Conclusions: In our study, we observed that the expression levels of Ki-67 and CD34 biomarkers were significantly elevated in psoriasis compared to psoriasiform dermatitis. Notably, four cases of psoriasiform dermatitis demonstrated positivity for CD34 in our analysis. This finding suggests a potential avenue for further research to explore the implications of CD34 positivity in psoriasis.

Keywords: Psoriasis, Psoriasiform dermatitis, Ki67, CD34.

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INTRODUCTION

Psoriasis, a chronic inflammatory condition driven by immune system dysfunction, affects approximately 2–3% of the global population, yet its exact cause remains elusive. The development of psoriasis involves a multifaceted interplay among genetic predispositions, immune responses, and environmental influences [1-4]. Diagnosis hinges on clinical observations, identifying scaly, red plaques on the skin's surface, often accompanied by joint and nail complications.

Psoriatic skin lesions exhibit distinctive histopathological traits, including thickening of the epidermis (acanthosis) and abnormal retention of nuclei in the outer skin layer (parakeratosis). These lesions also display increased formation of new blood vessels (angiogenesis) and a notable infiltration of inflammatory cells, particularly neutrophils and lymphocytes, within both the epidermal and dermal layers. Furthermore, there is an observed elevation in various cytokines, growth factors, inflammatory mediators, and angiogenic factors, contributing significantly to the inflammatory processes seen in psoriasis [5].

Psoriasiform lesions exhibit histological and clinical features that closely resemble those seen in psoriasis. Conditions, such as lichen simplex chronicus, pityriasis rosea, pityriasis rubra pilaris, seborrheic dermatitis, prurigo nodularis, and chronic eczema fall under this category. The shared clinical and histopathological characteristics between psoriasis and psoriasiform lesions present challenges in accurately diagnosing and differentiating between them, complicating the process of reaching a definitive diagnosis [3].

Immunohistochemistry serves as a crucial method for distinguishing between psoriasis and psoriasiform dermatitis, essential for diagnostic, prognostic, and therapeutic strategies. Psoriasis is characterized by a complex pathogenesis involving dysregulated keratinocyte proliferation and differentiation, immune-mediated inflammation, and aberrant angiogenesis with vascular remodeling. Angiogenesis plays a pivotal role in driving psoriasis, evident from early-stage lesions showing new blood vessel formation that diminishes as the disease resolves. This accentuated vascularity is corroborated by elevated CD34 expression and higher microvessel density values observed in psoriatic skin.

CD34 is a glycosylated transmembrane protein widely recognized as a marker for primitive progenitor cells originating from both blood and bone marrow, particularly endothelial cells. Its role extends to

functioning as a cell-cell adhesion factor, facilitating interactions with other adhesion molecules like selectins [7].

Psoriasis lesions demonstrate increased expression of the cell proliferation marker Ki-67 compared to normal skin, with higher levels of Ki-67 associated with greater disease severity [6]. The Ki-67 antigen is a protein complex weighing 345–395 kD, expressed throughout all phases of the cell cycle except G0, making it a reliable marker for actively proliferating cells [8].

In this study, our aim was to compare the expression levels of Ki-67 and CD34 markers to determine their relative levels of expression. Ki-67 serves as a well-established marker for cell proliferation and is notably abundant in psoriasis, where its expression correlates with the clinical severity of the condition. This marker is utilized to effectively demonstrate tissue proliferation across various phases of the cell cycle [9-11]. The primary focus of this investigation was to evaluate the differences in immunohistochemical expression of Ki-67 and CD34 between psoriasis and psoriasiform dermatitis.

