




Current Diagnostic and Therapeutic Practices in Alopecia Areata in Two Mediterranean Countries: A Survey-Based Study

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Received: January 29, 2024 / Accepted: March 11, 2024 / Published online: April 10, 2024
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ABSTRACT

Introduction: Alopecia areata (AA) affects approximately 2% of the general population and is associated with significant psychosocial morbidity and poor health-related quality of

life. Despite the high incidence of the disease the available clinical practice guidelines to help clinicians and improve patients' care are very poor and of a low methodological quality, as compared to other high-burden dermatoses. The aim of this survey is to capture the current clinical practice in AA management, as performed by dermatologists, in two

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s13555-024-01141-z>.

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Mediterranean countries to identify potential disparities and gaps in diagnosis and treatment.

Methods: A 50-item questionnaire was created in the English language and then translated into Greek and Italian language and sent to the Greek and Italian dermatologists via email.

Results: A total of 490 dermatologists from Italy and 234 from Greece participated in the survey. The diagnosis of AA is usually based on history and clinical examination, supported by trichoscopy. The rate of use of severity scores and scales to evaluate impact on quality of life by dermatologists was low. Treatment of patchy AA, in both adult and pediatric populations, is based on use of topical steroids as first-line treatment. Results on special site involvement (eyebrows, beard, and ophiasis), chronic cases, and the pediatric population highlight extreme heterogeneity in treatment approach.

Conclusions: Our results highlight that management of AA, in terms of diagnosis and treatment, is still challenging.

Keywords: Alopecia areata; Diagnosis; Management; Treatment

Key Summary Points

Alopecia areata (AA) is a common disorder that affects approximately 2% of the general population and is associated with strong psychosocial morbidity and poor health-related quality of life.

The available guidelines regarding the management of AA are outdated, very poor, and of a low methodological quality.

Capturing the current clinical practice in AA management in two Mediterranean countries is useful to identify potential disparities and gaps in diagnosis and treatment.

The management of AA in pediatric patients, chronic cases, and special areas is still challenging for a lot of dermatologists.

INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder characterized by non-scarring hair loss that affects approximately 2% of the general population, including all ethnic, gender, and age groups [1–3]. The disease results in significant psychosocial morbidity and poor health-related quality of life (QoL) [4–7]. Clinical manifestations of AA vary from a few, well-defined patches of alopecia to extensive scalp or body involvement [1].

Current treatments result in varying responses and are characterized by frequent relapses, reflecting the unmet clinical need. The level of evidence and strength of recommendation for their use are comparatively weak because of the lack of robust data and well-designed randomized controlled trials (RCTs). The latter obstacle is magnified when referring to the pediatric and adolescent population [8]. Recent advances in the field of AA have resulted in the development of a new class of drugs, the Janus kinase inhibitors (JAKi), that have shown promising results [9, 10].

Despite the high incidence of AA in the general population, the available clinical practice guidelines to help clinicians and improve patients' care are very poor and of a low methodological quality, as compared to other high-burden dermatoses [11, 12]. The latter paucity may result in a vague management landscape, turning the appropriate handling of AA into a challenging issue.

This survey-based study aimed towards capturing the current clinical practice/landscape of AA management, as performed by dermatologists, in two Mediterranean countries (Greece and Italy), in an effort to identify potential disparities and gaps in diagnosis and treatment of AA in different age groups and different clinical types of the disease.

