International Journal of Research in Medical Sciences
Siddique MRU et al. Int J Res Med Sci. 2025 Feb;13(2):646-650
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20250231

Original Research Article

Clinical outcomes of subcutaneous methotrexate in the management of chronic plaque psoriasis

Mohammad Rahmat Ullah Siddique*, Alauddin Khan, Sharmin Begum

Department of Dermatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Received: 11 December 2024
Accepted: 08 January 2025

***Correspondence:**
Dr. Mohammad Rahmat Ullah Siddique,
E-mail: rahmatskinexpert@gmail.com

ABSTRACT

Background: Chronic plaque psoriasis, also known as psoriasis vulgaris, is the most common form of psoriasis. Subcutaneous methotrexate has been utilized in the management of chronic plaque psoriasis, offering an alternative route of administration to the traditional oral method. The aim of this study was to evaluate the clinical outcomes of subcutaneous methotrexate in the management of chronic plaque psoriasis.
Methods: This cross-sectional observational study was conducted in department of dermatology, Bangabandhu Sheikh Mujib medical university, Dhaka, Bangladesh, during the period from November 2023 to May 2024. Total 70 participants were included in this study.
Results: The average age of participants was 42.3±11.8 years, with 52.9% males and 47.1% females. Baseline PASI scores averaged 18.5±4.2, indicating moderate-to-severe psoriasis. Mean psoriasis duration was 7.2±3.5 years. Depression (34.3%) was the most common comorbidity, followed by diabetes (15.7%) and hypertension (8.6%). Majority of the participants, 62.86% (n=44), had moderate psoriasis. Nausea (58.9%) was the primary reason for switching from oral to subcutaneous methotrexate, which led to progressive PASI reductions: 32.9% at Week 4, 53.0% at week 8, 69.7% at week 12, and 84.9% at week 16 ($p<0.001$). Adverse events were mild, with nausea (11.4%) and fatigue (8.6%) being most common.
Conclusions: This study demonstrated that subcutaneous methotrexate is a highly effective, safe, and well-tolerated treatment for moderate-to-severe chronic plaque psoriasis.

Keywords: Clinical outcomes, Subcutaneous methotrexate, Chronic plaque psoriasis

INTRODUCTION

Psoriasis, a chronic, immune-mediated inflammatory skin disorder, affects approximately 2-3% of the global population, with chronic plaque psoriasis accounting for 80–90% of cases.[1] Characterized by hyperproliferation of keratinocytes and immune system dysregulation, it presents as erythematous plaques with silvery scales, contributing to significant physical discomfort, pruritus, and quality-of-life impairment.[2] While psoriasis is often considered primarily a dermatological condition, its systemic nature-manifested through comorbidities such as psoriatic arthritis, cardiovascular diseases, and metabolic syndrome-underscores the complexity of its management.[1]

In Bangladesh, epidemiological data on psoriasis prevalence are sparse, yet regional studies suggest it mirrors South Asian trends, affecting 1-2% of the population.[3] The burden is exacerbated by underdiagnosis and limited access to dermatological resources, particularly in rural areas where cultural stigma and low awareness about advanced treatment options prevail.[4] The physical and psychological impact of psoriasis is profound, with symptoms such as pruritus and skin discomfort adversely affecting patients' quality of life.[5] Given the high prevalence of plaque-type psoriasis in low-resource settings such as Bangladesh, there is a pressing need for effective, accessible, and well-tolerated systemic treatments. Methotrexate, a folic acid antagonist that