METHODS

This retrospective study was conducted at Mediciti Institute of Medical Sciences in Ghanpur, spanning from January 1, 2020, to December 31, 2022, and based in the Department of Pathology at a tertiary care hospital. Clinical histories were extracted from requisition forms submitted by the department of dermatology. Patient consent obtained in the study included cases clinically diagnosed with psoriasis or where psoriasis was considered in the differential diagnosis, and these diagnoses were histologically confirmed as either psoriasis or psoriasiform dermatitis. The spectrum of psoriasiform dermatitis encompassed in the study included conditions such as lichen simplex chronicus, pityriasis rubra pilaris, pityriasis rosea, prurigo nodularis, chronic eczema, seborrheic dermatitis, and inflammatory linear verrucous epidermal nevus (ILVEN).

Patients undergoing treatment for Psoriasis or Psoriasiform dermatitis and those with inadequate biopsy samples less than 3 mm in size were excluded from the study.

The study included a total of 100 cases, comprising 50 cases of psoriasis and 50 cases of psoriasiform dermatitis.

The formalin-fixed paraffin-embedded blocks and slides were retrieved from the archives, and sections measuring 4 microns in thickness were cut and stained with hematoxylin and eosin. Additional sections were prepared from the paraffin blocks and mounted on two poly L-lysine-coated glass slides for immunohistochemical detection of Ki-67 and CD34 expression. Primary antibodies used included CD34 (Quartet clone QBEnd/10 Mouse Monoclonal antibody, Potsdam, Germany) and Ki-67 (Vitro, clone SP6 Rabbit Monoclonal antibody, Sevilla, Spain), following manufacturer protocols (Table 2).

The IHC slides underwent deparaffinization and rehydration using xylene and graded alcohols. Endogenous peroxidase activity was blocked with 0.3% hydrogen peroxide for 20 min. Antigen retrieval was achieved using a microwave oven followed by treatment with TRIS buffer and PBS washes (Figures 1-3 and Table 3). Slides were then incubated with monoclonal primary antibodies, followed by polymer HRP-labeled secondary antibodies, with PBS washes between each step. 3'-3'diaminobenzidine hydrochloride served as the chromogen for IHC staining. Following staining, all slides were counterstained with alcohol-free hematoxylin and rinsed with running tap water. Positive controls for Ki-67 and CD34 included squamous cell carcinoma and capillary hemangioma, respectively. Negative controls were appropriately utilized in our study.

Clinical, histological, and immunohistochemical criteria

The study assessed clinical characteristics including scaly lesions and the Auspitz sign. Histological criteria included evaluating acanthosis categorized as regular or irregular, suprapapillary plate thickness described as thick, normal, or thin, presence or absence of a granular layer (described as absent, normal, hypogranulosis, or hypergranulosis), presence or absence of Munro microabscesses, and the vertical orientation of collagen bundles (described as present or absent).

For CD34/MVD assessment, the slides were examined to identify highly vascularized areas in the papillary dermis using low-power magnification. Three areas with a high number of vessels were selected, and vessel counting was performed at high-power magnification. Each single endothelial cell or cluster of endothelial cells positive for CD34 in the membrane/cytoplasm was considered a distinct microvessel. The number of vessels was recorded and averaged, categorized as follows: 4–10 capillaries per high-power field (HPF) as 1+, 11–20 capillaries/HPF as 2+, and more than 21 capillaries/HPF as 3+ (Figures 4-6).

For Ki-67 staining, nuclei of keratinocytes in the epidermis were stained brown, indicating positive staining. Ki-67-positive cells were counted separately in the basal layer and suprabasal layer, as well as across the entire epidermis, in both psoriasis and psoriasiform dermatitis samples. The suprabasal Ki-67 positivity index, calculated as the ratio of suprabasal to total epidermal cell count, was determined using a light microscope.

Statistical analysis

The data were analyzed using SPSS version 22, and statistical significance was assessed using Chi-square and t-tests. CD34 and Ki67 data were categorized using mean values±standard deviation (SD). A $p<0.05$ was considered statistically significant.

