

# A Comparative Study of Histopathological Findings in Psoriatic Lesions with and without treatment

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## Abstract

**Background:** Psoriasis is a multifactorial chronic relapsing inflammatory dermatological disorder associated with significant comorbidities. It is characterized by sharply demarcated, erythematous papules, and plaques with abundant silvery-white scales. Due to its variable clinical presentation, histopathology remains the mainstay of diagnosis. However, these histologic features changes with treatment and may also guide in therapeutic decision-making. **Aim:** The aim is to evaluate and compare the histopathological features of psoriatic lesions before treatment with those receiving treatment for psoriasis. **Patients and Methods:** A total of 101 biopsies from selected consecutive patients of histopathologically confirmed psoriasis vulgaris were included in the study. These cases were then divided into two groups, Group A includes cases who never received treatment and Group B, those receiving treatment for psoriasis. These biopsies were histopathologically analyzed and compared for various morphological features. **Results:** Of 101 cases of psoriasis, 72 cases were included in Group A and 29 were included in Group B. Biopsies of Group A showed parakeratosis and acanthosis as a common feature in all of them with dilated or abnormal capillary pattern in dermal papillae in 93.1%. In Group B, in spite of uniform parakeratosis as noticed in Group A biopsies, focal parakeratosis was seen in 83.3%, acanthosis in 87.5%, and dilated/abnormal capillary pattern in dermis was observed to be a universal feature in biopsies of Group B. All other microscopic features of psoriasis also decreased in frequency in Group B. However, statistically significant difference is seen only in changes in morphological features of superficial epidermis that is, parakeratosis, acanthosis, and absent or decreased granular layer in both the groups. **Conclusion:** Treatment may lead to improvement in the histologic features in epidermis with significant difference in few of them. However, abnormal vasculature in the dermal papillae persists and does not show any improvement with therapy.

**Keywords:** Histopathology, methotrexate, phototherapy, psoriasis, treatment

## INTRODUCTION

Psoriasis is a chronic inflammatory papulosquamous skin disorder.<sup>[1]</sup> It is a lifelong ailment with exacerbations and remissions associated with significant comorbidities.<sup>[2]</sup> It has a worldwide distribution affecting about 1%–3% of the population<sup>[3-5]</sup> and is characterized clinically by well-demarcated erythematous plaques covered with silvery-white scales. These features are explained by epidermal hyperplasia and dilated superficial blood vessels.<sup>[6-8]</sup>

The pathogenesis of psoriasis includes hyperproliferation of keratinocytes with abnormal differentiation along with inflammatory infiltration of T-cells in epidermis and dermis.<sup>[9,10]</sup> Due to the variable clinical presentation in different types and stages, histopathological examination remains the gold standard for establishing the diagnosis.<sup>[11]</sup> The histologic spectrum of psoriasis is well established, but with the administration of

therapy, the cardinal histopathological features also change along with clinical improvement.<sup>[12]</sup>

Very few studies are documented in the literature which evaluates the response of psoriatic lesions histopathologically on treatment. Gordon *et al.*<sup>[13]</sup> studied the dynamics of psoriatic lesions on treatment. They concluded that on giving treatment Munro microabscesses, exocytosis, and parakeratosis disappear with the reappearance of stratum granulosum and orthokeratosis. Acanthosis and papillomatosis also decrease while the diameter of blood vessels reduces slowly.

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This prompted us to undertake this study to evaluate the histopathological changes in the lesions of psoriasis vulgaris on treatment and to compare with the histology of the lesions before therapy.

## PATIENTS AND METHODS

This prospective cross-sectional study was carried out for 3 years in the Department of Pathology in a tertiary care medical institute. A total of 101 consecutive biopsies of histopathologically-proven cases of psoriasis were included in the study.

### Inclusion criteria

1. All age groups and both gender are included
2. Biopsies of the patients with histologically confirmed diagnosis of psoriasis.

### Exclusion criteria

1. Inadequate biopsy samples defined as those <4 mm in maximum diameter or showing only epidermis or dermis on microscopic examination
2. Multiple biopsies from a single patient
3. Patients clinically diagnosed with other types of psoriasis than psoriasis vulgaris.