METHODS

A 50-item questionnaire was created in the English language by a group of experts in Italy and Greece and was used to serve the aims of the

study. The questionnaire was created in the English language, with the help of a native English speaker and translated into Greek and Italian languages, by Greek and Italian dermatologists, respectively (native speakers with excellent knowledge of the English language), and it received ethics approval from the Ethics Committee of The Medical School of The Aristotle University of Thessaloniki (protocol number 33/2022). The link to access the questionnaire was sent by email to dermatologist members of the National Societies of Dermatology (SIDE-MAST in Italy and HSDV in Greece). The dermatologists were asked to fill in the online survey anonymously to decrease biases. The web-based survey was conducted using a 50-question online form via Google Forms (Google LLC, Mountain View, CA, USA). The questionnaire was composed of three main parts: the first part included information about the demographics and work setting of the dermatologist, the second part referred to AA diagnosis and workup upon diagnosis, and the third part referred to AA treatment in different age groups and different disease topography. We analyzed the obtained data by performing descriptive analysis using Microsoft Excel 16.29 version. The questionnaire items are listed in the supplementary materials. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

Demographic Information and Work Setting

A total of 724 dermatologists, 490 from Italy and 234 from Greece, participated in the survey. Table 1 summarizes the participants' profiles.

Diagnosis and Workup

Most dermatologists (62.8%) based the diagnosis of AA on the history and clinical examination, while 37.2% declared the use of additional diagnostic tools, like trichoscopy (85.9%).

Scoring scales to record the disease severity and to evaluate the psychosocial impact of the

disease on patients' lives were used only by 21.9%, and 20.1%, respectively. Table 2 summarizes the requested laboratory examinations upon diagnosis, and the results regarding scoring indexes and additional diagnostic and follow-up tools.

Management of Patients Older than 12 Years of Age

Table 3 summarizes the results regarding management of patients older than 12 years of age.

Scalp Patchy Alopecia (< 50% involvement)

The most common first-line choice were topical steroids (69.7%) alone or in combination with topical calcineurin inhibitor (13.7%). As second-line treatment, intralesional steroid injection (36.1%) and systemic administration of steroids (28.3%) were preferred. As third-line treatment, systemic administration of steroids (26.6%) and systemic JAK inhibitors (10.5%) were the most reported therapeutic modalities. Interestingly, 8.9% of dermatologists reported that they do not prescribe any other treatment, if first- and second-line treatments fail.

Ophiasis

The preferred first treatment options were topical (32.2%) and systemic steroids (29.8%). As second-line treatment, systemic administration of steroids (21.6%), intralesional steroid injection (16.8%), and local immunotherapy (15.1%) were the most popular. As third-line treatment, a high rate of physicians (18.3%) declared no further treatment, followed by the use of systemic JAK inhibitors (14.4%).

Alopecia of the Beard

Topical steroid was the most preferred as first-line treatment (72.3%), whilst there was a diversity in the second-line modalities, with intralesional steroids (32.5%), combination of topical steroids with topical calcineurin

Table 1 Demographic information of participants

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Gender				
Male	42.9%	37.7%	298 (41.2%)	723
Female	57.1%	62.2%	425 (58.8%)	
Age				
20–29	2%	0.9%	12 (1.6%)	723
30–39	18.4%	12.9%	120 (16.6%)	
40–49	12.2%	37.3%	147 (20.3%)	
50–59	28.6%	32.2%	215 (29.7%)	
60–69	38.8%	16.7%	229 (31.6%)	
Working environment				
Private office	49%	65.2%	392 (54.2%)	723
Hospital	16.3%	20.2%	127 (17.6%)	
Both	34.7%	14.6%	204 (28.2%)	
Years of practicing as a specialist				
< 10	20.4%	32.3%	175 (24.2%)	722
10–20	20.4%	37.5%	187 (25.9%)	
> 20	59.2%	30.2%	360 (49.9%)	

inhibitor (16.0%), and monotherapy with topical calcineurin inhibitors (15.3%) being the most popular. Interestingly, 19.8% of the dermatologists declared no further treatment, after failure of the first and the second approach.

Alopecia of the Eyebrows

The most commonly reported first-line treatment was topical steroids (59.1%). As second-line treatment, topical calcineurin inhibitors (18.5%), intralesional steroid injection (17.0%), and topical steroids application (16.6%) were usually prescribed. After failure of the second step, the majority of physicians (27.2%) declared they do not continue with any kind of treatment.

