



# COMPARATIVE ANALYSIS OF CYCLOSPORINE AND METHOTREXATE IN TREATING EXTREME PSORIASIS

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## Abstract:

**Objective:** This study seeks to assess the effectiveness of cyclosporine and methotrexate in treating severe psoriasis, an autoimmune condition characterized by the formation of thick, red, scaly patches on the skin that recur over time. These two medications have been the gold standard for treating severe psoriasis for many years. This study's objective is to provide a comprehensive evaluation of their clinical outcomes as potential treatment options.

**Methods:** To gain insights into the treatment of severe psoriasis, this study conducted a retrospective analysis of medical records over three years for hospitalized patients. The study evaluating the effectiveness of methotrexate and cyclosporine in treating severe psoriasis examined various outcomes, including the Psoriasis Area and Severity Index (PASI) and length of hospital stay (LOS). This information is valuable in guiding clinicians toward the most effective management of this chronic autoimmune disease.

**Results:** Both methotrexate and cyclosporine were successful in lowering the psoriasis area and severity index in the study of 26 individuals with severe psoriasis (PASI). The average PASI decrease was 42.8% (or 24.64). In contrast to those who received methotrexate (mean 43.2224%), individuals who received cyclosporine had a higher decrease in PASI (mean 54.88±12.73%). The cyclosporine group required more time in the hospital 18.83 days with ±9.39 standard deviation than the methotrexate group which had 11.65 of hospital stay with ±5.91 standard deviation while having a better decrease in PASI.

**Conclusions:** The study demonstrated the efficacy of methotrexate and cyclosporine as treatments for extreme psoriasis. However, patients treated with cyclosporine may require longer hospital stays compared to those treated with methotrexate.

**Keywords:** cyclosporine, methotrexate, psoriasis



### Introduction:

The development of thick, red, scaly patches of skin that reoccur over time is a hallmark of the chronic inflammatory illness psoriasis. In addition to arthritis, cardiovascular morbidity, and psychological issues, it is often accompanied by hereditary vulnerability, immunological processes, and environmental variables. [1] Psoriasis prevalence varies from 0.09% to 11.4% globally, with an Asian frequency of around 0.4%. [2,3]Psoriasis may be treated with a variety of methods, including topical medications including anthralin, tar, corticosteroids, calcipotriene, psoralen with ultraviolet A (PUVA) and phototherapy using ultraviolet B (UVB), and immunosuppressant medications such acitretin, methotrexate, and cyclosporine. [4]Inhibiting DNA synthesis and having an antimitotic impact on the epidermis, methotrexate is a folic acid antagonist. Contrarily, the cyclic decapeptide cyclosporine has strong immunosuppressive qualities. In psoriasis, cyclosporine works by inhibiting the activation of T helper cells and cytokines such as interleukin-2 (IL-2). [5] In Pakistan, methotrexate and cyclosporine remain the first-line systemic therapies for moderate to severe psoriasis, indicating their continued importance in the management of this chronic autoimmune disease.

Despite its possible side effects, methotrexate and cyclosporine have been shown in clinical studies to be effective treatments for moderate to severe psoriasis. [6] Several studies have even combined these two medications to treat nail psoriasis and psoriasis vulgaris. [7-9] Yet according to a new meta-analysis, they may not be as effective as the more advanced and secure biologic treatments that are being employed more often in developed countries. [10] As biologics' relatively expensive price prevents them from being widely used in impoverished nations like Pakistan, methotrexate, and cyclosporine are the

preferred systemic treatments in clinical settings.As a result, it's critical to assess how well methotrexate and cyclosporine work to treat psoriasis, especially in Pakistani individuals. This research intends to analyze the clinical results of individuals with severe psoriasis who were cured with these two medications. The research will help physicians choose the best course of therapy for their patients by shedding light on how well these drugs work in the real world to treat severe psoriasis.

