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ORAL TOFACITINIB IN MODERATE AND SEVERE ALOPECIA AREATA: CASE SERIES OF 14 PATIENTS

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ABSTRACT

Background: Alopecia areata is an autoimmune disease that causes transient, non-scarring hair loss while maintaining the hair follicle. Tofacitinib citrate, a Janus kinase 1/3 inhibitor, has lately been used to treat alopecia areata in addition to rheumatoid arthritis (AA). We present the results of prolonged tofacitinib treatment in adult Indian patients with moderate-to-severe AA. **Materials and methods:** All patients with AA, AT, or AU assessed at a tertiary care center clinic had their records located between December 2021 and December 2022. The inclusion criteria was patients must be at least 18 years old, have a clinical diagnosis of AA, AT, or AU (defined as scalp hair loss of >90%), and have had a stable or deteriorating condition for at least six months. Each patient's clinical and demographic data, including age, gender, age at disease beginning, length of the current episode of disease, and severity of AA as determined by the Severity of Alopecia Tool (SALT), were collected. **Results:** The average age of the present sample was 32.24 years. Majority of them were males (71.43%). The re-growth rate among the present study was 64.29%. The re-growth rate correlated positively with age at onset of first episode[r=0.32; 0.031] and tofacitinib duration [r=0.55; 0.004] and correlated negatively with duration of current episode [r=-0.41; 0.022] and duration of disease since first onset [r=-0.42; 0.024]. **Conclusions:** More than ½ of the cases we studied had good regrowth rate in the present study. The re-growth rate correlated positively with age at onset of first episode and tofacitinib duration and correlated negatively with duration of current episode and duration of disease since first onset.

INTRODUCTION:

Alopecia areata is an autoimmune disease that causes transient, non-scarring hair loss while maintaining the hair follicle.[1] The various types of hair loss range from loss in distinct patches to diffuse or total hair loss, and they can affect all parts of the body that produce hair. Patchy hair loss on the scalp is the most common alopecia kind.[2,3] Alopecia areata will eventually affect 2% of the general population.[4] In skin biopsies of alopecia areata-affected skin, a lymphocytic infiltrate can be detected in and around the bulb or bottom portion of the hair follicle during the anagen (hair growth) phase. It is believed that a breakdown of the immune privilege of the hair follicle is one of the leading causes of alopecia areata.

Genetic studies in human patients and mouse models have shown that alopecia areata is a complex, polygenic disease. It was found that several genetic susceptibility loci were connected to signaling pathways essential for the growth and cycling of hair follicles.[2,5] Usually, alopecia areata is diagnosed based on its clinical symptoms. Dermoscopy and histology may be helpful. Two severe types of the disease, alopecia totalis, and universalis, might present clinically as patchy restricted alopecia, reticular pattern, ophiasis, sisaipho, diffuse, or incognito type.[2,6]

Some widely available therapeutic options include topical/intralesional steroids, topical immunotherapy, contact irritants, systemic steroids, and steroid-sparing drugs like cyclosporine, azathioprine, methotrexate, and JAK-STAT inhibitors. [7,8] Tofacitinib citrate, a Janus kinase 1/3 inhibitor, has lately been used to treat alopecia areata in addition to rheumatoid arthritis (AA). [8,9] We need information on the standard of care for patients in the Indian context and long-term tofacitinib monotherapy evidence. We present the results of prolonged tofacitinib treatment in adult Indian patients with moderate-to-severe AA.

MATERIALS AND METHODS:

All patients with AA, AT, or AU assessed at a tertiary care center clinic had their records located between December 2021 and December 2022. The inclusion criteria was patients must be at least 18 years old, have a clinical diagnosis of AA, AT, or AU (defined as scalp hair loss of >90%), and have had a stable or deteriorating condition for at least six months. Each patient's clinical and demographic data, including age, gender, age at disease beginning, length of the current episode of disease, and severity of AA as determined by the Severity of Alopecia Tool, were collected (SALT).