RESULTS

In the psoriasis group, there were 29 male and 21 female cases, resulting in a male-to-female ratio of 1.38:1 among the 50 cases studied. Similarly, in the psoriasiform dermatitis group, 32 cases were male, leading to a male-to-female ratio of 1.77:1. The mean age was 33.8 years for psoriasis and 34.8 years for psoriasiform dermatitis. The majority of psoriasis cases (Table 1) were observed in the 21–30 years age range, whereas for psoriasiform dermatitis, the predominant age range was 31–40 years.

In the present study, among psoriasiform dermatitis, most of the cases are pityriasis rosea and the least common is ILVEN.

In our study, the predominant clinical presentation among psoriasis patients was characterized by silvery scaly lesions and Auspitz signs. Conversely, in patients with psoriasiform dermatitis, hyperpigmented lesions were the most frequently observed clinical feature, with the Auspitz sign being the least commonly encountered.

In psoriasis cases, significant histological features included regular acanthosis, thinning of the suprapapillary layer, hypogranulosis, and the presence of Munro microabscesses. Conversely, features favoring psoriasiform lesions comprised irregular acanthosis, thickening of the suprapapillary plate, hypergranulosis, and vertical orientation of

Table 1: Distribution of cases in psoriasiform dermatitis

Histological diagnosis	No. of cases (%)
Pityriasis rosea	20 (40)
Chronic eczema	13 (26)
Lichen simplex chronicus	11 (22)
Prurigo nodularis	7 (14)
Pityriasis rubra pilaris	5 (10)
Seborrheic dermatitis	3 (6)
ILVEN	1 (2)
Total	50 (100)

Table 2: Comparison of clinical features in Psoriasis and Psoriasiform Dematitis

Clinical features	Psoriasis no. of cases (%)	Psoriasiform dermatitis no. of cases (%)	p-value
Auspitz sign			0.0001
Present	40 (80)	6 (12)	
Absent	10 (20)	44 (88)	
Type of lesion			0.00009
Scaly lesions	40 (80)	19 (38)	
Hyperpigmented lesions	10 (20)	31 (62)	

Table 3: Comparison of Histopathological findings in psoriasis and psoriasiform dermatitis

Histological characteristics	Psoriasis no. of cases (%)	Psoriasiform lesions no. of cases (%)	p-value
Acanthosis			
Regular	46 (92)	10 (20)	0.00001
Irregular	04 (8)	40 (80)	
Granular layer			
Absent	41 (82)	0 (0)	0.00001
Hypogranular	8 (16)	11 (22)	
Normal	0 (0)	3 (6)	
Hypergranular	1 (2)	36 (72)	
Suprapapillary plate			
Thin	42 (84)	1 (2)	0.000001
Normal	8 (16)	16 (32)	
Thick	0 (0)	33 (66)	
Munro microabscesses			
Present	50 (100)	4 (8)	0.0001
Absent	0 (0)	46 (92)	
Vertically oriented collagen bundles			
Present	0 (0)	26 (52)	0.00001
Absent	50 (100)	24 (48)	

collagen bundles.

Immunohistochemical staining with CD34 revealed intense positivity in psoriasis cases. The mean microvessel density (MVD) was 20±5.260 in psoriasis cases and 8.03±5.284 in psoriasiform dermatitis cases. Among psoriasis cases, 37 (74%) exhibited severe CD34 positivity, whereas only 4 (8%) cases of psoriasiform dermatitis showed similar intensity. Conversely, 41 (82%) cases of psoriasiform dermatitis displayed mild CD34 positivity, compared to 5 (10%) cases of psoriasis. The remaining 8 (16%) psoriasis cases and 5 (10%) psoriasiform dermatitis cases exhibited moderate CD34 positivity, as detailed in Table 4.

Ki-67 expression was identified by the presence of yellow to brown granules within the nucleus. Scoring for Ki-67 involved assessing the staining pattern of nuclei and counting the number of positive keratinocytes, resulting in a positivity index expressed as the percentage of Ki-67-positive cells.

The suprabasal Ki-67 positivity index, calculated as the ratio of suprabasal to total epidermal cell counts, was significantly higher in the psoriasis group (mean±SD: 73±1.91%) compared to the psoriasiform dermatitis group (mean±SD: 43±8.2%). This difference was statistically significant with a $p<0.001$, as shown in Table 5.

