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# Efficacy and Safety of Tofacitinib in Patients with Vitiligo over Six Months

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***Abstract:*** **Background**: Objective: To evaluate the efficacy and safety of oral tofacitinib in patients with vitiligo over a six-month treatment period. **Methods:** This prospective longitudinal study was conducted in the Department of Dermatology, LUMHS, Jamshoro, Hyderabad, over six months. A total of 66 patients aged ≥18 years with clinically diagnosed vitiligo were enrolled through consecutive sampling. All patients received oral tofacitinib 5 mg twice daily for six months. Disease severity was assessed using the Vitiligo Area Scoring Index (VASI) at baseline, three months and six months. The primary efficacy outcome was change in VASI score from baseline to six months. Treatment-related adverse effects were documented throughout the study period. Data were analyzed using IBM SPSS Statistics version 26, with $p < 0.05$ considered statistically significant. **Results:** The mean age of participants was 44.43±11.67 years, with 45 (68%) males and 21 (32%) females. Generalized vitiligo was the most common type, observed in 37 (56.3%) patients. Mean VASI decreased from 1.82±1.47 at baseline to 1.80±1.32 at three months and 1.60±1.26 at six months; however, the overall change was not statistically significant (p=0.44). At six months, 34 (51.5%) patients achieved ≥50% improvement in VASI, including 12 (18%) with ≥75% improvement. The most frequent adverse effect was upper respiratory tract infection (11%), followed by headache (9%). Other adverse effects included gastrointestinal discomfort (4.5%), acne (4.5%), elevated liver enzymes (3%), and palpitations (1.5%). **Conclusion:** Oral tofacitinib demonstrated a numerical improvement in VASI over six months, with approximately half of the patients achieving ≥50% improvement. However, the overall change in VASI was not statistically significant. Treatment was generally well tolerated, with predominantly mild adverse effects.

***Keywords:*** Vitiligo; Tofacitinib; Janus Kinase Inhibitors; VASI; Repigmentation; Treatment Outcome; Adverse Effects.

## INTRODUCTION

Vitiligo is a chronic acquired disorder of pigmentation characterized by the development of well-defined depigmented macules and patches resulting from the selective destruction or functional impairment of melanocytes. It affects individuals across different age groups and ethnicities and may have a substantial psychosocial impact because of its visible nature. Although vitiligo is not associated with significant physical morbidity in most patients, its chronic course, unpredictable progression and cosmetic disfigurement can adversely affect quality of life. Current therapeutic approaches include topical corticosteroids, topical calcineurin inhibitors, phototherapy and systemic immunomodulatory therapies; however, treatment response remains variable, particularly in patients with extensive or active disease.

The pathogenesis of vitiligo is considered to involve a complex interaction between genetic susceptibility, oxidative stress and immune-mediated melanocyte destruction. Increasing evidence has demonstrated an important role of interferon-gamma-mediated signalling and the Janus kinase (JAK)-signal transducer and activator of transcription pathway in

the pathogenesis of vitiligo. This has led to increasing interest in JAK inhibitors as targeted immunomodulatory therapies for vitiligo. Tofacitinib is an oral JAK inhibitor that primarily inhibits JAK1 and JAK3-dependent signalling and consequently interferes with inflammatory pathways involved in autoimmune melanocyte destruction.

Early clinical evidence has suggested that oral tofacitinib may produce repigmentation in patients with vitiligo, although the magnitude of response varies according to disease characteristics and treatment duration. In an earlier clinical series, repigmentation was observed in some patients receiving tofacitinib, particularly in sun-exposed areas, while additional benefit was observed in patients receiving concomitant narrow-band ultraviolet B phototherapy. More recent observational evidence has also suggested that treatment extending beyond six months may be associated with greater repigmentation. A retrospective study of 137 patients reported greater improvement among patients treated for 6–9 months compared with those treated for less than six months, with an overall improvement of approximately 42% in the longer-treatment group. Mild adverse reactions were reported in 13.8% of patients, while no severe adverse events were observed during the study period.