The study was approved by the Ethical and Research Committee of the Institute. Patients were selected in accordance with predefined inclusion and exclusion criteria of the study. All the selected patients for the study were briefed about the nature of study and written informed consent was obtained. The relevant clinical details, demographic data of the patients such as the name, age, and sex along with a questionnaire about the recent psychiatric disorders, known case of diabetes, cigarette smoking, skin cancer, any kidney or liver disease, pregnancy, and lactation were recorded from the requisite form accompanying the biopsy samples.

All cases were divided into two groups; the first group (Group A) comprised cases with no history of any treatment for psoriasis. The second group (Group B) included cases who are receiving treatment for psoriasis with phototherapy and oral methotrexate.

Punch biopsy was performed by a dermatologist on psoriasis patients as an outpatient procedure in the dermatology outpatient department. The tissue was immediately put into a container containing 10% buffered neutral formalin solution for fixation and was sent to the pathology department for further processing. All received punch biopsy samples were fixed in 10% formol saline overnight and then embedded in paraffin. After routine paraffin processing, blocks were made with the help of Leukhardt mold. 4–6  $\mu$  thick sections were obtained from each block. These were stained with hematoxylin and eosin and were subjected for histopathological examination. All the slides were thoroughly analyzed by two independent trained histopathologists. All the histological features were noted and recorded on predesigned pro forma. The findings were tabulated.

## Statistical analysis

Descriptive statistics was analyzed with SPSS version 17.0 software (SPSS Inc., Chicago, Illinois, United States). Categorical variables are expressed as frequencies and percentages. The Pearson's Chi-square test or Fisher's exact test was used to determine the relationship between two categorical variables.  $P < 0.05$  was considered statistically significant.

## RESULTS

A total of 101 biopsies were included with histopathologically proven cases of psoriasis vulgaris.

Seventy-two (71.3%) of 101 cases, had never received any treatment for psoriasis (Group A) while 29 (28.7%) were on treatment at the time of biopsy (Group B).

In Group A, maximum cases were noted in the age group of 31–40 years (33.3%) followed closely by 41–50 years (29.2%). Least number of cases was noted in 0–10 years' age group (0.9%). The youngest patient was 6 years old and the oldest was 89 years old at the time of biopsy. In Group B, majority of the cases were in the age group of 41–50 years (41.4%). Minimum cases were seen in >60 years (6.9%).

The study showed that there is male predominance in both groups. In Group A, sex ratio is 2.4:1, while in Group B, ratio is 1.6:1.

An attempt was made to correlate morphological changes observed on histopathological examination in biopsies of Group A and Group B which are shown in Table 1 and Graph 1.

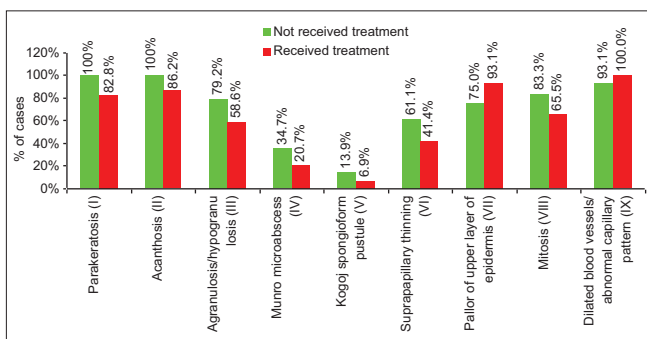
Even all the biopsy samples from Group A did not show all the classical histopathological features of psoriasis [Figure 1]. Parakeratosis and acanthosis were present in all the cases while majority of them (93.1%) show dilated blood vessels in dermal papillae. Absent or decreased granular layer along with mitosis was noted in 79.3% and 82.8% of the biopsies, respectively. About 75.9% of biopsies show pallor of the upper layer of the epidermis. Suprapapillary thinning was observed in 62.1% of biopsy samples. Munro microabscess and Kogoj spongiform pustule were present in 34.5% and 13.8% of the biopsies.

