



CLINICAL PROFILE AND RESPONSE TO TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO COMBINATION SYNTHETIC DMARDS

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized by persistent synovitis, progressive joint destruction, and extra-articular manifestations. Despite optimal use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), a subset of patients continues to have active disease. Tofacitinib, an oral Janus kinase (JAK) inhibitor, offers a targeted therapeutic option for such refractory cases.

Objectives: To evaluate the clinical profile and assess the efficacy and safety of tofacitinib in patients with rheumatoid arthritis refractory to combination synthetic DMARD therapy.

Methods: This was a prospective observational comparative study conducted at a tertiary care municipal hospital. A total of 74 patients fulfilling the ACR-EULAR 2010 criteria for RA and having DAS28-ESR >3.2 despite ≥3 months of csDMARD therapy were included. Patients were divided into two groups: Group I (n=26) received tofacitinib 5 mg twice daily along with csDMARDs, and Group II (n=48) continued csDMARDs alone. Disease activity was assessed at baseline and after 12 weeks using DAS28-ESR, CDAI, SDAI, ESR, and CRP.

Results: Group I showed a statistically significant reduction in inflammatory markers and disease activity scores at 12 weeks. Remission (DAS28-ESR <2.6) was achieved in 28.57% of patients, while 42.85% achieved low disease activity. In contrast, patients in Group II showed no significant improvement. Overall, 71.42% of tofacitinib-treated patients achieved the EULAR treatment target (p <0.0001). The drug demonstrated a favorable safety profile.

Conclusion: Tofacitinib is an effective and well-tolerated therapeutic option in RA patients refractory to combination synthetic DMARDs, enabling a substantial proportion of patients to achieve remission or low disease activity.

Keywords: Rheumatoid arthritis, Tofacitinib, JAK inhibitor, DAS28-ESR, DMARD-refractory RA

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune inflammatory disorder characterized by persistent synovitis, progressive joint destruction, functional disability, and extra-articular manifestations. It affects approximately 0.5–1% of the adult population worldwide and is associated with significant morbidity and increased mortality if inadequately treated (1).

Early diagnosis and aggressive treatment using a treat-to-target strategy are essential to prevent irreversible structural damage and improve long-term outcomes. Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), particularly methotrexate, remain the cornerstone of RA management; however, a substantial proportion of patients exhibit inadequate response or intolerance to these agents (2).

Biologic DMARDs targeting tumor necrosis factor- α (TNF- α) and other inflammatory cytokines, such as interleukin-6 and CD20, have significantly improved disease outcomes in patients with refractory RA. Despite their efficacy, limitations including parenteral administration, high cost, and increased risk of infections restrict their widespread use, especially in resource-limited settings (3).

Tofacitinib is an oral targeted synthetic DMARD that inhibits Janus kinase (JAK) pathways, primarily JAK1 and JAK3, and to a lesser extent JAK2, thereby modulating intracellular signaling of multiple pro-inflammatory cytokines involved in RA pathogenesis (4). Clinical trials have demonstrated that tofacitinib is effective as monotherapy as well as in combination with methotrexate in patients with moderate-to-severe RA who have an inadequate response to csDMARDs or biologic agents (5,6).

The European Alliance of Associations for Rheumatology (EULAR) recommends remission or low disease activity as the primary treatment goal in RA, emphasizing timely escalation of therapy in patients with persistent disease activity (7). Real-world studies have further supported the rapid and sustained efficacy of tofacitinib, with significant improvements in disease activity scores and functional outcomes (8).

In this context, the present study was undertaken to evaluate the clinical profile and assess the efficacy of tofacitinib in patients with rheumatoid arthritis refractory to combination synthetic DMARD therapy in a real-world tertiary care setting.

METHODOLOGY

Study Design: Prospective observational comparative study.

Study Setting: Tertiary care municipal hospital.

Sample Size: A total of 74 patients diagnosed with rheumatoid arthritis.

