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# A Clinical, Dermoscopic, Histopathological And Therapeutic Study Comparing Efficacy Of Methotrexate Versus Apremilast In The Treatment Of Palmoplantar Psoriasis

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***Abstract:***
***Background****: Palmoplantar psoriasis (PPP) is a chronic, debilitating variant of psoriasis that affects the palms and soles, accounting for 13–15% of all psoriasis cases. Despite limited body surface area involvement, PPP leads to significant functional impairment due to painful fissuring, scaling, and persistent inflammation. Dermoscopy and histopathology play important roles in differentiating PPP from clinically overlapping conditions. Owing to the poor response to topical therapies and limited clinical trials, systemic agents such as methotrexate and apremilast are frequently used. This study compares the therapeutic efficacy and safety of apremilast and methotrexate in biopsy-confirmed PPP cases.*
***Materials and Methods****: A hospital-based, randomized, prospective cross-sectional study was conducted in the DVL outpatient department Sixty-six patients fulfilling inclusion and exclusion criteria were randomized into two equal groups: Group A (apremilast) and Group B (methotrexate). All patients underwent clinical, dermoscopic, and histopathological evaluation. Apremilast was administered at 30 mg twice daily after dose titration, while methotrexate was given at 0.2 mg/kg/week with folic acid supplementation. Treatment response was assessed at baseline and at 4-week intervals up to 16 weeks using the Modified Palmoplantar Psoriasis Area and Severity Index (m-PPPASI) and Dermatology Life Quality Index (DLQI). Statistical analysis was performed using Chi-square and independent t-tests.*
***Results****: Baseline m-PPPASI scores were comparable between the apremilast (22.09 ± 1.98) and methotrexate (22.02 ± 1.58) groups. At 16 weeks, scores significantly decreased to 8.55 ± 1.55 and 7.75 ± 1.23, respectively, indicating a marginally greater improvement with methotrexate. DLQI scores also reduced significantly in both groups, with slightly better improvement in the methotrexate group.*
***Conclusion:*** *Both methotrexate and apremilast were effective and well tolerated in the management of palmoplantar psoriasis. Methotrexate demonstrated a slightly faster and greater clinical improvement compared to apremilast, although both agents significantly improved disease severity and quality of life. Dermoscopy and histopathology proved valuable in confirming diagnosis and guiding management. Systemic therapy should be considered in patients with significant functional impairment, inadequate response to topical agents, or extensive disease. Further multicentric studies with larger sample sizes are recommended to strengthen evidence for optimal PPP management.*
***Key Word:*** *Palmoplantar psoriasis, Apremilast, Methotrexate*

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## I. Introduction

Palmo plantar psoriasis (PPP), a localized subtype of psoriasis can occur either independently or in conjunction with other psoriatic lesions, affecting an estimated 2 to 3% of the global population [1]. Despite affecting only, a small portion of the body surface area, palmoplantar involvement in psoriasis can significantly reduce patients daily acitivities and hinder work productivity. This condition is recognized by fissuring, scaling, and well-defined erythema on the soles and palms, accounting for approximately 13-15% of all psoriasis cases. [1,2] Dermoscopy employs optical magnification to reveal a distinctive pattern of diffuse white scales and symmetrically distributed dotted vessels on a pale or dull red background. When the skin lesion is limited to the palmoplantar region, palmoplantar psoriasis (PPP) can easily be misdiagnosed and are difficult to treat

because of their chronicity and frequent exacerbations. Therefore, these diseases require dermoscopy, skin biopsy to confirm and use of systemic therapy to achieve adequate control.[3] Here we confirm by skin biopsy and compare therapeutic efficacy of Apremilast and Methotrexate in palmoplantar psoriasis.