The biopsies from Group B show some improvement in histopathological features [Figure 2]. About 83.3% of the biopsies had focal parakeratosis while few of them did not have parakeratosis at all. Acanthosis was seen in about 87% of biopsies. The granular layer was present in all biopsies. While around 40% of the biopsies showed normal, remaining had decreased granular layer. The pallor of the upper layer of the epidermis was seen in 93.1%. Thinning of suprapapillary layer was also noted in around 40% of biopsies. Munro microabscess and Kogoj spongiform pustule were observed in approximately 20% and 7% of cases, respectively. Mitosis was seen in 65.3% of biopsies and was limited to lower 3 layers of the epidermis. Dilated blood vessels in the dermal papillae were seen in all the cases.

**Table 1: Summary of histologic features present in biopsy samples according to treatment history**

Histological features	Not received treatment (n=72)	Received treatment (n=29)	P
	Group A	Group B	
Parakeratosis (%)	Uniform - 100	Focal - 83.3	0.002
Acanthosis (%)	100	87.5	0.006
Agranulosis/hypogranulosis (%)	79.3	59.7	0.035
Munro microabscess (%)	34.5	19.4	0.167
Kogoj spongioform pustule (%)	13.8	6.9	0.501
Suprapapillary thinning (%)	62.1	40.3	0.071
Pallor of upper layer of epidermis (%)	75.9	93.1	0.052
Mitosis (%)	82.8	65.3	0.050
Dilated blood vessels/abnormal capillary pattern (%)	93.1	100	0.318

Histopathological features (Parakeratosis, Acanthosis and Agranulosis/hypogranulosis) in superficial epidermis show significant improvement with treatment



**Graph 1:** Bar diagram showing histologic features present in biopsy samples according to treatment history

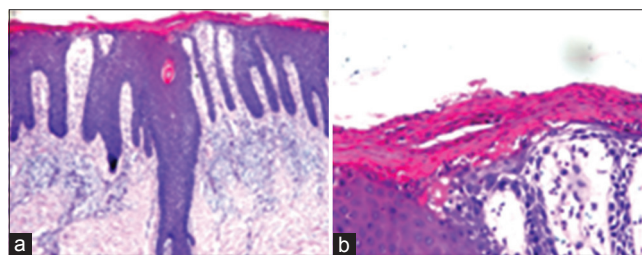
On statistical analysis, statistically significant difference ( $P < 0.05$ ) was observed in only three superficial epidermal features in both the groups. Rest of the features did not show any statistically significant difference ( $P > 0.05$ ).

## DISCUSSION

Although histopathology is the basis of the diagnosis of every disease and its remission, there are very few studies focused on changes noticed on histopathology of psoriasis after treatment. In this study, we have tried to evaluate and compare the histopathological features in the biopsies of lesions of psoriasis vulgaris patients who have never received treatment and those on treatment.

In this study, in Group A, maximum of the patients presented in the age group of 31–40 years with male predominance (2.4:1). As the age of onset depends on the patient’s recall, we recorded the age at the time of biopsy and hence, we cannot compare it with other studies. In the study of Kaur *et al.*<sup>[14]</sup> 67% of patients were male and 33% were female. A study from South India also observed male predominance. The ratio was 2.9:1 in their study.<sup>[15]</sup> Bilac *et al.*<sup>[16]</sup> reported slightly higher prevalence of psoriasis among females (51.7%) than that of males (48.3%).

Our findings are similar to the study of Kaur *et al.*<sup>[14]</sup> but differ from the study of Biliac *et al.*<sup>[16]</sup> Most of the Indian studies<sup>[14,15]</sup> have reported a higher incidence of psoriasis in