AA Totalis

Systemic (43.1%) followed by topical steroids (18.9%) were the top two choices, as a first-line approach. After first-choice failure, second-line treatments included systemic cyclosporine (15.4%), local immunotherapy (14.8%), and systemic steroids (14.6%). As third-line treatment option, systemic JAK inhibitors (31.7%) were the most preferred.

AA Universalis

For alopecia universalis the first treatment option was systemic steroids (36.4%). Surprisingly, 13.7% of the dermatologists would not prescribe any treatment even at baseline. The second most reported choice was systemic JAK

Table 2 Results regarding diagnosis and workup

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Diagnosis				
Only history and clinical examination				
Yes	63.3%	61.8%	454 (62.8%)	723
No (use also other tools)	36.7%	38.2%	269 (37.2%)	
Biopsy				
Yes	0	0.8%	2 (0.3%)	724
No	100%	99.1%	722 (99.7%)	
Trichogram				
Yes	8.2%	3%	47 (6.5%)	723
No	91.8%	97%	676 (93.5%)	
Other tests/workup				
Mycological test to rule out fungal infections				
Yes	4.1%	5.1%	32 (4.4%)	724
No	95.9%	94.9%	692 (95.5%)	
Blood tests				
Yes	87.8%	76.0%	84.0%	724
No	6.1%	10.7%	55 (7.6%)	
Only if the patient is scheduled for systemic treatment	6.1%	13.3%	61 (8.4%)	
Blood tests performed				
Thyroid function markers and antibodies	93.5%	96.4%	616 (94.3%)	653
CBC	87%	86.5%	567 (86.8%)	
ANA	82.6%	68.4%	512 (78.4%)	
AB anti-TG and anti-EMA	65.2%	11.9%	323 (49.5%)	
Indicators of inflammation	56.5%	61.1%	378 (57.9%)	
Dermatoscopy				
Yes	89.8%	77.8%	622 (85.9%)	724
No	2%	3.4%	18 (2.4%)	
Sometimes	8.2%	18.8%	84 (11.6%)	

Table 2 continued

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Severity scores				
Yes	26.5%	12.1%	158 (21.9%)	721
No	73.5%	87.9%	563 (78.1%)	
Scores used				
SALT	100%	96.4%	157 (99.4%)	158
SSA	0%	3.6%	1 (0.6%)	
ALODEX	0%	7.1%	2 (1.3%)	
AASI	15.4%	14.3%	24 (15.2%)	
QoL scales				
Yes	20.4%	19.5%	145 (20.1%)	721
No	79.6%	80.5%	576 (79.9%)	
Scales used				
DLQI	100%	91.1%	141 (97.2%)	145
Hairdex	0%	15.6%	7 (4.8%)	
PHQ 9	0%	4.4%	2 (1.4%)	
GAD 7	0%	4.4%	2 (1.4%)	
Other	10%	4.4%	12 (8.3%)	
Evaluation of AA activity				
Clinical overview only	46.9%	49.6%	346 (47.8%)	724
Pull test	65.3%	87.6%	525 (72.5%)	
Trichoscopy	87.8%	82.9%	624 (86.2%)	
Trichogram	10.2%	4.3%	60 (8.3%)	
Histology	6.1%	5.1%	42 (5.8%)	
Imaging for follow-up				
Clinical photos only	16.3%	15.9%	117 (16.2%)	722
Clinical and dermatoscopic photos	63.3%	62.1%	454 (62.9%)	
Not use any imaging method	20.4%	22.0%	151 (20.9%)	

AA alopecia areata, *ANA* antinuclear antibodies, *CBC* cell blood count, *Anti-TG* anti-tissue transglutaminase antibodies, *Anti-EMA* anti-endomysial antibodies, *SALT* Severity of ALoppecia Tool, *SSA* Scalp Surface Area, *ALODEX* Alopecia Density and Extent, *AASI* Alopecia Areata Severity Index, *DLQI* Dermatology Life Quality Index, *PHQ-9* Patient Health Questionnaire-9, *GAD-7* General Anxiety Disorder-7