### Methods:

**Research Design:** Retrospective research was carried out in Mayo Hospital Lahore, Pakistan, with the ethical committee's permission. Patients with severe psoriasis who were hospitalized in the Dermatovenereology ward from March 2021 to February 2023 and were treated with cyclosporine or methotrexate were involved in the research. Demographic data, the PASI, duration of hospital stay, and treatment history were all taken from medical records. In the research, a PASI score of more than 10 was considered to be severe psoriasis. The initial PASI score was computed at the time of admission, and the final PASI score was computed on the day of release. The duration of the hospital stay and the decline in PASI score were the outcomes assessed in this research. The goal for treating psoriasis is often viewed as a 75% decrease in PASI score (PASI-75).

**Statistical Analysis:** The open-source statistical program SPSS version 26 was used for the statistical analysis. The analysis of the clinical outcomes and demographic information using descriptive statistics. The researchers used the time-tested and trustworthy Pearson's correlation technique to investigate the correlations between the variables. The paired sample t-test was applied to data that were normally distributed. Where there was no normal distribution of the data, the Wilcoxon rank tests were performed to compare means.

The precision and rigor of the analysis of the study's results were ensured by the selection of these statistical techniques.

**Results:**

The study conducted at Mayo Hospital Lahore, Pakistan investigated the efficacy of methotrexate and cyclosporine in treating severe psoriasis. The study included 26 patients out of 30 hospitalized patients who met the inclusion criteria. At a mean age of 41.08 years

with ±16.04 years standard deviation, the research population comprised 26 people with severe psoriasis. Male prevalence was greater than female prevalence, with a ratio of 1.7:1 between the sexes. The average PASI score for these patients at the time of admission was 39.92 with a ±15.88 standard deviation, indicating a severe illness load. Table 1 lists the primary demographics and clinical characteristics of the research cohort.

Table 1: Table demographics characteristics of participants.

		Mean	SD	n	%
	<b>Age</b>	41.08	16.04		
<b>Gender</b>	<b>Female</b>			9	34.6
	<b>Male</b>			17	65.4
<b>Treatment</b>	<b>Cyclosporine</b>			6	20
	<b>Methotrexate</b>			20	66.7
	<b>Baseline PASI score</b>	39.92	15.88		

Twenty of the patients were given methotrexate, while six were given cyclosporine. Three times a week at 12-hour intervals, dosages of 2.5–5 mg of methotrexate were given. Contrarily, cyclosporine was given twice daily at a dose of 50–100 mg. The baseline PASI score for the methotrexate group was 37.81 with standard deviation of ±16.0, whereas it was 46.95 with ±14.50 standard deviation for the cyclosporine group. The mean

PASI score reduction in both groups was 45.91 (±22.59) percent, with both groups seeing considerable drops (Table 2). In comparison to the methotrexate group, the cyclosporine group exhibited a larger mean percentage decrease in PASI score (54.88±12.73%). Nevertheless, only 5% of methotrexate-treated individuals reached PASI-75, while most cyclosporine-treated patients reduced their PASI scores by 50% to 75%. (Figure 1).

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Table 2: Mean PASI scores for the two therapy groups with psoriasis.

	PASI baseline (±SD)	PASI after (±SD)	P-value
<b>Cyclosporine</b>	46.95 (±14.50)	21.08 (±8.25)	0.003
<b>Methotrexate</b>	37.81 (±16.00)	17.03 (±8.29)	<0.001

Hospital stays ranged from 4 to 34 days, with a mean length of 13.31 days with ±7.33 S.D for the patients. In comparison to those receiving

methotrexate for 11.65 days, those receiving cyclosporine had longer mean hospital stays (18.83 days).



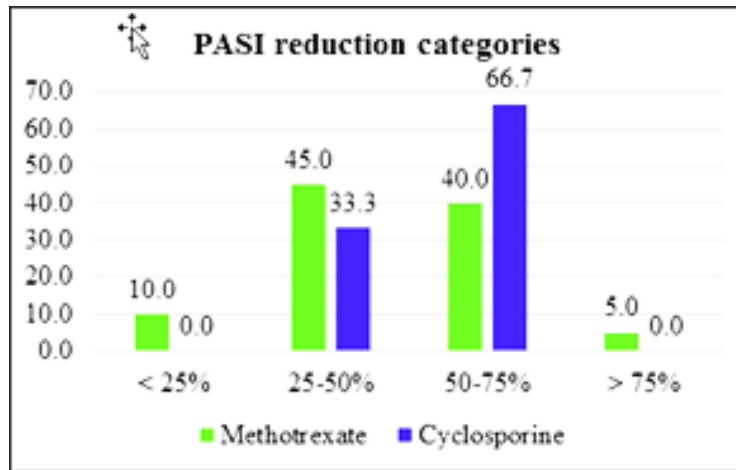


Figure 1: Score reduction categories for the PASI between two groups.