inhibits dihydrofolate reductase, is among the most widely used systemic therapies for moderate-to-severe psoriasis. First approved for psoriasis management in the 1960s, it remains a cornerstone of treatment due to its ability to suppress T-cell activity and keratinocyte proliferation, key drivers of psoriatic pathology.[6] However, oral methotrexate is associated with limitations such as gastrointestinal side effects and variable absorption, which can undermine patient adherence and clinical outcomes.[7] In recent years, subcutaneous (SC) methotrexate has emerged as a superior alternative, offering enhanced bioavailability, predictable pharmacokinetics, and improved tolerability. Clinical trials have demonstrated that SC methotrexate achieves faster reductions in psoriasis area and severity index (PASI) scores and prolongs remission compared to the oral form, while significantly reducing gastrointestinal adverse effects.[2,4] The cost-effectiveness of SC methotrexate further underscores its potential in resource-constrained settings. While biologics have revolutionized psoriasis treatment with unparalleled efficacy, their high-cost limits accessibility in low-income countries like Bangladesh. In contrast, SC methotrexate provides a more affordable option with comparable safety and efficacy for many patients.[8] Despite its global adoption, the generalizability of SC methotrexate's clinical outcomes to South Asian populations remains uncertain due to genetic, environmental, and lifestyle differences.[9] Local studies evaluating its efficacy, safety, and economic feasibility in the Bangladeshi healthcare context are conspicuously absent, creating a significant knowledge gap.[3] Addressing this unmet clinical need is essential for tailoring psoriasis management strategies that align with the unique challenges of the region, including cultural stigma, limited awareness, and constrained healthcare infrastructure. This study aims to evaluate the clinical outcomes of SC methotrexate in managing chronic plaque psoriasis in Bangladesh, focusing on its efficacy, safety, and cost-effectiveness compared to conventional therapies.

METHODS

This cross-sectional observational study was conducted in department of dermatology, Bangabandhu Sheikh Mujib medical university, Dhaka, Bangladesh, during the period from November 2023 to May 2024. Total 70 participants were included, selected based on the following inclusion criteria: adults aged 18-65 years with a diagnosis of chronic plaque psoriasis for at least six months, moderate-to-severe psoriasis (PASI ≥10), and no prior exposure to subcutaneous methotrexate therapy. Participants were required to provide informed consent. Exclusion criteria included pregnancy or lactation, severe systemic diseases or comorbidities (e.g., liver or kidney dysfunction), use of biologic therapies in the previous six months, and alcohol dependence or active substance abuse. The study patients received a weekly dose of SC MTX for 12 weeks. Insulin syringe was used for injection. It has marking from 10 to 100, the marking at 100 equals to 1 ml. The concentration of the vial was 25 mg/1 ml. The starting dose was 7.5 mg (30 units of syringe=0.3 ml) in mild cases recalcitrant to topical treatment and moderate cases while it was 10 mg (40 units of syringe=0.4 ml) in severe cases. The dose increased gradually by 2.5 mg (10 units of syringe=0.1 ml) every month, except four cases the dose in third month remained the same as second month due to good response, till reaching 10-15 mg/week. The study's primary outcome was the reduction in PASI scores from baseline to week 16, while secondary outcomes included assessment of safety and tolerability through adverse event monitoring and laboratory tests (including liver and renal function), and a cost-effectiveness analysis. Consent of the patients and guardians were taken before collecting data. Ethical approval was obtained from the institutional review board (IRB) of after collection of data, all data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with statistical packages for social sciences version 22. P value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 summarizes the demographic and clinical profiles of the study participants. The average age of the participants was 42.3±11.8 years, with a near-equal distribution of males (52.9%) and females (47.1%). The mean baseline PASI score was 18.5±4.2, indicating moderate-to-severe psoriasis. Participants had a mean psoriasis duration of 7.2±3.5 years, demonstrating the chronic nature of the condition. The most common comorbidity was depression (34.3%), followed by diabetes mellitus (15.7%) and hypertension (8.6%). Less frequently observed comorbidities included epilepsy (4.3%) and ischemic heart disease (2.9%). The table presents the distribution of psoriasis severity among the study participants. Figure 1 demonstrates that majority of the participants, 62.86% (n=44), had moderate psoriasis, indicating the prevalent severity level within the cohort. Severe psoriasis was observed in 24.29% (n=17) of the participants, highlighting a significant subset with high disease burden. Mild cases constituted the smallest group, comprising 12.86% (n=9) of the sample. These findings reflect the study's focus on patients with moderate-to-severe psoriasis, aligning with the inclusion criteria targeting those requiring systemic therapy. Table 2 identifies the reasons for transitioning from oral to subcutaneous methotrexate among the study subjects. The most frequent reason for switching was nausea (58.9%), followed by treatment ineffectiveness or partial response (27.1%) and gastrointestinal side effects (14.3%). Table 3 demonstrates the changes in PASI scores over time among the study subjects. The baseline PASI score was 18.5±4.2, and it decreased to 12.4±3.8 at week 4, representing a 32.90% reduction ($p<0.001$). At week 8, the PASI score further dropped to 8.7±3.1 (53.00% reduction, $p<0.001$). By week 12, the mean score was 5.6±2.5, reflecting a 69.70% reduction, and by week 16, the PASI score reached 2.8±1.9, an 84.90% reduction ($p<0.001$). These results indicate a robust improvement in disease severity over the

course of treatment. Table 4 reports the adverse events observed during the treatment period. The most commonly reported adverse event was nausea (11.4%), followed by fatigue (8.6%) and injection site pain (7.1%). Elevated ALT levels above the upper limit of normal were observed in 5.7% of patients, while gastrointestinal pain occurred in 4.3%.