All patients underwent baseline laboratory testing before starting tofacitinib therapy, which included a complete blood count with differential, a comprehensive metabolic panel, a fasting lipid panel (total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides), serum human chorionic gonadotropin (in women of childbearing age), and screening for HIV and hepatitis B and C viruses. The SALT score, a validated technique that measures the % of scalp hair loss, was used to assess effectiveness. A SALT score of 0 denotes no hair loss, whereas a SALT score of 100 denotes total baldness.

A SALT score change of 100% denotes total regrowth, whereas a score change of 0% denotes no regrowth. In all analyses, the percentage change in SALT score was employed. Safety was evaluated using a physical examination, system review, complete metabolic panel, fasting lipid panel, complete blood count with differential, and complete metabolic panel.[10]

Statistical Analysis:

The data was collected, compiled, and analyzed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantitative variables were categorized and expressed in percentages or terms of mean and standard deviations. Pearson's correlation coefficient was used to correlate the various characteristics with hair re-growth in the present study. All p values were two tailed and 0.05 was set as cut off for significance value.

RESULTS:

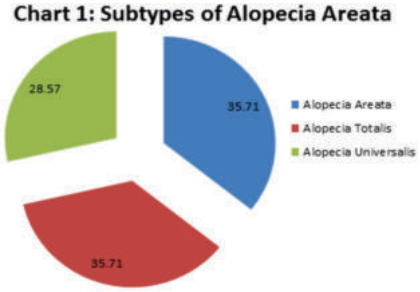
We have included 14 cases in the present study.

Table 1: Demographic and other characteristics of the present sample

Demographic particulars	Frequency	Percentage
Age group (years)		
<30	2	14.29
30 to 40	8	57.14
>40	4	28.57
Gender		
Male	10	71.43
Female	4	28.57
Duration of disease (years)		
<3	2	14.29
3 to 5	3	21.43
>5	9	64.29
Duration of current episode		
<12 month	1	7.14
12 to 24 months	2	14.29
2 to 5 years	3	21.43
>5 years	8	57.14

The average age of the present sample was 32.24 years. Majority of them were males (71.43%). The average duration of disease was 6.12 years and average duration of current episode was 5.67 years in the present study.

Chart 1: Subtypes of Alopecia Areata



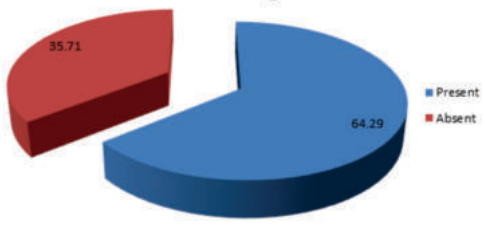
Of the 14 cases studied, five cases were alopecia areata, five cases were alopecia totalis and four cases were alopecia universalis.

Table 2:Treatment characteristics of the present sample

Treatment characteristics	Median	Inter quartile range
Initial SALT score	99.2	32.4 to 100
Tofacitinib duration (months)	6.5	4.2 to 14
Total Tofacitinib dose (mg)	1990	1300 to 4350

The initial SALT score was 99.20 [32.40 to 100], tocacitinib duration was 6.5 months and total dose was 1990 [1300 to 4350].

Chart 2: Total re-growth rate



The re-growth rate among the present study was 64.29%.

Table 5: Correlation of characteristics of alopecia areata patients (n = 14) treated with tofacitinib and percentage of hair re-growth at last visit

Patient characteristic	Hair re-growth	
	r	P value
Duration of current episode	-0.41	0.022
Age at onset of first episode	0.32	0.031
Duration of disease since first onset	-0.42	0.024
Age	0.03	0.712
Body mass index	-0.21	0.180
Initial severity of alopecia tool score	-0.12	0.562
Tofacitinib duration	0.55	0.004
Total Tofacitinib dose	0.08	0.662

The re-growth rate correlated positively with age at onset of first episode[r=0.32; 0.031] and tofacitinib duration [r=0.55; 0.004] and correlated negatively with duration of current episode [r=-0.41; 0.022] and duration of disease since first onset [r=-0.42;0.024].