Table 4: Distribution of CD34 intensity in psoriasis and psoriasiform dermatitis

Variables	Psoriaisis (No of cases and %)	Psoriasiform dermatitis (No of cases and %)
Mild	5 (10)	41 (82)
Moderate	8 (16)	5 (10)
Strong	37 (87)	4 (8)

Table 5: Comparison of ki67 and cd34 expression in psoriasis and psoriasiform dermatitis

	Psoriasis	Psoriasiform dermatitis	p-value
Ki67 Basal layer Suprabasal Suprabasal to total epidermis ratio (%)	69.56±2.29	28.62±7.8	<0.001
	189±16.78	20.54±3.02	<0.001
	73±1.91	43±8.2	<0.001
CD 34	20±5.260	8.03±5.284	<0.001

DISCUSSION

Based on the literature reviewed, histopathology is widely regarded as the gold standard for diagnosing most dermatological conditions, including psoriasis. Clinical criteria alone may not be reliable due to variations influenced by disease duration and treatment effects.

On the other hand, histological material provides definitive evidence that remains accessible for future review, if needed. However, there are instances where histopathology alone may not conclusively resolve diagnostic uncertainties. In such cases, establishing a clinicohistopathological correlation becomes essential. This approach allows dermatopathologists to differentiate between psoriasis and psoriasiform dermatitis, especially in the absence of typical features.

Even after clinicohistopathological correlation, when diagnostic challenges persist in certain cases, immunohistochemistry emerges as an invaluable tool. Advances in cell kinetics, immunology, and molecular biology have significantly enhanced our understanding of the etiopathogenesis involving keratinocyte proliferation, increased vascularity, and inflammation in psoriatic disorders. Previous literature extensively utilizes various IHC markers such as p53, cyclin D1, Ki-67,

Table 6: ki67 positivity index of psoriasis and psoriasiform dermatitis in comparison with other studies

Study	Year	KI67	
		Psoriasis	Psoriasiform dermatitis
Sezer *et al.* [6]	2015	77.1–92.4%	21–73.3%
Ramezani *et al.* [27]	2019	21.6±10	29±11.6
Sanasam *et al.* [25]	2021	71.65±4.99	39.47±3.37
Abdesalam *et al.* [26]	2022	94.4±11	21.1±5.7
Present study	2024	73±1.91	43±8.2

osteopontin, CD34, CD4, and CD8 to distinguish between psoriasis and psoriasiform dermatitis. In this study, we specifically investigated the differential immunohistochemical expression of Ki-67 as a proliferative marker and CD34 as a vascular endothelial marker in psoriasis and psoriasiform dermatitis.

Our study reviewed a total of 100 cases, comprising 50 cases of psoriasis and 50 cases of psoriasiform dermatitis.

In the studies by Dogra and Yadav [12] and Khandpur *et al*. [13], psoriasis and psoriasiform dermatitis were found to be twice as common in males compared to females, which aligns with the findings of the present study.

In Nisha *et al*.'s study [14], the most common age group for psoriasis was under 30 years of age, which aligns with our study where the majority were between 21 and 30 years old, and in their study, the most common age group for psoriasiform dermatitis was 30–50 years, whereas in our study, the majority were in the 31–40 years age range.

In the studies by Hellgren [15] and Mehta *et al*. [16], they noted that Auspitz signs, a commonly elicited clinical sign, are pathognomonic of psoriasis, which is consistent with our findings. In our study, the Auspitz sign was observed in 40 (80%) cases of psoriasis, whereas only 6 (12%) cases of psoriasiform lesions showed a positive Auspitz sign, with a significant p=0.0001.