## II. Material And Methods

**Study Design:** A hospital-based, randomized, prospective cross-sectional study.
**Study Location**: This was a tertiary care teaching hospital-based study done in Department of DVL outpatient department at GVPIHC&MT, Vizag, Andhra Pradesh.
**Study Duration:** August 2022 to February 2024.
**Sample size:** 66 patients.
**Sample size calculation:** The predicted sample size was calculated as 66 using the difference of means formula, with a power of 80%, $\alpha = 0.05$, and a 95% confidence interval.
**Subjects & selection method**: A hospital-based, randomized, prospective cross-sectional study was conducted on patients with palmoplantar psoriasis attending the DVL outpatient department at GVPIHC&MT, Vizag. The study was initiated after obtaining approval from the institutional ethics committee and was carried out from August 2022 to February 2024. The study was conducted over a period of 18 months, and sixty-six participants were enrolled after fulfilling the inclusion and exclusion criteria. Written informed consent was obtained from all participants after they were fully informed about the study. Participants were randomized equally into two groups of 33 each, with Group A receiving apremilast and Group B receiving methotrexate. Per-protocol analysis was followed, and two patients in Group A and three patients in Group B were lost to follow-up. Therefore, the final analysis included 31 cases in Group A and 30 cases in Group B.

**Inclusion criteria:**
All patients of 18 to 60 years. Patients diagnosed with skin biopsy of palmoplantar psoriasis

**Exclusion criteria:**
Patients with pustular psoriasis, palmoplantar pustulosis, erythrodermic psoriasis, guttate psoriasis, generalized pustular psoriasis, or eczema were excluded. Those receiving methotrexate, retinoids, or biologics; patients with acute or chronic infections; abnormal CBC, LFT, or renal function; pregnant or lactating women; and individuals with intolerance, hypersensitivity, or contraindications (absolute or relative) to methotrexate and/or apremilast were also excluded

**Procedure methodology**
All patients underwent a detailed general and cutaneous examination. Dermoscopic evaluation was performed at baseline and at the end of week 16 using a portable Heine dermoscope, and high-resolution images were captured using an iPhone 12 under standardized distance and position. Punch biopsies were obtained from all participants and processed for histopathological examination. Dermoscopic findings were correlated with histopathology.

Patients in the methotrexate group received a weekly dose of 0.2 mg/kg/week (upto maximum dose of 15mg/week), along with folic acid 5 mg supplementation on all days except the day of methotrexate administration. Patients in the apremilast group received 30 mg twice daily. Dose titration was carried out during the first week: a 10 mg initial dose was given on Day 0, followed by gradual escalation, and from Day 5 onward, patients received 30 mg twice daily for the 16-week treatment period.

Female patients of reproductive age underwent pregnancy testing prior to therapy and were counseled to use physical contraception during treatment and for one menstrual cycle after discontinuation of methotrexate. Male patients were advised to use contraception until three months after stopping methotrexate. Throughout the study, patients were instructed to use only bland emollients, and oral antihistamines were prescribed when required. Follow-up visits were scheduled every four weeks, resulting in a total of five visits over 16 weeks.

At the conclusion of the study, clinical, dermoscopic, and histopathological findings were correlated, and the therapeutic efficacy and safety of methotrexate and apremilast were evaluated. Baseline demographic characteristics of the study population are summarized in Table 1

**Table 1:** Baseline demographic characteristics of the study population

| Characteristics | Apremilast (n = 31) | Methotrexate (n = 30) |
|---|---|---|
| **Age, mean (years)** | 49.8 | 47.3 |
| **Gender** | | |
| **Male** | 15 | 19 |
| **Female** | 16 | 11 |
| **Family history of psoriasis** | 8 | 3 |

| | | |
|---|---|---|
| **Morphology of lesion** | | |
| **Palmar** | 7 | 3 |
| **Plantar** | 6 | 6 |
| **Both** | 18 | 39 |
| **Baseline m-PPPASI score** | 22.09 | 22.02 |
| **Baseline DLQI score** | 16.47 | 15.77 |
| **Duration of the disease (years)** | 2.32 | 2.20 |
| **Nail involvement** | 3 | 3 |
| **Joint involvement** | 15 | 11 |
| **History of smoking** | 6 | 10 |
| **History of Alcohol** | 7 | 11 |
| **History of Diabetes** | 13 | 6 |
| **History of Hypertension** | 10 | 13 |

**Treatment evaluation**:

The primary outcome measure was the change in Modified Palmo plantar Psoriasis Area and Severity Index (m-PPPASI) score, DLQI Score from baseline after 16 weeks of treatment, Safety analysis was done by recording and evaluating the adverse events.

