ARC Journal of Public Health and Community Medicine
Volume 10 Issue 1, 2025, PP 19-26
ISSN No. (Online) 2456-0596
DOI: https://doi.org/10.20431/2456-0596.1001004
www.arcjournals.org

Effect of Tofacitinib in Axial Spondyloarthritis in Physical Medicine & Rehabilitation Department in a Tertiary Level Hospital in Bangladesh

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Received: 16 April 2025 Accepted: 02 May 2025 Published: 10 May 2025

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Abstract

Background: *Axial Spondyloarthritis (AxSpA) is a chronic inflammatory disease affecting the axial skeleton, often resulting in pain, stiffness, and reduced quality of life. While several biologics exist, not all patients respond adequately. Janus kinase (JAK) inhibitors like Tofacitinib have emerged as promising alternatives due to their broad immunomodulatory effects.*

Methods: *This quasi-experimental study was conducted in the Department of Physical Medicine and Rehabilitation at Dhaka Medical College Hospital over a period of six months from January 2020 to June 2020. A total of 28 patients diagnosed with axial spondyloarthritis were enrolled using a purposive convenient sampling method. The study population included patients aged over 18 and under 48 years of both sexes who met the modified Assessment of SpondyloArthritis International Society (ASAS) criteria for axial spondyloarthritis.*

Results: *The mean age of participants was 35.32±6.62 years, with 79% male. ASDAS-CRP scores decreased significantly from 5.56±1.27 at baseline to 1.757±1.42 at 12 weeks ($p \leq 0.001$). BASDAI scores improved from 6.768±1.5 to 2.31±1.88, and VAS scores from 6.82±1.7 to 2.82±1.6. ASAS40 and ASAS5/6 responses were achieved in 71.43% of participants. Adverse events were minimal: upper respiratory tract infections (10.7%), diarrhea (7.1%), urinary tract infection and headache (3.5% each), while 75.2% experienced no adverse effects.*

Conclusion: *Tofacitinib 5 mg twice daily demonstrated significant short-term efficacy in reducing disease activity and improving clinical outcomes in AxSpA patients, with a favorable safety profile. Further large-scale, placebo-controlled studies are recommended to confirm these findings.*

Keywords: *Axial Spondyloarthritis, Tofacitinib, JAK inhibitors, BASDAI, ASDAS-CRP, ASAS40, Clinical Efficacy, Adverse Events*

1. Introduction

Axial Spondyloarthritis (AxSpA) is a chronic systemic inflammatory disease of the axial skeleton that significantly impacts quality of life [1]. It primarily affects musculoskeletal sites such as the synovium and entheses and can involve extra-articular targets including the uvea and the aortic valve root. AxSpA encompasses a spectrum of clinical manifestations, with ankylosing spondylitis (AS) representing its most severe phenotype, characterized by sacroiliac joint and spinal damage ranging from mild erosions to new bone formation and joint fusion [2].

AxSpA typically presents in the second to third decade of life and shows a male predominance, with a male-to-female ratio of approximately 2–

3:1. Disease onset occurs about five years earlier in individuals who are HLA-B27 positive compared to those who are HLA-B27 negative [3]. Most epidemiological studies to date have focused on AS, with an estimated prevalence of 0.5–1% [4]. The overall prevalence of AxSpA varies between 0.32% and 1.8%, depending on geographic region and ethnicity [3].

The pathophysiology of AxSpA is believed to involve dysfunction of antigen-presenting cells and misfolding of HLA-B27 molecules, which trigger the production of inflammatory interleukins, particularly IL-17 and IL-23 [5]. T-cell mediated immune responses, including both CD4+ and CD8+ T-cells, contribute to the release of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α), IL-17, and IL-22. These cytokines are associated with bony destruction, synovitis, and osteoproliferation. As structural damage progresses, compensatory bone formation may occur, leading to syndesmophyte development and eventual bony ankylosis—the hallmark of AS and the major cause of functional impairment [2].

