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Research Article

To Study Role of Azathioprine vs Tofacitinib in Treatment of Vitiligo at Tertiary Care Centre: A Comparative Study

Mahajabeen Madarkar[1*], D Purshotam B[1], Muskan Jain[2]

[1]Professor and Head of the Dermatology Department, S R Patil Medical College, Badagandi, Bagalkot, India

[2]Medical Intern, Himalayan Institute of Medical Sciences, Jollygrant, Dehradun, Uttarakhand, India

***Correspondence author:** Mahajabeen Madarkar, Associate Professor and Head of the Department, SR Patil Medical College, Badagandi, Bagalkot, India; Email: mahajabeenmadarkar@gmail.com

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Abstract

Background: Recent studies have confirmed that both hereditary and environmental influences contribute to the onset of vitiligo. Among the key immune elements involved are CD8+ T cells and Interferon-Gamma (IFN-γ), which play a critical role in melanocyte destruction. Immunomodulatory drugs like azathioprine, an oral agent with established suppressive effects on T-cell activity, have been introduced to help slow the progression of the disease. Another promising addition to the therapeutic options is tofacitinib, a Janus Kinase (JAK) inhibitor that works by blocking IFN-γ-driven inflammation-one of the central mechanisms in the formation of vitiligo patches. These developments offer new avenues for controlling immune-mediated skin damage in affected individuals. The purpose of this study was to compare the therapeutic efficacy of tofacitinib with azathioprine pulse therapy in reducing disease activity among patients with vitiligo.

Aims and objectives: The aim of this study was to compare the therapeutic efficacy of tofacitinib with azathioprine pulse therapy in reducing disease activity among patients with vitiligo, as measured by changes in the Vitiligo Area Severity Index (VASI) and Body Surface Area (BSA) involvement. The primary objective was to evaluate whether tofacitinib demonstrates superior clinical outcomes compared to azathioprine. The secondary objective was to assess the safety and tolerability of tofacitinib in the treatment of vitiligo.

Methodology: All patients aged above 12 years with a clinical diagnosis of vitiligo, attending the dermatology outpatient department of our institution and providing written informed consent, were enrolled in the study. Participants were randomly allocated into two groups: Group A received azathioprine at a dose of 50 mg on two non-consecutive days per week, while Group B was administered tofacitinib 5 mg twice daily. Both groups were advised to follow each dose with controlled sun exposure. Standardized clinical photographs were obtained at each monthly follow-up to monitor treatment response.

Results: The mean reduction in both VASI and BSA scores was consistently greater in the tofacitinib group compared to the azathioprine group at all follow-up visits. In the azathioprine group, the average VASI scores at baseline and at the 1st, 2nd and 3rd monthly visits were 13.82, 12.25, 10.43 and 7.56, respectively. Corresponding mean BSA values were 10.65, 9.58, 8.20 and 7.61. In contrast, the tofacitinib group demonstrated a more pronounced reduction, with mean VASI scores of 14.86, 12.30, 9.32 and 6.94 across the same time points and BSA values declining from 11.35 at baseline to 9.20, 7.10 and 5.10 by the third visit. As illustrated in Fig. 1,2, the average change in both VASI and BSA from baseline was significantly higher in the tofacitinib group at each visit. Importantly, no adverse effects were reported in either treatment arm throughout the study period.

Conclusion: Tofacitinib, when used in conjunction with controlled sun exposure, appears to induce more rapid repigmentation and better disease control compared to oral azathioprine pulse therapy in patients with vitiligo, as evidenced by the greater improvements in VASI and BSA scores over time.

Keywords: Oral Treatment; Tofacitinib; Azathioprine; Vitiligo; Immunosuppressive Agents

Introduction

Vitiligo poses a significant cosmetic and psychological burden on patients and their families. Over the years, dermatologists have gathered substantial clinical evidence supporting various therapeutic approaches for its management. Traditionally, treatment strategies have targeted melanocytes or inflammatory pathways, with interventions broadly classified into melanogenic agents and immunosuppressive therapies, such as azathioprine [1].

However, advancements in our understanding of the underlying pathogenesis of vitiligo have paved the way for novel therapeutic modalities. Among the most promising are Janus Kinase (JAK) inhibitors, including tofacitinib and ruxolitinib. These agents interfere with the JAK-STAT signaling cascade, a critical pathway mediating the effects of Interferon-Gamma (IFN-γ) and other pro-inflammatory cytokines. Upon cytokine stimulation, JAK1 and JAK2 activate STAT proteins, which then translocate to the nucleus and initiate transcription of genes involved in the autoimmune response. Given their direct role in IFN-γ signaling, JAK1 and JAK2 have become the primary focus of studies [2].