**Statistical analysis**

Data were compiled and analyzed using MS Excel 2019 and the SPSS trial version 25 software. Qualitative variables were compared using the Chi-square test, while quantitative variables were analyzed using the independent samples unpaired t-test. A p-value of $<0.05$ was considered statistically significant.

## III. Results

A total of 66 patients were recruited for the study, of whom 5 were lost to follow-up during the study period.

The majority of patients presented with painful fissuring associated with significant functional disability. Most patients belonged to the 41–50-year age group, followed by the 51–60year group **(Figure 1)**. Males outnumbered females in the study population. The mean duration of illness was 28.79 ± 13.3 months, with a range from 1 month to 10 years.

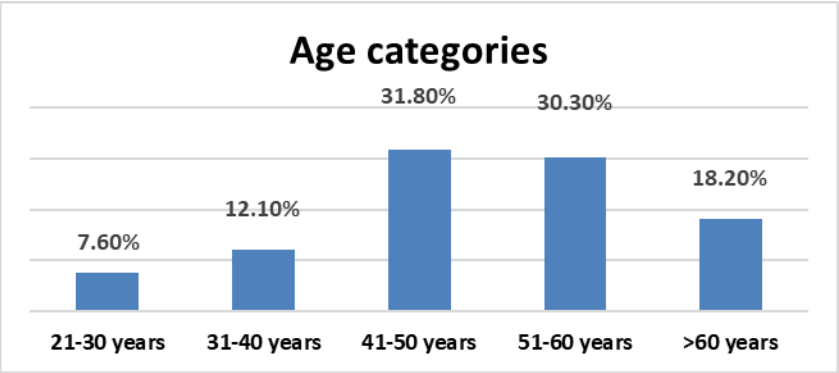


**Figure 1:** Distribution of the Age

Of the 66 patients, involvement of both palms and soles was observed in 42 (63.6%), while 12 (18.2%) had isolated palm involvement and 12 (18.2%) had isolated sole involvement.

**Distribution according to the dermoscopic findings (Figure 2)**

The most frequent dermoscopic feature observed was **white scaling** (80.3%), followed by **diffuse distribution of scales** (72.1%) and **dilated vessels** (67.2%). A **light red background** was noted in (45.9%), while a **dull red background** was seen (26.2%) and a **yellow-red background** (18%). Scales were **yellow** in (32.8%), and a combination of **white and yellow scales** was observed in (18%).

Vascular patterns included **regular distribution of vessels** (39.3%), **undifferentiated vessels** (19.7%), **linear vessels** (9.8%), and **patchy distribution of vessels** (13.1%). Patchy distribution of scales was noted in (27.9%).

