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REAL-WORLD EFFECTIVENESS AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS: A MULTICENTER RETROSPECTIVE STUDY FROM INDIA

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ABSTRACT **Objective-** Tofacitinib, first oral Janus kinase (JAK) inhibitor approved for the treatment of moderately to severely active rheumatoid arthritis (RA). This study aims to evaluate the real-world efficacy and safety of tofacitinib in Indian patients with RA across multiple centers. **Methods-** A Retrospective observational study was conducted across 287 centers in India, collecting data from Jan 2022 to June 2024 of patients who received tofacitinib for RA. The study was approved by the ethics committee. Descriptive statistics summarized demographics, and a paired t-test analyzed baseline and post-treatment data. **Results-** The study included 1,950 rheumatoid arthritis (RA) patients who were treated with tofacitinib. Tofacitinib was prescribed as 5 mg BID in 51% (n=992) and as 11 mg extended-release in 49% (n=958). The Tofacitinib treatment resulted in statistically significant improvements across all measured parameters, including joint pain, morning stiffness, joint stiffness severity, and daily activities. Adverse reactions were reported in only 8% (n=156) of patients, including headache, abdominal pain, nausea, vomiting, and URTI. **Conclusion-** This real-world study indicates that tofacitinib is an effective and well-tolerated treatment option for RA in the Indian population, either as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

KEYWORDS : Oral Janus kinase inhibitor, Joint Pain, Visual Analog Scale, Patient Global Assessment (PGA)

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disorder characterized by joint inflammation, pain, stiffness, and functional disability, leading to a significant decline in quality of life. Globally, the prevalence of RA is estimated to range between 0.3% and 1%, with variations across populations.[1] In India, recent data suggest a prevalence of approximately 0.75% among adults, posing a substantial burden on healthcare systems and patients alike.[2,3]

Despite advancements in RA management, many patients fail to achieve optimal disease control with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biologics, highlighting the need for additional therapeutic options. Tofacitinib is a Janus kinase (JAK) inhibitor that modulates the immune response by inhibiting JAK enzymes, which are involved in the signaling of pro-inflammatory cytokines, thereby reducing inflammation and joint damage in patients with rheumatoid arthritis. Tofacitinib has become a key targeted synthetic DMARD for managing moderate-to-severe rheumatoid arthritis, especially in patients who have an inadequate response or intolerance to conventional synthetic DMARDs (csDMARDs) or biologics.[4,5] Global clinical trials and real-world studies have demonstrated the efficacy and safety of tofacitinib in improving disease activity and functional outcomes in RA patients; however, real-world data from India remain limited.

The objective of this multicenter, retrospective study was to evaluate the effectiveness and safety of tofacitinib in Indian patients with RA in a real-world setting. This study aimed to provide valuable insights into the clinical outcomes and tolerability of tofacitinib, thereby supporting its practical application in routine RA management in India.

Methods

Study Design

This retrospective observational study was conducted across 287 centers in India, collecting data from January 2022 to June 2024 on RA patients treated with tofacitinib. Ethical approval was obtained from the life Point Research Ethics Committee, Pune. Informed consent from patients was waived, as the study involved anonymized retrospective data.

Study Population

The study included adult patients (≥18 years) diagnosed with RA according to the 2010 ACR/EULAR criteria who received tofacitinib (5 mg BID or 11 mg extended-release) for at least 12 weeks. Inclusion criteria were documented diagnosis of RA, treatment with tofacitinib during the study period, and availability of complete baseline and follow-up data. Exclusion criteria included patients with incomplete medical records, insufficient follow-up, or those who discontinued treatment before 12 weeks.

Outcome Measures

Primary outcomes included changes in joint pain, morning stiffness, joint stiffness severity, and daily activities. Joint pain was evaluated using the Visual Analog Scale (VAS), where patients rated their pain on a scale from 0 (no pain) to 10 (worst pain). Morning stiffness was recorded in minutes based on patient recall. Joint stiffness severity was measured on a numerical scale ranging from 0 (no stiffness) to 10 (severe stiffness). Additionally, the Patient Global Assessment (PGA) of daily activities was used. Adverse events such as headache, abdominal pain, nausea, vomiting, and URTI were recorded.

Data Analysis

Descriptive statistics summarized demographics; paired t-tests compared baseline and post-treatment outcomes. Statistical significance was set at $p < 0.05$, using SPSS version XX.

RESULTS

Demographic and Clinical Data

The study included 1,950 patients with a mean age of 57.21 ± 10.92 years (range: 22 to 85 years). The cohort consisted of 68% females (n=1,325) and 32% males (n=625). Regarding smoking status, 68% were non-smokers (n=1,326), 16% were current smokers (n=306), and 16% were former smokers (n=318). The average disease duration was 4.7 ± 4 years, indicating a population with moderate chronicity of RA.

