Original Article:

Comparison Of Outcome Between Tofacitinib and Baricitinib in Alopecia Areata: A Retrospective Observational Study

AN Asma[1], Md Mahabubur Rahaman[2], Md. Mostaque Mahmud[3], Mohammad Asifuzzaman[4], Md. Shah Zaman[5], Humaira Afreen[6]

1. Dr. Anzirun Nahar Asma, Associate Professor and Head , Department of Dermatology, Popular Medical College, Dhaka.
2. Prof. Md Mahabubur Rahaman, Professor, Dept. Of Dermatology, City Medical College, Gazipur, Dhaka.
3. Md. Mostaque MahmudAssociate Professor, Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Professor Mohammad Asifuzzaman, Professor & Head, Dermatology, Green Life Medical College Hospital.
5. Dr. Md. Shah Zaman, Dermatology & Venereology, Assistant Professor, Z.H. Shikder Women's Medical College.
6. Dr Humaira Afreen, Assistant Professor, Sir Salimullah Medical College Mitford Hospital.

Abstract

Introduction: Alopecia Areata is an immune-mediated, chronic inflammatory disorder that affects hair follicles, leading to nonscarring hair loss. Several treatment options are available, but none of them promise to cure. Recently, JAK inhibitors have been used as treatment options. Several studies provide data about the safety and efficacy of JAK inhibitors like Tofacitinib and Baricitinib. These drugs are also being used by dermatologists in Bangladesh. But to date, there is no published data about the comparison between Tofacitinib and Baricitinib in terms of safety and efficacy in our country. **Objective:** To compare the outcome of alopecia treatment with Tofacitinib and Baricitinib in terms of safety and efficacy. **Methodology:** In this retrospective observational study, 30 patients were included. Among them, 15 were administered Tofacitinib treatment, with 10 being female and 5 male. Where 15 patients received Baricitinib treatment, among which 8 were female and 7 male. **Results:** Both the Tofacitinib and Baricitinib groups exhibited positive responses, showing a mean improvement of 75.97% and 79.36% respectively. Despite a statistically significant difference, drawing conclusions is challenging due to the small sample size of this observational study.

Introduction

Alopecia Areata (AA) is an immune-mediated disorder that causes non-scarring alopecia on the scalp and other body parts that bear hair.[1] Up to 2% of the population lifetime chance of being affected by Alopecia Areata worldwide.[2] This disease mostly affects the scalp hair. However, it can involve any hair-bearing area of the body and progress into complete scalp hair loss known as Alopecia Totalis, or body known as Alopecia Universalis. Disfigurement from the unpredictable course of Alopecia Areata reduces the quality of life significantly.[3,4] Several complex immune-mediated dysregulations are involved in the pathogenesis of AA. Disruption of immune privilege in the hair follicle is thought to be mediated by autoantigen directed towards the hair follicle, both melanocyte and keratinocyte-related autoantigens have been proposed to be involved. The immune attack has been attributed to the activation of Th1, Th2, and Th17 cytokines, with Th1 cytokines (IL-2, TNF, IL-12) and Th17 (IL17 and IL17E) also correlating with the disease activity.[5,6]

Corresponding author
Dr. Anzirun Nahar Asma, Associate Professor and Head , Department of Dermatology, Popular Medical College, Dhaka. Mail – anzirun@gmail.com

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In recent years, significant progress has been made in understanding the underlying mechanisms of Alopecia Areata (AA), leading to more targeted therapeutic approaches utilizing small molecules. Among the various treatment options, the Janus Kinase (JAK) Inhibitor, Baricitinib, which inhibits JAK1 and JAK2, was recently approved by the US FDA in June 2022 for severe AA in adult patients. Off-label use of other JAK inhibitors like Tofacitinib and Ruxolitinib has also been observed in treating AA. Additionally, there's ongoing development of more selective second-generation JAK inhibitors such as Lkeupadacitinib, Brepocitinib, Ritlecitinib, Abrocitinib, Jaktinib, Deucravacitinib, Ifidancitinib, and Delgocitinib. However, determining the most suitable JAK inhibitor in terms of both safety and efficacy remains uncertain. Dermatologists in Bangladesh have incorporated JAK inhibitors into their AA treatment protocols, yet limited published data exists, particularly in comparing the safety and effectiveness of Tofacitinib and Baricitinib.

