

# IADVL SIG Pediatric Dermatology (Academy) Recommendations on Childhood Alopecia Areata

## Abstract

Alopecia areata (AA) is a chronic inflammatory disease characterized by nonscarring alopecia. In contrast to adult onset AA, the epidemiology, clinical characteristics, and therapy of childhood AA are less explored. This study aims at providing recommendations for the management of childhood AA. The special interest group (SIG) in pediatric dermatology under the Indian Association of Dermatology, Venereology and Leprosy (IADVL) conducted online meetings from February 2021 to September 2021, intending to identify the critical aspects in the diagnosis and treatment of AA. The classification, diagnosis, and tools for assessment of disease activity of childhood AA have been described in this study, along with recommendations for topical and systemic therapy, including newer therapeutic options.

**Keywords:** Alopecia areata, childhood, recommendations, trichoscopy

## Introduction

Alopecia areata (AA) is a chronic inflammatory disease characterized by nonscarring alopecia. Recent evidence suggests it is a T-cell-mediated autoimmune disease that occurs in genetically predisposed individuals. In contrast to adult-onset AA, the epidemiology, clinical characteristics, and therapy of childhood AA are less explored. This study aims at providing recommendations for the management of childhood AA.<sup>[1]</sup>

## Materials and Methods

The special interest group (SIG) in pediatric dermatology under the Indian Association of Dermatology, Venereology and Leprosy (IADVL) conducted online meetings from February 2021 to September 2021, intending to identify the critical aspects in the diagnosis and treatment of AA. The following keywords were used for the literature search: "Alopecia areata," "Childhood alopecia areata," "Treatment of alopecia areata," "Systemic treatments in alopecia areata," and "Trichoscopy of alopecia areata." Using these keywords, an extensive literature search was performed in MEDLINE, Google Scholar, Embase, and Cochrane databases. Relevant data

from articles published from January 2010 to January 2021 in English were compiled. Figure 1 demonstrates the preferred reporting items for systematic review and meta-analyses (PRISMA) flowchart.

As per the Oxford Centre for Evidence-Based Medicine (CEBM), a level of evidence and strength of recommendation were assigned to each component after a thorough discussion [Table 1].

## Results and Discussion

### Classification and diagnosis

The common presentation of AA is an asymptomatic circumscribed round to oval smooth alopecic patch without any surface changes. An exclamation mark hair, short and easily pluckable hair with distal end broader than proximal end, can be visualized at the margin of an active lesion. The scalp is the most common and initial site of involvement. Isolated involvement of the beard, eyebrows and eyelashes is less common. AA preferentially affects the pigmented hair, and non-pigmented hairs are spared. A patient with rapid progressive AA may produce a dramatic change in hair color called "going white overnight."<sup>[1,2]</sup>

**Bhumesh K. Katakam,**  
**Biswanath Behera<sup>1</sup>,**  
**Ranugha PSS<sup>2</sup>,**  
**Neerja Puri<sup>3</sup>,**  
**T. Narayana Rao<sup>4</sup>,**  
**Ram Gulati<sup>5</sup>,**  
**K.A. Seetharam<sup>6</sup>**

Department of Dermatology, Venereology and Leprosy, Government Medical College/Hospital, Suryapet, Telangana,

<sup>1</sup>Department of Dermatology and Venereology, AIIMS, Bhubaneswar, Odisha,

<sup>2</sup>Department of Dermatology, JSS Medical College and Hospital, JSSAHER, Mysore, Karnataka, <sup>3</sup>Department of Dermatology, GGS Medical College, Faridkot, Punjab,

<sup>4</sup>Department of Dermatology, MIMS, Vijayanagaram, Andhra Pradesh, <sup>5</sup>Department of Dermatology, Consultant Dermatologist, SDM Hospital, Jaipur, Rajasthan, <sup>6</sup>Department of Dermatology, Venereology and Leprosy, GSL Medical College, Rajahmundry, Andhra Pradesh, India

<sup>6</sup>Department of Dermatology, Consultant Dermatologist, SDM Hospital, Jaipur, Rajasthan, <sup>6</sup>Department of Dermatology, Venereology and Leprosy, GSL Medical College, Rajahmundry, Andhra Pradesh, India

### Address for correspondence:

Dr. Biswanath Behera,  
Department of Dermatology and Venereology, AIIMS, Bhubaneswar, Odisha, India.  
E-mail: biswanathbehera61@gmail.com

### Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.idoj\_54\_22

### Quick Response Code:



This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Katakam BK, Behera B, Ranugha PS, Puri N, Narayana Rao T, Gulati R, et al. IADVL SIG pediatric dermatology (Academy) recommendations on childhood alopecia areata. Indian Dermatol Online J 2022;13:710-20.