Approximately two-thirds of patients with AxSpA exhibit active disease that may warrant treatment with biologic disease-modifying anti-rheumatic drugs (bDMARDs), defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score >4 and a spinal Visual Analogue Scale (VAS) >4, or an Ankylosing Spondylitis Disease Activity Score (ASDAS) ≥2.1 [6,7]. According to the ASAS-European League Against Rheumatism (ASAS-EULAR) guidelines, bDMARD therapy is recommended for patients with persistently high disease activity despite treatment with at least two non-steroidal anti-inflammatory drugs (NSAIDs) over four weeks, especially in the presence of elevated CRP or radiologic/MRI evidence of sacroiliitis [8].

Tofacitinib is currently the only oral medication that closely resembles biologics in the treatment of AxSpA. As a Janus kinase (JAK) inhibitor, it preferentially inhibits JAK1 and JAK3, with some selectivity over JAK2, thereby affecting cytokine signaling pathways implicated in AS pathogenesis—including IL-17, IL-21, and IL-23 [9]. By modulating these immune responses, tofacitinib helps reduce or prevent inflammation [10–12].

Conventional DMARDs such as methotrexate and sulfasalazine have shown limited efficacy in AxSpA, and injectable biologics, though more effective, remain financially inaccessible to many patients in low-income countries like Bangladesh. Given its oral formulation and lower cost, tofacitinib may serve as a viable alternative to injectable biologics for the Bangladeshi population.

However, due to the scarcity of local and global data regarding the efficacy and safety of tofacitinib in AxSpA, further research is needed. Therefore, this study aimed to evaluate the therapeutic effects of tofacitinib in Bangladeshi patients with AxSpA.

2. Methodology & Materials

This quasi-experimental study was conducted in the Department of Physical Medicine and Rehabilitation at Dhaka Medical College Hospital over a period of six months from January 2020 to June 2020. A total of 28 patients diagnosed with axial spondyloarthritis were enrolled using a purposive convenient sampling method. The study population included patients aged over 18 and under 48 years of both sexes who met the modified Assessment of SpondyloArthritis International Society (ASAS) criteria for axial spondyloarthritis. All participants had a documented history of unsatisfactory response to conventional disease-modifying antirheumatic drugs (DMARDs) such as methotrexate and sulfasalazine.

Patients were excluded if they had any contraindication to the use of Tofacitinib, active infectious diseases such as tuberculosis, hepatitis B or C, or HIV, hematological disorders, abnormal liver function, an estimated glomerular filtration rate below 40 ml/min/1.73m², malignancies, overlapping autoimmune rheumatic diseases, a history of prior use of Tofacitinib, or if they were severely ill or immunocompromised.

Participants were thoroughly evaluated in the outpatient department, and the details of the study were clearly explained in the local language using a printed handout. Written informed consent was obtained from each participant. Patients were assured of confidentiality, informed that the study involved no invasive procedures, and that their participation would not influence their ongoing medical care.

Data were collected through a structured questionnaire that included demographic information and clinical variables. Pain levels

were assessed using the Visual Analogue Scale (VAS), and grip strength was measured with a hand dynamometer at baseline and during follow-up. Collected data were reviewed for completeness and accuracy before analysis.

Statistical analysis was performed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency and percentage. The chi-square test was used for categorical data, and ANOVA was applied to assess changes in VAS scores and grip strength over time. A p-value less than 0.05 was considered statistically significant.