Table 1: Baseline characteristics of the study subjects (n=70).

Characteristics	N	Percentage (%)
Age (in years)		
Mean±SD	42.3±11.8	
Sex		
Male	37	52.9
Female	33	47.1
Baseline PASI score		
Mean±SD	18.5±4.2	
Duration of psoriasis (in years)		
Mean±SD	7.2±3.5	
Co-morbidities		
Depression	24	34.3
Diabetes mellitus	11	15.7
Hypertension	6	8.6
Eepilepsy	3	4.3
Ischaemic heart disease	2	2.9

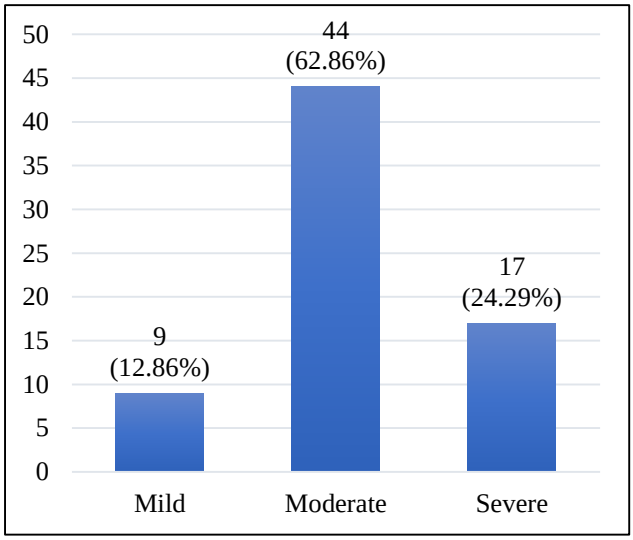

Figure 1: Psoriasis severity among the study subjects, (n=70).

Table 2: Reasons for switching from oral to subcutaneous methotrexate (n=70).

Reasons	N	Percentage (%)
Nausea	41	58.9
Ineffectiveness/ partial response	19	27.1
Gastrointestinal side effects	10	14.3

Table 3: Changes in PASI scores over time among the study subjects (n=70).

Time point	Mean PASI score±SD	Reduction (%)	P value
Baseline	18.5±4.2	-	-
Week 4	12.4±3.8	32.90%	<0.001
Week 8	8.7±3.1	53.00%	<0.001
Week 12	5.6±2.5	69.70%	<0.001
Week 16	2.8±1.9	84.90%	<0.001

Table 4: Adverse events during treatment (n=70).

Adverse event	N	Percentage (%)
Nausea	8	11.4
Fatigue	6	8.6
Elevated ALT (>ULN)	4	5.7
Injection site pain	5	7.1

DISCUSSION

This cross-sectional observational study was conducted in department of dermatology, Bangabandhu Sheikh Mujib medical university, Dhaka, Bangladesh, during the period from November 2023 to May 2024. The present study evaluated the clinical outcomes, tolerability, and quality-of-life improvements associated with subcutaneous methotrexate (SC MTX) in the management of chronic plaque psoriasis, enrolling 70 patients with a mean age of 42.3±11.8 years and a near-equal sex distribution (52.9% male, 47.1% female). Baseline disease severity was high, with a mean PASI score of 18.5±4.2, highlighting the significant impact of psoriasis on physical domains. A majority, 62.86% (n=44), were categorized as having moderate psoriasis, affirming its predominance in clinical practice, as highlighted in previous studies. For instance, Bonifati et al reported that 38% of first-time psoriasis patients attending a tertiary care clinic presented with moderate-to-severe psoriasis, emphasizing the high prevalence of this severity level among patients requiring systemic therapy.[10] Severe psoriasis was observed in 24.29% (n=17) of the current cohort, reflecting a notable subset with high disease burden. This aligns with Strober et al who found that severity definitions often capture patients with significant skin involvement and systemic symptoms, many of whom require advanced therapeutic options, including biologics.[11] Mild psoriasis constituted the smallest group, comprising 12.86% (n=9) of the participants, consistent with a study by Hoffmann and Enk.[12] This study demonstrated marked improvements in clinical outcomes and tolerability with SC MTX, aligning with findings from previous research, while providing important localized insights. The reduction in PASI scores in this study was both significant and progressive, starting with a 32.9% reduction at week 4 (mean PASI 12.4±3.8, $p<0.001$), followed by a 53.0% reduction at Week 8 (mean PASI 8.7±3.1, $p<0.001$). By week 12, the reduction was 69.7% (mean PASI 5.6±2.5, $p<0.001$), culminating in an 84.9% reduction at week 16 (mean PASI 2.8±1.9,