**Received:** 27-Jan-2022. **Revised:** 18-Jul-2022.  
**Accepted:** 20-Jul-2022. **Published:** 31-Oct-2022.

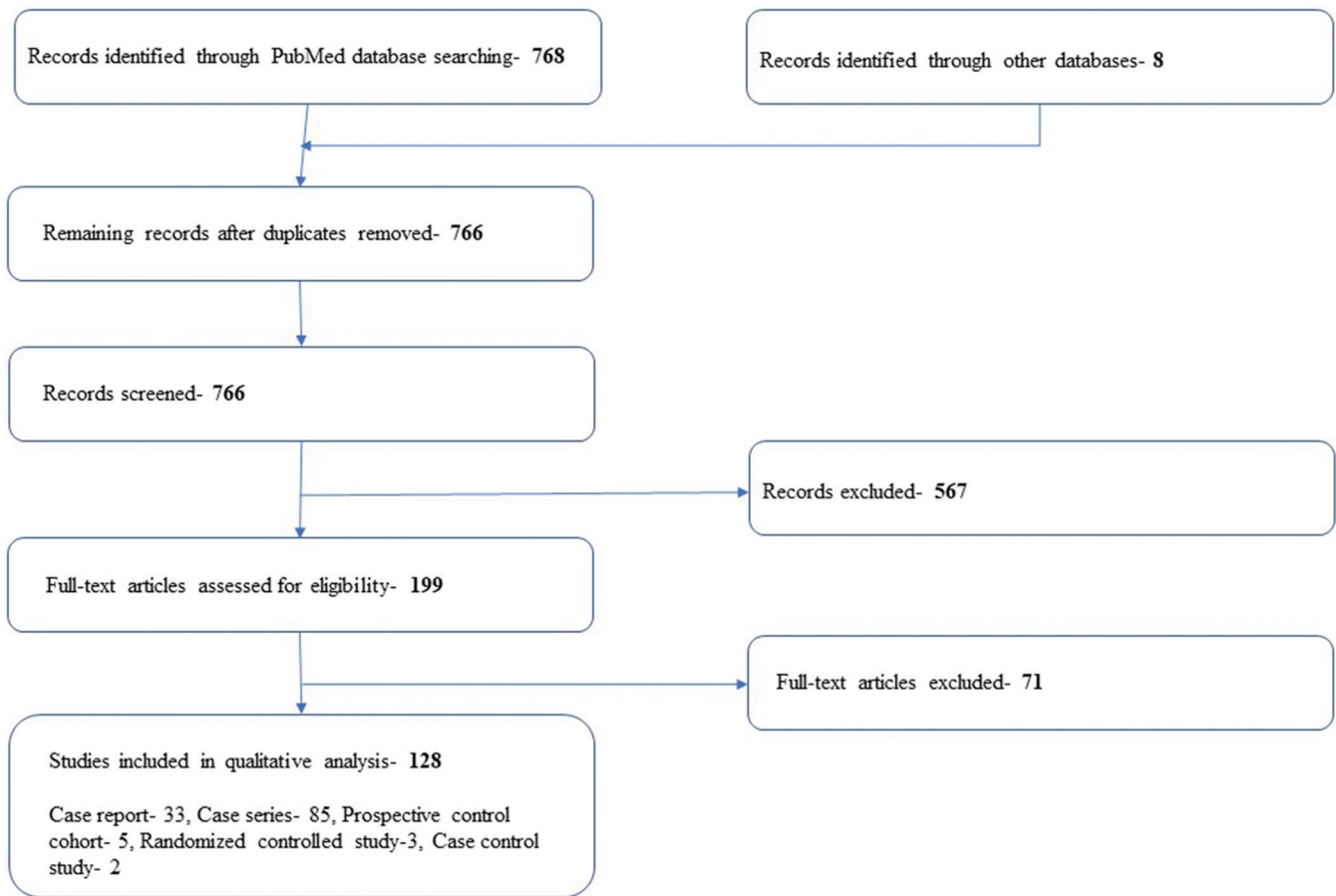


Figure 1: PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) flowchart

**Table 1: Levels of Evidence and Strength of Recommendation**

Levels of evidence from CEBM	Strength of recommendation
Level 1: Systematic reviews of randomized controlled trial (RCT) or individual RCT (with narrow confidence interval).	A=Consistent level 1 studies.
Level 2: Systematic reviews of cohort studies or individual cohort study.	B=Consistent level 2 or 3 studies or extrapolations from level 1 studies.
Level 3: Systematic reviews of case-control studies, and individual case-control study.	C=Level 4 studies or extrapolations from level 2 or 3 studies.
Level 4: Case-series and poor-quality cohort and case-control studies.	D=Level 5 evidence or troublingly inconsistent or inconclusive studies at any level.
Level 5: Expert opinion.	

### Clinical patterns of AA

The following patterns of AA have been described [Figure 2].<sup>[2-4]</sup>

1. Patchy (unifocal or multifocal): round or oval area of hair loss
2. Ophiasis pattern: hair loss in symmetric

- band-like pattern over the temporal and occipital areas
3. Saisipho pattern: loss of scalp hair sparing temporal and occipital areas
4. Alopecia totalis (AT): complete or near-complete loss of scalp hair
5. Alopecia universalis (AU): complete or near-complete loss of all body hair
6. Diffuse AA: diffuse loss of scalp hair without any patchy alopecia over a prolonged period
7. AA incognita: rapidly developing, widespread, and severe hair loss

### Nail changes

Nails are usually involved in severe AA, and changes include regular pitting, trachyonychia, longitudinal ridging, leukonychia, and dystrophy. Rare findings are mottled lunulae, onychomadesis, lamellar splitting, Beau's lines, ragged cuticles, onychorrhexis, shiny nails, and yellow-brown discoloration.<sup>[5]</sup>

### Differential diagnoses

1. **Patchy AA:** The various differential diagnoses of patchy AA are tinea capitis, trichotillomania, traction alopecia, congenital triangular alopecia, and loose anagen hair syndrome.<sup>[2-4]</sup>



Figure 2: (a) Solitary circumscribed round smooth alopecic patch without any surface changes. (b) Diffuse alopecia areata. (c) Ophiasis pattern with nail dystrophy. (d) Alopecia totalis [Image: AIIMS-Bhubaneswar]

2. **Diffuse AA/AA incognita/AA totalis:** The differential diagnoses of diffuse AA or AA incognita are telogen effluvium, androgenetic alopecia (AGA), loose anagen hair syndrome, and chemotherapy-induced alopecia.<sup>[2-4]</sup>

### Diagnosis

The diagnosis of AA is mostly clinical. The patient usually presents with a well-circumscribed round or oval patch(s) of alopecia without any surface changes. A hair pull test at the margin of the active AA patch is usually positive and white hairs are relatively spared. Nail abnormalities such as fine pitting, trachyonychia, and nail dystrophy provide additional clues. A history of waxing and waning course and spontaneous hair regrowth support the diagnosis. However, in doubtful cases, investigations are needed to rule out other causes of alopecia.

### Trichoscopy

In the case of AA, trichoscopy is useful in aiding the diagnosis and monitoring response to therapy. The common features are yellow dots, short vellus hairs, and dystrophic hairs, visible under the trichoscope as black dots, broken hairs, and exclamation mark hairs [Figures 3-6]. Other features noticed are coudability hairs or tapered hairs, upright regrowing hairs, pigtail or circle hairs, and Pohl–Pinkus constrictions, or pseudo monilethrix.<sup>[6,7]</sup> In children, yellow dots can be solitary or clustered (three or more adjacent hair follicles showing yellow dots).<sup>[8]</sup> There is no specific trichoscopic feature for AA, and a combination of features may help diagnose.<sup>[7]</sup>

### Histopathology

Pathological examination is the last resort in doubtful cases. Due to its dynamic nature, both horizontal and vertical

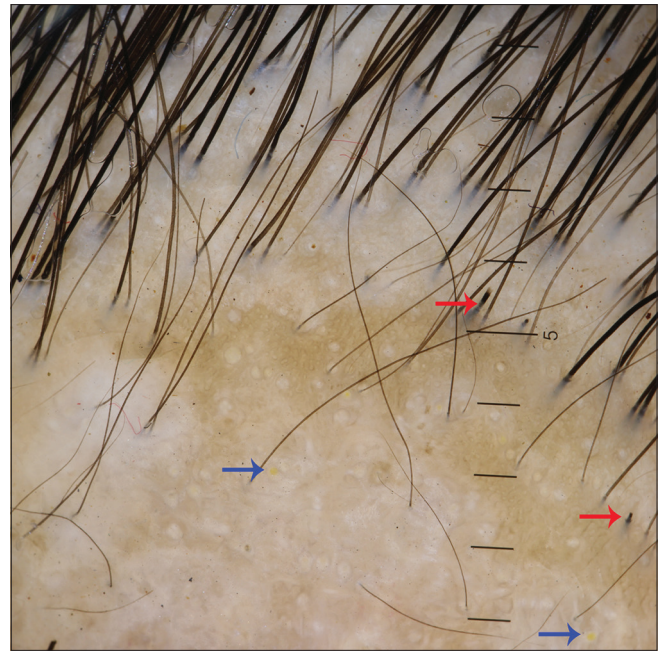


Figure 3: Trichoscopy (DermLite DL4, 10x magnification) shows yellow dots (blue arrows) and broken hairs (red arrow) [Image: AIIMS-Bhubaneswar]

sections from the margin of an active alopecic patch must be examined to arrive at a diagnosis of AA. A peribulbar lymphocytic inflammatory infiltrate resembling a “swarm of bees” is characteristic. Other features are increased catagen and telogen hairs, follicular miniaturization, pigment cast, and pigment incontinence.<sup>[9]</sup>

### Screening for associations

Atopic dermatitis (AD) is two to three times more common in patients with AA. Although some studies reported an earlier onset, severe disease, and longer duration of AA in patients with AD, others could not duplicate the same findings.<sup>[10]</sup>

An associated thyroid abnormality has been reported in 8%–28% of AA cases. Although high titers of antithyroid antibodies have been detected in AA patients, these do not correlate with disease severity.<sup>[11]</sup>

Other diseases associated with AA are vitiligo, psoriasis, Addison’s disease, diabetes mellitus, autosomal recessive autoimmune polyglandular syndrome, celiac disease, ulcerative colitis, multiple sclerosis, systemic lupus erythematosus, and Down’s syndrome. Patients with AA have an increased frequency of autoantibodies to follicular structures (especially to keratin 16 and trichohyalin).<sup>[12,13]</sup>

