

Predictors of Treatment Response in Localized Alopecia Areata: A Comparative Clinical Trial of Fractional CO₂ Laser versus Intralesional Corticosteroid Therapy

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ARTICLE INFO

Received: 9 June 2026
Accepted: 15 June 2026
Published Online: 19 June 2026

DOI: 10.5281/zenodo.20760826

Volume: 9, Number: 4, Page: 195-201

e-ISSN: 2789-5912
ISSN: 2617-0817

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ABSTRACT

Background: Alopecia areata is an autoimmune disorder causing patchy hair loss and is commonly treated with intralesional corticosteroids, though their use is limited by pain, adverse effects, and recurrence. Fractional CO₂ laser therapy is an emerging alternative with promising outcomes, with treatment response influenced by disease severity, duration, and trichoscopic features. This study compares both modalities and evaluates predictors of therapeutic response. **Methods & Materials:** A prospective clinical trial at Combined Military Hospital (Jan–Dec 2024) enrolled 60 treatment-naïve patients (age 12–50) with patchy alopecia areata, divided equally into two groups (n=30 each). Group A received fractional CO₂ laser therapy (10,600 nm, 20–30 mJ, 100 MTZ/cm²; 4 sessions at 4-week intervals), while Group B received intralesional triamcinolone acetonide (5 mg/mL) at the same interval. Treatment response was evaluated after 16 weeks, with an additional 3–4 months follow-up. Data were analyzed using SPSS-23. **Results:** Clinical improvement occurred in 90.0% of the fractional CO₂ laser group and 83.3% of the intralesional corticosteroid group (p>0.05), with moderate response most common and greater marked improvement in the laser group. Short disease duration (<6 months) was the only independent predictor of good response (p=0.047; OR=4.21). Adverse effects were more frequent and severe with corticosteroids (pain, erythema, burning, atrophy), while the laser group had fewer and milder effects. No recurrence was observed in either group during follow-up. **Conclusion:** Fractional CO₂ laser therapy shows efficacy comparable to intralesional corticosteroids in Alopecia areata, with better safety and tolerability. Early disease

duration is the strongest predictor of favorable response.

Keywords: Alopecia Areata, Fractional CO₂ Laser, Intralesional Corticosteroid Therapy, Treatment response, Predictors.

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INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder leading to patchy, non-scarring hair loss that follows a relapsing-remitting pattern and can become chronic in more severe situations. It ranks as the second most frequent non-scarring hair loss after pattern baldness ^[1,2]. It is mainly autoimmune, motivated by CD8⁺ NKG2D⁺ cytotoxic T cells targeting anagen hair follicles. This interrupts follicular immune privilege, provoking an early transition to the telogen phase and leading to hair loss ^[3]. Individuals with alopecia areata frequently pursue treatment for aesthetic reasons. A variety of local and systemic treatments exist with differing levels of effectiveness; thus, the selection of therapy should be directed by clinical evaluation ^[4]. Intralesional corticosteroids (ILCs) serve as the primary treatment for localized alopecia areata ^[5]. Intralesional corticosteroids inhibit local immune responses and

decrease follicular inflammation, facilitating hair regrowth, with response rates ranging from approximately 60–80% in localized conditions. They may lead to discomfort, skin thinning, telangiectasia, folliculitis, and relapse upon discontinuation, and frequent extensive injections tend to be impractical ^[6]. Given these constraints, alternative and complementary therapies for alopecia areata are under investigation.

Fractional lasers, particularly CO₂ lasers, induce precise microthermal damage that stimulates wound healing, cytokine production, and immune modulation near hair follicles. They might also improve drug absorption via transepidermal delivery when used alongside topical treatments, increasing therapeutic effectiveness ^[7,8]. Alopecia areata exhibits inconsistent reactions to corticosteroids and fractional laser therapy, probably owing to individual patient characteristics. Recognizing factors

that influence response is crucial for enhancing treatment and results ^[9].

Prasanna et al. (2024) found that the combination of fractional CO₂ laser and topical corticosteroids yielded better clinical results than ILC monotherapy, highlighting the effectiveness of laser-assisted drug delivery in improving treatment outcomes in AA ^[10]. Recent systematic and comparative studies additionally affirm that treatment response in AA is heavily impacted by initial severity, disease duration, and existence of trichoscopic activity indicators, with early-stage lesions exhibiting markedly higher regrowth rates for both corticosteroid and laser-based treatments ^[11].