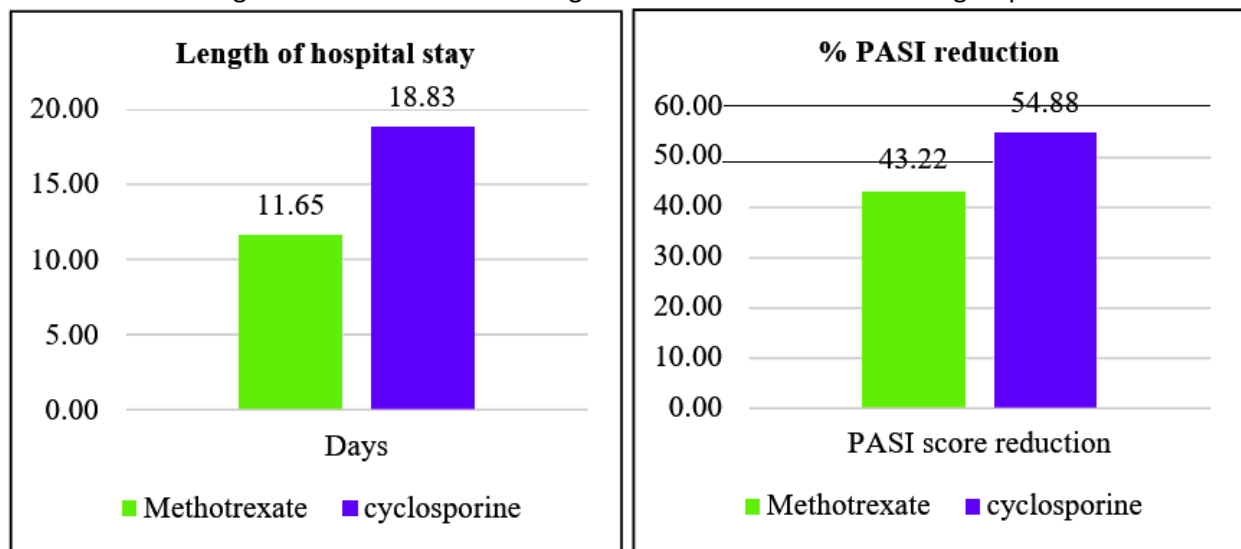


Figure 2: Hospitalization duration and decrease in PASI scores between two groups

**Discussions:**

Two systemic medications that have historically been employed to cure moderate-severe psoriasis include cyclosporine and methotrexate. [11] The intensity of the psoriasis must be determined in order to choose the best treatment. The most popular techniques for assessing the severity of psoriasis in clinical practice, particularly for patients receiving systemic medication, are PASI and DLQI. [12,13,14] In this research, the PASI score is utilized to evaluate clinical progress. In clinic, three severity categories are used based on the PASI score (mild, moderate, severe). Severe psoriasis is defined as PASI >10.13, mild psoriasis as PASI 5, moderate psoriasis as PASI 5–10, etc.

The effectiveness of cyclosporine and methotrexate in treating severe psoriasis was studied at the Mayo Hospital in Lahore. In this research, patients taking methotrexate or cyclosporine had substantially lower PASI scores. Despite the fact that the difference is not statistically significant, cyclosporine is more effective. Despite the lack of a statistically significant difference, it was found that cyclosporine was superior to methotrexate in achieving PASI-75. [15] According to studies, when given combined for 16 weeks at dosages of 3 mg/day for cyclosporine and 15 mg/week for methotrexate, respectively, 94% of patients see a drop in PASI scores of at least 25%. 60% of methotrexate group participants and 71% of cyclosporine group participants satisfied the