Inclusion Criteria

Age ≥ 18 years

Diagnosis of RA as per ACR-EULAR 2010 criteria

On combination synthetic DMARD therapy for ≥ 3 months

DAS28-ESR score > 3.2

Exclusion Criteria

Pregnant or lactating women

History of tuberculosis

History of thrombo-embolic events

Active infections or malignancy

Table 1: Baseline Clinical Characteristics

Parameter	Value
Total patients	74
Male	3 (4.05%)
Female	71 (95.95%)
Mean age	45 years
Mean disease duration	5.6 years
Moderate disease activity	53 (71.62%)
High disease activity	21 (28.38%)

Table 2: Treatment Outcomes at 12 Weeks

Outcome	Tofacitinib Group (n=21)	Non-Tofacitinib Group (n=43)
Remission	6 (28.57%)	0
Low disease activity	9 (42.85%)	0
Moderate disease activity	6 (28.57%)	43 (100%)
Significant DAS28 reduction (>1.2)	21 (100%)	0

Study Groups

Group I (n = 26): csDMARDs + Tofacitinib 5 mg twice daily

Group II (n = 48): csDMARDs alone

SR. NO	N=74			
1	Gender	Males	3	95.95%
		Females	71	4.05%
2	Age	Mean Age	43.9 years	
2	Disease Duration	Mean Disease Duration	5.66 years	
3	Arthritis	Erosive Arthritis	53	71.62%
		Non Erosive Arthritis	21	28.38%
4	With Tofacitinib(n=23)	Tofacitinib	26	
		Lost to Follow up with Tofacitinib	5	
	Remission	DAS ESR <2.6	15	
		LDA	9	
5	Without Tofacitinib (n=43)	Without Tofacitinib	48	
		Lost to Follow up without Tofacitinib	5	
6	Antibody Status	Sero Positive	71	
		Sero Negative	3	
7	Remission			
	DAS ESR<2.6	15		
	Low disease activity	9		

Outcome Measures

Patients were assessed at baseline and at 12 weeks for:

ESR and CRP

DAS28-ESR

Clinical Disease Activity Index (CDAI)

Simplified Disease Activity Index (SDAI)

Disease activity was categorized as remission, low, moderate, or high as per standard DAS28-ESR criteria.

Statistical Analysis

Data were analysed using appropriate statistical tests. A p-value <0.05 was considered statistically significant.