Methodology:

This retrospective observational study involved the collection of data from various dermatologists who treated cases of Alopecia Areata with a severity of alopecia tool (SALT) scoring of 50 or higher using oral Tofacitinib or Baricitinib from January to December 2022. These dermatologists maintained comprehensive clinical and biochemical records and monitored the outcomes of the treatments. Improvement in SALT scoring after 6 months of treatment served as the measure of outcome, with specific percentage ranges indicating levels of improvement. The study included a total of 30 patients: 15 received oral Tofacitinib (10 female, 5 male) and 15 received oral Baricitinib (8 female, 7 male). Patients receiving additional treatments alongside oral JAK inhibitors, as well as those with SALT scores below 50 or incomplete data, were excluded. Data on demographics, treatment response, and adverse events were collected from electronic medical records with proper permission. Statistical analysis, conducted using SPSS version 25, involved comparing outcomes between the two treatment modalities, with a significance level set at $p < 0.05$.

Result

In this retrospective observational study, a total of 30 patients were included: 15 received oral Tofacitinib treatment (5mg to 10mg) for six months, with 10 females and 5 males; and 15 patients received oral Baricitinib (2mg to 4mg) for the same duration, with 8 females and 7 males (as depicted in Figure-1).

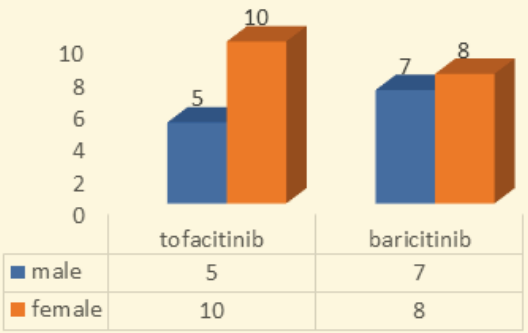

fig 1. Sex distribution of Tofacitinib and Baricitinib treated group

In both Tofacitinib and Baricitinib treated group female patient outnumber male.

The mean age of patients in the Tofacitinib group was 27.39 years (ranging from 13 to 48 years), and in the Baricitinib group, it was 22.73 years (ranging from 12 to 50 years) (Table 1).

Table-1:Distribution of age (in years) of included patients

	Tofacitinib	Baricitinib
Mean	27.93	22.73
Minimum	13	12
Maximum	48	50

In Tofacitinib treated group total number of patient 15 (n=15), in Baricitinib treated group total number of patient 15 (n=15)

In terms of alopecia types, 53% of the Tofacitinib-treated group had Alopecia Areata, 33% had Alopecia Totalis, and 13% had Alopecia Universalis, while in the Baricitinib-treated group, 67% had Alopecia Areata, 27% had Alopecia Totalis, and 7% had Alopecia Universalis (Figure 2).

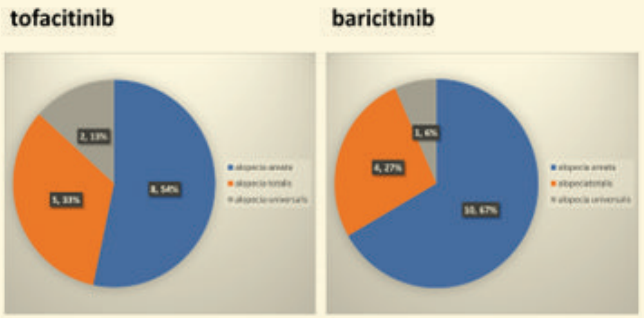

fig 2. Pattern of alopecia in both Tofacitinib and Baricitinib treated group

Total cases of Alopecia Areata outnumbers the cases of alopecia totalis and universalis in both Tofacitinib and Baricitinib treated cases.

