RESEARCH ARTICLE

Efficacy of oral tofacitinib in moderate to severe alopecia areata, totalis and universalis at the tertiary care hospital, Karachi

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Abstract

Objective: To evaluate the effectiveness and safety of oral tofacitinib in treating patients with different forms of alopecia.

Method: The prospective, interventional, open-label study was conducted at the Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi, from November 2023 to April 2024, and comprised cases of alopecia areata, totalis and universalis. Tofacitinib 5mg twice daily was prescribed, and the Severity of Alopecia Tool score was evaluated at baseline, and then again at 6 weeks, 12 weeks and 24 weeks. Data was analysed using SPSS 23.

Results: Of the 30 subjects with mean age 26.53±4.77 years (range: 19-36 years), 15(50%) were males and 15(50%) were females. The mean Severity of Alopecia Tool score at baseline was 88.41±11.59, which decreased to 74.75±13.88 at 6 weeks, 58.51±20.96 at 12 weeks, and 45.88±23.63 at 24 weeks. Overall, 24(80%) patients showed improvement at 24 weeks in terms of hair regrowth. No adverse events were noted in any patient.

Conclusion: The efficacy and safety of tofacitinib in the treatment of alopecia areata showed promising results, and it could be a viable treatment option for alopecia.

Key Words: Tofacitinib, Alopecia areata, Alopecia totalis, Alopecia universalis, Janus kinase inhibitor, Therapeutic efficacy.

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Introduction

Alopecia areata (AA) is a chronic autoimmune condition characterised by hair loss due to infiltration of autoreactive cluster of differentiation-8+ (CD8+) T cells, also called cytotoxic T cells, into hair follicles.[1] This condition can affect any area and can manifest in a variety of forms' from patchy diffuse alopecia to severe alopecia, such as alopecia totalis (AT) or alopecia universalis (AU).[2] The prevalence of AA varies from 0.1% to 0.2% and it is ranked as the second most common type of alopecia, following male and female pattern alopecia.[3] The major concern of alopecia is the psychological impact regardless of the fact that it is not life-threatening. Managing advanced AA poses significant challenges compared to milder cases, often necessitating treatment for patients to stimulate hair regrowth.[4] Steroids (intralesional, topical and systemic), squaric acid dibutyl ester (SADBE), topical minoxidil, topical immunotherapy (diphenylcyclopropenone [DPCP], topical immunosuppressants (tacrolimus, pimecrolimus), and topical prostaglandin analogues (bimatoprost, latanoprost).[5]

Janus Kinase inhibitors (JAKs) represent the new era of promising therapeutic agents based on advancements in human understanding of intracellular cytokine signalling pathways. JAKs exert their action by impeding the signalling of specific cytokines. This interruption effectively hinders the JAK/signal transducer and activator of transcription (STAT) pathway, subsequently leading to the suppression of pro-inflammatory cytokine production associated with AA.[6] Even with the rapid emergence of new JAK inhibitors, like baricitinib and ritlecitinib, tofacitinib continues to be effective and stands as the longest-utilised JAK inhibitor for AA treatment.[7] Tofacitinib predominantly targets JAK 1/3, weakening the immune response and subsequent inflammation.[7,8]

The initial instance of employing a JAK1/3 inhibitor, specifically tofacitinib citrate, for treating AU, was documented in a patient with concurrent plaque psoriasis. Remarkably, the patient achieved complete hair regrowth within 8 months.[9,10] Subsequently, the scientific comprehension of AA has advanced, underscoring the pivotal role of cytotoxic T lymphocytes in AA, and emphasising the potential efficacy of JAK inhibition in its treatment.[11,12]

The current study was planned to evaluate the

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effectiveness and safety of oral tofacitinib in treating patients with different forms of alopecia.