JAK inhibitors are also being explored for their efficacy in other autoimmune skin conditions, such as alopecia areata and psoriasis. Their emergence in vitiligo therapy marks a significant advancement, offering renewed hope to both patients and clinicians. Nonetheless, further large-scale studies and long-term safety data are required to validate their potential as safer alternatives to conventional immunosuppressants and systemic corticosteroids.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Methodology

Patients diagnosed with vitiligo, aged between 13 and 64 years, with a disease duration exceeding one year, Body Surface Area (BSA) involvement greater than 5% and a Vitiligo Area Severity Index (VASI) above 10, who were unresponsive to oral PUVA therapy, were enrolled from the dermatology outpatient department of our institute. Exclusion criteria included pregnancy or lactation, comorbid conditions such as diabetes mellitus, hypertension, hypothyroidism, cardiovascular disease, ongoing chemotherapy or immunosuppressive treatment (including investigational agents) and unwillingness to provide informed consent [3].

The recruitment phase spanned six months, from July 2024 to December 2024 during which a total of 28 patients were enrolled. Participants were alternately assigned to two treatment groups: Group A (consisting of the first patient and every alternate thereafter) received azathioprine 50 mg twice weekly, while Group B (second patient and every alternate thereafter) was administered tofacitinib 5 mg twice daily. Both groups were advised to undergo controlled sun exposure for 30 minutes daily between 10:00 a.m. and 12:00 p.m.

Follow-up evaluations were conducted monthly for a duration of three months from the date of enrollment, which was defined as the date of screening or upon availability of all baseline investigation results, whichever occurred earlier. Standardized digital photographs were taken at baseline and at each follow-up visit to document repigmentation progress. VASI and BSA scores were recorded at baseline and at the conclusion of the first, second and third months.

A reduction in VASI of ≥10% from baseline at each visit was considered indicative of a positive therapeutic response, while a cumulative reduction of ≥20% by the final visit was defined as significant recovery. Baseline and monthly laboratory investigations included complete blood count, liver and renal function tests, serum lipid profile, Mantoux test for Tofacitinib and TPMT activity for Azathioprine in selective cases showing abnormality in blood work all were performed within the institute's laboratory facilities.

Clinical assessments at each visit also included documentation of any cutaneous or systemic adverse events to evaluate the safety profile of the study drugs.

Outcome Measures: The primary outcome was defined by the degree of reduction in VASI and BSA scores. Secondary outcomes included the extent of repigmentation as assessed through photographic evidence.

Results

Demographic data presented in Table 1 indicate a nearly equal distribution of patients between the two treatment groups, with comparable age and gender profiles. A majority of participants exhibited vitiligo lesions on sun-exposed areas, which may have acted as a confounding variable in the study. Analysis of Tables 2,3 demonstrates a progressive decline in both BSA and VASI scores across all follow-up visits for patients receiving either tofacitinib or azathioprine pulse therapy. However, the intergroup difference reached statistical significance by the third visit (P = 0.002), favoring the tofacitinib group. At the conclusion of the follow-up period, clinical response was notably superior in the tofacitinib cohort.

Moreover, graphical representations in Fig. 1,2 illustrate that the mean changes in VASI and BSA at each visit were consistently greater in the tofacitinib group. Table 4 highlights that among patients with lesions predominantly on exposed body areas, a higher proportion achieved significant recovery in the tofacitinib group (75%) compared to the azathioprine group. Importantly, no patients in either treatment arm experienced any cutaneous or systemic adverse effects throughout the study duration.

Number of Participants	**Total 51**	**Azathioprine (27)**	**Tofacitinib (24)**
Mean	35.56	37	34
Standard Deviation	9.33	8.33	10.41
Gender, *n* (%)			
Male	21 (41.18%)	11 (40.74%)	10 (41.67%)
Female	30 (58.82%)	16 (59.26%)	14 (58.33%)
Exposed/Unexposed, *n* (%)			
Exposed	27 (52.94%)	9 (33.33%)	18 (75.00%)
Unexposed	4 (7.84%)	4 (14.81%)	0 (0.00%)
Exposed and unexposed	20 (39.21%)	14 (51.85%)	6 (25.00%)
Note: Total number of patients in azathioprine and tofacitinib groups were same with respect to sex and vitiligo was mostly present on exposed areas of the body.			