Table 3 Results regarding management of patients older than 12 years of age

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Patchy alopecia < 50% involvement				
First-line treatment				
Topical steroids	77.6%	53.0%	503 (69.7%)	722
Topical steroid + topical calcineurin inhibitor	10.2%	21.1%	99 (13.7%)	
Intralesional steroid injection	8.2%	12.1%	68 (9.4%)	
Second-line treatment				
Intralesional steroid injection	28.6%	51.9%	260 (36.1%)	721
Systemic steroids	36.7%	10.4%	204 (28.3%)	
Third-line treatment				
Systemic steroids	27.7%	24.3%	185 (26.6%)	696
Systemic JAK inhibitors	10.6%	10.2%	73 (10.5%)	
No treatment	8.5%	9.7%	62 (8.9%)	
Intralesional steroid injection	4.3%	11.1%	45 (6.5%)	
AA of the beard				
First-line treatment				
Topical steroids	77.6%	61.2%	522 (72.3%)	722
Intralesional steroid injection	6.1%	13.8%	62 (8.6%)	
Topical steroid + topical calcineurin inhibitor	0	17.2%	40 (5.5%)	
Second-line treatment				
Intralesional steroid injection	25%	48.1%	231 (32.5%)	711
Topical steroid + topical calcineurin inhibitor	16.7%	14.7%	114 (16.0%)	
Topical calcineurin inhibitors	16.7%	12.5%	109 (15.3%)	
Third-line treatment				
Systemic steroids	28.3%	18.1%	170 (24.9%)	682
No treatment	19.6%	20.3%	135 (19.8%)	
Topical steroid + topical calcineurin inhibitor	15.2%	4.1%	79 (11.5%)	
AA of the eyebrows				
First-line treatment				

Table 3 continued

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Topical steroids	61.2%	54.7%	428 (59.1%)	724
Topical calcineurin inhibitors	18.4%	14.5%	124 (17.1%)	
Intralesional steroid injection	12.2%	5.6%	73 (10.1%)	
Second-line treatment				
Topical calcineurin inhibitors	18.4%	19.0%	134 (18.5%)	722
Intralesional steroid injection	14.3%	22.8%	123 (17.0%)	
Topical steroids	22.4%	4.3%	120 (16.6%)	
Third-line treatment				
No treatment	25%	31.7%	180 (27.2%)	661
Local immunotherapy	15.9%	2.3%	75 (11.3%)	
Intralesional steroid injection	6.8%	14.0%	61 (9.2%)	
Ophiasis				
First-line treatment				
Topical steroids	34.7%	26.8%	232 (32.2%)	721
Systemic steroids	34.7%	19.5%	215 (29.8%)	
Intralesional steroid injection	12.2%	22.1%	111 (15.4%)	
Second-line treatment				
Systemic steroids	23.9%	17.0%	149 (21.6%)	689
Intralesional steroid injection	15.2%	20.1%	116 (16.8%)	
Local immunotherapy	19.6%	6.1%	104 (15.1%)	
Third-line treatment				
No treatment	18.2%	18.7%	122 (18.3%)	664
Other	20.5%	7.6%	107 (16.1%)	
Systemic JAK inhibitors	11.4%	20.5%	96 (14.4%)	
AAT				
First-line treatment				