Patients and Methods

The prospective, interventional, open-label study was conducted at the Department of Dermatology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from November 2023 to April 2024. The study protocol was approved by the institutional ethical review committee prior to conduction of the study. The sample was raised using non-probability consecutive sampling strategy after calculating the sample size using the World Health Organisation (WHO) calculator[13] with 95% confidence interval (CI) in the light of literature. Those included were AA patients of either gender aged 15-60 years. Patients with prior history of arthritis (seropositive or seronegative), connective tissue disorders, vasculitis, psoriasis, active infection, severe haematological abnormalities, having history of treatment with systemic agent, weight <25kg and those who were pregnant or lactating were excluded.

After taking informed consent from the patients, demographic and clinical data was obtained, and the Severity of Alopecia Tool (SALT) score was calculated.[14] Photographic evidence was also obtained with the consent of the patients. After appropriate examinations, oral tofacitinib 5mg twice daily was administered. The effectiveness of the intervention was evaluated using SALT score assessment at 6 weeks, 12 weeks and 24 weeks. The treatment response was graded as 0 = hair regrowth <10%, 1 = 11-25%, 2 = 26-50%, 3 = 51-75% and 4 =>75%. A score >2 represented efficacy of the intervention. Overall SALT score 0 indicated no hair regrowth, while 100 indicated complete hair regrowth. A composite score was calculated based on computed SALT score by measuring the hair loss percentage in four specific areas of the scalp; vertex (40%), right profile (18%), left profile (18%) and posterior (24%). Clinical comparison was also done at each of the visit.

Data was analysed using SPSS 23. Numerical variables were presented as mean ± standard deviation, whereas categorical variables were reported as frequencies and percentages. Chi-square test, paired t- test and student's t-test were used as appropriate. Age and gender were used for the stratification of effect modifiers. P<0.05 was considered significant.

Results

Of the 30 subjects with mean age 26.53±4.77 years (range: 19-36 years), 15(50%) were males and 15(50%) were females. There were 14(46.7%) patients aged 19-25 years, 9(30%) aged 26-30 years, 5(16.7%) aged 31-35

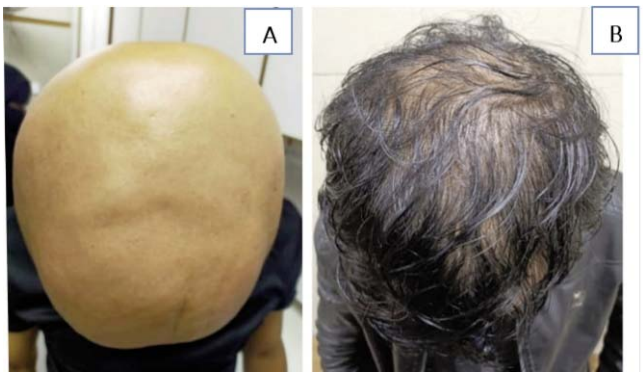

Figure-1: Severity of alopecia tool (SALT) score 100 at baseline (A) and 95% hair re-growth after treatment (B)

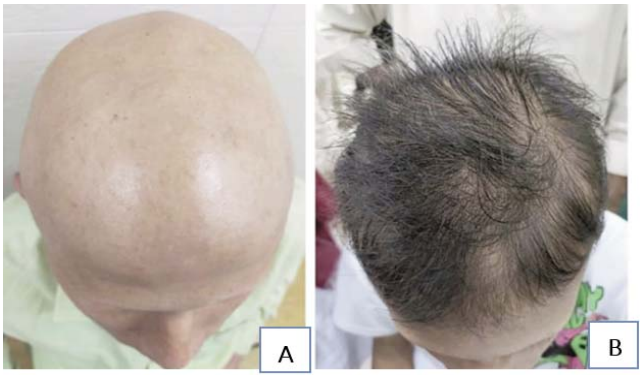

Figure-2: Severity of alopecia tool (SALT) score 100 at baseline (A) with 92% hair re-growth (B) after 6 month treatment with oral Tofacitinib.