Table 1: Demographic profile of the study participants.

Visit	**Azathioprine (Mean ± SD)**	**Tofacitinib (Mean ± SD)**	**Intergroup *P*-value**
Baseline	10.65 ± 2.64	11.35 ± 3.75	0.412
1st Visit	9.58 ± 2.15	9.20 ± 3.34	0.359
2nd Visit	8.20 ± 2.17	7.10 ± 2.51	0.048
3rd Visit	7.61 ± 2.13	5.10 ± 2.23	0.002
Note: The table suggests that BSA was consistently decreasing in both the groups and at the 3rd visit, it had decreased significantly more in the tofacitinib group (p = 0.002).			

Table 2: Mean Body Surface Area (BSA) scores across follow-up visits.

Visit	**Azathioprine (Mean ± SD)**	**Tofacitinib (Mean ± SD)**	**Intergroup *P*-value**
Baseline	13.82 ± 3.54	14.86 ± 3.67	0.376
1st Visit	12.25 ± 3.41	12.30 ± 3.73	0.912
2nd Visit	10.43 ± 3.35	9.32 ± 3.48	0.04
3rd Visit	7.56 ± 3.72	6.94 ± 3.59	0.0216
Note: At the 3rd visit, the intergroup P-value shows significant improvement in the tofacitinib group as compared to the Azathioprine group.			

Table 3: Mean Vitiligo Area Scoring Index (VASI) scores across follow-up visits.

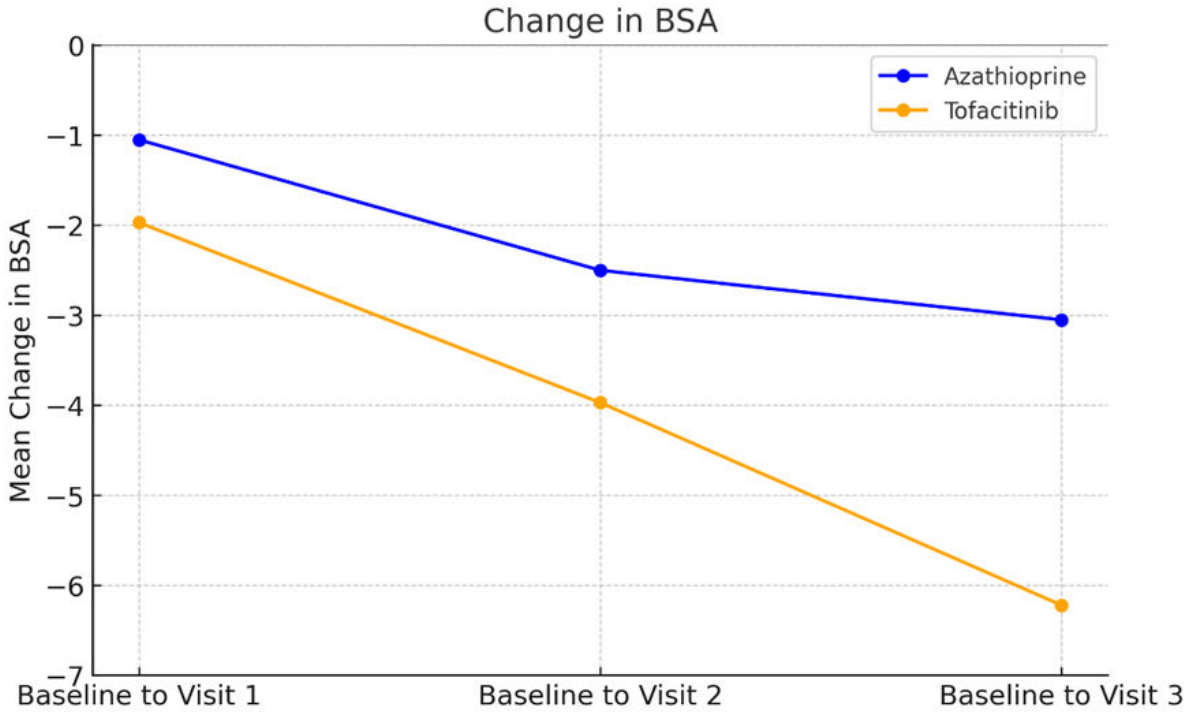

Figure 1: Change in BSA.