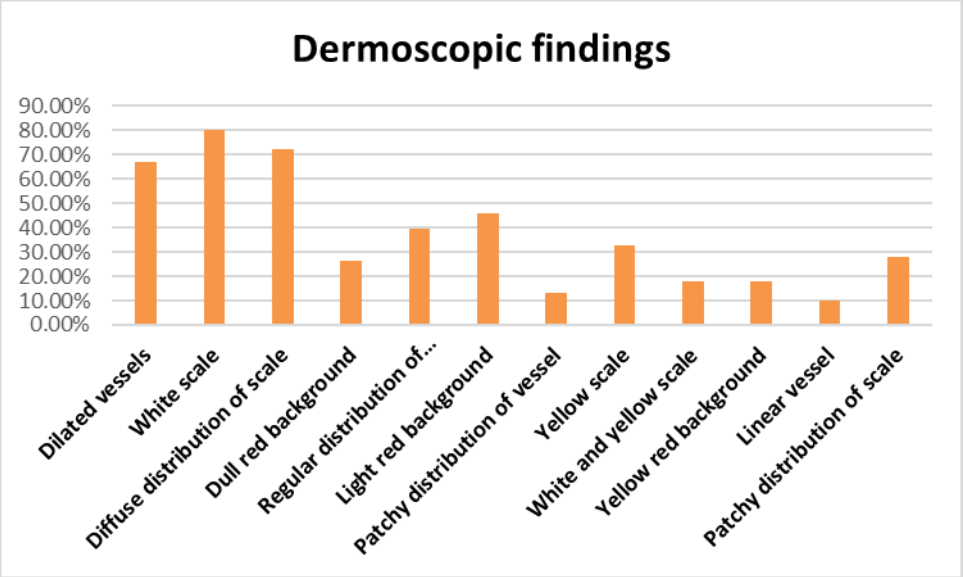


**Figure 2:** Distribution according to the dermoscopic findings

**Distribution according to the Histopathological findings (Figure 3)**

Histopathology most frequently revealed **perivascular infiltrates** (65.6%), **focal parakeratosis** (63.9%), and **spongiosis** (63.9%). **Hypogranulosis** was observed in 59% and **normal rete ridges** in 54.1% of cases. Other changes included **suprapapillary thinning** (45.9%), **dilated tortuous vessels** (32.8%), **tapered rete ridges** and **confluent parakeratosis** (27.9% each), **broad rete ridges** (21.3%), and **interstitial infiltrates** (19.7%). **Perivascular with interstitial infiltrates** were less common, seen in 14.8% of patients.

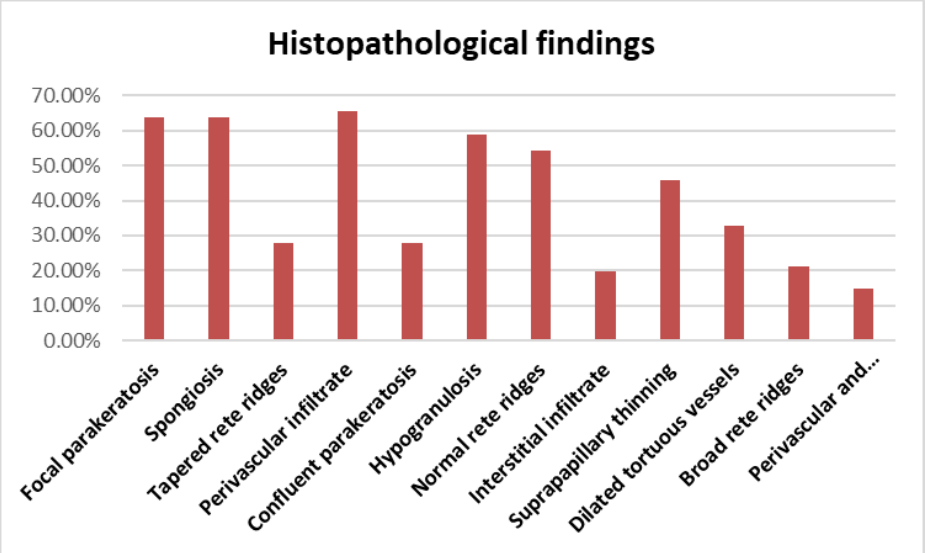


**Figure 3:** Distribution according to the Histopathological findings

**Association between m-PPPASI score and treatment**

The mean m-PPPASI scores at baseline were comparable between the Apremilast group (22.09 ± 1.98) and the Methotrexate group (22.02 ± 1.58). Both groups demonstrated a progressive reduction in scores over the 16-week period. At week 4, mean scores decreased to 15.96 ± 1.68 with Apremilast and 14.83 ± 1.88 with Methotrexate, showing a greater early response in the Methotrexate group. By week 8, scores further declined to 13.75 ± 1.51 (Apremilast) and 11.85 ± 1.75 (Methotrexate). At week 12, both groups showed comparable improvement, with mean scores of 10.99 ± 1.27 and 9.38 ± 1.42, respectively. By week 16, the lowest scores were recorded, with 8.55 ± 1.55 in the Apremilast group, reflecting a 61.29 % improvement. and 7.75 ± 1.23 in the Methotrexate group, showing a 64.8 % improvement. Overall, while both treatments were effective, Methotrexate achieved a slightly greater reduction in m-PPPASI scores compared to Apremilast. **(Table 2, Figure 4)**

| m-PPPASI | Apremilast | | Methotrexate | | Independent T test (p) |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| **Baseline** | 22.09 | 1.98 | 22.02 | 1.58 | **0.89** |
| **Week 4** | 15.96 | 1.68 | 14.83 | 1.88 | **0.02** |
| **Week 8** | 13.75 | 1.51 | 11.85 | 1.75 | **<0.001** |
| **Week 12** | 10.99 | 1.27 | 9.38 | 1.42 | **<0.001** |
| **Week 16** | 8.55 | 1.05 | 7.75 | 1.23 | **0.008** |

