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ORIGINAL RESEARCH

Efficacy of oral tofacitinib therapy in mild to severe alopecia areata

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ABSTRACT

Background: An autoimmune condition called alopecia areata produces temporary, non-scarring hair loss without destroying the hair follicle. Recently, alopecia areata has been treated with tofacitinib citrate, a Janus kinase 1/3 inhibitor, in addition to rheumatoid arthritis (AA). The outcomes of extended tofacitinib therapy for adult Indian patients with moderate-to-severe AA are reported.**Materials and methods:** Records for every patient assessed at a tertiary care center clinic with AA, AT, or AU were found between December 2022 and December 2023. Patients had to meet three requirements in order to be eligible: they needed to be at least eighteen years old, clinically diagnosed with AA, AT, or AU (which is defined as scalp hair loss exceeding ninety percent), and their disease needed to be stable or worsening for at least half a year. Clinical and demographic information on each patient was gathered. This information included age, gender, the age at the onset of the disease, the duration of the current episode of the disease, and the severity of AA as assessed by the Severity of Alopecia Tool (SALT).**Results:** The current sample's average age was 28 years. Males made up half of them (50%). In the current study, the regrowth rate was 74.00%. The re-growth rate showed a positive correlation with age at first episode onset (r=0.24; 0.036) and tofacitinib duration (r=0.43; 0.001), but a negative correlation with current episode duration (r=-0.34; 0.012) and disease duration from first onset (r=-0.15; 0.023).**Conclusion:** In the current study, a good regeneration rate was seen in more than half of the patients we looked at.The regrowth rate had a negative correlation with the length of the present episode and the time since the disease's onset, and a positive correlation with the age at the beginning of the first episode and the duration of tofacitinib.

INTRODUCTION

Alopecia areata is a chronic, immune-mediated polygenetic condition affecting hair follicles, nails, and, occasionally the retinal pigment epithelium with prevalence 2% [1] [2]

History of alopecia remains 3500 year old , in 30 CE Celsus described alopecia areata as "windings of a snake" and suggested treatment with caustic compounds.[3]

The hair cycle has 3 phases—anagen, catagen, and telogen. the anagen phase has 6 stages of hair growth. In individuals with alopecia areata the hair follicles is arrested in stages III or IV , prematurely reverting to the catagen or telogen phase leading to abrupt hair loss and a deficiency of hair regrowth.

Diagnosis is based on medical history and clinical findings of the patient characterised by Exclamation-mark hair which has narrower proximal end than the distal end.[4]

trichoscopy and histology can serve as a valuable complementary diagnostic tool. [5]

Various types of alopecia areata includes Ophiasis (involves the occipital region,) ,Sisaipho (involves the frontal, temporal, and parietal scalp except occipital region.),Diffuse (diffuse hair loss) [1]

In skin biopsy of alopecia areata reveals a distinctive "bee-swarm pattern" characterized by dense lymphocytic infiltrates surrounding the bulbar region of anagen hair follicles.[6]

Patients with extensive disease, typically defined as having more than 50% scalp hair loss, may consider treatment options such as topical immunotherapy or oral tofacitinib[7]

Tofacitinib primarily targets JAK 1/3 and reduces the immune response caused by the signaling JAK - STAT pathway necessary for hair follicle growth and cycling

The objectives of this study is to examine the efficacy and safety of tofacitinib for the treatment of alopecia areata.

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MATERIALS AND METHODS

All patients with AA, AT, or AU assessed at a tertiary care center clinic had their records located between December 2022 and December 2023. Patient who satisfied the inclusion and exclusion criteria were taken in the study.

Inclusion criterian

1. age above eighteen years old
2. clinically diagnosed with AA, AT, or AU (which is defined as scalp hair loss exceeding ninety percent)
3. Disease needed to be stable or worsening for at least half a year.

Exclusion criterian

1. Patients who did not give consent
2. Patients who lost follow-up

Clinical and demographic information about each patient was gathered, including age, gender, age at onset of disease, duration of the current episode, and severity of AA as assessed by the Severity of Alopecia Tool (SALT).

The efficacy of the treatment was evaluated using the SALT score, a proven method that calculates the percentage of scalp hair loss.

scalp is divided into 4 parts (top, posterior, right side, and left side), and a constant is assigned to each of these 4 parts based on surface area. Constant factor of 0.4 is given to top of the scalp a factor of 0.24 (24%) is given to posterior aspect of scalp, 0.18 (18%) each to right and left side of scalp. Then, percentage of area actually affected with hair loss in each of these 4 parts is assessed independently and multiplied by the constant factor of that part. Summation of the 4 multiplication products gives Alopecia Tools (SALT) score.