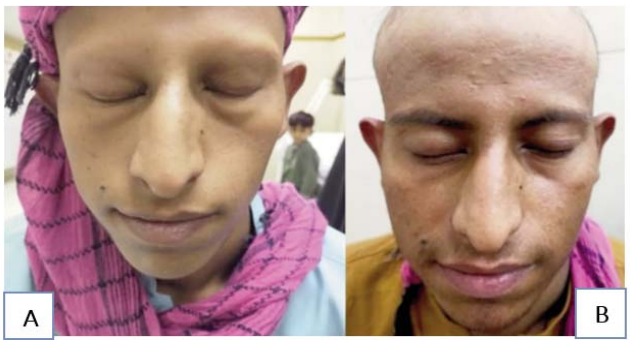

Figure-3: A case of alopecia universalis showing re-growth of hair over eyebrows, eyelashes and beard area.

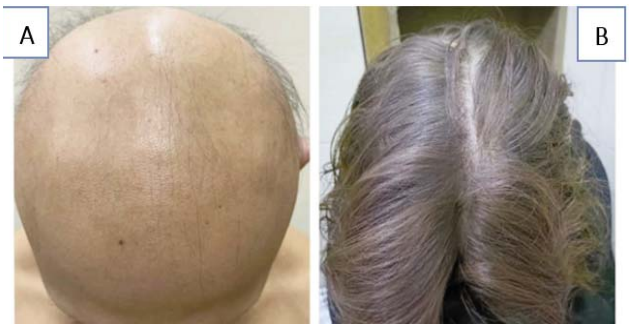

Figure-4: Severity of alopecia tool (SALT) score 98 at baseline (A) and 100% hair re-growth (B) in response to treatment with oral Tofacitinib.

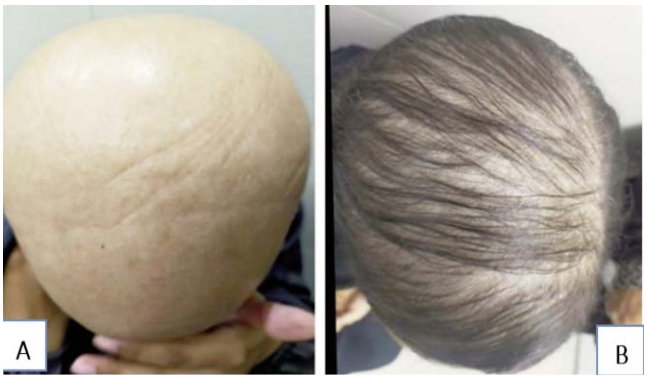

Figure-5: Severity of alopecia tool (SALT) score 100 at baseline (A) and 92% hair re-growth (B) after treatment.

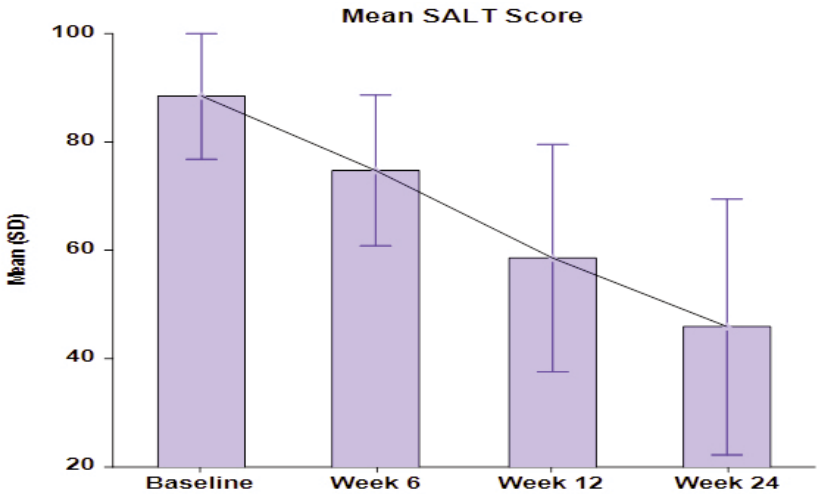

Figure-6: Decline in severity of alopecia tool (SALT) score from baseline to 24-week follow-up.