In Bangladesh, information on alopecia areata is scarce, particularly concerning fractional CO₂ laser treatment and factors influencing treatment outcomes. The majority of research centers on intralesional corticosteroids, lacking substantial

comparative or predictive evaluation of the two treatments. Thus, this research intends to evaluate fractional CO₂ laser versus intralesional corticosteroid treatment in alopecia areata and determine clinical and dermoscopic indicators of treatment efficacy.

METHODS & MATERIALS

This prospective randomized comparative clinical trial was conducted in the Department of Dermatology and Venereology at Combined Military Hospital, Dhaka, Bangladesh, from January 2024 to December 2024 to evaluate predictors of treatment response in patients with alopecia areata treated with Fractional CO₂ laser and intralesional corticosteroid therapy.

A total of 60 clinically diagnosed treatment-naïve patients with alopecia areata were enrolled in the study. The sample size was calculated using the standard formula for comparison of two proportions considering 80% statistical power and 5% level of significance. Based on previous published studies, the minimum required sample size was calculated as 29.29 patients per group, which was rounded to 30, resulting in a total sample size of 60 participants.

Patients were selected purposively from the outpatient department and subsequently randomized into two equal treatment groups using a computer-generated random allocation method. Group A consisted of 30 patients treated with Fractional CO₂ laser therapy, while Group B included 30 patients treated with intralesional corticosteroid therapy.

Patients aged 12–50 years of either sex with clinically diagnosed localized patchy non-scarring alopecia areata involving up to three patches were included in the study. Only treatment-naïve patients who provided written informed consent were enrolled. Patients with alopecia totalis, alopecia universalis, diffuse alopecia areata, pregnancy, keloidal tendency, active scalp infection, systemic autoimmune disease requiring immunosuppressive therapy, or extensive disease involving more than three patches were excluded.

Baseline evaluation included detailed history taking, clinical examination, Severity of Alopecia Tool (SALT) score assessment, and dermoscopic (trichoscopic) examination. SALT score was assessed by a single trained dermatologist at baseline and follow-up to reduce inter-observer variability. Dermoscopic findings including yellow dots, black dots, exclamation mark hairs, broken hairs, short vellus hairs, and

perifollicular scaling were recorded before treatment initiation.

Primary outcome measure was percentage hair regrowth assessed after completion of therapy using SALT score improvement and standardized clinical photographs.

Secondary outcome measures included:

- Dermoscopic/trichoscopic improvement
- Adverse effects
- Recurrence during follow-up
- Predictors of favorable treatment response

Treatment Protocol

Group A: Fractional CO₂ Laser Therapy
Patients in Group A received Fractional CO₂ laser therapy using a 10,600 nm fractional CO₂ laser device (SmartXide DOT®, DEKA, Italy). Treatment parameters included:

- Mode: Fractional ablative mode
- Energy: 20–30 mJ
- Density: 100 MTZ/cm²
- Pulse duration: 0.6–1.0 ms
- Spot size: 120 µm
- Fluence: 15–20 J/cm²

A single pass was applied over alopecic patches at 4-week intervals for a total of four sessions.

Group B: Intralesional Corticosteroid Therapy

Patients in Group B received intralesional triamcinolone acetonide (5 mg/mL). Injections were administered intradermally using a 30-gauge insulin syringe at 1 cm intervals throughout the lesion. Maximum dose per session did not exceed 20 mg, and the total injected volume per session ranged from 1–4 mL depending on lesion size. Treatment sessions were repeated every 4 weeks for four sessions.

Clinical Evaluation

Treatment response was assessed after 16 weeks using:

1. Percentage hair regrowth
2. SALT score reduction
3. Dermoscopic improvement

Percentage regrowth was categorized as:

- No response: <10% regrowth
- Slight response: 10–25% regrowth
- Moderate response: 26–50% regrowth
- Marked response: 51–75% regrowth
- Excellent response: >75% regrowth

Dermoscopic response was evaluated by reduction in black dots, yellow dots, broken

hairs, and appearance of upright regrowing hairs and terminal hairs. Patients were followed for an additional 3–4 months after completion of treatment to assess maintenance of regrowth and recurrence. Immediate and delayed adverse effects including erythema, burning sensation, pain, irritation, pruritus, hypopigmentation, telangiectasia, and skin atrophy were recorded during each visit.