3. RESULTS

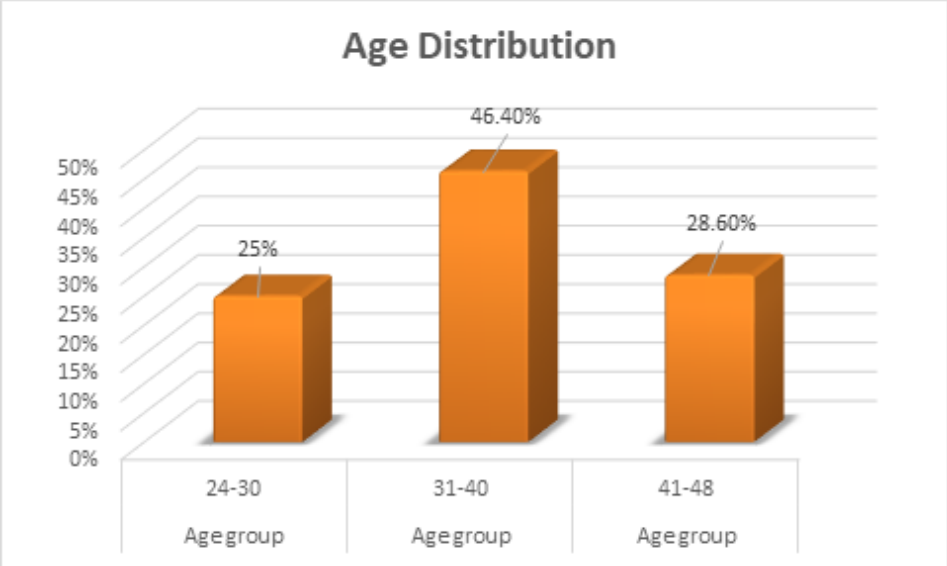

Figure 1. *Age distribution of patients with Axial Spondyloarthritis (n=28).*

Figure 1 shows the distribution of respondents by age. The age of the respondents was in between 24 to 48 year and the mean age was 35.32± 6.62 year. Most (46.4%) respondents were31-40 year of age. 28.6% respondents belonged to >40 years age group Rest 25% belonged to ≤30 year age group.

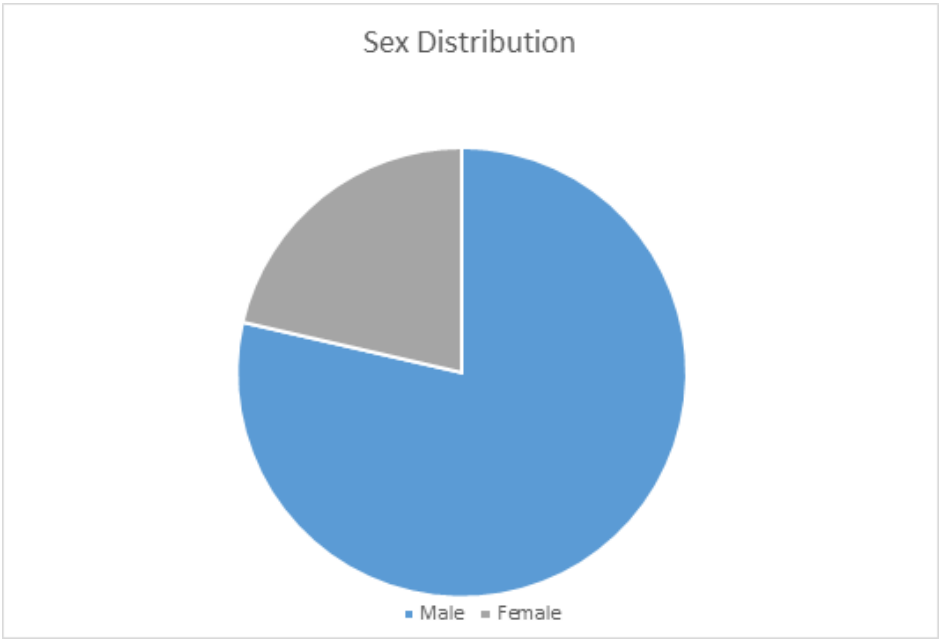

Figure 2. *Distribution of study population according to sex (n=28).*

Figure 2 shows distribution of the respondents by sex. Most respondents (79%) were male. Rest 21% respondents were female. Ratio of male and female 4:1.