years, and 2(6.7%) were aged 36-40 years. Of the 30(100%) AA, 25(83.3%) had AU and 5(16.7%) had AT. The SALT score showed a significant decrease at every stage of follow-up both in overall cases and types of alopecia (Figures 1-5) The mean SALT at baseline was 88.41±11.59, which decreased to 74.75±13.88 at 6 weeks, 58.51±20.96 at 12 weeks, and 45.88±23.63 at 24 weeks. The mean decrease in SALT score from baseline to 24-week follow-up was 42.53±19.84 (p=0.001) AU and AT groups showed the same pattern (Table 1). The improvement was consistent across all follow-up visits compared to the baseline SALT score (Figure 6).

Overall, 24(80%) patients showed improvement at 24 weeks in terms of hair regrowth; 21(84%) of the AU patients, and 3(60%) of the AT patients.

There was a significant difference in efficacy with respect to SALT scores (p=0.001) and response percentage (p=0.001). The current alopecia episode's mean duration was 5 months (range: 2-8 months). Efficacy of tofacitinib was not associated with alopecia duration, age and gender (Table 2). No adverse events were reported in any patient.

Table-1: SALT score at baseline and post-intervention.

Evaluation stage	Overall Mean ± SD (n=30)	Alopecia universalis Mean ± SD (n=25)	Alopecia totalis Mean ± SD (n=5)	Mean comparison between type of alopecia evaluation stage P-value
Baseline	88.40 ±1 1.59	88.26 ± 11.49	89.12 ± 13.42	0.883
At 6 weeks	74.75 ± 13.88	74.90 ± 13.23	74.04 ± 18.59	0.902
At 12 weeks	58.51 ± 20.96	58.95 ± 19.54	56.28 ± 29.74	0.800
At 24 weeks	45.87 ±23.63	45.77 ± 21.95	45.87 ± 23.63	0.956
Average decrease in SALT score with follow-up duration				
Change in SALT score with follow-up duration	**Overall (n=30)**	**Alopecia universalis (n=25)**	**Alopecia totalis (n=5)**	
Baseline to week 6	(-)13.65 ± 7.20 P=0.001	(-)13.37 ± 6.74 P=0.001	(-)15.08 ± 10.05 P=0.02	
Week 6 to week 12	(-)16.24 ± 10.71 P=0.001	(-)15.94 ± 9.86 P=0.001	(-)17.76 ± 15.67 P=0.06	
Week 12 to week 24	(-)12.63 ± 5.76 P=0.001	(-)13.18 ± 5.78 P=0.001	(-)9.86 ± 5.33 P=0.01	
Baseline to week 24	(-)42.53 ± 19.84 P=0.001	(-)42.50 ± 18.18 P=0.001	(-)42.70 ± 27.03 P=0.02	

(-): shows decrease in SALT score with the follow-up duration.
SALT: Severity of alopecia tool, SD: Standard deviation.

Table-2: Efficacy of oral tofacitinib in patients with alopecia.

Efficacy	Type of alopecia	SALT score (at 24 weeks)	Response (%)	Duration of Alopecia (months)	Age (years)	Gender	
						Male	Female
Yes (n=24)							
	Alopecia universalis (n=21)	40.22 ± 19.32	55.73 ± 18.02	4.76 ± 1.87	26.23 ± 5.18	11	10
	Alopecia totalis (n=3)	23.70 ± 17.49	78.83 ± 7.50	3.33 ± 1.53	26.67 ± 3.21	1	2
	Overall (n=24)	38.15 ± 19.55	58.62 ±18.66	4.58 ± 1.83	26.29 ± 4.93	12	12
Comparison between type of alopecia with efficacy		**t=1.39 P=0.170**	**t=2.16 P=0.04**	**t=1.26 P=0.022**	**t=1.3 P=0.89**	**Fisher's Exact test=1.00 P=0.50**	
No (n=6)							
	Alopecia universalis (n=4)	74.87 ± 4.83	14.49 ± 2.79	4.75 ± 0.50	27.5 ± 4.79	3	1
	Alopecia totalis (n=2)	80.50 ± 12.02	15.05 ± 5.73	6.00 ±2.82	27.5 ± 4.94	0	2
	Overall (n=6)	76.75 ± 7.17	14.67 ±3.37	5.17 ± 1.47	27.5 ± 4.32	3	3
Comparison between type of alopecia without efficacy		t=0.887 P=0.425	t=1.720 P=0.871	t=0.976 P=0.384	t=0.00 P=1.000	Fisher's Exact test=0.40 P=0.21	
Comparison between Efficacy (Yes and No)		P=0.001* t=4.70	P=0.001* t=5.67	P=0.483 t=0.710	P=0.588 t=0.54	P=1.000 Fisher's Exact test=1.00	