### Monitoring parameters and scoring in alopecia areata

#### Clinical examination

The following clinical features are suggestive of active disease. The presence of exclamation mark hairs at the periphery, positive hair pull test, daily hair fall count >100 hairs, and hair pluck test with more telogen hairs.<sup>[14]</sup>





Figure 4: Trichoscopy (DermLite DL4, 10× magnification) shows exclamation mark hair (blue arrow) [Image: AIIMS-Bhubaneswar]

#### Clinical scale to assess the severity of AA

The severity of AA can be graded into the following three types.<sup>[14,15]</sup>

- i. Mild: Three or fewer patches of alopecia with the largest diameter of <3 cm or disease limited to eyelashes and eyebrows
- ii. Moderate: The existence of more than three patches of alopecia or a patch greater than 3 cm at the widest diameter without AT or alopecia universalis
- iii. Severe: AT or alopecia universalis

#### Severity of alopecia tool score (SALT score)

It is a quantitative assessment of hair loss. The SALT (severity of alopecia tool) score is determined by visually determining the amount of terminal hair loss in each of the four views of the scalp (right, left, top, and back) and adding these together with a maximum score of 100%. One can determine the percentage of scalp hair loss in a given quadrant, multiply this by the total scalp area delineated by that quadrant (right, left-18% each, top-40%, back-24%), and sum the resultant numbers for each quadrant to give the total percentage of scalp hair loss. The SALT score may be determined at the bedside by the investigator or by reviewing representative photographs by the investigator, or expert panel. Further subgrouping of percentage of scalp hair loss into the following SALT subclasses has also been suggested: S0 = no hair loss, S1 = <25% hair loss, S2 = 25–49% hair loss, S3 = 50–74% hair loss, S4 = 75–99% hair loss (a = 75–95% hair loss, b = 96–99% hair loss), S5 = 100% hair loss.<sup>[16]</sup>

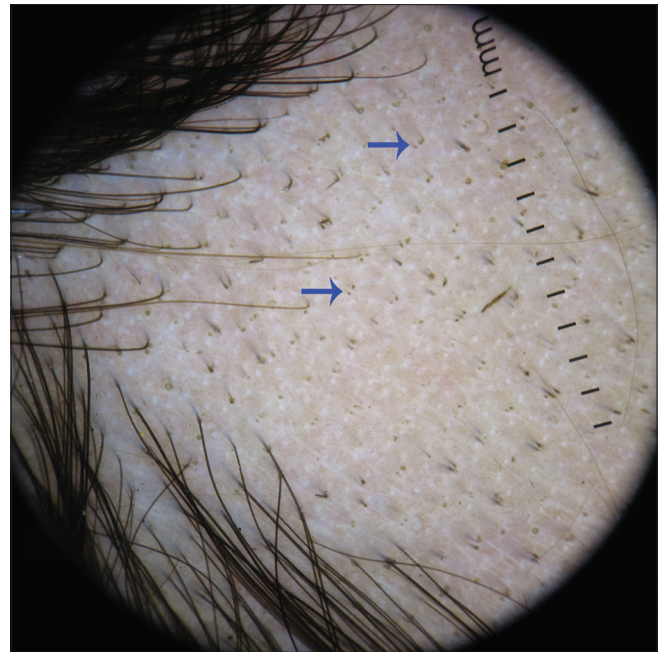


Figure 5: Trichoscopy (DermLite DL4, 10× magnification) shows black dots (blue arrows) [Image: AIIMS-Bhubaneswar]

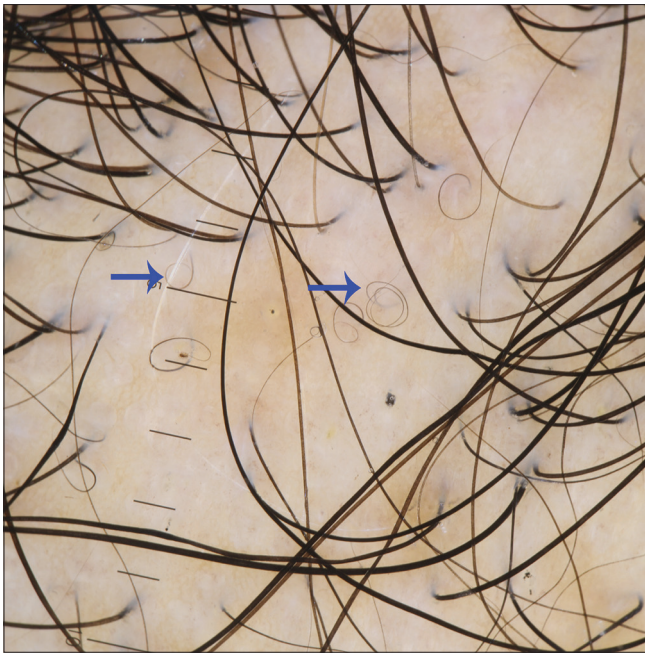
#### Histopathology

A biopsy can predict the prognosis in AA. It is essential to assess the proportion of hair follicles in various stages, the level of hair follicles in the dermis, and to quantify the density and diameter of hair follicles. A mean count of less than one follicle/mm<sup>2</sup> usually indicates lower chances of regrowth.<sup>[14]</sup>

- i. In acute cases: Peribulbar and intrabulbar, predominantly, lymphocytic infiltration along with eosinophils, mast cells, plasma cells, and Langerhans cells are noticed along with reduced anagen to telogen ratio (A:T ratio). A dense lymphocytic inflammation can cause weakening of the hair shaft, resulting in a trichorrhexis nodosa-like fracture, leading to the exclamation mark hairs.
- ii. In subacute lesions: A high proportion of catagen/telogen hair follicles is seen.
- iii. In chronic cases: Follicular miniaturization with variable papillary dermal inflammatory infiltrate is seen

#### Trichoscopy

In patchy AA, the presence of black dots, broken hairs, exclamation mark hairs, and tapered hairs (negative prognostic factors) following therapy indicate nonresponse to therapy, whereas the presence of upright regrowing hair and pigtail hair (positive prognostic factors) suggests a good response to therapy.<sup>[14,17-18]</sup> Alopecia Areata Predictive Score (AAPS) is a new trichoscopy-based tool to predict treatment outcomes in patients with patchy AA. The score is calculated by adding the positive and negative predictive trichoscopic markers. It ranges from -4 to +2, a higher score indicates better hair growth. Recently, Brigham Eyebrow Tool for Alopecia (BETA) has



**Figure 6:** Trichoscopy (DermLite DL4, 10× magnification) shows pigtail hairs (blue arrows) [Image: AIIMS-Bhubaneswar]

been developed for the quantitative evaluation of eyebrow AA.<sup>[19]</sup> Wyrwic *et al.*<sup>[20]</sup> developed clinician-reported outcome (ClinRO) and patient-reported outcome (PRO) measures and accompanying photoguides to aid in assessing AA-related eyebrow, eyelash, and nail signs/symptoms.

Also, Alopecia Areata Investigator Global Assessment (AA-IGA) has been developed to measure five clinically meaningful gradations of AA scalp hair loss. The AA-IGA can be used to determine clinically meaningful treatment success for AA.<sup>[21]</sup>

#### Optical coherence tomography (OCT)

This is a recently evaluated non-invasive technique to detect hair shaft abnormalities in AA. Bartels *et al.*<sup>[22]</sup> demonstrated that a cross-section of hairs from an AA patch is significantly lower than from hairs of an unaffected area.