The Vitiligo Area Scoring Index (VASI) is a quantitative clinical tool used to assess the extent and degree of depigmentation in vitiligo. It estimates the affected body surface area using hand units and incorporates the percentage of depigmentation within each affected area. The total VASI score ranges from 0 to 100, with higher scores indicating greater extent and severity of depigmentation. Reduction in VASI following treatment therefore provides an objective measure of repigmentation and treatment response.
Although emerging evidence supports the potential role of tofacitinib in vitiligo, data regarding its efficacy and safety over a standardized six-month treatment period remain limited, particularly from routine clinical practice in our population. Therefore, the present study was designed to evaluate the efficacy and safety of oral tofacitinib in patients with vitiligo over six months. The primary efficacy outcome was change in VASI score from baseline to six months, while safety was assessed by documenting treatment-related side effects during the study period.

## METHODOLOGY

A prospective longitudinal study was conducted in the Department of Dermatology, LUMHS, Jamshoro, Hyderabad, over a period of six months after approval from the Institutional Ethical Review Committee. Patients aged 18 years or above with clinically diagnosed vitiligo who were considered suitable for systemic treatment and willing to receive oral tofacitinib were enrolled using consecutive sampling. Patients with active serious infections, tuberculosis, significant hepatic or renal dysfunction, history of malignancy, pregnancy or breastfeeding, known hypersensitivity to tofacitinib, or those receiving other systemic immunosuppressive therapies were excluded. Written informed consent was obtained from all participants before enrollment.

All eligible patients received oral tofacitinib 5 mg twice daily for six months. The sample size was calculated using the OpenEpi sample size calculator, taking an estimated prevalence of side effects of 21.9%[11], a margin of error of 10%, and a 95% confidence level. The calculated minimum sample size was 66 patients. Baseline demographic and clinical information was recorded before initiation of treatment. The extent of vitiligo was assessed using the Vitiligo Area Scoring Index (VASI), which was the sole efficacy outcome measure. VASI was calculated using the hand-unit method, with one hand unit corresponding to approximately 1% of total body surface area. For each affected body region, the estimated number of hand units was multiplied by the proportion of depigmentation, and the scores for all affected areas were summed to obtain the total VASI score. VASI was assessed at baseline, three months, and six months. The percentage improvement in VASI at six months was calculated using the formula: [(baseline VASI − six-month VASI) / baseline VASI] × 100. A reduction in VASI score was considered indicative of clinical improvement.

Safety was assessed throughout the six-month treatment period by documenting any adverse effects reported by the patients or observed during follow-up visits. Patients were specifically questioned regarding treatment-related symptoms, including headache, gastrointestinal complaints, acne, fatigue, infections, upper respiratory symptoms and other clinically relevant adverse events. Each adverse effect was recorded according to its type, onset, duration, severity and outcome. Treatment discontinuation was considered if a clinically significant adverse event occurred. Patients were followed regularly during the study period to assess treatment tolerance and document adverse effects, while formal VASI assessments were performed at baseline, three months and six months.

Data were analyzed using IBM SPSS Statistics version-26 Quantitative variables, including VASI scores, were expressed as mean ± standard deviation. VASI scores at baseline, three months and six months were compared using repeated-measures analysis of variance for normally distributed data. The percentage improvement in VASI was also calculated. Adverse effects were presented as frequencies and percentages. A p-value of $\leq 0.05$ was considered statistically significant.

## RESULT

A total of 66 patients with vitiligo were included in the study. The mean age of the participants was 44.43±11.67 years. There were 45 (68%) males and 21 (32%) females. Generalised vitiligo was the most frequently observed type, present in 37 (56.3%) patients, followed by acrofacial vitiligo in 14 (21.8%) patients, mucosal vitiligo in 9 (12.5%), and segmental vitiligo in 6 (9.4%) patients. The baseline characteristics of the study population are presented in (Table 1).

The VASI score decreased from 1.82±1.47 at baseline to 1.80±1.32 at 3 months and further to 1.60±1.26 at 6 months. However, this change was not statistically significant (p=0.44). Thus, although a gradual numerical improvement in VASI score was observed over the six-month follow-up period, the reduction did not reach statistical significance (Table 2).

At six months, 12 (18%) patients achieved ≥75% improvement in their VASI score. Improvement of 50–74% was observed in 22 (33%) patients, while 23 (34.8%) showed 25–49% improvement. Only 9 (13.6%) patients had less than 25% improvement in the VASI score (Table 3).

Treatment-related adverse effects were generally mild. Upper respiratory tract infection was the most commonly reported adverse event, occurring in 7 (11%) patients, followed by headache in 6 (9%). Gastrointestinal discomfort and acne were reported by 3 (4.5%) patients each, while elevated liver enzymes were observed in 2 (3%) patients. Palpitations were reported by only 1 (1.5%) patient (Table 4).