DISCUSSION:

Phosphotransferases and Janus kinases are activated by cytokines when their receptors are engaged. Therefore, a novel approach to the treatment of immunological and inflammatory illnesses is represented by Janus kinase inhibitors.[5] A specific synthetic small chemical called tofacitinib inhibits Janus kinases when taken orally (JAKs). It is a (JAK) inhibitor that the FDA approved in April 2012 and is indicated for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PA), ulcerative colitis (UC), and juvenile idiopathic arthritis with a polyarticular course (pcJIA). The non-receptor tyrosine kinase JAK enzymes are more favorably affected by tofacitinib than JAK-1 and JAK-3 enzymes. In the current case series, we have treated AA with this medication (moderate to severe). The following compares our study's re-growth rates with various studies conducted around the world.

Table 6: Re growth rate compared with various studies and our study

Studies	Re-growth rate
Our study	64.29%
Jabbari et al[11]	66.70%
Kennedy et al[12]	31.80%
Pultterman et al[13]	27.30%
Shin et al[14]	44.40%
Ibrahim et al[15]	46.20%
Park et al[16]	56.30%
Liu et al[17]	58.50%

In the current study, the regrowth rate correlated favorably with age at first episode onset (r=0.32; 0.031), duration of tofacitinib (r=0.55; 0.004), and duration of the disease since first onset (r=-0.42; 0.024). It correlated unfavorably with the current episode's length and the latter two variables. The growth rate, defined as (final SALT score initial SALT score)/(initial SALT score) 100, ranged from 2% to 90% in a study by Ibrahim et al.[15], with a mean (SD) of 44.3% (31.9) and a median (range) of 50.5%. (90 [0-90]). Seven individuals (53.8%) had at least 50% of their hair grow back. With a mean (SD) of 4.2 (2.6) months, response time—the interval between the start of treatment and the first sign of hair regrowth—ranged from 1 to 9 months. Ninety patients matched the inclusion criteria in Liu et al. On average, 77% of the 65 potential therapy responders— those with alopecia totalis, alopecia universalis, or alopecia areata—achieved a clinical response, with 58% of patients experiencing a higher than 50% reduction in SALT score throughout 4 to 18 months of therapy. Individuals with AA saw a more significant percentage change in their SALT score (81.9% vs. 59.0%) than those with alopecia totalis or universalis. No severe adverse events were associated with tofacitinib, which was well tolerated in research by Hogan et al.[18], 3.85 months on average passed before regrowth occurred. 70% of individuals demonstrated regrowth three months after starting treatment. Regrowth percentages ranged from 1% to 100%, with a mean of 42.6% and a median of 55%. Eleven patients (55%) saw a more than 50% SALT score improvement. During the trial period, 25% of the patients experienced complete regrowth (>90% improvement in SALT score). By the end of the research period, 91.7% of patients who had received treatment for more than 12 months had experienced regrowth. Three patients failed to improve their SALT score by more than 5% and were considered nonresponders. Lab abnormalities appeared in seven patients. Elevated cholesterol, triglycerides, and low-density lipoprotein levels were observed in four patients dose-dependently. Although one patient was started on a statin, these were resolved with

dose reduction or continuing treatment. Each of the six clinically significant adverse effects (such as palpitations, herpes zoster, and upper respiratory infection) happened to a separate patient. Data at six months were reported to be available for 45 patients by AlMarzoug A et al[19]. 62.2% had a SALT score of greater than 50%. Patients with a score of 50% had a baseline SALT score that was considerably greater than patients with a score of >50%. Systemic steroid use in the past was linked to a lower level of therapeutic response (P = 0.015). Compared to patients with alopecia totalis and alopecia universalis, people with AA had a considerably stronger response to medication.

CONCLUSION:

More than ½ of the cases we studied had good regrowth rate in the present study. The re-growth rate correlated positively with age at onset of first episode and tofacitinib duration and correlated negatively with duration of current episode and duration of disease since first onset. Randomized controlled trials and observational studies with larger sample have to be conducted to understand the safety and efficacy of this drug in Indian setup.