The mean duration of disease was 20.27 months in the Tofacitinib group and 17.53 months in the Baricitinib group (Table 2),

Table -2: Duration of disease in months

Duration of disease in months	Tofacitinib	Baricitinib
Mean	20.27	17.53
Minimum	6	6
Maximum	60	54

with the maximum duration being 60 months for Tofacitinib and 54 months for Baricitinib. Most cases were not associated with other autoimmune diseases, although hypothyroidism was the most common among associated diseases, alongside Vitiligo, Atopic Dermatitis, and Psoriasis (Figure 3).

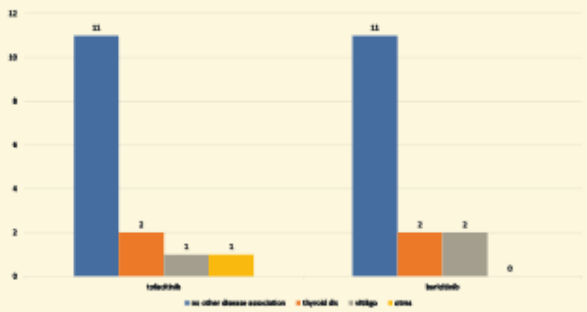

fig 3. Other disease association along with Alopecia Areata

Among the associated disease condition, thyroid diseases are most commonly found in both Tofacitinib and Baricitinib treated group.

In the Tofacitinib group, 33.3% had previously been treated with systemic steroids, while 40% had been treated in the Baricitinib group. Additionally, intralesional steroids, MTX, and Cyclosporine were attempted before initiating JAK inhibitor treatment (Figure 4).

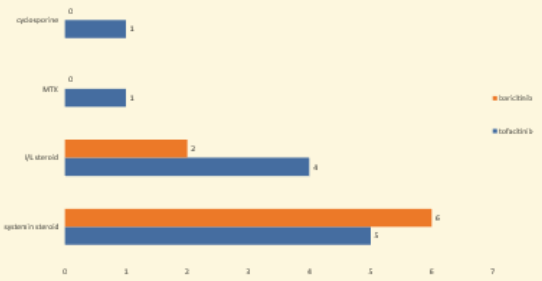

fig 4. Previous treatment modalities

In Tofacitinib group 33.3 % ware previously treated with systemic steroid and 40% in Baricitinib group. Il steroid , MTX and Cyclosporine also tried

Both the Tofacitinib and Baricitinib treatment groups demonstrated favorable responses, with an average improvement of 75.97% and 79.36% respectively (Table 3).

Table- 3: Treatment outcome (changes in SALT score from baseline):

Response	Tofacitinib (n-15)	Baricitinib (n-15)	P value
Mean ± SD	75.97 ± 19.13	79.36 ± 19.99	0.04
Low (0 -24%)			
Medium (25-49%)	1(6.7%)	0(0%)	
Good (50-74%)	4(26.7%)	8(53.3%)	
Excellent (75-99%)	8(53.3%)	2(13.3%)	
Complete (100%)	2(13.3%)	5(33.3%)	

Despite the statistically significant difference in outcomes between these two groups (p-value of 0.04), drawing definitive conclusions is challenging due to the small size of this observational study. However, it's noteworthy that fewer complications were observed in the Baricitinib-treated group compared to the Tofacitinib-treated group. Specifically, there was only one case of upper respiratory tract infection in the Baricitinib-treated group, whereas three cases were observed in the Tofacitinib-treated group.

Other complications noted included urinary tract infections, folliculitis, and headache in the Tofacitinib group, and abdominal pain and weight gain in the Baricitinib group (Figure-5).

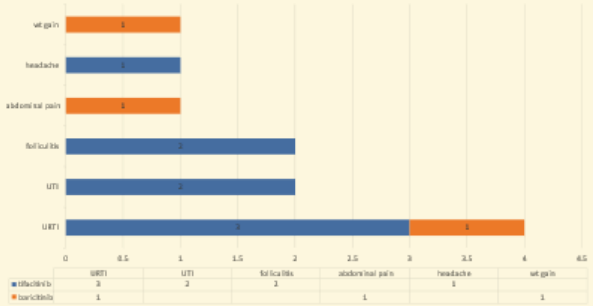

fig 5. Complications during treatment with Tofacitinib and Baricitinib

P value is < 0.05 that is statically significant. In both Tofacitinib and Baricitinib treated group upper respiratory tract infection commonly encountered complication.