p<0.001). These findings are consistent with Warren et al where PASI 75 was achieved by 41% of patients treated with SC MTX over 16 weeks.[4] Similarly, Attwa et al reported PASI reductions from 23.4 to 2.55 over 12 weeks with SC MTX, underscoring its superior efficacy compared to oral formulations.[8] The results from the current study surpass the PASI reductions of 60.2% achieved with oral MTX reported by Lajevardi et al highlighting the potential of SC MTX as a preferred first-line systemic therapy.[13] The tolerability of SC MTX was reflected in the low frequency of adverse events. The most common were nausea (11.4%), fatigue (8.6%), and injection site pain (7.1%). Elevated ALT levels occurred in 5.7% of patients, while gastrointestinal pain was reported by 4.3%. This aligns with findings by Dolan and Joshi where nausea and gastrointestinal symptoms resolved in 63.6% of patients who switched from oral to SC MTX.[14] Kromann et al further corroborated that SC MTX significantly reduces gastrointestinal adverse effects compared to oral formulations.[15] The current study's adverse event rates were lower than those reported by Nakarmi et al where nausea occurred in 19.4% of patients on MTX monotherapy, highlighting the relative tolerability of the SC route.[16] The findings of this study substantiate the advantages of SC MTX over oral formulations in terms of efficacy and safety. The higher bioavailability and predictable pharmacokinetics of SC MTX, as demonstrated by Schiff et al likely underpin the superior clinical outcomes observed.[17] The 84.9% PASI reduction at Week 16 in the current study are comparable to outcomes achieved with biologics such as secukinumab in the study of Houghton et al but at a fraction of the cost, making SC MTX a more accessible option in resource-limited settings like Bangladesh.[18] Despite these encouraging findings, this study highlights the challenges of managing psoriasis in Bangladesh, including limited access to dermatology specialists and a lack of national treatment guidelines tailored to the local population. The cost-effectiveness of SC MTX positions it as an essential alternative to biologics in low-resource settings, though further research is needed to optimize dosing and address patient-specific barriers to adherence. Combining SC MTX with adjunct therapies, such as narrowband UVB phototherapy, could further enhance outcome.[19]

Limitations

In our study, there was small sample size and absence of control for comparison. Study population was selected from one center in Dhaka city, so may not represent wider population. The study was conducted at a short period of time.