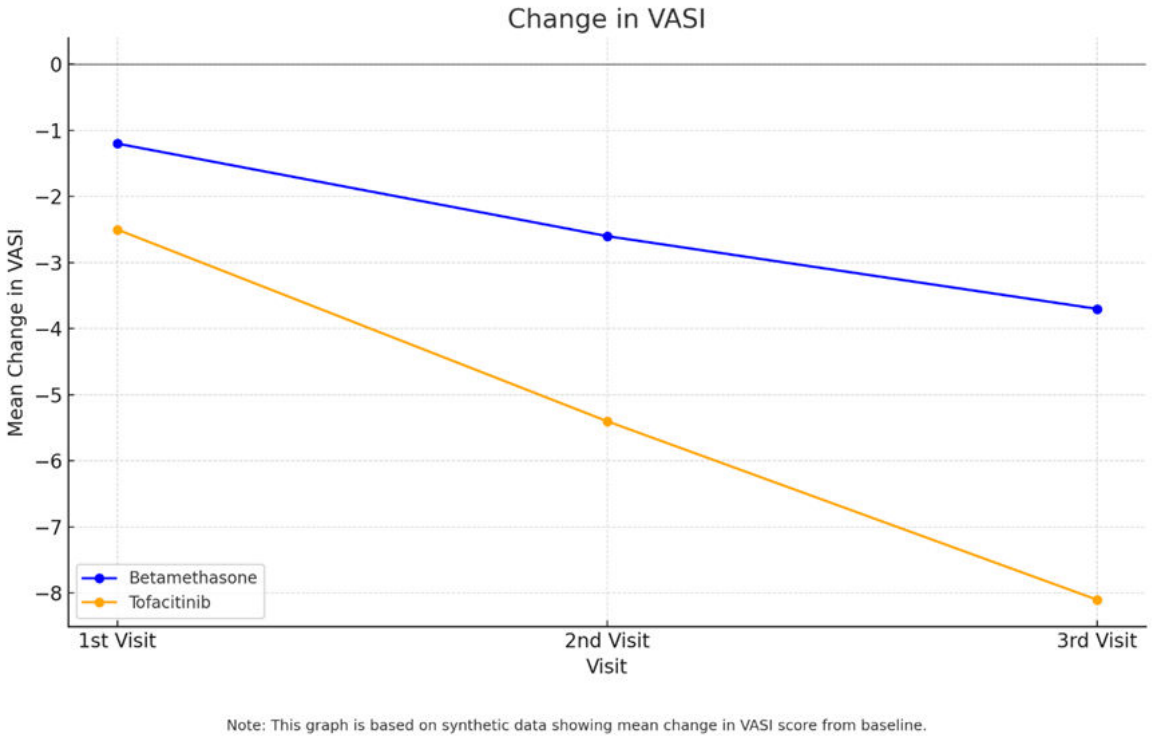

Figure 2: Change in VASI.

Discussion

A review of the current literature supports our findings. Recent studies have elucidated that the pathogenesis of vitiligo is primarily driven by IFN-γ production by CD8+ T cells, which induces CXCL9/10 expression by keratinocytes. This cascade recruits more CD8+ T cells, culminating in melanocyte destruction [4-6]. JAK inhibitors, such as tofacitinib, effectively interrupt this pathogenic pathway by targeting IFN-γ signaling.

Liu, et al., reported improved repigmentation outcomes in patients receiving tofacitinib along with sun exposure in affected areas. Similarly, our study showed enhanced responses in sun-exposed areas. However, since a greater number of participants had lesions predominantly on exposed sites, this may have acted as a confounding factor in our analysis [7].

Craiglow, et al., reported a significant clinical response in a 50-year-old female with facial vitiligo who received tofacitinib 5 mg twice daily with brief NB UVB exposure [8]. However, pigmentation was lost upon treatment discontinuation after five months. In contrast, our patients-maintained pigmentation even after dose reduction. Nonetheless, long-term outcomes post-discontinuation remain uncertain and represent a limitation of our study.

JAK inhibitors are also being explored for their efficacy in other autoimmune skin conditions, such as alopecia areata and psoriasis. Their emergence in vitiligo therapy marks a significant advancement, offering renewed hope to both patients and clinicians. Nonetheless, further large-scale studies and long-term safety data are required to validate their potential as safer alternatives to conventional immunosuppressants and systemic corticosteroids [9].