**Table 2:** Association between m-PPPASI score and treatment

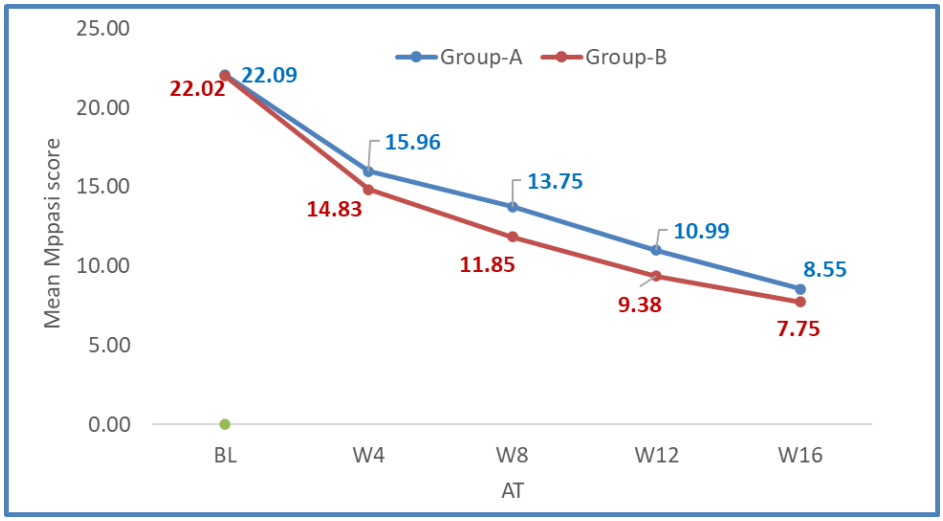


**Figure 4:** Association between m-PPPASI score and treatment

**Association between DLQI score and treatment**

At baseline, the mean DLQI scores were similar in the Apremilast group (16.47 ± 1.85) and the Methotrexate group (15.77 ± 1.81), indicating comparable impairment in quality of life. After 16 weeks of treatment, both groups showed marked improvement, with mean scores reduced to 7.40 ± 1.07 for Apremilast and 6.97 ± 1.09 for Methotrexate. This demonstrates that both treatments significantly enhanced patients' quality of life, with Methotrexate showing a marginally greater reduction in DLQI scores. **(Table 3)**

| DLQI | Apremilast | | Methotrexate | | Independent T test (p) |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| **Baseline** | 16.47 | 1.85 | 15.77 | 1.81 | **0.14** |
| **Week 16** | 7.40 | 1.07 | 6.97 | 1.09 | **0.12** |

**Table 3:** Association between DLQI score and treatment

**Adverse Events**

In the **Methotrexate group**, adverse events included nausea in 10% (3 patients), headache in 3% (1 patient), and abnormal liver function tests in 3% (1 patient).

In the **Apremilast group**, nausea was reported in 10% (3 patients), diarrhoea in 6.6% (2 patients), and weight loss in 3.2% (1 patient). Headache was observed in 6.4% (2 patients).

Overall, **most adverse effects were mild and well tolerated**, with no serious events necessitating treatment discontinuation.

## IV. Discussion

Palmoplantar psoriasis (PPP) is a form of psoriasis that specifically affects the palms and soles, manifesting in diverse morphological patterns ranging from thick hyperkeratotic plaques to pustular lesions.[5] The hyperkeratotic variant is often associated with psoriasis vulgaris and may present with characteristic disc-like lesions elsewhere on the body. The volar and palmar aspects of the fingers are most commonly involved, with occasional extension to the plantar surfaces. Despite affecting a relatively small body surface area, PPP causes significant functional impairment and compromises quality of life by limiting both occupational and recreational activities.[6]

Dermoscopy has emerged as a valuable non-invasive tool for diagnosing PPP, with key features including scaling patterns, background colors, vascular morphology, and specific structural changes. Histopathologically, psoriasis is characterized by parakeratosis with neutrophilic abscesses, hypogranulosis, suprapapillary thinning, and dilated tortuous capillaries in the papillary dermis. [6,7]

Treatment of PPP remains challenging due to limited penetration of topical agents through the thick stratum corneum. In this study, we compared the therapeutic efficacy and safety of methotrexate and apremilast in histopathologically confirmed cases of PPP. Apremilast, being a relatively newer systemic therapy, has limited head-to-head comparisons with methotrexate in PPP.