SALT score = (% of hair loss on top of scalp × 0.4) + (% of hair loss in posterior part of scalp × 0.24) + (% of hair loss in right side of scalp × 0.18) + (% of hair loss in left side of scalp × 0.18)

A SALT score of 100 indicates complete baldness, while a score of 0 indicates no hair loss at all. Complete regrowth is indicated by a SALT score change of 100%, while no regrowth is indicated by a score change of 0%. The % change in SALT score was used in all studies.[8]

Prior to beginning tofacitinib therapy, every patient had baseline laboratory testing, which included a full metabolic panel, a complete blood count with differential, a fasting lipid panel (total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides),serum human chorionic gonadotropin (in women of childbearing age), and HIV and hepatitis B and C virus screening.

Statistical Analysis

The data was collected, compiled, and analyzed using EPI info (version 7.2).Percentages were used to express the qualitative factors. The quantitative variables were divided into groups and given numerical values either as mean and standard deviations or as percentages.In the current study, the various features were correlated with hair regrowth using Pearson's correlation coefficient. Every p-value had two tails, and the significance threshold was set at 0.05.

RESULTSAND DISCUSSION

We have included 40 cases in the present study.

The current samples reveales 19-30 yr age group has the highest percentage, constituting 60% of the total patients. This indicates a significant skew towards younger adults in the patient population. average age was 28 years and married males made up half of them (50%). [TABLE 1]

The data suggests that the majority of patients are in the early stages of their disease (1-5 years), constituting 65% of the total. This indicates a need for healthcare strategies focused on early diagnosis and treatment. [TABLE1]

The data shows that 60% of patients are experiencing current episodes lasting less than a year, with the largest group (35%) in the 4-12 months range. However, a notable portion (35%) have very long-term episodes lasting more than 2 years. This indicates a bimodal distribution where a substantial number of patients have either short-term or very long-term episodes [TABLE1]

In the current study the median score of 99.1 indicates that half of the patients have a SALT score below 99.1, Interquartile range shows the middle 50% of patients have initial SALT scores between 32.4 and 100.The high median SALT score indicates that a large proportion of patients start treatment with severe alopecia. The wide IQR highlights the diversity in initial disease severity, which could affect treatment response and outcomes.[TABLE 2]

The median duration of Tofacitinib treatment is 7.5 months, meaning half of the patients were treated for less than 7.5 months and half for more,The IQR of 4.2 to 14 months indicates that the middle 50% of patients received treatment for this duration range.[TABLE 2]

The median total dose of Tofacitinib administered is 1880 mg. The IQR of 1300 to 4350 mg indicates significant variability in total dosages, with the middle 50% of patients receiving doses within this range.The variation in total doses reflects differences in treatment regimens, possibly due to patient-specific factors such as disease severity, response to treatment, and duration of therapy.[TABLE 2]

In the current study, the regrowth rate was 74.00%. The re-growth rate showed a positive correlation with age at first episode onset (r=0.24; 0.036) and tofacitinib duration (r=0.43; 0.001), but a negative correlation with current episode duration (r=-0.34; 0.012) and disease duration from first onset (r=-0.15; 0.023).[TABLE 3]

The data highlights significant differences in hair re-growth rates across various studies. In our study, with

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a 74% re-growth rate, suggests a particularly effective treatment regimen. This comparison underscores the importance of identifying the key factors contributing to successful outcomes and suggests areas for further research to optimize treatment protocols for alopecia.[TABLE4]

The pie chart effectively highlights the distribution of alopecia subtypes within a patient population, showing that AA is the most prevalent at 60%, followed by AU at 30%, and AT at 10%. This distribution is important for guiding treatment approaches [CHART 1]

The presence of a high number of patients with over 50% improvement (51percentage of patients) demonstrates the potential effectiveness of the treatment regimen being evaluated.The larger group with over 5% improvement (74 percentage of patients) suggests that while not all patients achieve dramatic improvements, many still benefit from the treatment to some extent.The chart provides a clear visual representation of the changes in SALT scores among patients, highlighting the effectiveness of treatment.[CHART 2]

The chart shows that 74% of patients experienced total hair regrowth, suggesting that the treatment being analyzed was highly effective for the majority of patients. Despite the high success rate, 26% of patients did not experience total regrowth [CHART 3]

When cytokines bind to their receptors, they activate Janus kinases and phosphotransferases. Therefore, Janus kinase inhibitors represent a fresh approach to the treatment of inflammatory and immunological diseases.5 When taken orally, a particular synthetic tiny molecule known as tofacitinib inhibits Janus kinases (JAKs). In April 2012, the FDA approved this (JAK) inhibitor, which is recommended for the treatment of ulcerative colitis (UC), psoriatic arthritis (PA), rheumatoid arthritis (RA), and juvenile idiopathic arthritis with a polyarticular course (pcJIA). Tofacitinib has a higher positive effect on the non-receptor tyrosine kinase JAK enzymes than on JAK-1 and JAK-3 enzymes. We have used this medicine to treat AA in the current case series (moderate to severe).