Tofacitinib was prescribed as 5 mg BID in 51% of the patients (n=992), and as 11 mg extended-release in 49% (n=958). Tofacitinib was prescribed as monotherapy in 14% of cases (n=278), while the remaining 86% (n=1,672) received it in combination with other medications, including methotrexate (84%, n=1,643), hydroxychloroquine (2.96%, n=59), and leflunomide (0.30%, n=6).

Table 1: Demographic & Clinical Data

Parameters	Total (n)1950
Age (Years)	57.21 ± 10.92
Female	1325 (68%)
Male	625 (32%)
Current Smoker	16 %
Non smoker	68 %
Former smoker	16 %
Average duration of RA(Years)	4.7 ± 4
Tofacitinib Monotherapy	14% (n=278)
Combination therapy	84% (n=1,643)
Clinical Symptoms	
Joint Pain	1879 (96.36%)

Morning Stiffness	1498 (76.8%
Joint stiffness	1907 (97.8%)

Efficacy Parameters

The study showed significant clinical improvement after 4 months of tofacitinib treatment. There was a marked reduction in joint pain (VAS score decreased from 8.12 to 6.49; p = 0.012) and morning stiffness duration (from 124 to 40.29 minutes; p = 0.001). Joint stiffness severity also improved significantly (from 7.53 to 5.61; p = 0.027). Additionally, patients reported better overall functioning in daily activities, as reflected by the Patient Global Assessment (PGA), which improved from 8.47 to 6.65 (p = 0.001).

Table 2: Efficacy Parameters

Parameter	Baseline	After 4 months	P value
Patient's Assessment of Joint pain VAS score	8.12 ± 1.45	6.49 ± 1.58	0.012
Morning stiffness duration (Minutes)	124 ± 34	40.29 ± 50	0.001
Joint stiffness severity score	7.53 ± 1.45	5.61 ± 1.27	0.027
Patient Global Assessment (PGA) Daily Activities	8.47 ± 1.32	6.65 ± 1.50	0.001

Safety

In terms of safety, adverse reactions were reported in 8% (n=156) of patients. The most commonly observed adverse events included headache (n=3.5%), abdominal pain(n=2.6%), nausea(n=3%),, vomiting(n=3%),, and upper respiratory tract infections (URTI) (n=0.7%),

DISCUSSION

This large real-world, retrospective multicenter study evaluated the effectiveness and safety of tofacitinib in 1,950 patients with rheumatoid arthritis (RA) across India. Our findings demonstrated significant improvements in joint pain, morning stiffness, joint stiffness severity, and daily activity scores after 4 months of treatment. Importantly, the safety profile was consistent with prior clinical experience, with adverse events reported in only 8% of patients, mostly mild in nature.

Our results align with data from pivotal phase 3 trials such as ORAL Standard and ORAL Sync, which reported significant reductions in disease activity and improvement in patient-reported outcomes with tofacitinib in combination with methotrexate or other conventional synthetic DMARDs.[6,7] In our cohort, combination therapy, predominantly with methotrexate, was used in 84% of cases, reflecting real-world practice patterns.

A study by Cohen et al. also demonstrated sustained improvements in joint pain and function over 12 months with tofacitinib, reporting safety events similar to ours, including mild infections and gastrointestinal symptoms.[8] Additionally, a real-world study from Japan by Takeuchi et al. found comparable reductions in morning stiffness and disease activity scores, supporting the generalizability of tofacitinib efficacy across different populations.[9]

Our study expands on these findings by providing evidence from a diverse Indian population with varying smoking status, disease duration, and treatment histories. Notably, the reduction in morning stiffness duration (from 124 to 40 minutes) and improvement in daily activity scores mirror the functional benefits reported in prior observational studies.[10,11]

The safety profile in our study was reassuring, with adverse events consistent with prior reports, particularly the low rates of serious infections, cardiovascular events, or thromboembolism over this short-term follow-up.[12] However, long-term monitoring is essential, as highlighted in post-marketing surveillance studies.

This large, multicenter study reflects real-world use of tofacitinib in India, with a diverse patient population and both monotherapy and combination therapy groups. Multiple key clinical outcomes were evaluated, enhancing the practical relevance of the findings. However retrospective, observational design limits the ability to establish causality between tofacitinib use and clinical outcomes. There was no control or comparator group, which restricts direct comparisons to other treatment modalities. The relatively short follow-up period (4 months) does not allow assessment of long-term efficacy, safety, or rare adverse events.

CONCLUSION

This large real-world study demonstrates that tofacitinib is an effective and well-tolerated treatment for rheumatoid arthritis in Indian patients, leading to significant improvements in joint symptoms and daily function, with a low rate of adverse events. These findings support its role as a valuable option in routine clinical practice.

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