Data were analyzed using SPSS version 23. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Independent sample t-test, Chi-square test, and Fisher's exact test were used where appropriate. Logistic regression analysis was performed to identify independent predictors of favorable treatment response. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. A p-value <0.05 was considered statistically significant.

Ethical approval was obtained from the institutional ethical review committee prior to commencement of the study. Written informed consent was obtained from all participants, and confidentiality was strictly maintained throughout the study.

RESULTS

A prospective randomized comparative clinical trial was conducted to evaluate predictors of treatment response among patients with alopecia areata treated with Fractional CO₂ laser and intralesional corticosteroid therapy. A total of 60 clinically diagnosed patients were enrolled and equally randomized into two treatment groups. Group A received Fractional CO₂ laser therapy, while Group B received intralesional corticosteroid therapy.

Baseline Characteristics of the Study Participants

Table 1 presents the baseline demographic and clinical characteristics of the study participants. Most participants were older than 15 years (78.3%), while patients aged ≤15 years constituted 21.7% of the study population. Female patients were predominant in both groups, accounting for 53.3% in Group A and 63.3% in Group B. Family history of alopecia areata was absent in the majority of participants (91.7%). Approximately half of the patients in each group presented with multiple lesions. The mean duration of illness was 10.0±7.24 months in Group A and 8.2±6.54 months in Group B, with an overall mean duration of 9.1±6.9 months.

Table I
Baseline demographic and clinical characteristics of the study participants (n=60).

Variables	Group A (n=30), n (%)	Group B (n=30), n (%)	Total (n=60), n (%)
Age			
≤15 years	6 (20.0)	7 (23.3)	13 (21.7)
>15 years	24 (80.0)	23 (76.7)	47 (78.3)
Sex			
Male	14 (46.7)	11 (36.7)	25 (41.7)
Female	16 (53.3)	19 (63.3)	35 (58.3)
Family history			
Present	2 (6.7)	3 (10.0)	5 (8.3)
Absent	28 (93.3)	27 (90.0)	55 (91.7)
Number of lesions			
Single	15 (50.0)	14 (46.7)	29 (48.3)
Multiple	15 (50.0)	16 (53.3)	31 (51.7)
Duration of illness (months)	10.0 ± 7.24	8.2 ± 6.54	9.1 ± 6.9

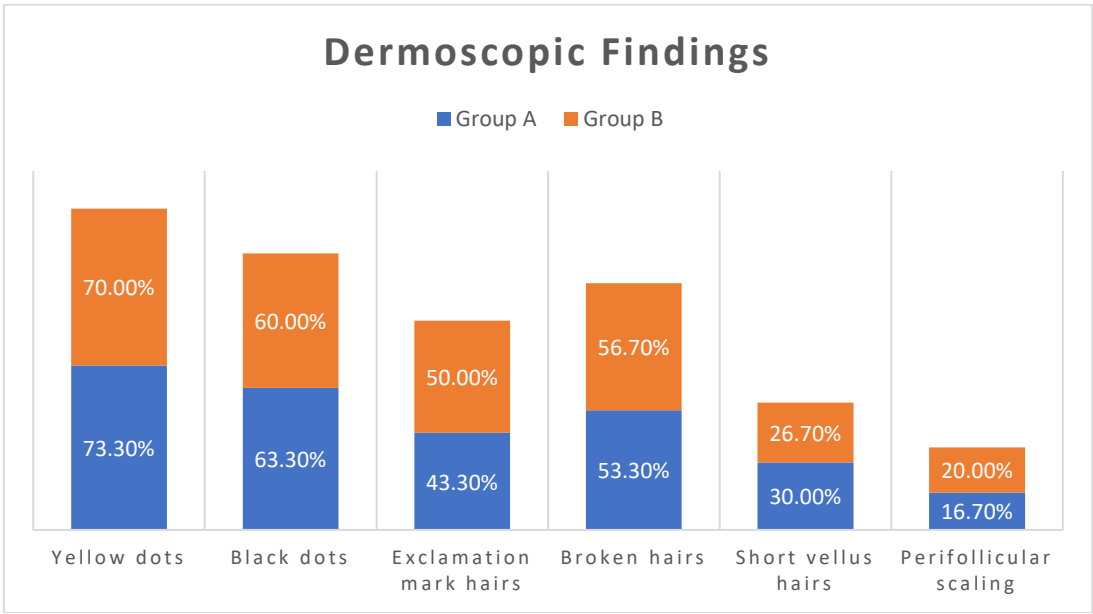


Figure 1 Baseline dermoscopic findings among study participants.