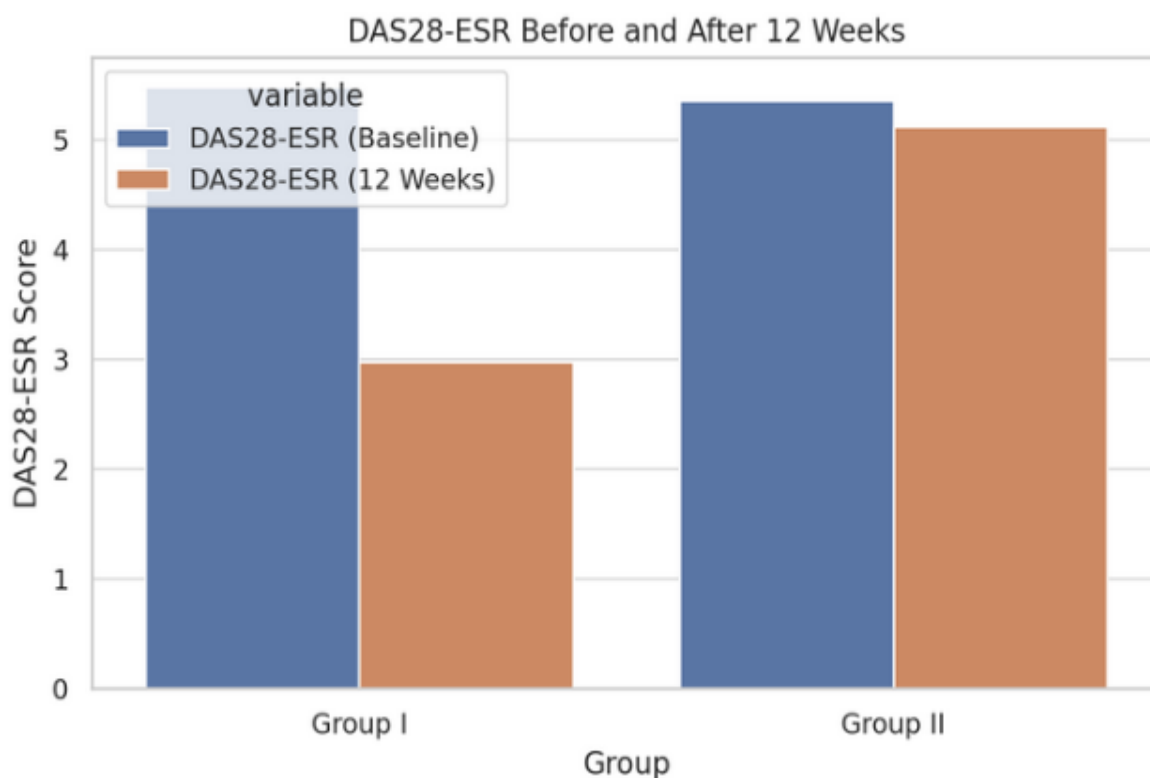
RESULTS

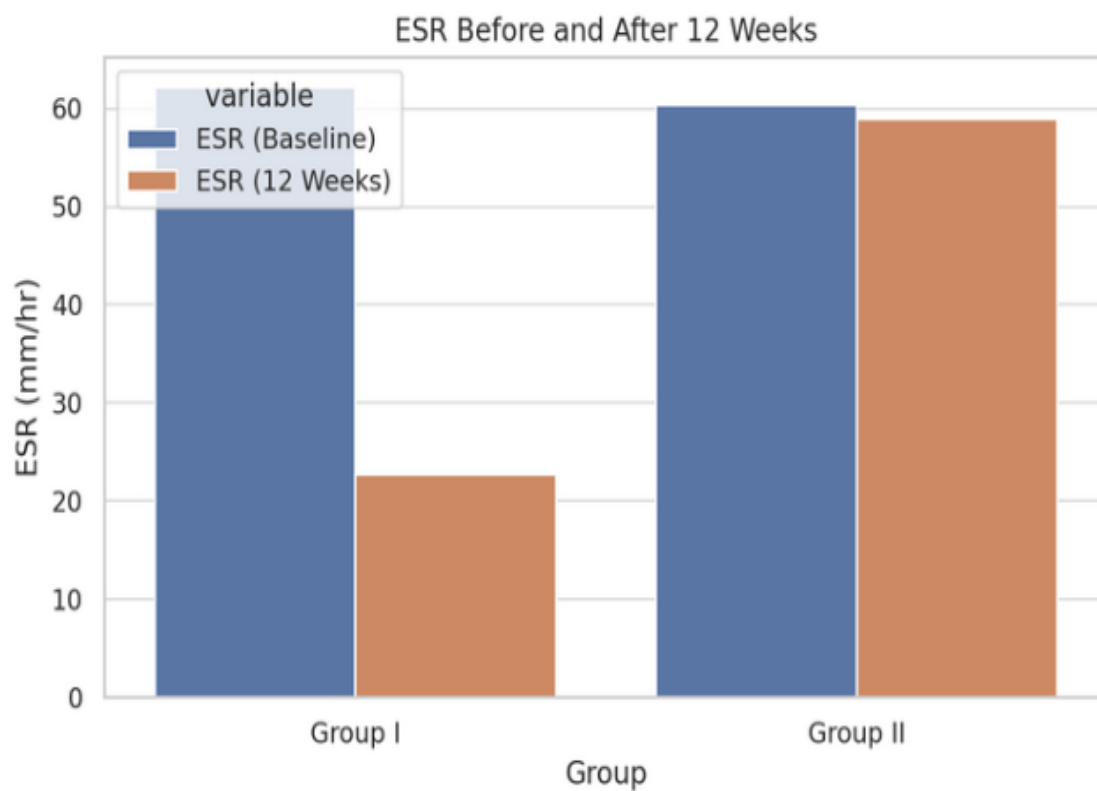
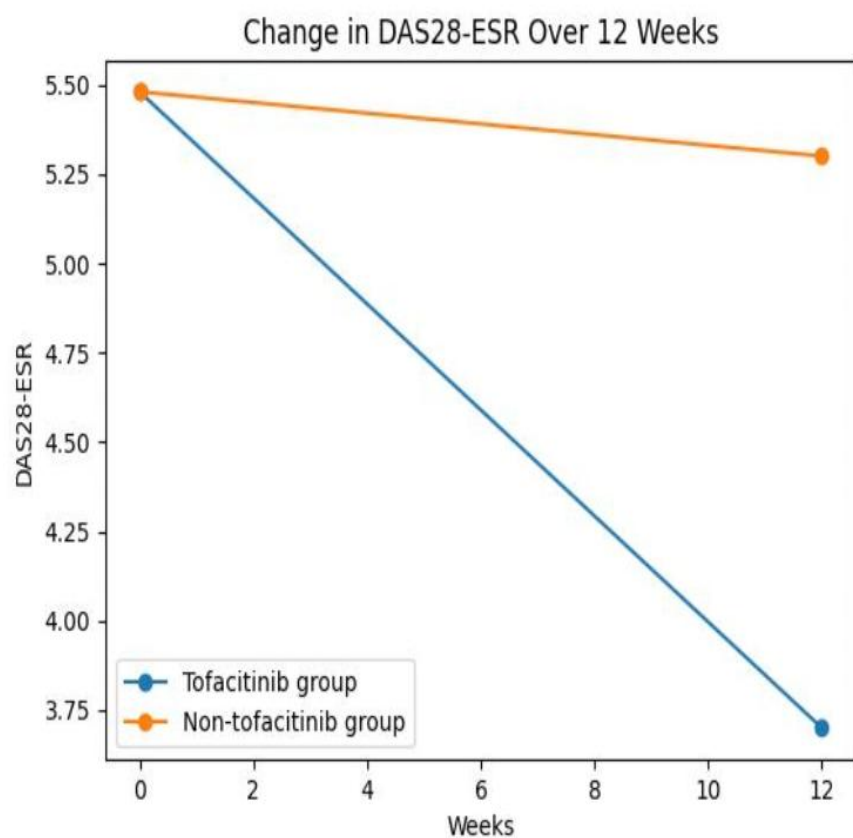
In Group I, there was a significant reduction in ESR, CRP, DAS28-ESR, CDAI, and SDAI scores after 12 weeks of tofacitinib therapy ($p < 0.0001$).