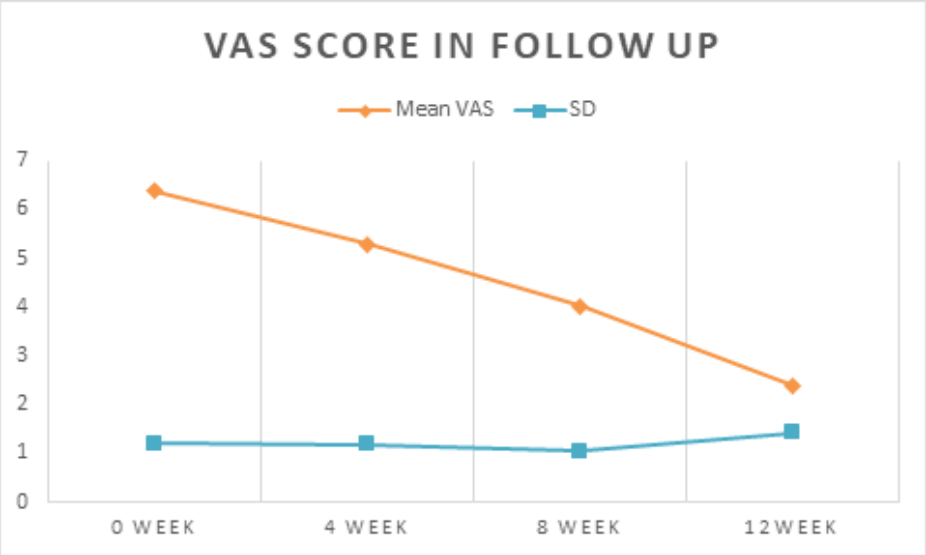

Figure 3. *Pattern of VAS score in Different week of follow up*

Figure 3 shows distribution of the respondent according to their VAS scale score in different weeks. Score at 0,4, 8 and 12 weeks were 6.39±1.2, 5.29±1.18, 4.03±1.04 and 2.39±1.42 respectively.

Table I. *VAS scale score difference at different weeks*

Difference between weeks	VAS scale score difference		p value
	Mean	Standard deviation	
Difference between 0 & 4 week	1.107	0.875	≤.001
Difference between 0 & 8 week	2.36	1.13	≤.001
Difference between 0 & 12 week	4	1.68	≤.001

Table I shows VAS scale score difference at different weeks. Scale score difference between 0 & 4 week was 1.107±0.875, between 0 & 8 week was 2.36±1.13 and 0&12 week was 4±1.68. Difference between 0 &12 week was greater than difference between 0 & 8 week and 0 & 4 week. Paired t test showed all the differences were statistically significant (p≤0.001).

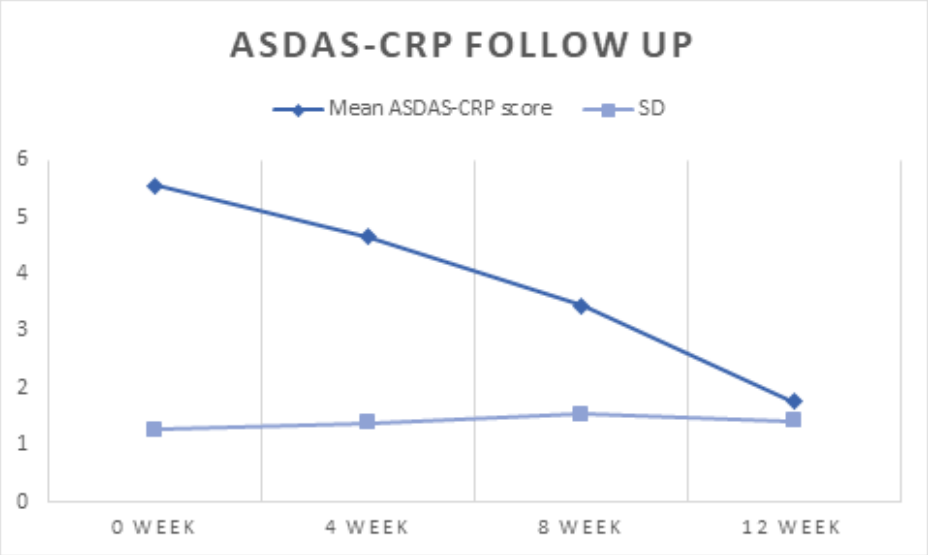

Figure 4. *Showing ASDAS-CRP score variation in different weeks of follow up*

Figure 4 shows distribution of the respondent according to their ASDAS-CRP scale score in different weeks. Score at 0, 4, 8 and 12 weeks were 5.56±1.27, 4.65±1.38, 3.45±1.54 and 1.757±1.42 respectively.