Figure 2 Dermoscopic Findings of Alopecia Areata.

Baseline Dermoscopic Findings

Figure 1 and 2 demonstrates the dermoscopic findings among the study participants in both treatment groups. Yellow dots were the most common trichoscopic feature observed, present in 22 (73.3%) patients in Group A and 21 (70.0%) patients in Group B. Black dots were identified in 19 (63.3%) patients treated with Fractional CO₂ laser and 18 (60.0%) patients receiving intralesional corticosteroids. Broken hairs were observed in more than half of the patients in both

groups, occurring in 16 (53.3%) patients in Group A and 17 (56.7%) patients in Group B. Exclamation mark hairs, a characteristic marker of active alopecia areata, were found in 13 (43.3%) and 15 (50.0%) patients in Groups A and B respectively. Short vellus hairs were present in approximately one-third of participants, while perifollicular scaling was the least common finding in both groups. Table II demonstrates the comparison of overall treatment outcomes between the two

treatment groups. Clinical response was achieved in the majority of patients in both groups, with a numerically higher response rate observed in the Fractional CO₂ laser group (90.0%) compared to the intralesional corticosteroid group (83.3%). Mean percentage hair regrowth was higher in the laser group (58.6 ± 18.4%) compared to corticosteroid group (49.8 ± 20.6%), although not statistically significant (p > 0.05). Mean SALT reduction was also higher in Group A.

Table II
Comparison of overall treatment outcomes between treatment groups.

Variables	Group A (n=30), n (%)	Group B (n=30), n (%)	p value
Responders	27 (90.0)	25 (83.3)	0.448
Non-responders	3 (10.0)	5 (16.7)	
Mean percentage regrowth	58.6 ± 18.4	49.8 ± 20.6	0.087
Baseline SALT score	12.8 ± 5.6	13.4 ± 5.9	0.681
Post-treatment SALT score	5.2 ± 3.8	7.1 ± 4.6	0.091
Mean SALT reduction	59.4 ± 19.2	47.0 ± 21.4	0.064

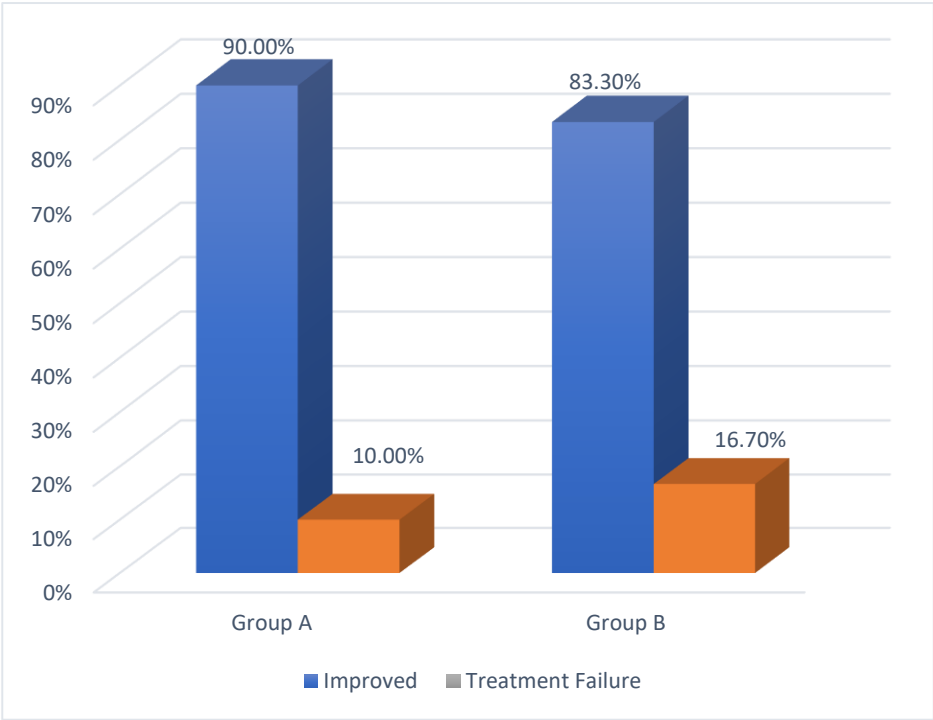


Figure 3 Overall treatment response among study participants.