No biochemical abnormalities were detected in any patient treated with either Tofacitinib or Baricitinib, except for a single case of lipid abnormality in the Tofacitinib-treated group. Children were also included in this observational study, with two in the Baricitinib-treated group and one in the Tofacitinib-treated group, aged between 12 and 15 years. No severe complications were observed, and the outcomes ranged from good to excellent in these children.

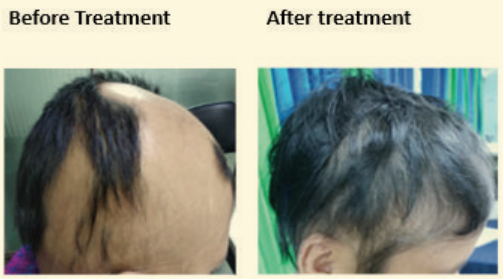

fig 6. Photograph showing before and after 6 months treatment with Baricitinib

fig 7. Photograph showing before and after 6 months treatment with Tofacitinib

Discussion

JAK inhibitors are immune modulating medications, which inhibits the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2), thereby interfering with the JAK-STAT signaling pathway in lymphocytes. There are several JAK inhibitors like Tofacitinib, Baricitinib, Ruxolitinib, that work on Alopecia proved by several published studies.[7,8,9]

The first case report on efficacy of Tofacitinib on a young male suffering from Alopecia Universalis and psoriasis was published by Craiglow and King in 2014 and was treated with oral Tofacitinib,15mg daily for 8 months and achieved complete regrowth of hair on all affected areas after completion of therapy.[10] Since then, a good number of research regarding the safety and efficacy of Tofacitinib in the treatment of Alopecia Areata, Alopecia Totalis and Universalis, in both adult and pediatric age group.[11,12]

Oral Baricitinib, selective JAK1/JAK2 inhibitor, found superior to placebo on hair growth after 36 weeks of treatment in adults with severe AA, in a phase 2 trial and recently in two phase 3 trials (BRAVE-AA1 and BRAVE-AA2).[13] On the basis of these trial results, Baricitinib approved by FDA for the treatment of adults with severe AA, On 13th June 2022.[14,15]

Liu et al. in their retrospective study of 90 AA, AU, or Alopecia Totalis (AT) patients on oral Tofacitinib 5-10 mg with or without prednisone and demonstrated >50% regrowth in 77% of patients. Of the 90 patients, 20% were complete responders (>90% reduction in SALT),[16] whereas 56.9% were intermediate to moderate responders (51%-90% reduction in SALT for intermediate responders and a 6%-50% reduction in SALT for moderate responders), and 23.1% were non-responders (≤5% reduction in SALT) . Jabbari et al 2018, in their recent open-label single-arm trial consisting of 12 patients (18–52 years) with moderate to severe AA or its variants, demonstrated that administering oral Tofacitinib ≥10mg daily for 6–12 months resulted in ≥90% regrowth.[13] In our study, with Tofacitinib 5mg to 10 mgfor 6 months in patient(total) , age ranges from 13 to 45 years, with severe Alopecia, Alopecia Totalis and Universalis we found medium response (based on is improvement of SALT scoring from baseline) that is 25 to 49% improvement in 6.7%, good response that is 50 to 74% improvement of SALT scoring seen in 26.7% cases , excellent response that is 75 to 99%

improvement of SALT scoring seen in 53.3% and complete response that 100 % improvement of SALT scoring seen in 13.3% cases.