PASI-75 standard. [16] Without utilizing a placebo, different research examined the effects of methotrexate and cyclosporine. The statistically significant mean PASI score change for the cyclosporine group was 72%, whereas the change for the methotrexate group was 58%. [17] Both medications were found to be efficient in treating severe psoriasis in a previous trial. After a 12-week course of treatment, the PASI score was lowered by 98.5% in the methotrexate group and by 85.6% in the cyclosporine group. [18]

A thorough study discovered that systemically administered biological drugs, such as infliximab, adalimumab, ustekinumab, and etanercept, are very successful in treating moderate to severe psoriasis. According to the research, these biological treatments were more effective than conventional drugs such as methotrexate, cyclosporine, fumaric acid, retinoids, alefacept, and alefacept. [19] Current psoriasis recommendations advise adopting biological therapy for individuals with moderate-to-severe psoriasis who are resistant to conventional treatments or cannot tolerate them because of adverse effects. [20-21] Conventional systemic therapy is often used as the initial line of treatment since it is less expensive, especially in underdeveloped nations like Pakistan. [22] The most important question is how to tell whether a biological agent should be employed in place of traditional systemic treatment, as per published international consensus guidelines. [23]

In Pakistani hospitals, the average length of stay (LOS) for patients with psoriasis seems to be greater than in wealthy nations. In comparison to patients who got cyclosporine, those who took methotrexate had a reduced mean LOS. In the United States, individuals with simple psoriasis spent an average of 4.6 days in the hospital, regardless of the disease's severity. In psoriasis patients with acute infections, it may increase to 6.6 days. [24] The average LOS for those with psoriasis was 8.6 days, according to further data from the United States. [25] Hospitalization for diagnostic or therapeutic procedures that cannot be performed at a main

or secondary referral hospital is advised for patients with moderate to severe psoriasis. [26] People with severe psoriasis often have underlying medical issues that need treatment from other medical specialists. Hospitalized psoriasis patients may have a worse quality of life and physical discomfort, especially if they are older. [27] A qualitative study found that the reduction in quality of life began to improve right away after hospital release and persisted for three months. [28] There are side effects to be cautious of with both methotrexate and cyclosporine, and some studies have shown that they affect more than 50% of individuals. [29] 14 participants in the methotrexate group withdrew from the trial due to an unusually elevated liver enzyme, revealing methotrexate adverse effects. Additional side effects mentioned in the reports included nausea, especially on the day the medicine was administered, as well as muscle pain, fatigue, and paranoia in the fingers. [30] The most frequent adverse effect of cyclosporine is elevated creatinine levels, which are then followed by headache, depression, hypertriglyceridemia, and hypertension. The study's shortcomings include the difficulty in establishing methotrexate and cyclosporine's long-term side effects after discharge due to a number of patients skipping outpatient follow-up appointments.

#### **Conclusions:**

Both methotrexate and cyclosporine have been shown to effectively reduce the severity of severe psoriasis in clinical settings. While patients receiving cyclosporine show a higher decline in their Psoriasis Area and Severity Index (PASI) scores, they may need to remain in the hospital for a longer period of time. Before contemplating moving to more costly biological medications, it is critical to assess the clinical response to these therapies. Careful consideration of the benefits and risks of each treatment option is essential to achieving optimal outcomes for psoriasis patients.