Overall Treatment Response

Figure 3 and Table II demonstrates the overall treatment response among the study

participants. Clinical improvement was observed in 27 (90.0%) patients in Group A and 25 (83.3%) in Group B. Treatment

failure occurred in 3 (10.0%) patients in the laser group and 5 (16.7%) patients in the corticosteroid group.

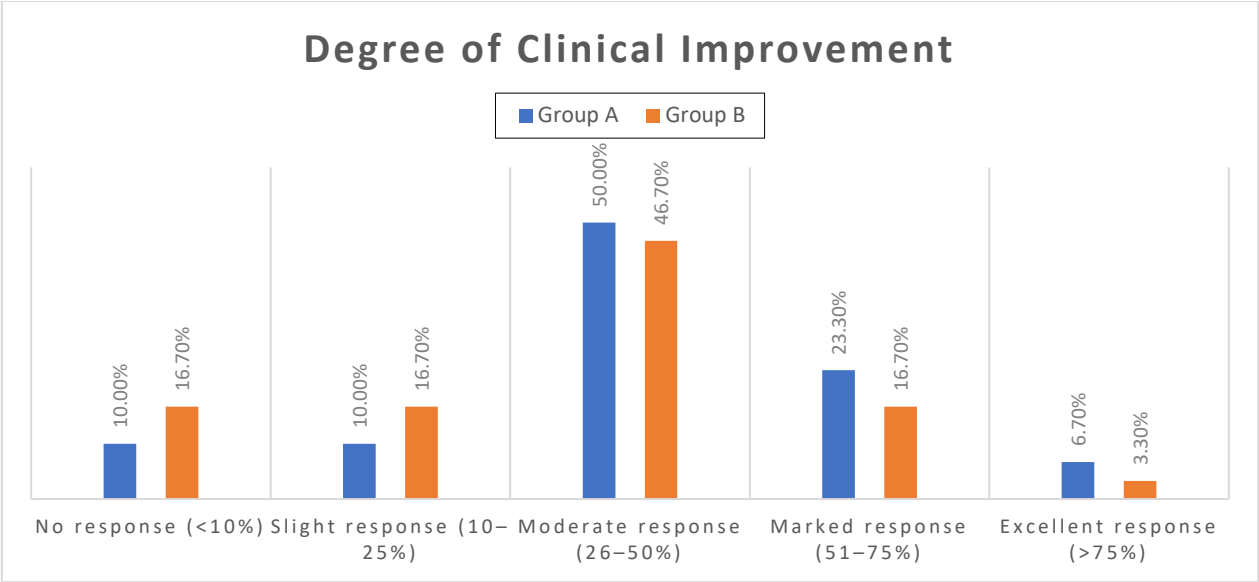


Figure 4 Degree of clinical improvement after 16 weeks of treatment.

Degree of Clinical Improvement After 16 Weeks

Figure 4 shows that moderate response (26–50% regrowth) was the most common outcome in both groups, observed in 50.0% patients in Group A and 46.7% patients in Group B. Marked response (23.3% vs 16.7%) and excellent response (6.7% vs 3.3%) were higher in the Fractional CO₂ laser group. No response was slightly higher in the corticosteroid group (16.7% vs 10.0%). Overall, Fractional CO₂ laser

therapy showed better trend but not statistically significant.

Predictors of Favorable Treatment Response

Table III shows the association between clinicodemographic variables and favorable treatment response. Shorter duration of illness (<6 months) was significantly associated with favorable treatment outcome (p=0.048). Among responders, 24 (46.2%) patients had disease duration less

than 6 months, whereas only 1 (12.5%) non-responder belonged to this category. Other variables including age, sex, family history, number of lesions, and treatment modality did not demonstrate statistically significant association with treatment outcome (p>0.05). Although patients in the Fractional CO₂ laser group showed a higher proportion of responders, treatment modality was not an independent predictor of outcome in regression analysis.

Table III
Association between clinicodemographic variables and favorable treatment response.

Variables	Responders (n=52), n (%)	Non-responders (n=8), n (%)	p value
Age ≤15 years	12 (23.1)	1 (12.5)	0.401
Female sex	30 (57.7)	5 (62.5)	0.801
Positive family history	4 (7.7)	1 (12.5)	0.651
Single lesion	27 (51.9)	2 (25.0)	0.171
Duration <6 months	24 (46.2)	1 (12.5)	0.048*
Fractional CO ₂ laser therapy	27 (51.9)	3 (37.5)	0.448

*Statistically significant.