In two phase 3 trial BRAVE-AA1 (NCT03570749) and BRAVE-AA2 (NCT03899259) are parallel-group, randomized, double-blind, 36-week, placebo-controlled trials that included 654 and 546 patients, respectively.[15] At week 36, the percentage of patients achieving a SALT 20 score was 38.8%, 35.9% in the Baricitinib 4 mg group, 22.8%, 19.4% in the Baricitinib 2 mg group, and 6.2%, 3.3% in the PBO group, in BRAVE-AA1 and BRAVE-AA2, respectively15.In our study there was 15 patient, age ranges from 12 to 50 years with severe Alopecia Areata , Alopecia Totalis or Alopecia Universalis treated with 2mg to 4 mg Baricitinib for 6 months. We got good response that is 50 to 74% improvement of SALT scoring in 53.3% patient, excellent response that is 75 to 99% improvement of SALT scoring from baseline in 13.3% patient and complete response that is total regrowth of hair seen in 33.3% patient.

Upper respiratory tract infection was the most common complication found in both group but more commonly seen in Tofacitinib treated group (20%) compared to Baricitinib treated group (6.7%). Other complications in Tofacitinib treated group were UTI, folliculitis, and headache. In the Baricitinib group there were fewer complications found, except for upper respiratory tract infection we got only one case of abdominal pain and one case of weight gain. According to the statistical analysis, we found the p-value of 0.04 which is <.05 which means there is a significant difference between the outcome (percentage of improvement of SALT scoring) of treatment response between Tofacitinib and Baricitinib treated group. There are also fewer complications found in the Baricitinib group. So, we found both Tofacitinib and Baricitinib are effective in the treatment of AA. As our study was retrospective and only 15 patients were included in each group, we cannot conclude that Baricitinib is better than Tofacitinib in treating severe Alopecia Areata, Alopecia Totalis or Universalis based on this study.

Conclusion

According to various research and published findings, JAK inhibitors emerge as promising treatments for Alopecia Areata, offering potential alternatives to systemic steroids with their associated side effects.

Beyond Tofacitinib and Baricitinib, other JAK inhibitors like Ritlecitinib, Deuruxolitinib, and Brepocitinib have also shown promising outcomes in Alopecia Areata treatment. While both Baricitinib and Tofacitinib demonstrate effectiveness in treating Alopecia Areata with minimal side effects, further studies are warranted to ascertain which one provides superior efficacy and safety, along with considerations of cost-effectiveness and their suitability for pediatric populations.

Limitations of the study

Small sample size and no follow up about recurrence after discontinuation of drug.

Conflict of interest

There is no conflict of interest.

References

1. Sibbald C. Alopecia Areata: An Updated Review for 2023. J Cutan Med Surg. 2023 May-Jun;27(3):241-259. doi: 10.1177/12034754231168839. PMID: 37340563; PMCID: PMC10291119.

2. Zhou C, Li X, Wang C, Zhang J. Alopecia Areata: an Update on Etiopathogenesis, Diagnosis, and Management. Clin Rev Allergy Immunol. 2021 Dec;61(3):403-423. doi: 10.1007/s12016-021-08883-0. Epub 2021 Aug 17. PMID: 34403083.

3. Haughton RD, Herbert SM, Ji-Xu A, Downing L, Raychaudhuri SP, Maverakis E. Janus kinase inhibitors for Alopecia Areata: A narrative review. Indian J Dermatol Venereol Leprol. 2023 Nov-Dec;89(6):799-806. doi: 10.25259/IJDVL_1093_2022. PMID: 37436019.

4. Toussi A, Barton VR, Le ST, Agbai ON, Kiuru M. Psychosocial and psychiatric comorbidities and health-related quality of life in Alopecia Areata: A systematic review. J Am Acad Dermatol. 2021 Jul;85(1):162-175. doi: 10.1016/j.jaad.2020.06.047. Epub 2020 Jun 17. PMID: 32561373; PMCID: PMC8260215.

5. Jadeja SD, Tobin DJ. Autoantigen Discovery in the Hair Loss Disorder, Alopecia Areata: Implication of Post-Translational Modifications. Front Immunol. 2022 Jun 3;13:890027. doi: 10.3389/fimmu.2022.890027. PMID: 35720384; PMCID: PMC9205194.