### Management

All children with AA should be considered for active treatment. Topical therapy is the most appropriate first-line treatment in children with AA. Combining two or three of topical treatments is considered second-line management. Systemic therapy is considered a third-line option in children.<sup>[23]</sup> Various treatment modalities, indications, side effects, duration of therapy, and levels of evidence (LoE) are mentioned in Table 2. Figure 7 depicts the SIG-Pediatric Dermatology recommendations for the managements of childhood alopecia areata.

#### Topical therapy

Indications of topical therapy are single or limited number of patches and a short duration of AA.

#### Topical corticosteroids

The use of topical corticosteroids, particularly high-potency topical corticosteroids, is supported by the literature (strongest levels of evidence [LoE] 1) and is considered a safe and effective first-line treatment option in children with patchy AA.<sup>[24]</sup> High-potency topical corticosteroids showed higher efficacy than low-potency topical corticosteroids in an RCT (randomized controlled trial) that included 41 pediatric patients.<sup>[25]</sup> They were also superior to topical tacrolimus and anthralin.<sup>[26,27]</sup> Results from a study with a predominantly pediatric population (19/28) revealed that those more than 10 years of age and those with an AA duration of less than 1 year tended to respond more frequently to treatment with topical corticosteroids (0.2% fluocinolone acetonide cream) with a 60% response rate.<sup>[28]</sup> In an RCT on 34 patients with moderate to severe AA, hair regrowth was noted in 89% of scalp sites treated with clobetasol foam compared to 11% sites with placebo after 12 weeks of treatment.<sup>[29]</sup>

Side effects include folliculitis (more with ointment than with foam preparation), rarely skin atrophy, and telangiectasia.<sup>[30]</sup>

#### Intralesional corticosteroids

Studies of intralesional steroid injections (triamcinolone acetonide 2.5-10mg/ml) in children with AA are rare due to the pain associated with the injections. Intralesional steroids can be considered the first line in children above 10 years of age and with limited disease. Though intralesional steroids as monotherapy may be inadequate for extensive AA, in the experience of the authors, this treatment can be used as adjunctive therapy to systemic treatment and may accelerate the effects of oral corticosteroids and response to Janus kinase (JAK) inhibitors.<sup>[31]</sup>

Side effects can be prevented by using smaller concentrations and volumes, minimizing the number of injections per site, and avoiding injections too superficially.<sup>[32,33]</sup>

#### Contact immunotherapy

Both diphenylcyclopropenone (DPCP) and squaric acid dibutyl ester (SADBE) have been tried safely in the pediatric population. The painless application makes DPCP the preferred option. A recent systematic review reported complete response rates between 0 and 37% with recurrence rates of 12.5% to 58.3% (strongest level of evidence 3) for DPCP. With SADBE also, a similar response rate was seen in 78 pediatric patients (strongest level of evidence 4).<sup>[15]</sup> DPCP is cheaper and stable in acetone, and irritation is less than SADBE. A meta-analysis including adult and pediatric patients demonstrated slightly better complete response rates with SADBE (38.4%) than with DPCP (30.7%).<sup>[34]</sup> One case-control study noted the potential of imiquimod to improve DPCP efficacy.<sup>[35]</sup> Durdu *et al.*<sup>[36]</sup> reported that the efficacy of DPCP may be enhanced by combination therapy with anthralin (0.5–1.0%), which causes irritant dermatitis.

**Table 2: Indication, side-effect, and duration of therapy of various treatment modalities of alopecia areata**

Treatment modalities	Indications	Side-effects	Duration of therapy	Level of evidence (LoE)
Clobetasol or Halobetasol	Limited patch AA	Atrophy Telangiectasia Folliculitis	3 months	LoE 1
Intralesional triamcinolone	Limited patch AA	Atrophy Telangiectasia Folliculitis	Once in 2 to 3 weeks for 3 months	LoE 1
Topical diphenyl cyclopropenone	Extensive AA Therapy-resistant AA	Irritation Itching Contact dermatitis	3 to 6 months	LoE 3
Topical anthralin	Limited patch AA	Irritation Folliculitis Regional lymphadenopathy Skin staining	Minimum 9 months	LoE 4
Topical minoxidil	As an adjuvant	Hypertrichosis Itching Dermatitis	-	LoE 4
Bimatoprost and Latanoprost	Localized AA	-	-	LoE 1-2
Oral Prednisolone, or IV Methyl Prednisolone, or Oral mini pulse	Rapidly progressing and extensive AA	Hypertension Impaired glucose tolerance Cushingoid features	T3 to 6 months	LoE 2
Methotrexate	Rapidly progressing and extensive AA	Hepatotoxicity Bone marrow suppression	3 months	LoE 4
Azathioprine	Rapidly progressing and extensive AA	Bone marrow suppression	3 months	LoE 4
Cyclosporine	Rapidly progressing and extensive AA	Nephrotoxicity Hypertension	3 months	LoE 3
Hydroxychloroquine	Refractory AA	Retinopathy Abdominal discomfort	-	LoE 4
Sulfasalazine and Mesalazine	Refractory AA	Dizziness	-	LoE 4
Tofacitinib	Refractory AA	Nasopharyngitis Headache Gastrointestinal disturbance	-	LoE 4
Phototherapy PUVA (Psoralen with ultraviolet light A) Excimer laser 308 nm	Refractory AA	Cataract Photoonycholysis	3 months	LoE 4
Cryotherapy	Recalcitrant AA	Skin necrosis Depigmentation	3 months	LoE 4

AA- alopecia areata

In a large series, cosmetically acceptable regrowth (>75%) was achieved in 17.4% of patients with AT/AU, 60.3% with 75–99% AA, 88.1% with 50–74% AA, and 100% with 25–49% AA following DPCP.<sup>[37]</sup>

Side effects of SADBE include irritation, itching, lymphadenopathy, and contact dermatitis.<sup>[38,39]</sup> Contact immunotherapy should be tapered gradually and not stopped suddenly to reduce the chances of relapse.