Table 3 continued

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Systemic steroids	49%	30.4%	310 (43.1%)	720
Topical steroids	24.5%	7.0%	136 (18.9%)	
Local immunotherapy	10.2%	8.7%	70 (9.7%)	
Second-line treatment				
Systemic cyclosporine	13%	20.9%	105 (15.4%)	683
Local immunotherapy	19.6%	4.9%	101 (14.8%)	
Systemic steroids	15.2%	13.4%	100 (14.6%)	
Third-line treatment				
Systemic JAK inhibitors	36.4%	22.2%	207 (31.7%)	652
Other	20.5%	9.4%	110 (16.9%)	
No treatment	6.8%	6.6%	95 (14.6%)	
AAU				
First-line treatment				
Systemic steroids	36.7%	35.6%	262 (36.4%)	720
No treatment	14.3%	12.6%	99 (13.7%)	
Systemic cyclosporine	8.2%	12.2%	68 (9.4%)	
Second-line treatment				
No treatment	23.8%	18.2%	139 (21.9%)	634
Systemic JAK inhibitors	21.4%	21.5%	136 (21.4%)	
Systemic cyclosporine	16.7%	18.2%	109 (17.2%)	
Third-line treatment				
No treatment	38.5%	45.6%	244 (40.9%)	596
Systemic JAK inhibitors	20.5%	20.9%	123 (20.6%)	
Other	20.5%	10.7%	42 (7.0%)	

inhibitors (21.5%). The rate of physicians who declared they would not proceed with a second treatment was 21.9%, which reached 40.9%

after failure of the first two lines of treatment. In this last scenario, 20.6% reported they would prefer systemic JAK inhibitors.

Table 4 Results regarding management of patients younger than 12 years of age

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Patchy alopecia < 50% involvement				
First-line treatment				
Topical steroids	79.6%	70.6%	553 (76.7%)	721
Topical steroid + topical calcineurin inhibitor	2%	16.0%	47(6.5%)	
Second-line treatment				
Topical calcineurin inhibitors	27.7%	19.6%	175 (25.0%)	699
Topical steroid + topical calcineurin inhibitor	8.5%	24.0%	95 (13.5%)	
Topical irritants (e.g., anthralin, dithranol)	12.8%	11.8%	87 (12.4%)	
Topical steroids	12.8%	5.2%	72 (10.3%)	
Third-line treatment				
No treatment	30.2%	31.0%	197 (30.4%)	646
Systemic steroids	7%	12.5%	57 (8.8%)	
Topical immunotherapy	18.6%	3.7%	88 (10.5%)	
AA of the eyebrows				
First-line treatment				
Topical steroids	59.2%	59.6%	424 (59.3%)	718
Topical calcineurin inhibitors	18.4%	18.4%	132 (18.4%)	
Second-line treatment				
Topical calcineurin inhibitors	31.1%	24.9%	197 (29.0%)	679
Topical steroid + topical calcineurin inhibitor	13.3%	25.3%	118 (17.4%)	
Third-line treatment				
No treatment	25%	46.6%	197 (32.4%)	608
Other	20%	9.62%	100 (16.4%)	
Topical steroid + topical calcineurin inhibitor	15%	13.9%	89 (14.6%)	
Ophiasis				
First-line treatment				

Table 4 continued

	Italy (<i>N</i> = 490) (%)	Greece (<i>N</i> = 234) (%)	Overall population (<i>N</i> = 724) <i>N</i> (%)	Number of dermatologists that answered
Topical steroids	75.5%	49.8%	484 (67.3%)	719
Topical steroid + topical calcineurin inhibitor	6.1%	20.5%	77 (10.7%)	
Second-line treatment				
Topical calcineurin inhibitors	28.3%	15.0%	164 (23.9%)	687
Topical steroid + topical calcineurin inhibitor	13%	18.5%	102 (14.8%)	
Intralesional steroid injection	2.2%	14.5%	43 (6.2%)	
Third-line treatment				
No treatment	31.8%	38.0%	221(33.8%)	653
Other	20.5%	12.7%	117 (17.9%)	
Systemic steroids	13.6%	11.7%	85 (13.0%)	
AAT				
First-line treatment				
Topical steroids	28.6%	20.35%	186 (26.6%)	698
Systemic steroids	22.4%	19.0%	153 (21.9%)	
Second-line treatment				
Systemic steroids	18.6%	9.4%	100 (15.6%)	642
No treatment	14%	22.6%	108 (16.8%)	
Third-line treatment				
No treatment	31%	42.3%	212 (34.5%)	614
Other	26.2%	13.4%	136 (22.1%)	
AAU				
First-line treatment				
Systemic steroids	34.7%	30.0%	238 (33.2%)	717
No treatment	16.3%	19.4%	124 (17.3%)	
Second-line treatment				
No treatment	28.6%	37.6%	194 (31.4%)	617
Other	16.7%	11.7%	93 (15.1%)	
Third-line treatment				
No treatment	33.3%	56.7%	232 (40.7%)	570
Other	30.8%	13.3%	144 (7.0%)	