CONCLUSION

This study demonstrated that subcutaneous methotrexate is a highly effective, safe, and well-tolerated treatment for moderate-to-severe chronic plaque psoriasis. Significant reductions in PASI scores highlight its clinical benefits. With a low frequency of adverse events compared to oral formulations, subcutaneous methotrexate offers enhanced tolerability and adherence. Its affordability and efficacy make it a viable first-line therapy in resource-limited settings like Bangladesh. These findings support the development of localized treatment guidelines to optimize psoriasis management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. J Eur Academy Dermatol Venereol. 2012;26(s2):3-11.
2. Dogra S, Mahajan R. Psoriasis: Epidemiology, clinical features, co-morbidities, and clinical scoring. Indian Dermatol Online J. 2016;7(6):471.
3. Bhuiyan MSI, Sikder MS, Mahmud M, Nandy AK, Haque MM. Prevalence of psoriasis in Bangladesh: A community-based survey. J Pak Assoc Dermatologists. 2020;30(1):39-45.
4. Warren RB, Mrowietz U, Kiedrowski R von, Niesmann J, Wilsmann-Theis D, Ghoreschi K, et al. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet. 2017;389(10068):528-37.
5. Da Silva N, Augustin M, Hilbring C, Braren-von Stülpnagel CC, Sommer R. Psychological (co)morbidity in patients with psoriasis: the impact of pruritus and anogenital involvement on symptoms of depression and anxiety and on body dysmorphic concerns - a cross-sectional study. BMJ Open. 2022;12(9):e055477.
6. Cronstein BN, Aune TM. Methotrexate and its mechanisms of action in inflammatory arthritis. Nat Rev Rheumatol. 2020;16(3):145-54.
7. Pichlmeier U, Heuer KU. Subcutaneous administration of methotrexate with a prefilled autoinjector pen results in a higher relative bioavailability compared with oral administration of methotrexate. Clin Exp Rheumatol. 2014;32(4):563-71.
8. Attwa EM, Elkot RA, Abdelshafey AS, Hafez AR. Subcutaneous methotrexate versus oral form for the treatment and prophylaxis of chronic plaque psoriasis. Dermatol Ther. 2019;32(5):e13051.
9. Berger EM, Gottlieb AB. Developments in systemic immunomodulatory therapy for psoriasis. Curr Opin Pharmacol. 2007;7(4):434-4.
10. Bonifati C, Graceffa D, Lora V, Maiani E. Clinical characteristics and systemic therapies administered to first-time patients at a tertiary psoriasis outpatient clinic. Giornale Italiano di Dermatologia e

Venereologia: Organo Ufficiale, Societa Ital Dermatologia Sifilografia. 2015;151(6):596-602.
11. Strober B, Ryan C, van de Kerkhof P, van der Walt J, Kimball AB, Barker J, et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. J Am Academy Dermatol. 2020;82(1):117-22.
12. Hoffmann JH, Enk AH. Evaluation of psoriasis area and severity index thresholds as proxies for systemic inflammation on an individual patient level. Dermatology. 2022;238(4):609-14.
13. Lajevardi V, Hallaji Z, Daklan S, Abedini R, Goodarzi A, Abdolreza M. The efficacy of methotrexate plus pioglitazone vs. methotrexate alone in the management of patients with plaque-type psoriasis: a single-blinded randomized controlled trial. Int J Dermatol. 2015;54(1):95-101.
14. Dolan L, Joshi A. AB0498 A True to Life Study on Effects of Switching from Oral to Subcutaneous Methotrexate. Ann Rheumat Dis. 2015;74(2):1065-5.
15. Kromann CB, Lage-Hansen PR, Koefoed M, Jemec GBE. Does switching from oral to subcutaneous administration of methotrexate influence on patient reported gastro-intestinal adverse effects? J Dermatolog Treat. 2015;26(2):188-90.
16. Nakarmi S, Pudasaini K, Adhikari B, Vaidya B. Adverse Events Profile of Low-dose Methotrexate in Nepalese Patients with Rheumatoid Arthritis: an Observational Study. J Nepal Health Res Council. 2020;18(3):360-5.
17. Schiff MH, Jaffe JS, Freundlich B. Head-to-head, randomised, crossover study of oral versus subcutaneous methotrexate in patients with rheumatoid arthritis: drug-exposure limitations of oral methotrexate at doses ≥15 mg may be overcome with subcutaneous administration. Ann Rheumatic Dis. 2014;73(8):1549-51.
18. Houghton K, Patil D, Gomez B, Feldman SR. Correlation Between Change in Psoriasis Area and Severity Index and Dermatology Life Quality Index in Patients with Psoriasis: Pooled Analysis from Four Phase 3 Clinical Trials of Secukinumab. Dermatol Ther (Heidelb). 2021;11(4):1373-84.
19. Khadka DK, Agrawal S, Dhali TK. Methotrexate plus narrow band ultraviolet B (NBUVB) versus methotrexate alone in the treatment of moderate to severe plaque psoriasis: A randomized clinical trial. Nep J Dermatol Venereol Leprol. 2015;13(1):12-23.

Cite this article as: Siddique MRU, Khan A, Begum S. Clinical outcomes of subcutaneous methotrexate in the management of chronic plaque psoriasis. Int J Res Med Sci 2025;13:646-50.