#### **References:**

1. Kearns, D. G., Chat, V. S., Zang, P. D., Han, G., & Wu, J. J. (2021). Review of



- treatments for generalized pustular psoriasis. *Journal of Dermatological Treatment*, 32(5), 492-494.
2. Armstrong, A. W., & Read, C. (2020). Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *Jama*, 323(19), 1945-1960.
  3. Elmas, Ö. F., Demirbaş, A., Kutlu, Ö., Bağcıer, F., Metin, M. S., Özyurt, K., ... & Lotti, T. (2020). Psoriasis and COVID-19: a narrative review with treatment considerations. *Dermatologic Therapy*, 33(6), e13858.
  4. Arora, S., Das, P., & Arora, G. (2021). Systematic review and recommendations to combine newer therapies with conventional therapy in psoriatic disease. *Frontiers in Medicine*, 8, 696597.
  5. Sadeghinia, A., & Daneshpazhooh, M. (2021). Immunosuppressive drugs for patients with psoriasis during the COVID-19 pandemic era. A review. *Dermatologic Therapy*, 34(1), e14498.
  6. Boh, E., Joselow, A., & Stumpf, B. (2021). Traditional Systemic Therapy I: Methotrexate and Cyclosporine. *Advances in Psoriasis: A Multisystemic Guide*, 103-118.
  7. Masson Regnault, M., Shourick, J., Jendoubi, F., Tauber, M., & Paul, C. (2022). Time to relapse after discontinuing systemic treatment for psoriasis: a systematic review. *American Journal of Clinical Dermatology*, 23(4), 433-447.
  8. Falto-Aizpurua, L. A., Martin-Garcia, R. F., Carrasquillo, O. Y., Nevares-Pomales, O. W., Sánchez-Flores, X., & Lorenzo-Rios, D. (2020). Biological therapy for pustular psoriasis: a systematic review. *International Journal of Dermatology*, 59(3), 284-296.
  9. Shah, S., Nikam, B., Kale, M., Jamale, V., & Chavan, D. (2021). Safety and efficacy profile of oral cyclosporine vs oral methotrexate vs oral acitretin in palmoplantar psoriasis: A hospital based prospective investigator blind randomized controlled comparative study. *Dermatologic Therapy*, 34(1), e14650.
  10. Lansang, P., Bergman, J. N., Fiorillo, L., Joseph, M., Lara-Corrales, I., Marcoux, D., ... & Landells, I. (2020). Management of pediatric plaque psoriasis using biologics. *Journal of the American Academy of Dermatology*, 82(1), 213-221.
  11. Daudén, E., Carretero, G., Rivera, R., Ferrándiz, C., Llamas-Velasco, M., de la Cueva, P., ... & de Vega Martínez, M. (2020). Long-term safety of nine systemic medications for psoriasis: A cohort study using the Spanish Registry of Adverse Events for Biological Therapy in Dermatological Diseases (BIOBADADERM) Registry. *Journal of the American Academy of Dermatology*, 83(1), 139-150.
  12. Thatiparthi, A., Martin, A., Liu, J., & Wu, J. J. (2022). Risk of Skin Cancer with Phototherapy in Moderate-to-Severe Psoriasis: An Updated Systematic Review. *The Journal of Clinical and Aesthetic Dermatology*, 15(6), 68.
  13. Zangrilli, A., Bavetta, M., & Bianchi, L. (2020). Adalimumab in children and adolescents with severe plaque psoriasis: a safety evaluation. *Expert Opinion on Drug Safety*, 19(4), 433-438.
  14. Aljefri, Y. E., Ghaddaf, A. A., Alkhumani, T. A., Alkhamisi, T. A., Alahmadi, R. A., Alamri, A. M., & Alraddadi, A. A. (2022). Efficacy and safety of apremilast monotherapy in moderate-to-severe plaque psoriasis: A systematic review and meta-analysis. *Dermatologic Therapy*, 35(7), e15544.
  15. Corazza, V., Cusano, F., De Pità, O., Rossi, L., & Virno, G. G. (2022). Methotrexate in the therapeutic pathway of patients with psoriasis. Analysis of clinical practice data and