The mean age of patients in our study was 50.24 years, which aligns with the findings of Hassanandani et al. who reported mean ages of 40.87, 54, and 65 years in different cohorts.[8] In our cohort, 54.5% were male and 45.5% female, consistent with existing literature suggesting a slightly higher prevalence in men. This may be attributed to greater occupational exposure and mechanical trauma to palms and soles, as well as increased likelihood of men seeking medical attention when functional disability interferes with work. Tubanur Cetinarslan et al. similarly reported male predominance (60% vs. 40%).

Dermoscopy in our study revealed white diffuse scaling in 80.3% and dilated vessels in 67.2% of patients. Regular dotted vessels were observed in 39.3%, while diffuse scaling was present in 72.1%. These findings are in concordance with Errichetti and Stinco, who reported vessels in 40% and diffuse white scaling in 80% of PPP cases.[9] Background colors varied, with yellow/yellow-brown seen in 18% and dull red/pink in 26.2%, consistent with previous studies identifying dull red as the most common background hue.

Histopathologically, focal parakeratosis was the predominant feature (63.9%), in agreement with Cesinaro et al. [10] Confluent parakeratosis was less frequent (27.9%). Hypogranulosis was observed in 59%, while suprapapillary thinning was seen in 45.9%, supporting earlier reports by Hesari et al.[11] Abnormal vascularity in the form of dilated tortuous vessels was seen in 32.8%, though this was less reliable as a diagnostic marker compared to other histological features. The inflammatory infiltrate was predominantly lymphocytic.[12]

Therapeutically, both apremilast and methotrexate demonstrated significant clinical improvement. In the apremilast group, the mean baseline m-PPPASI score of 22.09 reduced to 8.55 at 16 weeks, reflecting a 61.29 % improvement. In the methotrexate group, the baseline score of 22.02 decreased to 7.75 at week 16, showing a 64.8 % reduction. Previous studies, such as those by Hassanandani et al. and Sham Samkit [13]et al., also demonstrated 60–80% improvement within 12–16 weeks.

Adverse events were generally mild and tolerable. In the methotrexate group, nausea (10%), headache (3%), and abnormal liver function (3%) were noted. In the apremilast group, nausea (10%), diarrhoea (6.6%), headache (6.4%), and weight loss (3.2%) were observed. These results are consistent with prior studies, including Soufia et al., where gastrointestinal complaints were the most frequent adverse events with apremilast [14], while methotrexate-related toxicities were less pronounced in our cohort. Importantly, no severe adverse effects necessitated treatment discontinuation.

In summary, both methotrexate and apremilast are effective options for PPP, with methotrexate offering a slightly faster clinical response and a manageable safety profile.

## V. Conclusion

In the present study red dots, white scales in patchy distribution, light red background were significant dermoscopic findings in PPP. In this study, features such as confluent parakeratosis and hypogranulosis were significant in biopsies of palmoplantar psoriasis. We conclude that dermoscopy acts as a handy tool that aids in the clinical diagnosis and to differentiate overlapping clinical entities to a moderate extent The present study was attempted to observe the dermoscopic characters and histopathological findings and comparing the therapeutic efficacy in semi-urban Indian population of palmoplantar psoriasis attending tertiary care hospital. This shows that the systemic treatment with methotrexate and apremilast were equally effective, with methotrexate offering a slightly faster clinical response and minor side effects in both the groups. Systemic treatment can be considered when there is severe involvement, interference with day-to-day activity or non-response with topical medications with cost factor in consideration. More such multicentric studies should be carried out with a larger sample size to throw more light into this research area to further draw to conclusions.

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