Management of Patients Younger than 12 Years of Age

Scalp Patchy Alopecia (< 50% involvement)

The most common first-line treatments were topical steroids (76.7%) and combination of topical steroid with topical calcineurin inhibitor (6.5%). As second therapeutic options, topical application of calcineurin inhibitor (25.0%), combination of topical steroid with topical calcineurin inhibitor (13.5%), and topical irritants (12.4%), such as dithranol, were the most popular treatments. As third-line treatment, most dermatologists (30.4%) declared no further treatment, while 10.5% and 8.8% reported prescription of topical immunotherapy and systemic steroids, respectively.

Ophiasis

In children under 12 years old, the first treatment option was topical steroids (67.3%) and topical steroids with topical calcineurin inhibitor application (10.7%). After failure of the first treatment, the second most reported treatments were topical calcineurin inhibitors (23.9%), topical steroids with topical calcineurin inhibitor combination (14.8%), and intralesional steroid injection (6.2%), while as third-line treatment, the use of systemic steroids was reported by 13.0% of the participants. A high rate of physicians (33.8%) declared they do not proceed with a third therapeutic attempt after failure of the first two.

Alopecia of the Eyebrows

Topical steroids (59.3%) and topical calcineurin inhibitors (29.0%) were the most preferable first- and second-line treatments in this localization. After failure of two therapeutic interventions, the majority of physicians (32.4%) reported no further treatment.

AA Totalis

Topical steroids (26.6%) followed by systemic steroids (21.9%) were the first-choice treatments of preference. After failure of the first therapeutic attempt, the most commonly reported second treatment options were no further treatment by 16.8% and systemic steroids by 15.6% of dermatologists. After failure of the first two therapeutic attempts, 34.5% of the physicians declared they do not proceed with any other modalities.

AA Universalis

In patients with AA involving all hair-bearing areas, the first reported treatment option was systemic administration of steroids (33.2%). The percentage of dermatologists declaring they do not prescribe any treatment from the first visit was 17.3%. Similarly, 31.4% of those that start with a treatment are not willing to continue with a second attempt if the first therapeutic modality fails. The latter rate increased to 40.7% after failure of the second therapeutic attempt. Table 4 summarizes the results regarding management of patients less than 12 years of age.

DISCUSSION

Our results highlight that management of AA, in terms of diagnosis and treatment, is still challenging and the available guidelines are outdated. According to our records, there are numerous fields, especially in regard to treatment choices of AA in pediatric population, in chronic cases and in special localization, in which there is a significant diversity in specialists' approaches.

We recorded a broad use of trichoscopy in clinical practice in both Greece and Italy [3, 14, 15]. Despite the high level of evidence supporting trichoscopy as an effective, easy-to-apply, and cheap diagnostic tool for the evaluation of AA, the method has been incorporated only into the Italian guidelines. Integration of trichoscopy in all guidelines is a need that

would act towards harmonization in the way dermatologists handle patients with AA [13, 16].

On the other hand, trichogram was chosen only by 6.5% of dermatologists. Indeed, nowadays trichogram tends to be replaced by trichoscopy, which is a non-invasive technique and gives more information regarding the activity of the disease [17, 18].

Regarding blood tests upon diagnosis, about half (49.5%) of the dermatologists follow the recommendation for investigation of celiac disease with a laboratory search for antibodies [13, 14].