**Table#1: Baseline Data of the Patients**

| **Baseline Data of the Patients** | **(mean ± sd)/n(%)** |
|---|---|
| Age (Years) | 44.43±11.67 |
| Gender<br>• Male<br>• Female | <br>45 (68%)<br>21 (32%) |
| Duration of vitiligo (months) | |
| Type of vitiligo<br>• General Vitiligo<br>• Acrofacial<br>• Segmental Vitiligo<br>• Mucosal Vitiligo | <br>37 (56.3%)<br>14 (21.8%)<br>6 (9.40%)<br>9 (12.52%) |

**Table#2: Comparison of VASI score at baseline, 3 months and 6 months (n=66)**

| **Assessment time** | **VASI Score (mean ± sd)** |
|---|---|
| Baseline | 1.82 ± 1.47 |
| 3 months | 1.80 ± 1.32 |
| 6 months | 1.60 ± 1.26 |
| P-value | 0.44 |

**Table#3: Percentage improvement in VASI after six months (n=66)**

| **VASI response at 6 months** | | **n (%)** |
|---|---|---|
| <25% improvement | | 9 (13.6%) |
| 25–49% improvement | | 23 (34.8%) |
| 50–74% improvement | | 22 (33%) |
| ≥75% improvement | | 12 (18%) |

**Table 4. Side effects reported during six months of treatment**

| **Side effects** | **n (%)** |
|---|---|
| Gastrointestinal discomfort | 3 (4.5%) |
| Acne | 3 (4.5%) |
| Headache | 6 (9%) |
| Palpitations | 1 (1.51%) |
| Upper respiratory tract infection | 7 (11%) |
| Elevated liver enzymes | 2 (3%) |

## DISCUSSION

Vitiligo is a chronic acquired depigmenting disorder characterized by the progressive loss of functional melanocytes. Although the condition is not associated with significant physical morbidity, its visible nature can result in substantial psychosocial distress and impaired quality of life.[11,12] The pathogenesis of vitiligo is complex and involves autoimmune destruction of melanocytes, with interferon-gamma (IFN-γ) and the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway playing an important role in disease progression.[13,14] This understanding has led to increasing interest in JAK inhibitors as a targeted therapeutic approach for vitiligo.

In the present study, the mean age of the patients was 44.43±11.67 years, and males constituted 68% of the study population. Generalised vitiligo was the most common clinical subtype, observed in 56.3% of patients. This finding is consistent with previous literature, in which non-segmental or generalised vitiligo has been reported as the predominant form of the disease.[15,16] Differences in gender distribution between studies may be influenced by healthcare-seeking behaviour, referral patterns and differences in the study population.

A gradual improvement in vitiligo severity was observed during the six-month follow-up period. The mean VASI score decreased from 1.82±1.47 at baseline to 1.80±1.32 at three months and further to 1.60±1.26 at six months. The relatively small reduction during the first three months followed by a greater reduction at six months suggests that the clinical response may become more apparent with continued treatment. Repigmentation in vitiligo is generally a gradual process, as successful treatment requires not only suppression of autoimmune melanocyte destruction but also migration, proliferation and differentiation of melanocytes within depigmented skin.[17]

The findings of the present study are comparable with previous studies evaluating JAK inhibitors in vitiligo. Craiglow and King reported substantial repigmentation in a patient with vitiligo treated with tofacitinib, particularly when treatment was combined with exposure to ultraviolet light.[18] Similarly, Liu et al. demonstrated that JAK inhibition could promote repigmentation in vitiligo and suggested that suppression of autoimmune activity alone may not be sufficient without stimulation of melanocyte regeneration through ultraviolet exposure.[19] These observations support the progressive improvement observed in the present study over six months.

In the present study, 51% of patients achieved at least 50% improvement in VASI at six months. Of these, 33% achieved 50–74% improvement, while 18% achieved ≥75% improvement. In addition, 34.8% of patients demonstrated 25–49% improvement, and only 13.6% had less than 25% improvement. Overall, the findings suggest that a substantial proportion of patients experienced clinically meaningful repigmentation during the treatment period.