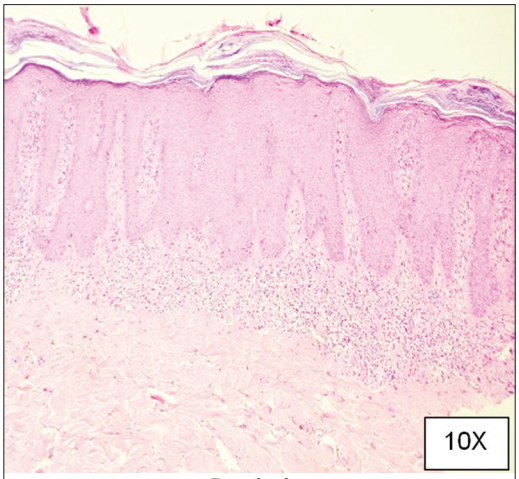
In the study by Meier and Seth [17], silvery scaly plaques were identified as clinically significant for psoriasis, which aligns with our study findings.

In the studies by Nisha *et al*. [14] and Maize *et al*. [18], hyperpigmented lesions were highlighted as significant in psoriasiform lesions, which mirrors our findings in the present study. They also noted that the characteristic silvery scales of psoriasis histologically correlate with parakeratosis in the cornified layer of the skin.

In the studies by Mehta *et al*. [16] and Nisha *et al*. [14], the predominant histopathological findings included regular acanthosis, suprapapillary thinning, hypogranulosis, and Munro microabscesses, which were observed to be significant in psoriasis cases, consistent with our findings in the present study.

In studies by Venna *et al*. [19], Lal *et al*. [20], Gordon and Johnson [21], Mehta *et al*. [16], and Pandit and Narayankar [22], as well as standard histopathology textbooks on Dermatopathology [23,24], it was consistently observed that psoriasiform dermatitis exhibits irregular acanthosis, thick suprapapillary plate, hypergranulosis, and vertical orientation of collagen bundles. These findings are in concordance with the results of our present study.

In our study, the distribution of psoriasiform dermatitis cases by frequency was as follows: 40% - pityriasis rosea, 26% - chronic eczema, 22% - lichen simplex chronicus, 14% - prurigo nodularis, 10% - pityriasis rubra pilaris, and 6% - seborrheic dermatitis.



Psoriasis

Fig. 1: In psoriasis demonstrates hyperkeratosis, parakeratosis, regular elongation of rete ridges, suprapapillary thinning, hypogranulosis, and inflammatory infiltrate

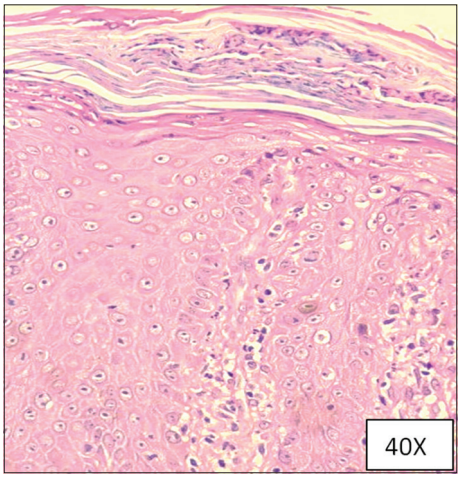
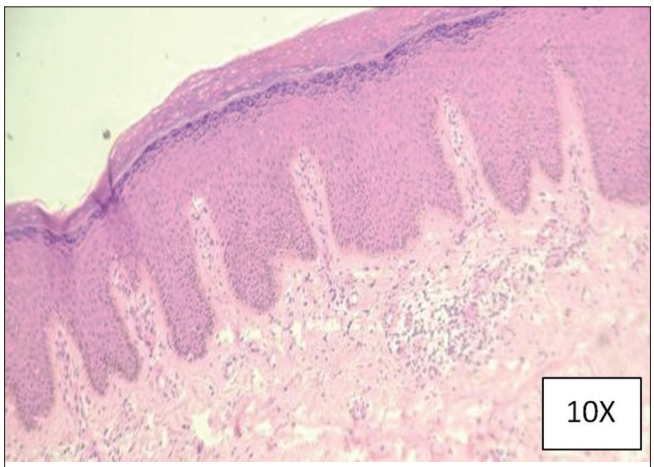