Further support for the role of JAK inhibition in vitiligo comes from a case report documenting repigmentation following baricitinib-a selective JAK1/JAK2 inhibitor therapy [10,11]. Another case involving a 17-year-old boy with treatment-resistant non-segmental vitiligo showed substantial improvement with topical tofacitinib [12]. Similarly, near-complete facial repigmentation has been reported after 3-6 months of oral tofacitinib (5 mg BID) combined with low-dose NB UVB phototherapy (Fig. 3-5) [13].

In our study, participants received tofacitinib for three months in combination with natural sunlight exposure instead of narrowband UVB, yielding consistently positive results. A contrasting case report of a 40-year-old female with rheumatoid arthritis and vitiligo treated with tofacitinib without any phototherapy also demonstrated satisfactory results. However, in our cohort, excellent responses were noted both in sun-exposed and sun-protected areas [14].

In our study, we observed that the tofacitinib group demonstrated faster and more consistent repigmentation of vitiliginous patches compared to the betamethasone (now azathioprine) group. This was accompanied by a more rapid reduction in both the Vitiligo Area Scoring Index (VASI) and Body Surface Area (BSA) involvement, indicating that the tofacitinib group effectively met both primary study objectives.

These findings reinforce the growing body of evidence supporting the efficacy of JAK inhibitors, especially tofacitinib, in inducing repigmentation in vitiligo. However, larger, long-term randomized controlled trials are essential to confirm sustained benefits and establish guidelines for optimal phototherapy regimens and maintenance strategies.

	Overall (N = 51)	**Exposed (N = 27)**	**Unexposed (N = 4)**	**Exposed and Unexposed (N = 20)**
Azathioprine (N = 27)				
Recovered	26(96.30%)	8 (29.63%)	4 (7.41%)	14 (51.85%)
Not recovered	1 (3.70%)	1 (3.70 %)	0 (0.00%)	0 (0.00%)
Tofacitinib (N = 24)				
Recovered	24 (100.00%)	18 (75.00%)	0 (0.00%)	6 (25.00%)
Not recovered	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Note: More number of patients in tofacitinib group have recovered (75%) as compared to Azathioprine group (29.63%) with vitiligo lesions on exposed areas of body.				

Table 4: Summary statistics of patient recovery status.

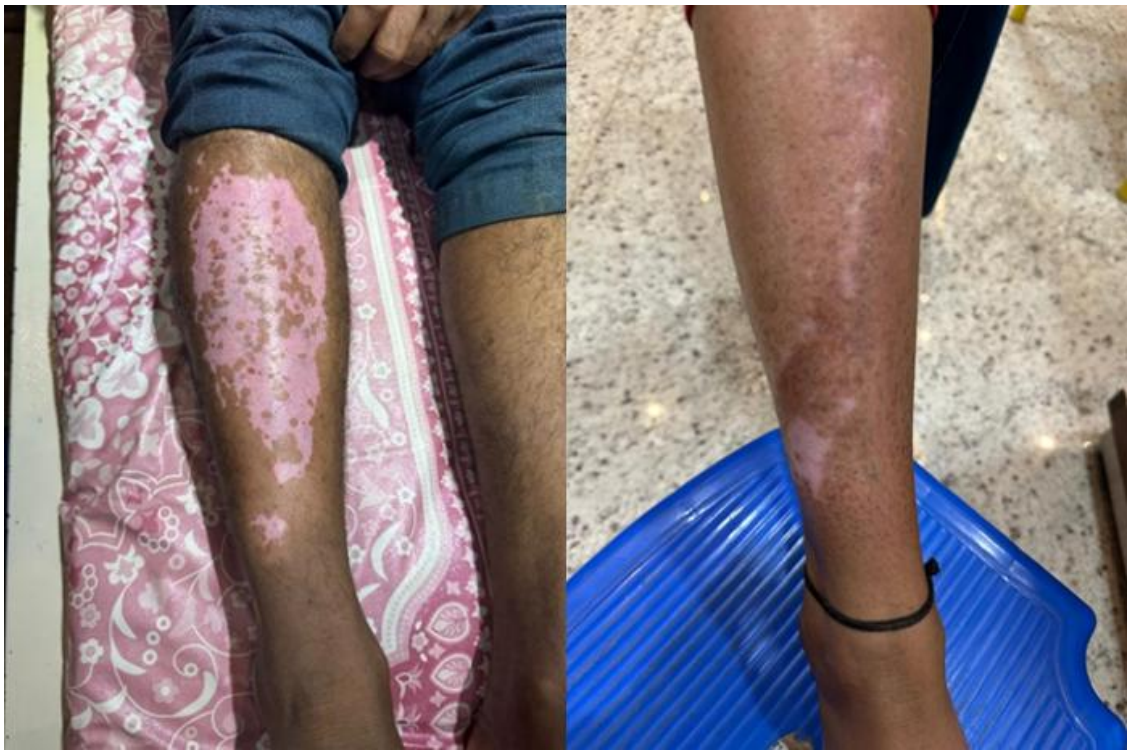

Figure 3: Photographs of extensor aspect of leg before and 2 months after oral tofacitinib.