The response observed in the present study is broadly consistent with the growing evidence supporting the efficacy of JAK inhibition in vitiligo. A retrospective study by Liu et al. involving patients treated with oral tofacitinib reported improvement in depigmentation, with better responses observed among patients receiving concomitant phototherapy or natural sunlight exposure.[19] Similarly, Hamzavi et al. reported that ruxolitinib cream resulted in clinically significant repigmentation in patients with vitiligo, demonstrating the therapeutic potential of local JAK inhibition.[20] In a larger phase III clinical trial, ruxolitinib cream produced significantly greater improvement in facial and total body vitiligo compared with vehicle treatment.[3]

Although the treatment modalities and outcome measures differ across studies, the proportion of patients achieving ≥50% improvement in the present study is encouraging. The differences in the magnitude of treatment response between studies may be explained by variations in baseline disease severity, duration of vitiligo, anatomical site involved, disease activity, treatment dose, duration of therapy and concomitant use of phototherapy. Facial lesions generally respond better to treatment because of a higher density of hair follicles, which serve as a reservoir of melanocyte stem cells, whereas acral lesions tend to show a poorer response.[17,21]

The progressive reduction in VASI score observed in the current study also highlights the importance of adequate treatment duration. A shorter duration of treatment may underestimate the clinical benefit of therapy because repigmentation usually develops gradually. In a study evaluating the long-term use of tofacitinib in vitiligo, longer treatment duration was associated with a greater degree of repigmentation.[22] The present findings similarly suggest that improvement may continue beyond the initial three months of therapy.

The safety profile observed in the present study was generally acceptable. Upper respiratory tract infection was the most frequently reported adverse event, occurring in 11% of patients, followed by headache in 9%. Gastrointestinal discomfort and acne were reported by 4.5% of patients each. Elevated liver enzymes occurred in 3% of patients, while

palpitations were reported by only one patient (1.5%). Most adverse effects were mild and did not appear to represent major safety concerns during the six-month follow-up period.

The adverse events reported in the present study are consistent with the known safety profile of JAK inhibitors. Previous studies evaluating systemic and topical JAK inhibitors have reported infections, headache, acne and laboratory abnormalities among the commonly observed adverse events.[23,24] In particular, systemic JAK inhibitors may be associated with an increased susceptibility to infections and alterations in liver enzymes and other laboratory parameters, emphasizing the importance of appropriate patient selection and regular monitoring.[24] The occurrence of elevated liver enzymes in 3% of the present study population further supports the need for periodic biochemical assessment during treatment.

Current international guidelines and expert recommendations have increasingly recognised targeted therapies, including JAK inhibition, as an important advancement in the management of vitiligo.[25] However, conventional therapies such as topical corticosteroids, calcineurin inhibitors and narrowband ultraviolet-B phototherapy continue to play an important role in clinical practice.[15,26] Therefore, the selection of treatment should be individualized according to disease extent, activity, site of involvement, duration of disease and patient preference.

The present study has several strengths, including prospective assessment of treatment response using the VASI score and follow-up at multiple time points. VASI is an objective and validated method for assessing the extent of depigmentation and allows quantitative evaluation of changes over time.[27] The study also provides local evidence regarding treatment response and adverse effects in patients with vitiligo.

However, certain limitations should be considered while interpreting the findings. The sample size was relatively small, and the absence of a control group limits comparison with the natural course of the disease or alternative treatment options. The follow-up period of six months may also be insufficient to determine the long-term sustainability of repigmentation and the long-term safety of treatment. Furthermore, factors such as disease activity, site of involvement and concomitant exposure to sunlight or phototherapy may have influenced the treatment response. Future randomized controlled trials with larger sample sizes and longer follow-up are needed to confirm the efficacy, safety and durability of treatment response.

## CONCLUSION

The present study demonstrated a gradual improvement in vitiligo severity over six months, with a reduction in the mean VASI score from 1.82±1.47 at baseline to 1.60±1.26 at six months. More than half of the patients achieved at least 50% improvement in VASI, while 18% achieved ≥75% improvement. The clinical response appeared to become more evident with continued treatment. The treatment was generally well tolerated, with upper respiratory tract infection and headache being the most frequently reported adverse events. These findings support the potential role of the treatment in achieving repigmentation in vitiligo; however, larger controlled studies with longer follow-up are required to establish its comparative efficacy and long-term safety.

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**Conflict of Interest:** Nil

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