Table 1: Present sample demographics and additional features

Characteristics	Frequency (n=40)	Percentage (%)
Age(yrs)		
12-18	**10**	**25**
19-30	**24**	**60**
>50	**6**	**15**
Gender		
Female	**20**	**50**
Male	**20**	**50**
Marital Status		
Married	**28**	**70**
Single	**12**	**30**
Duration of disease(Years)		
1-5	**26**	**65**
6-10	**4**	**10**
11-20	**6**	**15**
>20	**4**	**10**
Duration of current episodes		
<3 months	**10**	**25**
4-12 months	**14**	**35**
13-24 months	**2**	**5**
>2-5yrs	**7**	**17.5**
>5yrs	**7**	**17.5**

The average age of the sample was 32.2 years with average duration of disease of 6.12 years and average duration of current episode of 5.67 years in my study

Table 2: Features of the current sample's treatment

Treatment characteristics	Median	Inter quartile range
Initial SALT score	**99.1**	**32.4 to 100**
Tofacitinib duration (months)	**7.5**	**4.2 to 14**
Total Tofacitinib dose (mg)	**1880**	**1300 to 4350**

The tofacitinib duration was 7.5 months, the total dose was 1880 [1300 to 4350], and the baseline SALT score was 99.10 [32.40 to 100].

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Table 3: The percentage of hair regrowth at the final visit and the features of the 40 alopecia areata patients receiving tofacitinib are correlated.

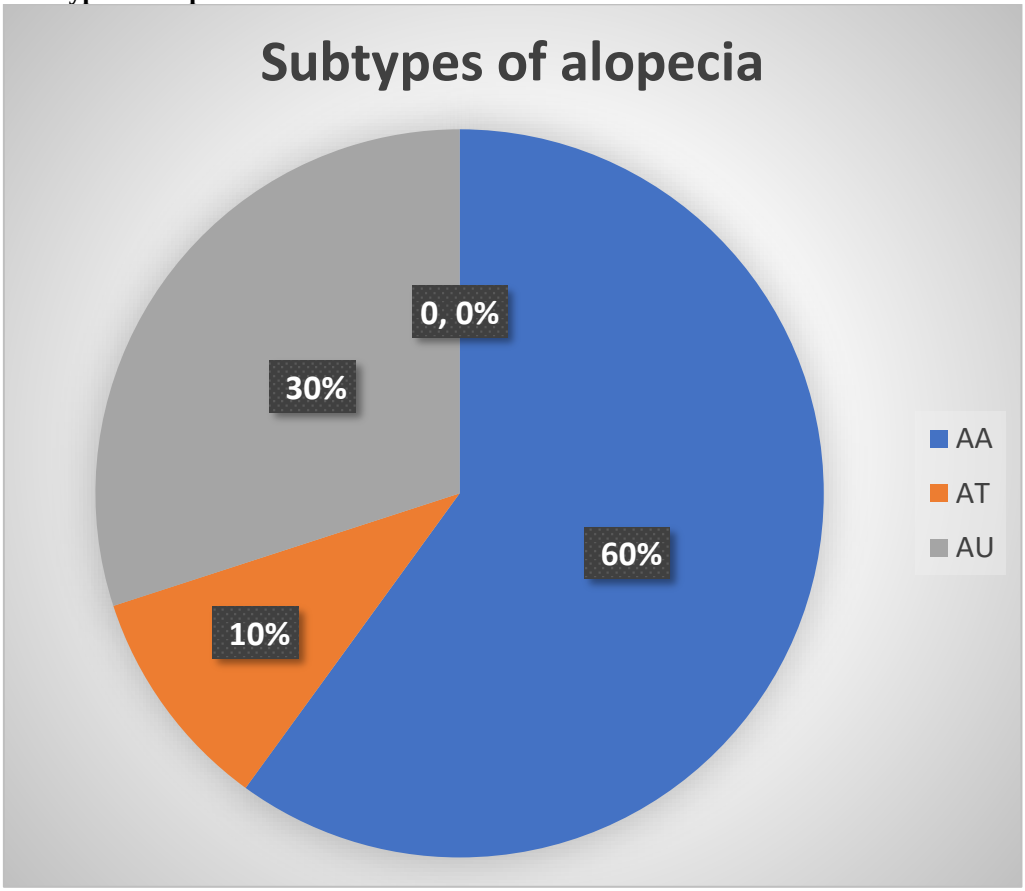
Correlation between characteristics of the patients and treatment response		
Patient characteristic	**Percent change in SALT score**	
	Correlation Coff (R)	**P**
Age	**0.196**	**0.84**
Duration of current episode	**-0.34**	**0.012**
Age at onset of first episode	**0.242**	**0.0361**
Duration of diseaseSince first onset	**−0.154**	**0.0203**
Initial SALT score	**−0.165**	**0.015***
Duration of tofacitinib treatment	**0.436**	**0.001***