- comparison with guidelines. *Dermatology Reports*, 14(1).
16. Singh, S. K., & Singnarp, S. R. (2021). Safety and efficacy of methotrexate (0.3 mg/kg/week) versus a combination of methotrexate (0.15 mg/kg/week) with cyclosporine (2.5 mg/kg/day) in chronic plaque psoriasis: A randomised non-blinded controlled trial. *Indian Journal of Dermatology, Venereology and Leprology*, 87(2), 214-222.
  17. Behrang, E., Sadeghzadeh-Bazargan, A., Salimi, N., Shaka, Z., FeyzKazemi, M. H., & Goodarzi, A. (2022). Erythrodermic flare-up of psoriasis with COVID-19 infection: A report of two cases and a comprehensive review of literature focusing on the mutual effect of psoriasis and COVID-19 on each other along with the special challenges of the pandemic. *Clinical case reports*, 10(4), e05722.
  18. Bellinato, F., Gisondi, P., Mantovani, A., Girolomoni, G., & Targher, G. (2022). Risk of non-alcoholic fatty liver disease in patients with chronic plaque psoriasis: an updated systematic review and meta-analysis of observational studies. *Journal of Endocrinological Investigation*, 45(7), 1277-1288.
  19. Schaap, M. J., van Winden, M. E., Seyger, M. M., de Jong, E. M., & Lubbeek, S. F. (2020). Representation of older adults in randomized controlled trials on systemic treatment in plaque psoriasis: a systematic review. *Journal of the American Academy of Dermatology*, 83(2), 412-424.
  20. Hader, E., Mosca, M., Hong, J., Brownstone, N., Bhutani, T., & Liao, W. (2021). Nail psoriasis: a review of effective therapies and recommendations for management. *Dermatology and therapy*, 11(3), 799-831.
  21. Mehta, M., O'Toole, A., & Gooderham, M. (2021). Real-world experience with risankizumab in patients with plaque psoriasis: a retrospective study. *Journal of the European Academy of Dermatology and Venereology*, 35(10), e685-e688.
  22. Pandey, S., Tripathi, P., Gupta, A., & Yadav, J. S. (2022). A comprehensive review on possibilities of treating psoriasis using dermal cyclosporine. *Drug Delivery and Translational Research*, 1-15.
  23. Armstrong, A., Fahrback, K., Leonardi, C., Augustin, M., Neupane, B., Kazmierska, P., ... & Warren, R. B. (2022). Efficacy of Bimekizumab and other biologics in moderate to severe plaque Psoriasis: a systematic literature review and a network meta-analysis. *Dermatology and Therapy*, 12(8), 1777-1792.
  24. Mahé, E., Beauchet, A., Hadj-Rabia, S., Mazereeuw-Hautier, J., Mallet, S., Phan, A., ... & Groupe de Recherche sur le Psoriasis (GrPso) of the Société Française de Dermatologie (SFD), Groupe de Recherche de la Société Française de Dermatologie Pédiatrique (GR SFDP), and Societá Italiana di Dermatologia Pediatrica (SI Der. P.). (2022). Biologics combined with conventional systemic agents for the treatment of children with severe psoriasis. Real-life data from the BiPe cohorts and a practice survey among French and Italian pediatric dermatologists. *Dermatologic Therapy*, 35(11), e15828.
  25. Aslam, N., Saleem, H., Murtazaliev, S., Quazi, S. J., & Khan, S. (2020). FDA approved biologics: can etanercept and ustekinumab be considered a first-line systemic therapy for pediatric/adolescents in moderate to severe psoriasis? A systematic review. *Cureus*, 12(8).
  26. Gisondi, P., Bellinato, F., Chiricozzi, A., & Girolomoni, G. (2020). The risk of COVID-19 pandemic in patients with



- moderate to severe plaque psoriasis receiving systemic treatments. *Vaccines*, 8(4), 728.
27. Balak, D. M., Piaserico, S., & Kasujee, I. (2021). Non-Alcoholic Fatty Liver Disease (NAFLD) in patients with psoriasis: a review of the hepatic effects of systemic therapies. *Psoriasis: Targets and Therapy*, 151-168.
  28. Felquer, M. L. A., LoGiudice, L., Galimberti, M. L., Rosa, J., Mazzuocolo, L., & Soriano, E. R. (2022). Treating the skin with biologics in patients with psoriasis decreases the incidence of psoriatic arthritis. *Annals of the Rheumatic Diseases*, 81(1), 74-79.
  29. SakthiPriyadarsini, S., Vani, P. B., & Kumar, P. R. (2020). A Comparative Review on Conventional and Traditional medicine in the Treatment of Psoriasis. *Research J. Pharm. and Tech*, 13(11), 5642-5646.
  30. Ghalamkarpour, F., Pourani, M. R., Abdollahimajd, F., & Zargari, O. (2022). A case of severe psoriatic erythroderma with COVID-19. *Journal of Dermatological Treatment*, 33(2), 1111-1113.