Table II. *ASDAS-CRP scale score difference at different weeks*

Difference between weeks	ASDAS scale score difference		p value
	Mean	Standard deviation	
Difference between 0 & 4 week	0.914	0.83	≤.001
Difference between 0 & 8 week	2.11	1.06	≤.001
Difference between 0 & 12 week	3.81	1.5	≤.001

Table II shows ASDAS-CRP scale score difference at different weeks. Scale score difference between 0 & 4 week was 0.914±0.83, between 0 & 8 week was 2.11±1.06 and 0&12 week was 3.81±1.5. Difference between 0 &12 week was greater than difference between 0 & 8 week and 0 & 4 week. Paired t test showed all the differences were statistically significant (p≤0.001).

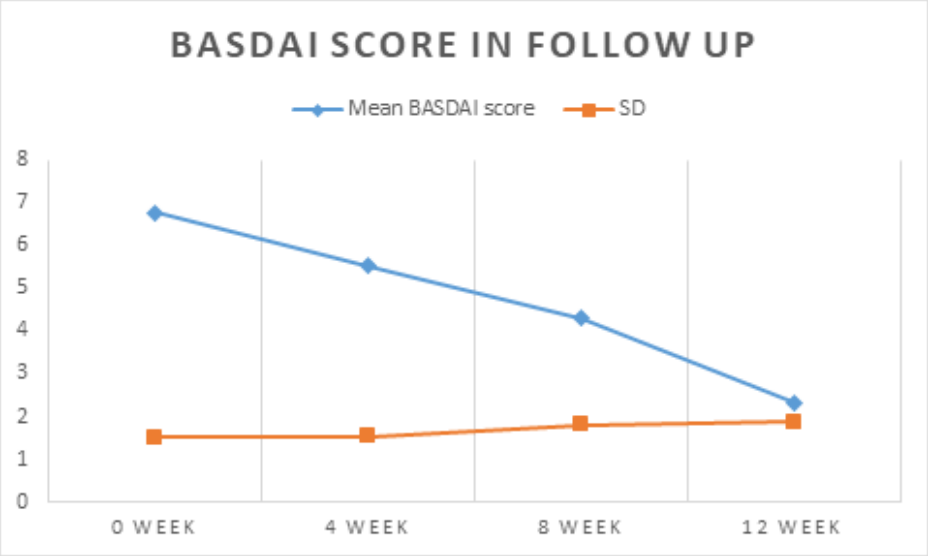

Figure 5. *BASDAI score in different weeks of follow up showing a trend to fall down of the value.*

Table 5 shows distribution of the respondent according to their BASADAI scale score in different weeks. Score at 0, 4, 8 and 12 weeks were 6.768±1.5, 5.53±1.53, 4.3±1.81 and 2.31±1.88 respectively.