6. Waśkiel-Burnat A, Osińska M, Salińska A, Blicharz L, Goldust M, Olszewska M, Rudnicka L. The Role of Serum Th1, Th2, and Th17 Cytokines in Patients with

Alopecia Areata: Clinical Implications. Cells. 2021 Dec 2;10(12):3397. doi: 10.3390/cells10123397. PMID: 34943905; PMCID: PMC8699846.

7.Renert-Yuval Y, Guttman-Yassky E. The Changing Landscape of Alopecia Areata: The Therapeutic Paradigm. Adv Ther. 2017 Jul;34(7):1594-1609. doi: 10.1007/s12325-017-0542-7. Epub 2017 Jun 23. PMID: 28646393; PMCID: PMC5504208.

8. Triyangkulsri K, Suchonwanit P. Role of janus kinase inhibitors in the treatment of Alopecia Areata. Drug Des Devel Ther. 2018 Jul 27;12:2323-2335. doi: 10.2147/DDDT.S172638. PMID: 30100707; PMCID: PMC6067625.

.Xing L, Dai Z, Jabbari A, Cerise JE, Higgins CA, Gong W, de Jong A, Harel S, DeStefano GM, Rothman L, Singh P, Petukhova L, Mackay-Wiggan J, Christiano AM, Clynes R. Alopecia Areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. Nat Med. 2014 Sep;20(9):1043-9. doi: 10.1038/nm.3645. Epub 2014 Aug 17. PMID: 25129481; PMCID: PMC4362521.

9. Craiglow BG, King BA. Killing two birds with one stone: oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. J Invest Dermatol. 2014 Dec;134(12):2988-2990. doi: 10.1038/jid.2014.260. Epub 2014 Jun 18. PMID: 24940651.

10. Jabbari A, Sansaricq F, Cerise J, Chen JC, Bitterman A, Ulerio G, Borbon J, Clynes R, Christiano AM, Mackay-Wiggan J. 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 Jul;138(7):1539-1545. doi: 10.1016/j.jid.2018.01.032. Epub 2018 Feb 13. PMID: 29452121; PMCID: PMC6564681.

11. Jerjen R, Meah N, Trindade de Carvalho L, Wall D, Eisman S, Sinclair R. Treatment of Alopecia Areata in pre-adolescent children with oral tofacitinib: A retrospective study. Pediatr Dermatol. 2021 Jan;38(1):103-108. doi: 10.1111/pde.14422. Epub 2020 Oct 25. PMID: 33099833.

12. King B, Ohyama M, Kwon O, Zlotogorski A, Ko J, Mesinkovska NA, Hordinsky M, Dutronc Y, Wu WS, McCollam J, Chiasserini C, Yu G, Stanley S, Holzwarth K, DeLozier AM, Sinclair R; BRAVE-AA Investigators. Two Phase 3 Trials of Baricitinib for Alopecia Areata. N Engl J Med. 2022 May 5;386(18):1687-1699. doi: 10.1056/NEJMoa2110343. Epub 2022 Mar 26. PMID: 35334197.

13. Freitas E, Guttman-Yassky E, Torres T. Baricitinib for the Treatment of Alopecia Areata. Drugs. 2023 Jun;83(9):761-770. doi: 10.1007/s40265-023-01873-w. Epub 2023 May 17. PMID: 37195491; PMCID: PMC10191081.

14. FDA approves first systemic treatment for Alopecia Areata 2022 [cited 2022 06/22] https://www.fda.gov/news-events/press-announcements/fda-approves-first-systemic-treatment-alopecia-areata Available from.

15. Liu LY, King BA. Tofacitinib for the Treatment of Severe Alopecia Areata in Adults and Adolescents. J Investig Dermatol Symp Proc. 2018 Jan;19(1):S18-S20. doi: 10.1016/j.jisp.2017.10.003. PMID: 29273099.

16. Bretz F, Posch M, Glimm E, Klinglmueller F, Maurer W, Rohmeyer K. Graphical approaches for multiple comparison procedures using weighted Bonferroni, Simes, or parametric tests. Biom J. 2011 Nov;53(6):894-913. doi: 10.1002/bimj.201000239. Epub 2011 Aug 12. PMID: 21837623; PMCID: PMC3427907.