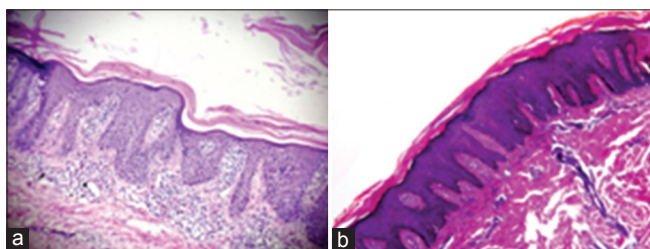


**Figure 1:** (a) Pretreatment microphotograph shows acanthosis along with club-shaped rete ridges and subepidermal lymphocytic infiltrate. (b) Pretreatment microphotograph shows uniform parakeratosis

males as compared to females. However, there is no definite sex predilection as observed from most studies in the literature. There is a paucity of data in literature about the age and sex distribution of psoriasis patients receiving treatment. However, we tried to study the preponderance of age and sex in this group. We found majority of cases in 41–50 years with sex ratio of 1.6:1.

In the present study, there was a significant decrease in parakeratosis on treatment. Uniform parakeratosis was noticed in all the biopsies of Group A, while in Group B, it was noticed in 83% of biopsies but in focal manner. Our study is in concordance with the study of Bhat *et al.*,<sup>[5]</sup> Ozkanli *et al.*<sup>[17]</sup> and Eskicirak *et al.*<sup>[18]</sup> who observed a significant decrease in parakeratosis with therapy. Puri *et al.*<sup>[3]</sup> reported complete absence of parakeratosis with therapy. The study is also similar to the study conducted by Talwar *et al.*<sup>[19]</sup> who documented that parakeratosis became patchy initially following methotrexate treatment. Weedon<sup>[20]</sup> has described psoriasis as a dynamic process and consequently, the picture varies during evolution and subsequent resolution of individual lesions. The epidermis is initially normal, but soon there is the formation of mounds of parakeratosis. Therefore, keratosis, especially parakeratosis is a consistent feature in all cases of psoriasis.

In this study, acanthosis which was a universal feature in all biopsies of Group A, was present in around 87% of cases in Group B. The difference was statistically significant. The results are similar to the studies of Puri *et al.*<sup>[3]</sup> and Ozkanli *et al.*<sup>[17]</sup> who documented a significant decrease in acanthosis.



**Figure 2:** (a) Posttreatment microphotograph shows mild acanthosis with focal parakeratosis. (b) Posttreatment microphotograph shows mild acanthosis with mild subepidermal inflammatory infiltrate

Other investigators such as Talwar *et al.*<sup>[19]</sup> and Braverman *et al.*<sup>[21]</sup> also noticed reduction in acanthosis in their studies.

Moorchung *et al.*<sup>[6]</sup> reported a strong correlation between acanthosis and parakeratosis. This was explained on the basis of common pathogenesis of rapid proliferation and differentiation of keratinocytes shared by them.

In this study, we observed a statistically significant decrease in agranulosis/hypogranulosis on treatment. This finding was seen in around 80% of the biopsies of Group A, while in Group B, the granular layer was present in all biopsies although around 60% of them had decreased granular layer. Our study is similar to the studies of Puri *et al.*,<sup>[3]</sup> Bhat *et al.*,<sup>[5]</sup> Ozkanli *et al.*,<sup>[17]</sup> and Talwar *et al.*,<sup>[19]</sup> in which the granular layer increased or became normal in comparison to pretreatment biopsies. Braverman *et al.*<sup>[21]</sup> noticed a few focal areas of agranulosis on treatment with methotrexate. Talwar *et al.*<sup>[19]</sup> and Braverman *et al.*,<sup>[21]</sup> in their study, stated that the appearance of the granular layer can be taken as the first sign for improvement in those responding to therapy.

Few studies stated that first change noted on microscope in psoriasis which correlates with clinical findings is the reappearance of the granular layer.<sup>[22-24]</sup> Bhat *et al.*<sup>[5]</sup> also documented that change in percentage of parakeratosis and thickness of the granular layer can be taken as reliable markers of consideration of improvement with therapy in the psoriatic patient.