#### Topical anthralin

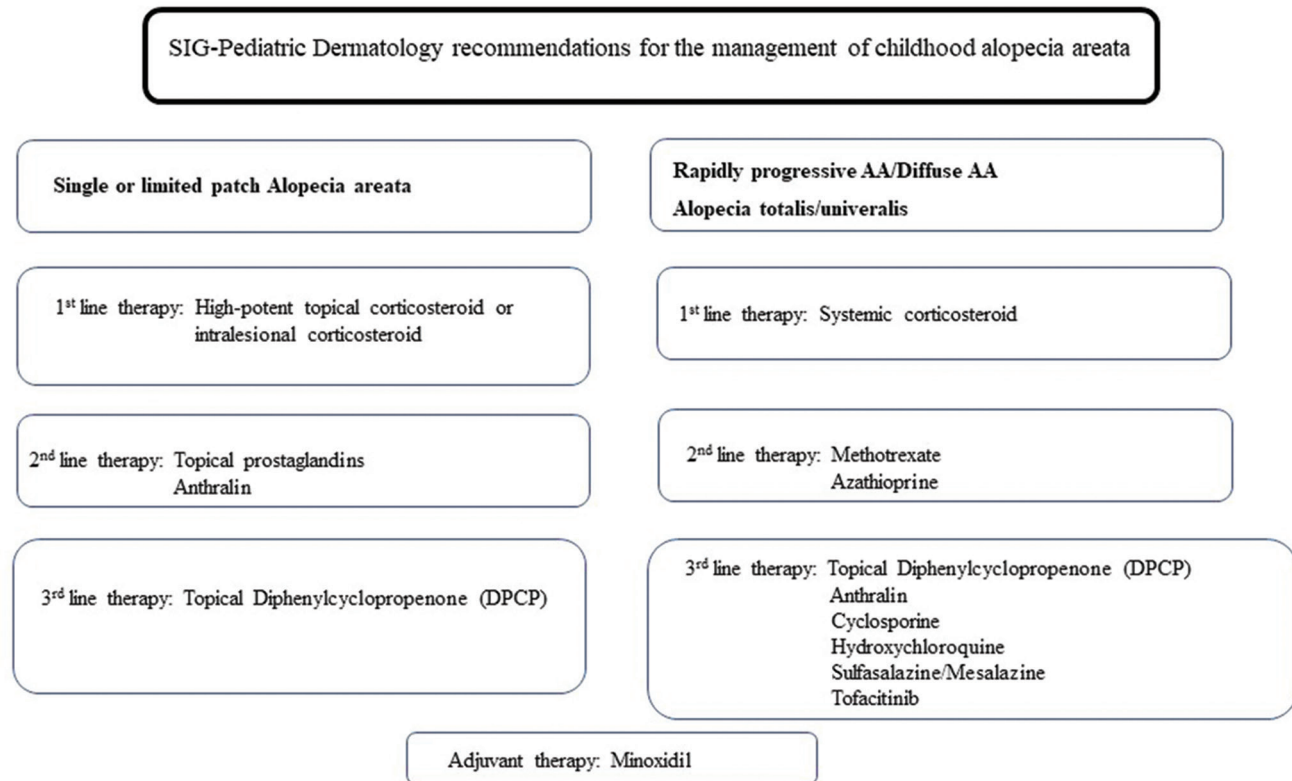
Anthralin 1% can be used as short contact therapy. It is applied daily for 15–20 min initially and then washed off.

The contact time is increased by 5 min weekly up to 1 h, or until low-grade dermatitis develops. The contact time is then fixed and continued daily for at least 3 months before judging the response to treatment. The treated area should be protected from the sun. Anthralin should produce a mild irritant reaction to being effective.<sup>[40]</sup> Side effects include severe irritation, folliculitis, regional lymphadenopathy, skin staining, staining of clothes, and fair hair.<sup>[41-43]</sup>

#### Topical calcineurin inhibitors

A consensus of four studies that included seven pediatric AA patients concluded that topical calcineurin inhibitors,





**Figure 7: SIG Pediatric Dermatology recommendations for the treatment of childhood alopecia areata**

tacrolimus, and pimecrolimus are not effective for the treatment of AA (strongest LoE 2).<sup>[15]</sup>

#### Topical minoxidil

Five percent minoxidil can be used as adjuvant therapy in AA in adults.<sup>[15]</sup> Topical minoxidil may benefit patients with AA although it is unlikely to alter the disease course or induce remission. Minoxidil may help maintain hair growth stimulated by other treatments.<sup>[30]</sup> Only case reports exist evaluating its use in nine children (strongest LoE 4).

Both 2% and 3% minoxidil are beneficial.<sup>[44]</sup> Some authors have recommended 5% minoxidil as opposed to lower strengths because higher concentrations have been reported to be more effective although there may be an increased likelihood of unwanted hair growth on other parts of the body compared to lower concentrations.<sup>[45]</sup>

#### Prostaglandins

Topical prostaglandins such as bimatoprost and latanoprost have been used in AA.<sup>[46]</sup> In a recent RCT in adults, topical latanoprost 0.005% ophthalmic solution was found to be less effective but safer than topical betamethasone dipropionate 0.05% lotion in the treatment of localized AA.<sup>[47]</sup> In another RCT comparing latanoprost 0.1%, minoxidil 5%, betamethasone valerate 0.1%, and a combination of latanoprost with steroid, all were found to be safe and effective in patchy AA. The use of latanoprost added to the therapeutic efficacy of topical betamethasone

valerate in the treatment of AA and could be an effective adjunctive topical therapy for AA.<sup>[48]</sup>

#### Phototherapy

Psoralen and ultraviolet A therapy after topical application of 0.1% 8-MOP is an effective treatment option for resistant AA. There were 6 reports involving 26 pediatric AA patients treated with psoralen and ultraviolet A therapy (strongest LoE 4). All adolescents showed partial responses.<sup>[15]</sup> In an RCT, a phototoxic regimen of topical PUVA (psoralen with ultraviolet light A) was found to be equally efficacious as intralesional steroid (ILS) with successful regrowth in 45% of cases.<sup>[49]</sup>

Excimer laser 308 nm was tried in children with recalcitrant AA and AT, with a 60% hair regrowth. Treatment was given twice weekly for 12 weeks, and there were no relapses 6 months after stopping the treatment.<sup>[50]</sup> In another study on the use of excimer laser in patients aged 12 years and above, good improvement was seen in patients with alopecia areata partialis (AAP) with no response in AT and AU after 24 sessions of treatment. Side effects included mild scalp erythema and desquamation.<sup>[51]</sup> Narrow-band ultraviolet B therapy was largely ineffective in pediatric patients,<sup>[52]</sup> similar to the results in adults.<sup>[15]</sup>

#### Cryotherapy

An RCT demonstrated superficial liquid nitrogen cryotherapy to be effective in managing recalcitrant AA.

Eight to ten seconds and dual freeze–thaw cycles were optimum, improving 76% of cases.<sup>[53]</sup> In a comprehensive retrospective review involving 353 patients, hair regrowth was seen in 60.9% of cases after 3 months. The response was superior when the treatment interval was less than 2 weeks and in the first occurrence of the disease.<sup>[54]</sup>

Although cryotherapy is less effective than topical and intralesional steroids, it has been an effective adjuvant modality along with topical steroids and contact immunotherapy for multiple patches and eyebrow lesions, respectively.<sup>[55-57]</sup>

#### Other treatment options

Plate-rich plasma (PRP) - A recent systematic review on the use of PRP for AA and AGA concluded that PRP is a safe and easy method of treatment with minimal adverse events and a low recurrence rate. Pain was the main side effect noted during PRP treatment. The highest efficacy in patients with AA was 76%, and the lowest efficacy was 31.7%.<sup>[58]</sup>

Compared with intralesional triamcinolone, some have found PRP to be less efficacious, whereas others have found it equally effective.<sup>[59,60]</sup>

Trichloroacetic acid (TCA) 35% and phenol 88% peels once in 3 weeks have been tried in multifocal patchy AA patients between 6 and 43 years of age and found to be efficacious with TCA showing higher efficacy and tolerability.<sup>[61,62]</sup>

Topical Janus kinase inhibitors - 2% tofacitinib and 1% ruxolitinib have shown some efficacy in AA patients in retrospective series and a pilot RCT.<sup>[62-64]</sup> However, conclusive efficacy data in AA is lacking, and large-scale RCTs are required.

#### Systemic therapy

Indications of systemic therapy are the following: rapidly progressive AA, multiple patches, alopecia totalis, AU, diffuse AA and AA incognita.

#### Systemic corticosteroids

Systemic corticosteroids are indicated in rapidly progressive disease, extensive disease, and children who do not respond to topical therapies. These can be used for the short term, 1 to 6 months and are beneficial in halting the progression of AA. Various studies have shown benefits in children, but randomized trials are lacking. It is tapered as soon as hair loss is stabilized. However, relapses are common.<sup>[24]</sup>

#### Intravenous pulse corticosteroid therapy

Various studies have shown poor outcomes in children, with 66% of patients having less than 30% regrowth after a median of 12 months.<sup>[65]</sup> Because the side effect profile of IV methylprednisolone is higher in children, it is reserved for recalcitrant cases only.