*P<0.05. SALT: Severity of alopecia tool

Table 4: Re growth rate compared with various studies and our study

Studies	Re-growth rate
Our study	**74%**
Jabbari et al11	**66.70%**
Kennedy et al12	**31.80%**
Pultterman et al13	**27.30%**
Shin et al14	**44.40%**
Ibrahim et al15	**46.20%**

Chart 1: Subtypes of alopecia areata



Out Of the 40 cases studied, 24 cases were alopecia areata, 12 cases were alopecia totalis and 4 cases were alopecia universalis

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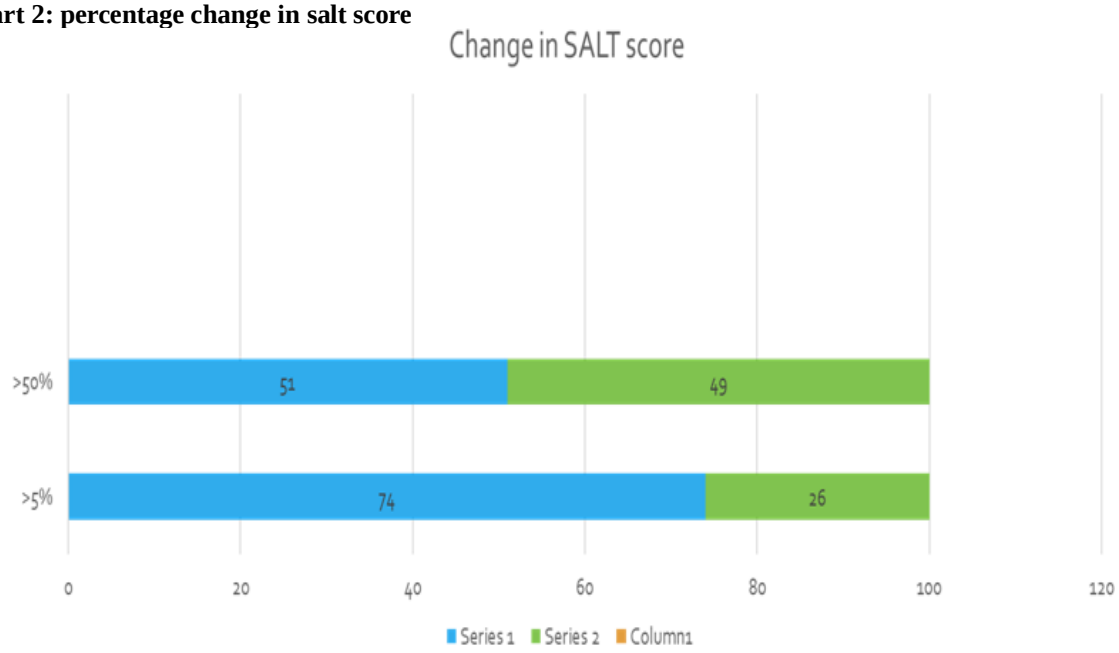
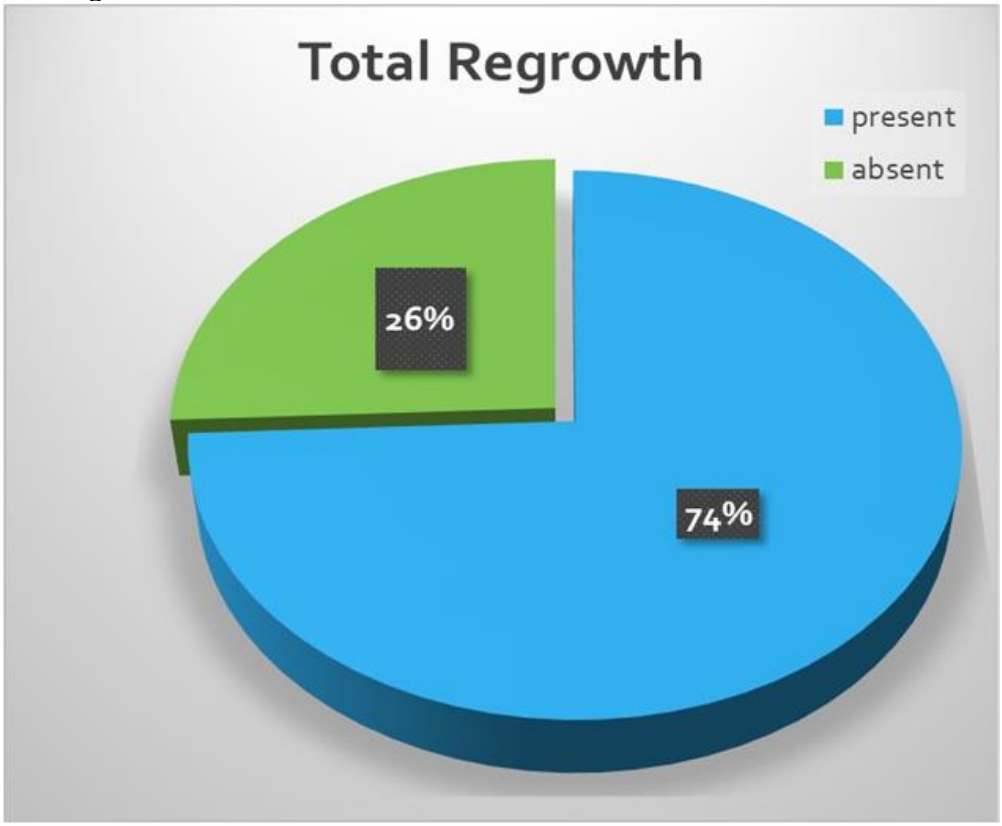
Chart 2: percentage change in salt score