REFERENCES:

1. Pratt CH, King LEJ, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nat Rev Dis Prim. 2017;3:17011.
2. Darwin E, Hirt PA, Fertig R, Doliner B, Delcanto G, Jimenez JJ. Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options. Int J Trichology. 2018;10(2):51–60.
3. Hordinsky MK. Overview of alopecia areata. J Investig dermatology Symp Proc. 2013;16(1):S13-5.
4. Spano F, Donovan JC. Alopecia areata: Part 1: pathogenesis, diagnosis, and prognosis. Can Fam Physician. 2015;61(9):751–5.
5. Alsantali A. Alopecia areata: a new treatment plan. Clin Cosmet Investig Dermatol. 2011;4:107–15.
6. Brzezińska-Wcisło L, Bergler-Czop B, Wcisło-Dziadecka D, Lis-□wi□ty A. New aspects of the treatment of alopecia areata. Postep dermatologii i Alergol. 2014;31(4):262–5.
7. Cada DJ, Demaris K, Levien TL, Baker DE. Tofacitinib. Hosp Pharm. 2013;48(5):413–24.
8. Sonthalia S, Aggarwal P. Oral Tofacitinib: Contemporary Appraisal of Its Role in Dermatology. Indian Dermatol Online J. 2019;10(5):503–18.
9. Padda IS, Bhatt R, Parmar M. Tofacitinib. In Treasure Island (FL); 2022.
10. King BA, Senna MM, Ohyama M, Tosti A, Sinclair RD, Ball S, et al. Defining Severity in Alopecia Areata: Current Perspectives and a Multidimensional Framework. Dermatol Ther (Heidelb). 2022;12(4):825–34.
11. Jabbari A, Sansaricq F, Cerise J, Chen JC, Bitterman A, Ulerio G, et al. An Open-Label Pilot Study to Evaluate the Efficacy of Tofacitinib in Moderate to Severe Patch-Type Alopecia Areata, Totalis, and Universalis. J Invest Dermatol. 2018;138(7):1539–45.
12. Kennedy Crispin M, Ko JM, Craiglow BG, Li S, Shankar G, Urban JR, et al. Safety and efficacy of the JAK inhibitor tofacitinib citrate in patients with alopecia areata. JCI insight. 2016;1(15):e89776.
13. Putterman E, Castelo-Soccio L. Topical 2% tofacitinib for children with alopecia areata, alopecia totalis, and alopecia universalis. Vol. 78, Journal of the American Academy of Dermatology. 2018. p. 1207-1209.e1.
14. Shin J-W, Huh C-H, Kim M-W, Lee J-S, Kwon O, Cho S, et al. Comparison of the Treatment Outcome of Oral Tofacitinib with Other Conventional Therapies in Refractory Alopecia Totalis and Universalis: A Retrospective Study. Acta Derm Venereol. 2019;99(1):41–6.
15. Ibrahim O, Bayart CB, Hogan S, Piliang M, Bergfeld WF. Treatment of Alopecia Areata With Tofacitinib. JAMA dermatology. 2017;153(6):600–2.
16. Park H-S, Kim M-W, Lee JS, Yoon H-S, Huh C-H, Kwon O, et al. Oral tofacitinib monotherapy in Korean patients with refractory moderate-to-severe alopecia areata: A case series. Vol. 77, Journal of the American Academy of Dermatology. 2017. p. 978–80.
17. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. J Am Acad Dermatol. 2017;76(1):22–8.
18. Hogan S, Wang S, Ibrahim O, Piliang M, Bergfeld W. Long-term treatment with tofacitinib in severe alopecia areata: an update. J Clin Aesthet Dermatol. 2019;12(6):12–4.
19. AlMarzoug A, AlOrainy M, AlTawil L, AlHayaza G, AlAnazi R, AlIssa A, et al. Alopecia areata and tofacitinib: a prospective multicenter study from a Saudi population. Int J Dermatol. 2022;61(7):886–94.