#### Oral pulse therapy

Oral mini pulse (OMP) therapy has shown efficacy in children with minimal side effects and is well tolerated in most patients. Oral prednisolone 5 mg/kg/month for 3 months in patients aged 3–11 years and 5 mg/kg twice/month for children more than 12 years have been used. In a study, results were seen in 60% of patients, and minimal side effects were reported except headache and giddiness in two patients.<sup>[24]</sup>

#### Oral immunosuppressive agents

##### Methotrexate

Methotrexate is shown to be efficacious when combined with oral steroids and is mainly used in children with severe AA. The response rate is poor in children, with only a 38.4% response rate.<sup>[66]</sup>

##### Azathioprine and cyclosporine

Azathioprine has been used at a dose of 2 mg/kg/day. It has been shown to have significant regrowth after 3 months.<sup>[67]</sup>

Cyclosporine helps to suppress T-helper cells and interferon-gamma (IFN- $\gamma$ ). So it is an effective drug for severe AA in children. However, its use in children is limited due to its serious side effects.<sup>[68]</sup>

#### Sulfasalazine and mesalazine (strongest LoE 4)

The role of sulfasalazine and mesalazine in the management of pediatric AA is limited. Only a single case series of five patients had a complete response with or without additional oral/topical steroids and minoxidil. They possibly exert their effect by affecting T lymphocytes.<sup>[24]</sup>

#### Biologics

It is seen that tumor necrosis factor (TNF)- $\alpha$  levels are elevated in AA patients. However, TNF antagonists are not effective in AA. Thus, no biologics are recommended for the treatment of AA. Biologics such as infliximab, etanercept, adalimumab, and efalizumab have been tried, and all of them were unsuccessful. Some showed worsening or occurring of AA while on treatment with biologics.<sup>[24]</sup>

#### JAK inhibitors

Tofacitinib is given in a dose of 5 mg once daily in children less than 6 years of age, for patients in the age group 6 to 12 years, tofacitinib can be started with 5mg once daily and can be increased to twice daily as per the response and 5 mg twice daily in children more than 12 years of age. It is seen that children on tofacitinib experience up to 80% hair growth in 6 months to 1 year, but chances of relapse are high after the stoppage of this drug.<sup>[69]</sup>

#### Complementary treatment

Complementary therapies with some evidence and efficacy in AA include studies on aromatherapy, topical garlic, oral glucosides of paeony with compound glycyrrhizin, hypnotherapy, and psychotherapy.<sup>[70]</sup>



## Hair prostheses (Wigs)

Hair prostheses or wigs improve the quality of life in patients with severe AA by boosting self-esteem and social adjustment. A recent study using objective parameters such as the Psychosocial Impact of Assistive Device Scale (PIADS) and Hair Specific Skindex-29 (Hairdex-29) reported that the use of wigs was associated with a positive effect on psychosocial aspects of severe AA patients.<sup>[71]</sup>

## Prognosis

The prognosis of AA can be variable. Spontaneous hair regrowth can occur in about 50–80% of patients with patchy alopecia. A subset of patients may not recover or may progress to AT or AU.<sup>[14]</sup>

- Poor prognostic factors are early age of onset, positive family history, history of atopy, associated autoimmune disease, long duration of the disease, alopecia totalis, AU, ophiasis pattern, and nail involvement.<sup>[14,72-75]</sup>

## SIG recommendations for screening investigations in children with AA

Appropriate investigations to rule out underlying associated autoimmune disease to be done on a case-to-case basis depending upon the accompanying symptoms.

## Quality of life (QOL)

The QOL of children with AA is impaired similar to adult patients. A recent study demonstrated around 76% of childhood AA cases had impaired QOL.<sup>[76]</sup>

## Counseling

It is important to counsel patients and families regarding the chronicity of AA and the relapsing and remitting nature of the disease. Because of the lack of an evidence-based treatment algorithm, we recommend counseling patients and their families on the wide range of severity and varied responses to treatment among different AA subtypes. Clinicians should also highlight the existence and impact of comorbidities, particularly co-occurring autoimmune conditions, such as vitiligo, which add to the psychological impact of an AA diagnosis and can have long-lasting effects on self-esteem during childhood. In addition, psychological support may be advised in patients with demonstrable symptoms of psychosocial disturbance.

## Future research directions in alopecia areata

Future research priorities include the following: Microbiome studies to identify mechanisms of the microbiome-associated induction and development of AA, roles of regulatory T cells and other immune cells in the pathogenesis of AA, genetic architecture studies to identify biomarkers, epigenetic studies of environmental factors that interact with gene expression, and identification of T-cell receptor (TCR) antigens and/or epitopes driving the disease.<sup>[77,78]</sup>

## Conclusion

AA is a chronic inflammatory disorder with a remitting and relapsing course. There are sparse interventional studies in pediatric AA. Clinicians have to choose from the limited available therapeutic options based on the extent of alopecia and possible side effects. There is a need for more interventional studies, especially RCTs to find out the efficacy and safety of various treatment modalities in the pediatric age group.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Wohlmuth-Wieser I, Osei JS, Norris D, Price V, Hordinsky MK, Christiano A, *et al.* Childhood alopecia areata-Data from the National alopecia areata registry. *Pediatr Dermatol* 2018;35:164-9.
2. Hegde SP, Naveen KN, Athanikar SB, Reshme P. Clinical and dermatoscopic patterns of alopecia areata: A tertiary care centre experience. *Int J Trichology* 2013;5:132-6.
3. Fonda-Pascual P, Vano-Galvan S, Garcia-Hernandez MJ, Camacho F. Alopecia areata sisaipho: Clinical and therapeutic approach in 13 patients in Spain. *Int J Trichology* 2016;8:99-100.
4. Alessandrini A, Starace M, Bruni F, Brandi N, Baraldi C, Misciali C, *et al.* Alopecia areata incognita and diffuse alopecia areata: Clinical, trichoscopic, histopathological, and therapeutic features of a 5-year study. *Dermatol Pract Concept* 2019;9:272-7.
5. Chelidze K, Lipner SR. Nail changes in alopecia areata: An update and review. *Int J Dermatol* 2018;57:776-83.
6. Lacarrubba F, Micali G, Tosti A. Scalp dermoscopy or trichoscopy. *Curr Probl Dermatol* 2015;47:21-32.
7. Waśkiel A, Rakowska A, Sikora M, Olszewska M, Rudnicka L. Trichoscopy of alopecia areata: An update. *J Dermatol* 2018;45:692-700.
8. Rakowska A, Zadurska M, Czuwara J, Warszawik-Hendzel O, Kurzeja M, Maj M, *et al.* Trichoscopy findings in loose anagen hair syndrome: Rectangular granular structures and solitary yellow dots. *J Dermatol Case Rep* 2015;9:1-5.
9. Dy LC, Whiting DA. Histopathology of alopecia areata, acute and chronic: Why is it important to the clinician? *Dermatol Ther* 2011;24:369-74.
10. Thomas EA, Kadyan RS. Alopecia areata and autoimmunity: A clinical study. *Indian J Dermatol* 2008;53:70-4.
11. Kasumagić-Halilović E. Thyroid autoimmunity in patients with alopecia areata. *Acta Dermatovenerologica Croatica* 2008;16:123-5.
12. Tan E, Tay YK, Glam YC. A clinical study of childhood alopecia areata in Singapore. *Pediatr Dermatol* 2002;19:298-301.
13. Xiao FL, Yang S, Liu JB, He PP, Yang J, Cui Y, *et al.* The epidemiology of childhood alopecia areata in China: A study of 226 patients. *Pediatr Dermatol* 2006;23:13-8.
14. Seetharam KA. Alopecia areata: An update. *Indian J Dermatol Venereol Leprol* 2013;79:563-75.
15. Meah N, Wall D, York K, Bhojru B, Bokhari L, Asz-Sigall D, *et al.* The Alopecia areata consensus of experts (ACE) study part II: Results of an international expert opinion on diagnosis and laboratory evaluation for alopecia areata. *J Am Acad*