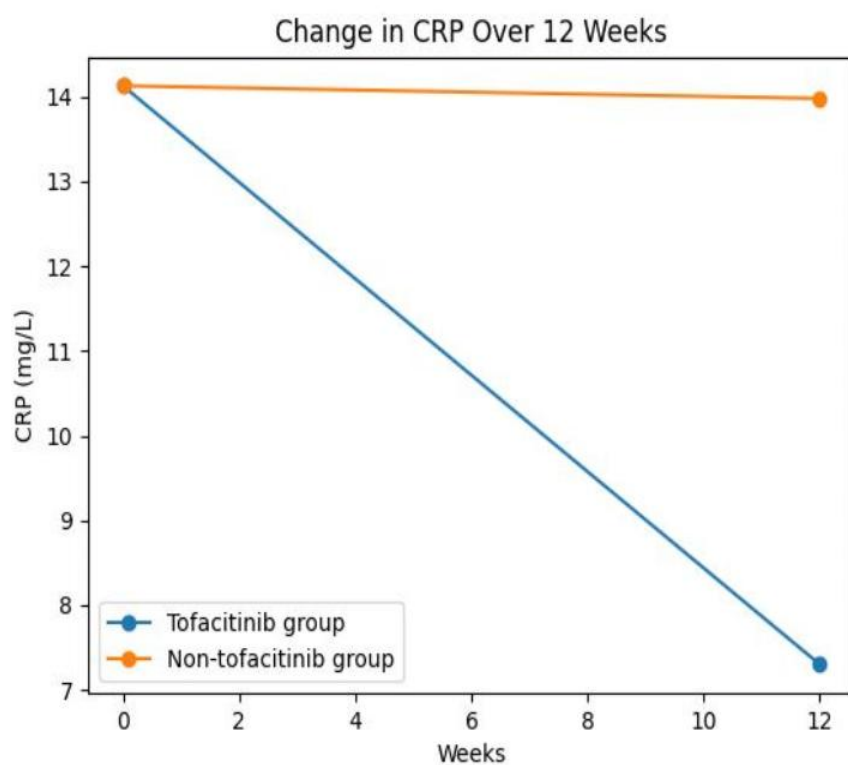
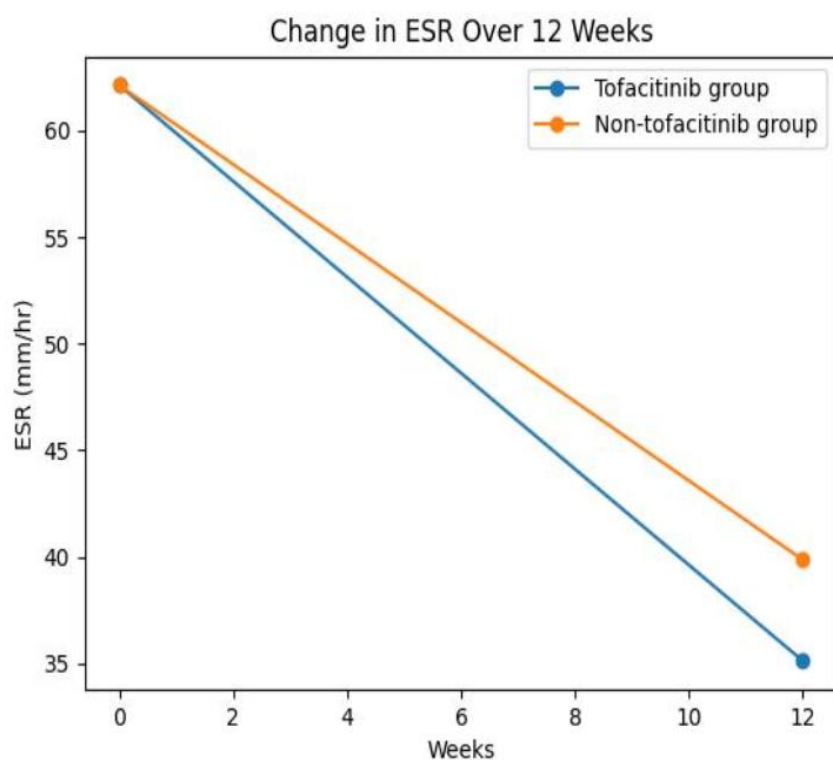
- Remission: 6 patients (28.57%)
- Low disease activity: 9 patients (42.85%)
- Total achieving treatment target: 71.42%