Figure 4: Photographs of dorsum of hand before and 2 months after oral tofacitinib.

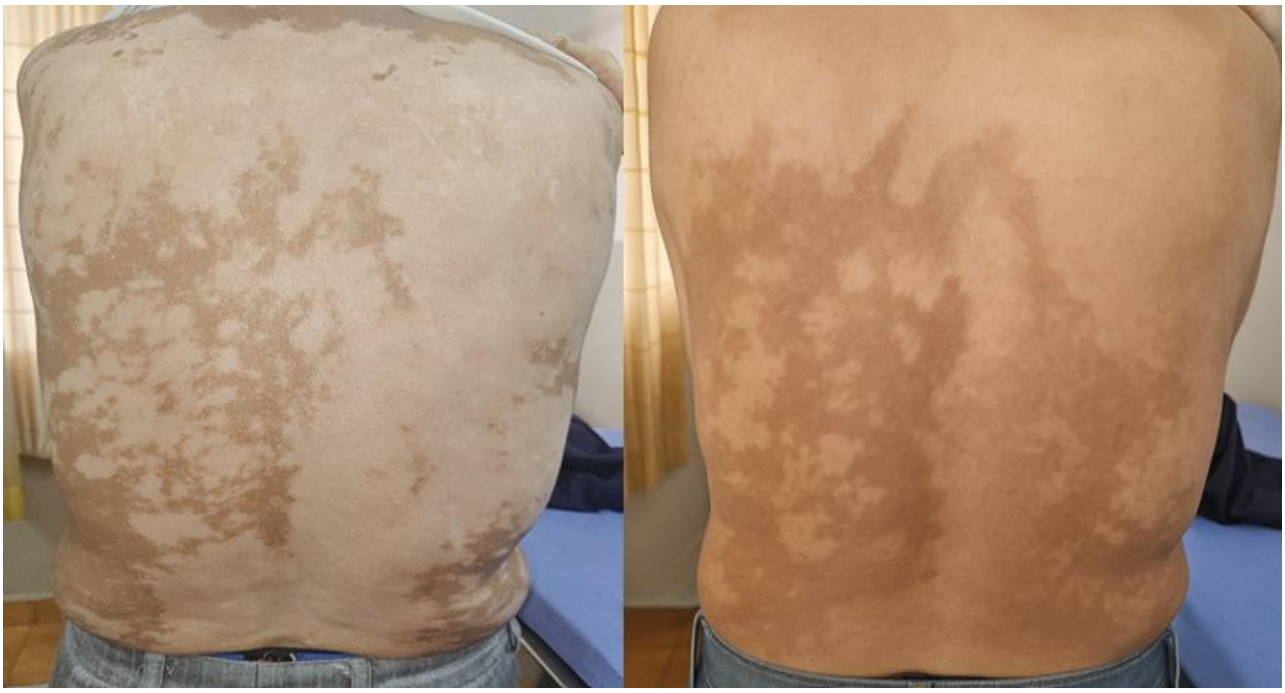

Figure 5: Photographs of patient's back at 3 months of oral tofacitinib.

Strengths

Head-to-head comparison of two active therapies, Controlled sunlight exposure, Clear group allocation process, Defined dosages and regimens.

Limitations

Small sample size, short follow-up period are a few limitations of this study.

Future Prospects

Long-term follow-up of patients receiving combination therapy with tofacitinib and betamethasone is essential to assess the durability of repigmentation and to monitor for any recurrence of vitiligo lesions over time.

Conclusion

Upon completion of this study, it was noted that patients with vitiligo receiving tofacitinib therapy exhibited earlier onset of repigmentation, as supported by both photographic documentation and significant reductions in VASI and BSA scores. These findings suggest that tofacitinib may facilitate more rapid disease activity suppression compared to conventional treatments, potentially accelerating the repigmentation process.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Consent To Participate

The authors certify that they have obtained all appropriate patient consent.

Data Availability and Consent of Patient

Data is available for the journal. Informed consents were not necessary for this paper.

Author's Contribution

All authors contributed equally in this paper.

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