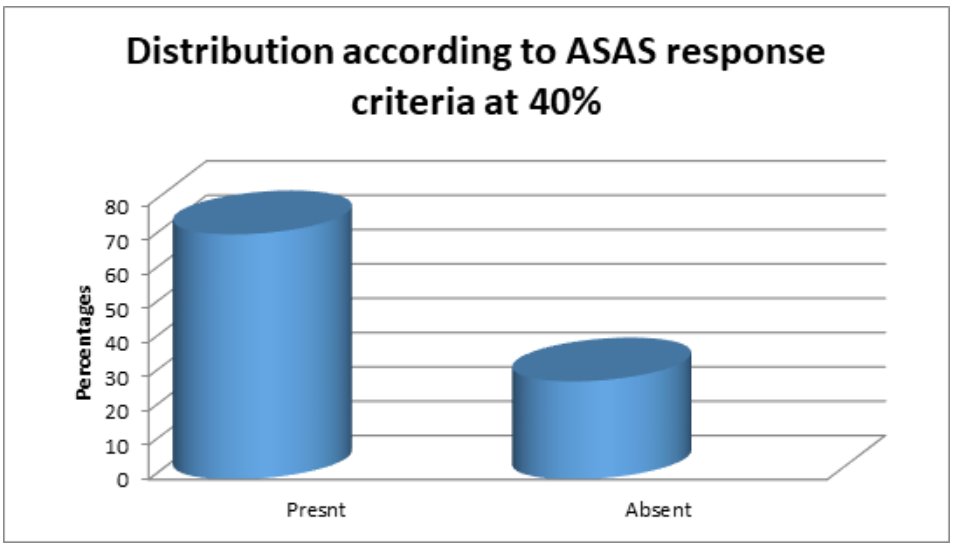

Figure 6. *Shows distribution of the respondent according to ASAS40 response criteria at 12 weeks of treatment*

Figure 6 illustrates the distribution of respondents based on the Assessment of SpondyloArthritis International Society 40% improvement criteria (ASAS40) after 12 weeks

of Tofacitinib treatment. A significant proportion of patients (71.43%) achieved ASAS40 response, indicating substantial clinical improvement. Conversely, 28.57% of the patients did not meet the ASAS40 response threshold.

Table III. *Adverse Events of the treatment noticed among the respondents (n=28)*

Adverse Events	Frequency(n=28)	Percentage
Upper Respiratory Tract Infection(URTI)	3	10.7%
Diarrhea	2	7.1%
Urinary Tract Infection(UTI)	1	3.5%
Headache	1	3.5%
No adverse Event	21	75.2%

*** All side effects were noticed within 2 weeks of starting the drug.*

Table III presents the adverse events observed among the 28 patients treated with Tofacitinib. A majority of the respondents (75.2%) did not experience any adverse effects during the treatment period. Among the reported side effects, upper respiratory tract infection (URTI) was the most common, observed in 10.7% of patients, followed by diarrhea in 7.1%. Urinary tract infection (UTI) and headache were each reported in 3.5% of patients. Notably, all adverse events occurred within the first two weeks of initiating therapy.

4. Discussion

JAK inhibitors are a novel class of therapies that have shown considerable efficacy in treating inflammatory diseases due to their broad effects on cytokine signaling pathways. Among these, Tofacitinib has emerged as a potential option for patients with Axial Spondyloarthritis (Axial SpA), especially those unresponsive to conventional treatment modalities. In our study, we evaluated the short-term effectiveness and safety profile of Tofacitinib (5 mg twice daily) in patients with active Axial SpA.

A total of 28 patients were enrolled, with a mean age of 35.32 ± 6.62 years (range: 24–48 years). The majority (46.4%) were aged 31–40 years, 28.6% were above 40 years, and 25% were aged ≤30 years. Most participants (79%) were male. These demographics are consistent with previous studies by Maneiro JR et al., Walter P et al., and Stolwijk et al., where the mean age ranged from 28–38 years, and individuals over 40 years constituted approximately 23.4% of the population [13-15].

In terms of disease duration, 42.9% of patients reported pain for less than 12 months, while 57.1% had pain for 12–28 months. The mean duration was 22.7 ± 23.3 months, comparable to the findings by Buraun et al., who reported a mean disease duration of 28–30 months in Axial SpA patients [16].

We observed significant clinical improvement over 12 weeks of treatment with Tofacitinib. The ASDAS-CRP scores progressively declined from a baseline of 5.56±1.27 to 1.757±1.42 at week 12, indicating a shift from high to low or inactive disease activity. The week-wise score reductions were statistically significant ($p \leq 0.001$), with differences of 0.914±0.83 at 4 weeks, 2.11±1.06 at 8 weeks, and 3.81±1.5 at 12 weeks. Similar improvements were documented in studies by Inman RD et al., Landewé R et al., and Van der Heijde et al., where ASDAS-CRP scores reached comparable levels after treatment with Certolizumab, Infliximab, and Tofacitinib [17-20].