Adverse Effects Following Therapy

Table IV shows that adverse effects were significantly more frequent in the intralesional corticosteroid group compared to the Fractional CO₂ laser group. Symptoms such as irritation, burning sensation, erythema, and pain were

markedly higher in Group B (96.7% each) than in Group A. Pruritus was also significantly lower in the laser group (3.3% vs 20.0%, p=0.044). In contrast, hypopigmentation, atrophy, and telangiectasia were observed only in the corticosteroid group, with statistically

significant differences for atrophy and telangiectasia (p=0.038). Overall, Fractional CO₂ laser therapy showed a significantly better safety profile with fewer and milder adverse effects.

Table IV
Comparison of adverse effects between treatment groups.

Adverse effects	Group A (n=30), n (%)	Group B (n=30), n (%)	p value
Pruritus	1 (3.3)	6 (20.0)	0.044*
Irritation	15 (50.0)	30 (100.0)	<0.001*
Burning sensation	7 (23.3)	29 (96.7)	<0.001*
Erythema	10 (33.3)	29 (96.7)	<0.001*
Pain	4 (13.3)	29 (96.7)	<0.001*
Hypopigmentation	1 (3.3)	4 (13.3)	0.161
Atrophy	0 (0.0)	4 (13.3)	0.038*
Telangiectasia	0 (0.0)	4 (13.3)	0.038*

*Statistically significant.

Trichoscopic Improvement Following Therapy

Table V demonstrates trichoscopic improvement following treatment in both groups. Reduction of black dots, yellow dots, and broken hairs was more frequently

observed in the Fractional CO₂ laser group compared with the intralesional corticosteroid group. Appearance of upright regrowing hairs was noted in 80.0% patients in Group A and 66.7% patients in Group B, while terminal hair regrowth was observed

in 60.0% and 46.7% patients respectively. Although the improvements were numerically higher in the laser-treated group, the differences were not statistically significant ($p>0.05$).

Table V
Trichoscopic improvement after treatment.

Trichoscopic changes	Group A (n=30), n (%)	Group B (n=30), n (%)	p value
Reduction of black dots	23 (76.7)	19 (63.3)	0.260
Reduction of yellow dots	21 (70.0)	18 (60.0)	0.417
Reduction of broken hairs	20 (66.7)	16 (53.3)	0.292
Appearance of upright regrowing hairs	24 (80.0)	20 (66.7)	0.243
Appearance of terminal hairs	18 (60.0)	14 (46.7)	0.301

Multivariate Logistic Regression Analysis

Table VI presents the multivariate logistic regression analysis of predictors of favorable treatment response. Among all variables, only shorter duration of illness (<6 months) was identified as a statistically significant independent predictor of

favorable outcome (Adjusted OR = 4.21, 95% CI: 1.02–17.38, $p = 0.047$), indicating that patients with early disease had significantly higher odds of achieving good clinical response. Other factors, including age, sex, family history, number of lesions, and treatment modality, did not show statistically significant association with

treatment response ($p > 0.05$). Although Fractional CO₂ laser therapy showed a higher odds ratio, it was not statistically significant after adjustment for confounders.

Table VI
Logistic regression analysis of predictors of favorable treatment response.

Variables	Adjusted OR	95% CI	p value
Age >15 years	1.42	0.31–6.48	0.651
Female sex	1.18	0.29–4.73	0.812
Positive family history	0.74	0.08–6.51	0.785
Single lesion	2.36	0.51–10.81	0.268
Duration of illness <6 months	4.21	1.02–17.38	0.047*
Fractional CO ₂ laser therapy	1.76	0.39–7.91	0.458

*Statistically significant.