A recent meta-analysis found that serum interleukin-6 (IL-6) and C-reactive protein (CRP) levels are significantly increased in patients with AA, compared to healthy controls, whilst serum vitamin D levels are significantly decreased [19]. More than half of Greek and Italian dermatologists prescribe indicators of inflammation (57.9%) such as CRP, while dosage of serum IL-6 is not usually prescribed.

On the basis of our results, dermatologists in Italy and Greece are not familiar with the use of scoring scales, since only 21.9% declared their use in daily practice. The low integrity of measuring tools in both private and public settings is not surprising, since these practices are generally time-consuming and increase the workload of the physicians [20]. However, measuring AA severity with the use of scoring systems is fundamental because the percentage of scalp involvement drives treatment decisions. Moreover, SALT score is the strongest predictor of long-term outcomes, especially in severe forms. A complete assessment of patients with AA should also include evaluation of the disease impact on patient's QoL [21, 22]. In our survey only two out of 10 participants declared the use of any tool to evaluate psychosocial impact on patients' lives. Among them the most popular index was the DLQI. The very low use of indexes could potentially result in "under-grading" of AA severity, since as doctors, we may fail to capture the overall burden of disease. In this context, familiarization of physicians with the use of at least DLQI and SALT score is essential, in order to improve holistic grading of AA severity, facilitate treatment decisions, and

optimize follow-up. In this context, development of fast and easy-to-apply tools is highly needed.

Impressively, 20.9% of the respondents declared they do not use any imaging documentation, neither for grading nor for follow-up, even if there is cumulative evidence supporting the use of digital photography to quantify and evaluate hair loss [23–27].

Management of Patients Older than 12 Years of Age

Interestingly, even though guidelines recommend intralesional steroids in localized AA [28], only 9.4% of the participants declared their use as first-line treatment. Another surprising point emerging from our study was the use of combination of topical steroid and topical calcineurin inhibitor as first-choice treatment by 13.7% of the dermatologists, although it has been proven that neither topical pimecrolimus nor tacrolimus has any beneficial effect on AA [29–31]. Intralesional steroid injection (36.1%) and systemic administration of steroids (28.3%) were chosen as second-line treatment. The existing guidelines stress that systemic glucocorticoids should be only used as a temporary measure to constrain rapidly progressing active disease. Even if topical immunotherapy is recommended by guidelines, especially in chronic stages or in patients not responding to topical corticosteroids, their use remains low among Italian and Greek dermatologists. Only one out of 10 (10.5%) physicians reported the use of systemic JAK inhibitors as a treatment option, and only after failure of the previous two modalities.

In AA of the beard, the first and second treatment options reported were topical and intralesional steroid injection, respectively, confirming what is recommended by the existing literature [32, 33]. The use of topical steroids is not the best option for long-term use in this area, as a result of adverse event like folliculitis [16], and a meta-analysis of 12 studies, according to the British Association of Dermatologists' guidelines, reported intralesional triamcinolone acetonide as the most effective treatment in

patients with limited AA and short course of disease [34]. The use of topical calcineurin, in association or not with topical steroids, was chosen by several dermatologists, even if it is well known that topical calcineurin inhibitors are not effective in AA. In addition, two out of 10 decide not to prescribe any treatment, highlighting that the management of AA of special sites, like beard, is still difficult for dermatologists.

In alopecia of the eyebrows the most common first-line treatments were topical steroids (59.1%) and calcineurin inhibitors (17.1%), whilst after failure of the second treatment, three out of 10 (27.2%) physicians declared they do not proceed with any other modality. These results reflect the lack of safe and effective treatment options for AA involving special sites. Even though topical and intralesional steroids have been linked to several site-related adverse events, they are—thus far—considered the most widely accepted therapeutic modalities. It has been documented that intralesional corticosteroids may cause cataract and elevation of intraocular pressure [35].