The BASDAI scores also showed a statistically significant reduction from 6.768±1.5 at baseline to 2.31±1.88 at 12 weeks ($p \leq 0.001$). Score differences were 1.24±0.94 (week 4), 2.47±1.27 (week 8), and 4.45±1.92 (week 12). These results align with a prior study of Tofacitinib in Axial SpA, which found a BASDAI score change of 4.32±1.8 over 12 weeks [21].

VAS scores decreased from baseline with significant differences observed at all follow-up points: 1.107±0.875 (week 4), 2.36±1.13 (week 8), and 4±1.68 (week 12). These reductions were also statistically significant ($p \leq 0.001$) and support findings from Van der Heijde et al., and Walter P et al., where VAS changes ranged from 2.66 to 4.36 over 12 weeks of treatment with Tofacitinib and Adalimumab [20, 22].

Regarding response criteria, ASAS40 and ASAS 5/6 responses were observed in 71.43% of patients at 12 weeks, indicating substantial clinical benefit. These findings are consistent with other biologic trials in Axial SpA, where ASAS40 responses ranged from 63.9% to 64.7%

and ASAS5/6 responses from 62.4% to 65.4% [20, 21].

Adverse events were minimal and manageable. URTI was the most frequent (10.7%), followed by diarrhea (7.1%), UTI (3.5%), and headache (3.5%). No adverse events were reported in 75.2% of patients. Our results are supported by Davis et al., who also found that 79% of patients reported no side effects with Tofacitinib 5 mg [23]. Furthermore, Baeten et al. reported serious infections in only 3.4% of patients treated with Tofacitinib, which reinforces the relatively safe profile observed in our study [24].

In summary, this study contributes valuable insight into the short-term effectiveness and tolerability of Tofacitinib in Axial SpA. The drug demonstrated significant clinical improvement in disease activity indices (ASDAS-CRP, BASDAI, VAS) and favorable ASAS response rates. These findings align with previous biologic trials and support the potential role of JAK inhibitors like Tofacitinib in managing Axial SpA [25]. However, larger, controlled, long-term studies are needed to fully establish its efficacy and safety profile. Given its oral route, affordability, and availability, Tofacitinib may represent a promising addition to the current treatment landscape for Axial Spondyloarthritis.

5. Limitations Of The Study

This study had several limitations that should be acknowledged. Firstly, the sample size was relatively small, which may limit the generalizability of the findings. Secondly, the absence of a placebo control group restricts the ability to compare the observed outcomes directly and definitively attribute them to Tofacitinib. Additionally, the study did not include a long-term follow-up, making it difficult to assess the sustained efficacy and safety of the drug over time. Therefore, future research should focus on conducting larger, multicenter randomized controlled trials with extended follow-up periods to validate these findings and establish more robust evidence for the use of Tofacitinib in Axial Spondyloarthritis.

6. Conclusion

In this study, it was observed that the following 5mg Tofacitinib twice daily for treatment of Axial Spondyloarthritis showed significant improvement like VAS, ADL improvement by assessing some recognised criteria related to Axial Spondyloarthritis was noted at 3 months follow up of the patients. Comparison of this study with other case control studies of Tofacitinib in Axial Spondyliarthritis also shows significant resemblance in the outcome of diseases. Based on the findings, it can be said that for the treatment of Axial SpA, Tofacitinib 5mg twice daily is a suitable alternative. However, further large multicenter randomized controlled trial is required.

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Citation: *Dr. Md. Mominul Islam et al. Effect of Tofacitinib in Axial Spondyloarthritis in Physical Medicine & Rehabilitation Department in a Tertiary Level Hospital in Bangladesh. ARC Journal of Public Health and Community Medicine. 2025; 10(1):19-26. DOI: https://doi.org/10.20431/2456-0596.1001004.*