- Dermatol 2021;84:1594-601.
16. Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, *et al.* National alopecia areata foundation. Alopecia areata investigational assessment guidelines-Part II. National alopecia areata foundation. *J Am Acad Dermatol* 2004;51:440-7.
  17. Kibar M, Aktan Ş, Lebe B, Bilgin M. Trichoscopic findings in alopecia areata and their relation to disease activity, severity and clinical subtype in Turkish patients. *Australas J Dermatol* 2015;56:e1-6.
  18. Waśkiel-Burnat A, Rakowska A, Sikora M, Olszewska M, Rudnicka L. Alopecia areata predictive score: A new trichoscopy-based tool to predict treatment outcome in patients with patchy alopecia areata. *J Cosmet Dermatol* 2020;19:746-51.
  19. Tkachenko E, Huang KP, Ko JM, Liu KJ, Scott DA, Senna MM, *et al.* Brigham eyebrow tool for alopecia: A reliable assessment of eyebrow alopecia areata. *J Investig Dermatol Symp Proc* 2020;20:S41-4.
  20. Wyrwich KW, Kitchen H, Knight S, Aldhouse NVJ, Macey J, Nunes FP, *et al.* Development of Clinician-reported outcome (ClinRO) and Patient-reported outcome (PRO) measures for eyebrow, eyelash and nail assessment in alopecia areata. *Am J Clin Dermatol* 2020;21:725-32.
  21. Wyrwich KW, Kitchen H, Knight S, Aldhouse NVJ, Macey J, Nunes FP, *et al.* The alopecia areata investigator global assessment scale: A measure for evaluating clinically meaningful success in clinical trials. *Br J Dermatol* 2020;183:702-9.
  22. Bartels NG, Jahnke I, Patzelt A, Richter H, Lademann J, Blume-Peytavi U. Hair shaft abnormalities in alopecia areata evaluated by optical coherence tomography. *Skin Res Technol* 2011;17:201-5.
  23. Cranwell WC, Lai VW, Photiou L, Meah N, Wall D, Rathnayake D, *et al.* Treatment of alopecia areata: An Australian expert consensus statement. *Australas J Dermatol* 2019;60:163-70.
  24. Barton VR, Toussi A, Awasthi S, Kiuru M. Treatment of pediatric alopecia areata: A systematic review. *J Am Acad Dermatol* 2022;86:1318-34.
  25. Lenane P, Macarthur C, Parkin PC, Krafchik B, DeGroot J, Khambalia A, *et al.* Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata in children: A randomized clinical trial. *JAMA Dermatol* 2014;150:47-50.
  26. Jung KE, Gye JW, Park MK, Park BC. Comparison of the topical FK506 and clobetasol propionate as first-line therapy in the treatment of early alopecia areata. *Int J Dermatol* 2017;56:1487-8.
  27. Torchia D, Schachner LA. Bilateral treatment for alopecia areata. *Pediatr Dermatol* 2010;27:415-6.
  28. Pascher F, Kurtin S, Andrade R. Assay of 0.2% fluocinolone acetonide cream for alopecia areata and totalis. *Dermatology* 1970;141:193-202.
  29. Tosti A, Iorizzo M, Botta GL, Milani M. Efficacy and safety of a new clobetasol propionate 0.05% foam in alopecia areata: A randomized, double-blind placebo-controlled trial. *J Eur Acad Dermatol Venereol* 2006;20:1243-7.
  30. Strazzulla LC, Wang EHC, Avila L, Lo Sicco K, Brinster N, Christiano AM, *et al.* Alopecia areata: An appraisal of new treatment approaches and overview of current therapies. *J Am Acad Dermatol* 2018;78:15-24.
  31. Strazzulla L, Avila L, Lo Sicco K, Shapiro J. Image gallery: Treatment of refractory alopecia universalis with oral tofacitinib citrate and adjunct intralesional triamcinolone injections. *Br J Dermatol* 2017;176:e125.
  32. Shapiro J. Current treatment of alopecia areata. *J Investig Dermatol Symp Proc* 2013;16:S42-4.
  33. Chang KH, Rojhirunsakool S, Goldberg LJ. Treatment of severe alopecia areata with intralesional steroid injections. *J Drugs Dermatol* 2009;8:909-12.
  34. Lee S, Kim BJ, Lee YB, Lee WS. Hair regrowth outcomes of contact immunotherapy for patients with alopecia areata: A systematic review and meta-analysis. *JAMA Dermatol* 2018;154:1145-51.
  35. Wasylyszyn T, Borowska K. Possible advantage of imiquimod and diphenylcyclopropenone combined treatment versus diphenylcyclopropenone alone: An observational study of nonresponder patients with alopecia areata. *Australas J Dermatol* 2017;58:219-23.
  36. Durdu M, Özcan D, Baba M, Seçkin D. Efficacy and safety of diphenylcyclopropenone alone or in combination with anthralin in the treatment of chronic extensive alopecia areata: A retrospective case series. *J Am Acad Dermatol* 2015;72:640-50.
  37. Wiseman MC, Shapiro J, MacDonald N, Lui H. Predictive model for immunotherapy of alopecia areata with diphenylpyrone. *Arch Dermatol* 2001;137:1063-8.
  38. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: Part II. Treatment. *J Am Acad Dermatol* 2010;62:191-202.
  39. Shapiro J, Tan J, Ho V, Abbott F, Tron V. Treatment of chronic severe alopecia areata with topical diphenylcyclopropenone and 5% minoxidil: A clinical and immunopathologic evaluation. *J Am Acad Dermatol* 1993;29:729-35.
  40. MacDonald Hull SP, Wood ML, Hutchinson PE, Sladden M, Messenger AG. Guidelines for the management of alopecia areata. *Br J Dermatol* 2003;149:692-9.
  41. Alkhalifah A. Topical and intralesional therapies for alopecia areata. *Dermatol Ther* 2011;24:355-63.
  42. Nasimi M, Ghandi N, Abedini R, Mirshamsi A, Shakoei S, Seirafi H. Efficacy and safety of anthralin in combination with diphenylcyclopropenone in the treatment of alopecia areata: A retrospective case series. *Arch Dermatol Res* 2019;311:607-13.
  43. Ibrahim SA, Esawy AM, Abdelshafy AS. Treatment of chronic extensive alopecia areata by diphenylcyclopropenone alone versus in combination with anthralin. *Dermatol Ther* 2019;32:e13010.
  44. Peloquin L, Castelo-Soccio L. Alopecia areata: An update on treatment options for children. *Paediatr Drugs* 2017;19:411-22.
  45. Fiedler-Weiss VC. Topical minoxidil solution (1% and 5%) in the treatment of alopecia areata. *J Am Acad Dermatol* 1987;16:745-8.
  46. Borchert M, Bruce S, Wirta D, Yoelin SG, Lee S, Mao C, *et al.* An evaluation of the safety and efficacy of bimatoprost for eyelash growth in pediatric subjects. *Clin Ophthalmol* 2016;10:419-29.
  47. Bhat S, Handa S, De D. A randomized comparative study of the efficacy of topical latanoprost versus topical betamethasone dipropionate lotion in the treatment of localized alopecia areata. *Indian J Dermatol Venereol Leprol* 2021;87:42-8.
  48. El-Ashmawy AA, El-Maadawy IH, El-Maghraby GM. Efficacy of topical latanoprost versus minoxidil and betamethasone valerate on the treatment of alopecia areata. *J Dermatolog Treat* 2018;29:55-64.
  49. El-Mofty M, Rasheed H, El-Eishy N, Hegazy RA, Hafez V, Shaker O, *et al.* A clinical and immunological study of phototoxic regimen of ultraviolet A for treatment of alopecia areata: A randomized controlled clinical trial. *J Dermatolog Treat* 2019;30:582-7.
  50. Al-Mutairi N. 308-nm excimer laser for the treatment of alopecia areata in children. *Pediatr Dermatol* 2009;26:547-50.
  51. Zakaria W, Passeron T, Ostovari N, Lacour JP,