Fig. 2: Illustrates Munro microabscesses



Psoriasiform dermatitis

Fig. 3: Exhibits hyperkeratosis, irregular acanthosis, and hypergranulosis

In the study by Sanasam *et al*. [25], the suprabasal Ki-67 positivity index (suprabasal/total epidermal cell count ratio) was significantly higher in the psoriasis group (mean±SD: 71.65±4.99%) compared to

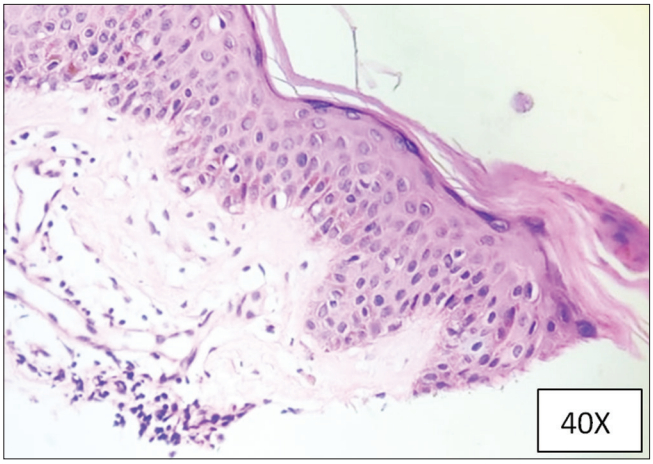


Fig. 4: Displays perivascular lymphomononuclear infiltrates

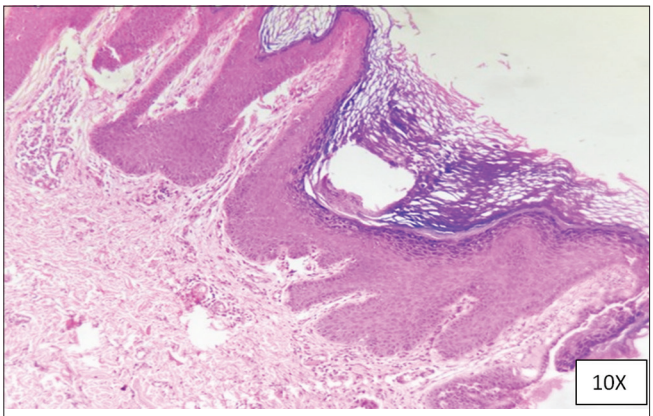


Fig. 5: Depicts ILVEN, demonstrating hyperkeratosis, irregular acanthosis, alternating areas of hypogranulosis with parakeratosis, and areas of depressed hypergranulosis with orthokeratosis

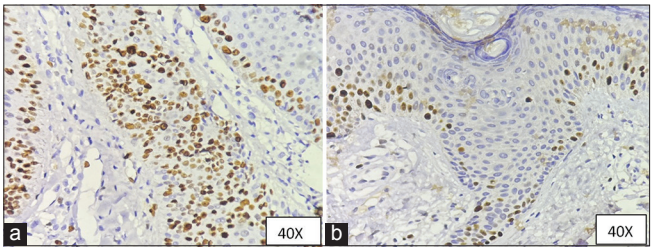


Fig. 6: Depicts Ki67 immunoexpression: (a) In Psoriasis, there is suprabasal positivity of Ki67. (b) In Psoriasiform Dermatitis, Ki67 shows basal positivity

the psoriasiform dermatitis group (mean±SD: 39.47±3.37%) with a p<0.05. Similarly, in our present study, we found a significant difference in the suprabasal Ki-67 positivity index between psoriasis (mean ± SD: 73±1.91%) and psoriasiform dermatitis (mean±SD: 43±8.2%), with a p<0.001, consistent with the findings of Sanasam *et al*. [25] (Table 6).