Follow-up Outcome

Patients were followed for approximately 3–4 months after completion of therapy. Sustained hair regrowth and maintenance of clinical improvement were observed in most patients during this short-term follow-up period. No recurrence was observed in either treatment group during follow-up evaluation

DISCUSSION

In this study, a majority of participants were over 15 years old, with females making up the larger portion, and most reported no family history of alopecia areata. In 51.7% of patients, there were several lesions, and the average illness duration was 9.1 ± 6.9 months. Comparable results were observed by Yeasmin DM et al., (2022) with the average age of cases being 27.67 ± 4.25 years and a significant number of patients being female and absence of family history in most patients. They also noted that the majority of patients experienced a disease duration exceeding 6 months [12]. In this study, yellow dots emerged as the predominant dermoscopic finding in both groups, with black dots, broken hairs, and exclamation mark hairs following. Short vellus hairs and perifollicular scaling were observed less often. Comparable results

were noted by Bains P et al., (2020) with black dots (82.7%), broken hairs (69.2%), and yellow dots (61.5%) being the most prevalent dermoscopic characteristics. They also discovered notable correlations between yellow dots, damaged hairs, and the severity of alopecia areata [13]. In this study, most patients in both groups showed clinical improvement, with a greater response rate in the Fractional CO₂ laser group than in the intralesional corticosteroid group. Mean percentage hair regrowth and mean SALT reduction were greater in the laser group, although the differences lacked statistical significance. El-Husseiny R et al., (2020) reported comparable results, showing improved clinical outcomes and enhanced hair regrowth with fractional CO₂ laser in alopecia areata patients compared to intralesional steroid treatment. Their research also indicated a notable decrease in SALT scores after laser therapy [14]. In the current study, the most frequent outcome after 16 weeks was a moderate response in both groups, with Group A showing a greater percentage compared to Group B. Marked and outstanding responses were also more common in the Fractional CO₂ laser group, whereas no response was marginally higher in the corticosteroid group. Comparable results

were noted by Metwally D et al., (2022) where the majority of patients experienced moderate enhancement, with improved overall response patterns seen in more advanced or combination therapy groups [15]. In this study, a shorter illness duration was notably linked to a better treatment response, whereas age, gender, family history, number of lesions, and treatment method exhibited no statistically significant relationship with the outcome. Comparable results were noted by Majid I et al., (2018) who found that patients with a shorter duration of disease had a more favorable response to fractional CO₂ laser therapy, while a longer disease duration correlated with a less effective response [16]. In this study, negative effects were notably greater in the intralesional corticosteroid group than in the Fractional CO₂ laser group. Skin irritation, burning, erythema, and pain were more prevalent in Group B, whereas atrophy and telangiectasia were exclusive to this group, suggesting Fractional CO₂ laser therapy has a superior safety profile. Comparable results were observed by Shen Y et al., (2023) who discovered that fractional laser treatments exhibited fewer steroid-associated adverse effects and were typically well tolerated in

comparison to intralesional corticosteroids [17].

In this study, trichoscopic enhancements were observed in both groups, with a more significant decrease in black dots, yellow dots, and broken hairs in the Fractional CO₂ laser group. Upright regrowing and terminal hairs were more common in the laser group, but the differences were not significant. In a similar vein, Meguid AM et al. (2023) noted considerable dermoscopic enhancement with Fractional CO₂ laser, demonstrating a decrease in dystrophic hairs and an increase in regrowing terminal hairs, indicating improved follicular recovery relative to baseline [18].

In this study, multivariate logistic regression indicated that only shorter disease duration significantly predicted a favorable outcome, whereas other variables, including treatment modality, were not significant. The majority of patients continued to show improvement during follow-up without any recurrence. El-Husseiny R (2020) and Meguid AM (2023) reported comparable results, indicating that a shorter disease duration correlated with enhanced treatment response and better clinical outcomes in alopecia areata [14,18]. In summary, both Fractional CO₂ laser and intralesional corticosteroid treatment enhanced alopecia areata, with the laser group showing better, though not statistically significant, results, and a shorter disease duration being the key predictor of positive response.

CONCLUSION

Fractional CO₂ laser therapy and intralesional corticosteroid therapy both demonstrated satisfactory effectiveness in the management of alopecia areata. However, Fractional CO₂ laser therapy showed comparatively better clinical improvement, fewer treatment failures, and a higher proportion of marked hair regrowth with better tolerability and fewer adverse effects. Importantly, no cases of skin atrophy or telangiectasia were observed in the laser-treated group. Shorter disease duration (<6 months) was identified as the only independent predictor of favorable treatment response. Additionally, sustained clinical improvement without recurrence was observed during the 3–4 months follow-up period in both treatment groups. These findings suggest that Fractional CO₂ laser therapy may serve as a safe, effective, and promising alternative to intralesional corticosteroids for patients with localized alopecia areata.

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