All patients demonstrated a clinically meaningful improvement in DAS28-ESR (>1.2 reduction).

In Group II, out of 48 patients, 5 were lost to follow-up. The remaining 43 patients showed no significant change in disease activity after 12 weeks.







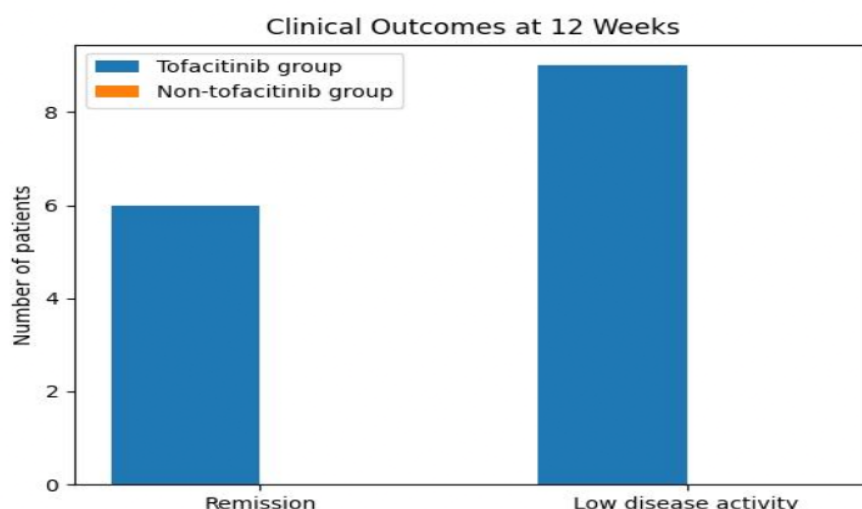
Assessment of Disease Activity and Comparison Between the Two Groups

S.No	Parameter	With Tofacitinib (n=21)	Without Tofacitinib (n=43)	P (Baseline)	With Tofacitinib (n=21)	Without Tofacitinib (n=43)	P (12 weeks)
1	ESR	62.14 (30.72)	22.71 (13.52)	<0.0001	50.13 (29.35)	39.86 (25.7)	0.7007
2	CRP	14.13 (12.61)	6.8 (7.547)	0.0122	17.30 (24.11)	13.39 (14.83)	0.1770
3	DAS-28 ESR	5.48 (0.81)	2.84 (0.53)	<0.0001	4.92 (1.13)	3.46 (1.19)	<0.0004
4	CDAI	25.16 (7.55)	6.42 (2.8)	<0.0001	24.98 (15.42)	22.81 (13.3)	<0.0001
5	SDAI	26.41 (7.17)	7.17 (2.67)	<0.0001	28.47 (15.5)	26.07 (13.73)	<0.0001

DISCUSSION

This study demonstrates that the addition of tofacitinib in RA patient's refractory to combination synthetic DMARDs leads to significant improvement in disease activity within 12 weeks. The proportion of patients achieving remission or low disease activity aligns with results from pivotal clinical trials and real-world observational studies.

Tofacitinib's oral administration, rapid onset of action, and targeted mechanism of action make it an attractive alternative to biologic DMARDs, particularly in resource-limited settings. The favourable safety profile observed in this study further supports its use in routine clinical practice.



CONCLUSION

Tofacitinib is a safe and effective treatment option for patients with rheumatoid arthritis refractory to combination synthetic DMARD therapy. A substantial proportion of patients achieved remission or low disease activity within a short duration, fulfilling the EULAR treat-to-target recommendations.

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