In the study by Sezer *et al*. [6], similar findings were observed regarding Ki-67 immunostaining. An important and interesting feature noted was the establishment of a cut-off value for the suprabasal/total epidermal cell count ratio of 75% for Ki-67 staining. This ratio was consistently higher in all patients with psoriasis (range, 77.1–92.4%) compared to psoriasiform dermatitis cases, where it ranged from 21.0% to 73.3%. This distinction highlights the diagnostic utility of Ki-67

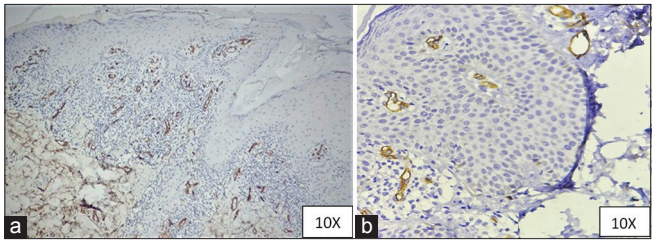


Fig. 7: Illustrates CD34 immunoexpression in dermal vessels: (a) Increased microvessel density (MVD) in Psoriasis compared to (b) Psoriasiform dermatitis

immunostaining in differentiating between psoriasis and psoriasiform dermatitis.

In Abdesalam *et al*.'s study [26], the average Ki-67 expression was markedly elevated in psoriasis (94.4±11) compared to psoriasiform dermatoses (21.1±5.7), demonstrating a significant difference (p<0.001). This highlights Ki-67 as a valuable marker for distinguishing between psoriasis and psoriasiform dermatoses based on their proliferative activity.

In contrast to our findings, Ramezani *et al*. [27] reported a higher mean Ki-67 expression in psoriasiform dermatoses (29±11.6) compared to psoriasis (21.6±10), with a statistically significant difference (p=0.002). This discrepancy can be attributed to their utilization of a 25% cut-off value for Ki-67 expression in their research, whereas in our study, we assessed Ki-67 expression based on the suprabasal/total epidermal cell count ratio.

CD34

In studies by Gupta *et al*. [28] and Sujatha *et al*. [30], strong CD34 positivity and increased microvessel density were observed in psoriasis compared to psoriasiform dermatitis, consistent with our findings.

In the study conducted by Gupta *et al*. [28], they observed higher CD34 positivity through routine microscopy and noted a tendency toward increased microvessel length density in psoriasis compared to psoriasiform lesions, although this difference did not achieve statistical significance (p>0.05). Our study, as depicted in Table 5, similarly reveals these trends with a significant (p<0.001).

In Amin *et al*. [29] study, significant differences were found in the expression of OPN, Ki-67, and CD34 between lesional and non-lesional skin, as well as between non-lesional skin and control groups (p≤0.001). In addition, significant differences were observed in the expression of OPN, Ki-67, and CD34 between the control group and the lesional group (p=0.02, p=0.02, and p=0.04, respectively). Unlike our study, they categorized samples into lesional, non-lesional, and control groups.

In contrast, our findings differ from those of Ramezani *et al*. [27], where strong CD34 positivity was reported in psoriasiform dermatitis compared to psoriasis.

CONCLUSION

The prototypical features of psoriasis on histopathology include regular acanthosis, Munro microabscesses, absence of the granular layer, suprapapillary plate thinning, club-shaped enlargement, and dermal inflammatory infiltrates. Psoriasiform dermatoses comprise a spectrum of disorders with overlapping clinical and histomorphological characteristics.

Immunohistochemical markers such as CD34 and Ki67 are valuable for distinguishing between psoriasis and psoriasiform dermatitis. However, our study revealed CD34 positivity in four cases of psoriasiform dermatitis. Further investigations focusing on CD34 expression in psoriasis are warranted to better understand its role in differentiating these conditions.

CONFLICTS OF INTERESTS

Nil.

AUTHORS FUNDING

Nil.

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