Munro microabscess and kogoj spongiform pustule were noticed in approximately 35% and 14% in biopsies of Group A which was reduced to 20% and 7%, respectively, in Group B, but there was no significant decrease. The low incidence of microabscess even in pretreatment biopsies can be attributed to continuous exfoliation of stratum corneum.<sup>[25]</sup> Not many authors have studied the change in frequency of Munro microabscess and kogoj spongiform pustule on treatment. Results of our study are in contrast to the study conducted by Puri *et al.*<sup>[3]</sup> and Ozkanli *et al.*<sup>[17]</sup> who reported a significant decrease in Munro microabscess and spongiform pustules in the biopsies after treatment. However, it is necessary to evaluate multiple sections for demonstration of Munro microabscess.<sup>[26]</sup> Moorchung *et al.*,<sup>[6]</sup> in their study, demonstrated that these microabscesses are significantly correlated with pustules of Kogoj.

Other epidermal features which did not show any statistically significant difference were mitosis, thinning of suprapapillary plates and pallor of the upper layer of the epidermis.

We observed less frequency of mitosis (65.3%) in biopsies of Group B as compared to mitosis (82.8%) in Group A. The result of our study differs from a few other studies. Bhat *et al.*<sup>[5]</sup> noticed a significant decrease in mitotic figures post treatment and Talwar *et al.*<sup>[19]</sup> reported normalization of mitosis by 4–6 days after treatment. Bhat *et al.*<sup>[5]</sup> though found in their study that mitosis reduced after therapy but concluded that it cannot be used as a marker for those responding to therapy as it is decreased in both responders and nonresponders to treatment. The epidermal hyperproliferation described in patients of psoriasis is due to increase in number of germinative cells and mitotic figures. Mitosis indicates active hyperproliferation and this may also indicate fluctuation in activity of psoriasis.<sup>[27]</sup>

Suprapapillary thinning was noticed in approximately 62% of biopsies in Group A which was only seen in around 40% biopsies in Group B. The present study is comparable with the study of Talwar *et al.*<sup>[19]</sup> who reported decrease in thinning of suprapapillary epidermis on methotrexate therapy. The results of this study did not match with the study conducted by Puri *et al.*<sup>[3]</sup> and Ozkanli *et al.*<sup>[17]</sup> They demonstrated significant decrease in suprapapillary plate thinning on therapy. Although we noticed the percentage decrease in suprapapillary thinning on administration of treatment, our results are not statistically significant. The reason for this could be that the suprapapillary epidermal thinning is a relative observation on comparison with markedly elongated rete ridges.

On the contrary, where all histopathologic features decreased in biopsies of patients who were on treatment, dilated/abnormal capillary pattern in the dermal papillae became consistent feature in them and there was no statistically significant difference noted. In general, studies in literature documented that changes which occur in vessels were minimal on giving treatment.<sup>[21-23]</sup> Our results are in concordance with the study of Puri *et al.*<sup>[3]</sup> who reported no significant decrease in vascularity in dermal papillae in biopsies on treatment. In contrast, Ozkanli *et al.*<sup>[17]</sup> demonstrated a significant decrease in dilated tortuous vessels in the papillary dermis on treatment with phototherapy but not with methotrexate. Few studies<sup>[22,23]</sup> in literature have demonstrated the persistence of abnormal capillary pattern till 5 months on treatment with methotrexate. However, we did not take treatment duration into account while evaluating biopsies in the group receiving treatment. The reason for the persistence of dilated tortuous vessels in the dermis with phototherapy could be the inability of the wavelength to sufficiently penetrate the dermis.

### Limitation

There is a need for sequential histological assessment of the biopsies of psoriatic lesions in the patients undergoing treatment on large sample size for a better understanding of histopathological changes.

## CONCLUSION

This study indicates that with treatment certain histopathological features in epidermis show reversal to normal, especially in the superficial epidermis (i.e., diminution of parakeratosis, appearance of the granular layer and recovery of the normal thickness of epidermis) which is responsible for the clinical improvement of psoriatic lesions (i.e., healed lesions). Some of the histological features in the epidermis also decrease in frequency though no statistically significant difference is observed. However, the vascular changes in the dermis may persist. This may account for relapses on discontinuation of therapy. Hence, a clinicopathological correlation is must to determine the duration of therapy.

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## Conflicts of interest

There are no conflicts of interest.

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