- Ortonne JP. 308-nm excimer laser therapy in alopecia areata. *J Am Acad Dermatol* 2004;51:837-8.
52. Jury CS, McHenry P, Burden AD, Lever R, Bilsland D. Narrowband Ultraviolet B (UVB) phototherapy in children. *Clin Exp Dermatol* 2006;31:196-9.
  53. Abdel Motaleb AA, Sayed DS. Different freezing time of superficial liquid nitrogen cryotherapy in treatment of recalcitrant alopecia areata: Randomized clinical trial. *Dermatol Ther* 2020;33:e13640.
  54. Jun M, Lee NR, Lee WS. Efficacy and safety of superficial cryotherapy for alopecia areata: A retrospective, comprehensive review of 353 cases over 22 years. *J Dermatol* 2017;44:386-93.
  55. Amirnia M, Mahmoudi SS, Karkon-Shayan F, Alikhah H, Piri R, Naghavi-Behzad M, *et al.* Comparative study of intralesional steroid injection and cryotherapy in alopecia areata. *Niger Med J* 2015;56:249-52.
  56. Jun M, Lee WS. Therapeutic effect of superficial cryotherapy on alopecia areata: A prospective, split-scalp study in patients with multiple alopecia patches. *Ann Dermatol* 2017;29:722-7.
  57. Choe SJ, Lee WS. Efficacy of superficial cryotherapy on the eyebrows of patients with alopecia universalis also treated with contact immunotherapy on the scalp: A prospective, split-face comparative study. *Int J Dermatol* 2017;56:184-9.
  58. Roohaninasab M, Goodarzi A, Ghassemi M, Sadeghzadeh-Bazargan A, Behrangi E, NajarNobari N. Systematic review of platelet-rich plasma in treating alopecia: Focusing on efficacy, safety, and therapeutic durability. *Dermatol Ther* 2021;34:e14768.
  59. Kapoor P, Kumar S, Brar BK, Kukar N, Arora H, Brar SK. Comparative evaluation of therapeutic efficacy of intralesional injection of triamcinolone acetonide versus intralesional autologous platelet-rich plasma injection in alopecia areata. *J Cutan Aesthet Surg* 2020;13:103-11.
  60. Balakrishnan A, Joy B, Thyvalappil A, Mathew P, Sreenivasan A, Sridharan R. A comparative study of therapeutic response to intralesional injections of platelet-rich plasma versus triamcinolone acetonide in alopecia areata. *Indian Dermatol Online J* 2020;11:920-4.
  61. Mahgoub D, MohyeEldeen R, Saadi D, El-Samanoudy S, Ibrahim S. Clinical and trichoscopic evaluation of trichloroacetic acid 35% vs phenol 88% peels in treatment of alopecia areata. *J Cosmet Dermatol* 2021;20:143-9.
  62. Wang EHC, Sallee BN, Tejada CI, Christiano AM. JAK inhibitors for treatment of alopecia areata. *J Invest Dermatol* 2018;138:1911-6.
  63. Bayart CB, DeNiro KL, Brichta L, Craiglow BG, Sidbury R. Topical Janus kinase inhibitors for the treatment of pediatric alopecia areata. *J Am Acad Dermatol* 2017;77:167-70.
  64. Bokhari L, Sinclair R. Treatment of alopecia universalis with topical Janus kinase inhibitors—a double blind, placebo, and active controlled pilot study. *Int J Dermatol* 2018;57:1464-70.
  65. Friedli A, Labarthe MP, Engelhardt E, Feldmann R, Salomon D, Saurat JH. Pulse methylprednisolone therapy for severe alopecia areata: An open prospective study of 45 patients. *J Am Acad Dermatol* 1998;39:597-602.
  66. Joly P. The use of methotrexate alone or in combination with low doses of oral corticosteroids in the treatment of alopecia totalis or universalis. *J Am Acad Dermatol* 2006;55:632-6.
  67. Farshi S, Mansouri P, Safar F, Khiabanloo SR. Could azathioprine be considered as a therapeutic alternative in the treatment of alopecia areata? *Int J Dermatol* 2010;49:1188-93.
  68. Shapiro J, Lui H, Tron V, Ho V. Systemic cyclosporine and low dose prednisone in the treatment of chronic severe alopecia areata: A clinical and immunopathologic evaluation. *J Am Acad Dermatol* 1997;36:114-7.
  69. Craiglow BG, King BA. Tofacitinib for the treatment of alopecia areata in preadolescent children. *J Am Acad Dermatol* 2019;80:568-70.
  70. Tkachenko E, Okhovat J-P, Manjaly P, Huang KP, Senna MM, Mostaghimi A. Complementary & alternative medicine for alopecia areata: A systematic review. *J Am Acad Dermatol* 2019;S0190-9622 (19) 33304-3.
  71. Park J, Kim DW, Park SK, Yun SK, Kim HU. Role of hair prostheses (Wigs) in patients with severe alopecia areata. *Ann Dermatol* 2018;30:505-7.
  72. Uchiyama M, Egusa C, Hobo A, Irisawa R, Yamazaki M, Tsuboi R. Multivariate analysis of prognostic factors in patients with rapidly progressive alopecia areata. *J Am Acad Dermatol* 2012;67:1163-73.
  73. Jiménez-Herrera EA, Rios-Garza Z, Peralta-Pedrero ML, Jurado-Santa Cruz F, Morales-Sánchez MA. Prognostic factors in Mexican patients with patchy and other types of alopecia areata. *Skin Appendage Disord* 2020;6:296-303.
  74. Cho HH, Jo SJ, Paik SH, Jeon HC, Kim KH, Eun HC, *et al.* Clinical characteristics and prognostic factors in early-onset alopecia totalis and alopecia universalis. *J Korean Med Sci* 2012;27:799-802.
  75. Alabdulkareem AS, Abahusseini AA, Okoro A. Alopecia areata: Prognostic factors. *Ann Saudi Med* 1996;16:87-9.
  76. Vélez-Muñoz RDC, Peralta-Pedrero ML, Jurado-Santa Cruz F, Morales-Sánchez MA. Psychological profile and quality of life of patients with alopecia areata. *Skin Appendage Disord* 2019;5:293-8.
  77. Hon KL, Luk DCK, Leung AKC, Ng C, Loo SKF. Childhood alopecia areata: An overview of treatment and recent patents. *Recent Pat Inflamm Allergy Drug Discov* 2020;14:117-32.
  78. Ellison A, Kranz D, Mesinkovska NA, Christiano AM, Shapiro J, Norris DA. Forging the future: 2018 alopecia areata research summit summary report. *J Investig Dermatol Symp Proc* 2020;20:S1-5.