>50% change in salt score is seen in 20 patients and > 5% change in salt score is seen in 29 patients.

Chart 3: Total regrowth



The re-growth rate among the present study was 74%

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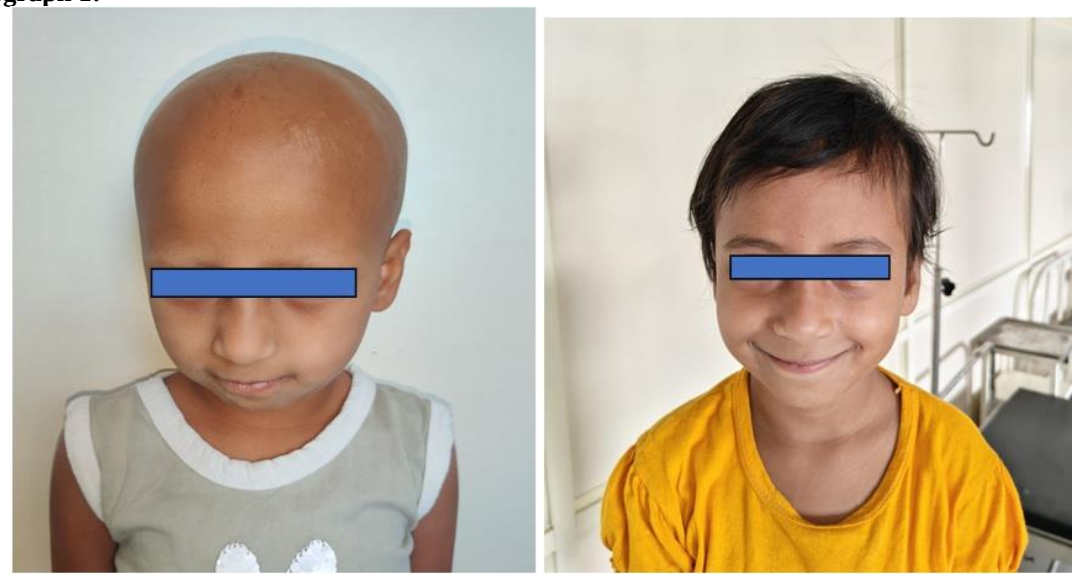
Photograph 1:



Photograph 2:

CONCLUSION

In the current study, a good regeneration rate was seen in more than half of the patients we looked at. The regrowth rate had a negative correlation with the length of the present episode and the time since the disease's onset, and a positive correlation with the age at the beginning of the first episode and the duration of tofacitinib. 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.

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