*: Highly significant
SALT: Severity of alopecia tool

Discussion

The present study investigated 30 AA patients and found that treatment with tofacitinib was effective and safe.

Craiglow et al. in 2016[15] studied 13 AA patients aged 12-17 years who were treated with tofacitinib, and reported that hair regrowth was observed in 9(69.2%) of them. The SALT score median change were 93% over mean treatment duration of 6.5 months. There were mild adverse events. Funda et al.[16] also reported a case study of a woman aged 23 years wo had presented with AU and was treated with tofacitinib.

Shin et al.[17] compared the outcome of oral tofacitinib with conventional treatment for AT and reported that after a 6-month treatment, oral tofacitinib demonstrated superior effectiveness compared to diphenylcyclopropenone immunotherapy, and greater tolerability than conventional oral treatments. Similarly, Guo et al. in 2019[18] reported tofacitinib was the promising treatment option for AA with mild adverse events.

A study in 2021[18] assessed tofacitinib safety, survival and efficacy in treating AA, and identified key factors affecting long-term outcomes. It was concluded that tofacitinib was safe and effective in AA, whereas survival rate was satisfactory. The result was comparable to the current findings.

Zhang et al. in 2021[19] compared the effectiveness of systemic corticosteroids with oral tofacitinib monotherapy and their combination in moderate to severe AA, and observed that tofacitinib was a safe, well-tolerated and effective treatment than systemic corticosteroids. A combination of both may have higher efficacy than corticosteroids alone.

El Ahmed et al. in 2022[20] analysed data related to 47 participants of Arab-Asian heritage. The incidence of complete, partial, and no regrowth was observed in 18(41.9%), 11(25.6%) and 12(27.9%) patients, respectively. Majority of no regrowth cases (66.7%) was from the AU group.

Al Marzoug et al. in 2021 carried out a multi-centre study[21] to measure the efficacy and response rate of tofacitinib in the treatment of AA patients, and observed that SALT score >50% was achieved by 62.2% patients. In comparison with AU and AT, there were significantly higher response of tofacitinib by AA patients.

Asilian et al.[22] conducted a study in Iran to assess the efficacy of oral tofacitinib in the treatment of moderate to severe AA patients. The findings suggested that using tofacitinib in AA treatment was advisable, as it proved effective in hair loss reduction, and the side-effects were reversible.

The current study has limitations as it was a single-centre, single-arm trial, which makes it challenging to attribute the improvement to the treatment rather than other factors. Besides, a more extended follow-up period and a

more comprehensive study design could have established the efficacy of tofacitinib, while detecting potential relapses, and assessing long-term benefits and risks. Extensive, randomised controlled trials (RCTs) with extended durations are required to validate the current findings.

Further studies are also needed to be carried out to mainly focus on the key questions, such as optimal duration of treatment, the longevity of treatment response, factors influencing response variability, rates of relapse, and potential side-effects associated with the use of JAK inhibitors in this specific population.

Conclusion

The efficacy and safety of tofacitinib in AA treatment showed promising results in patients. Due to its therapeutic potential, the JAK inhibitor is being considered a viable option in AA treatment.

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Conflict of Interest: None.

Source of Funding: None.

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AUTHOR'S CONTRIBUTION:
MZQ, RG, MKS, PS, NJ & KA: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.