In ophiasis, systemic corticosteroids have shown good results; however, in our study, they were chosen as first-line treatment only by 29.8% of the dermatologists [36–38]. The treatment of choice in AA totalis, as declared by 43.1% of the respondents, was systemic corticosteroids. The Italian guidelines suggest topical corticosteroids under occlusion or systemic corticosteroids if there are signs of activity, whilst in the chronic phase the recommendation is the use of topical immunotherapy. In our survey only a minority of physicians reported the use of local immunotherapy (9.7%) in AA totalis. In a similar manner, despite the favorable outcomes with the use of JAK inhibitors in moderate and severe AA, these drugs represented the most preferred treatment only as a third option (31.7%) [39, 40].

The responses regarding treatment of AA universalis were similar to AA totalis. Unexpectedly, a large number of dermatologists (21.9%) declared they would not prescribe any treatment as first line, whilst only a small percentage of them would apply topical immunotherapy. These inconsequential results

are associated not only with a potential gap of knowledge in the field of AA therapeutics by the dermatologists but also to the lack of widely accepted, harmonized guidelines and the lack of robust data and RCTs in AA treatment.

Management of Patients Younger than 12 Years of Age

Although the majority of children with limited AA recover spontaneously, the variability of the disease course and the unpredictable response to therapy make AA challenging to treat.

In patchy alopecia, topical steroids were the most popular (76.7%), confirming what is recommended by the existing guidelines [11, 41, 42, 43]. Topical immunotherapy, which is also strongly supported in this age group, was chosen only by 10.5% of dermatologist, as a third-line option [37, 44, 45]. Topical calcineurin inhibitors, with or without topical steroids, were also popular choices (25.3% and 13.5%, respectively). While Jung et al. [46] and Sotiriou et al. [47] observed hair regrowth after topical application of tacrolimus in children with AA, in a study performed by Price et al. [30], topical application of tacrolimus 0.1% proved ineffective in both adults and children with AA. According to the Alopecia Areata Expert Consensus, intralesional corticosteroids are recommended for children older than 13 years of age with limited AA (SALT 0–30%) [43]. Italian guidelines suggest intralesional corticosteroids for children over 10 years of age with active patchy AA [10]. In contrast, according to the Australian Expert Consensus [41], intralesional corticosteroid injections are not recommended for children because their use is generally not feasible without sedation. The aforementioned conflicting data and recommendations certainly contribute to the inconsequential and diverse approaches the dermatologist follow for their pediatric patients with AA.

For eyebrow AA in children, dermatologists prefer topical steroids (59.3%) followed by topical calcineurin inhibitors (18.4%), while after failure of two approaches, most physicians (32.4%) do not prescribe any treatment.

Literature data in this field are extremely poor and of low quality [43]. Topical calcineurin inhibitors may be applied to treat eyebrow AA but should not be considered the first-line topical treatment.

While Alopecia Areata Consensus of Experts (ACE) recommends contact immunotherapy before systemic therapy for ophiasis in children, only a small percentage of dermatologists declared they use this modality. Robust data in childhood ophiasis are vastly missing.

The recommendations in respect of AA universalis and totalis are inconsistent. ACE for AA [43] suggests topical immunotherapy before systemic therapy, while the Italian guidelines support topical immunotherapy only for children over the age of 10 years, with chronic disease. The Australian expert consensus suggests topical therapies (i.e., steroid, minoxidil, or immunotherapy as described below) as the most appropriate first-line treatments, in particular, minoxidil is mainly used as an add-on modality in AA and not as monotherapy [41]. On the other hand, systemic corticosteroids provide the most rapid response of any systemic therapeutic option [40, 45]. According to the ACE, oral corticosteroids are recommended for acute AA with SALT > 50% and > 30% in children aged 7–12 and 13–18 years, respectively. In chronic AA, oral corticosteroids are recommended for patients aged 13–18 years with SALT > 50%. The responses we received are not in complete agreement with the literature, since the dermatologists favored topical steroids (26.6%) and systemic steroids (21.9%) as first options. Similarly in AA universalis, the first treatment option chosen was systemic steroids (33.2%), while 17.3% of the dermatologists do not prescribe any treatment.

The very low rate of dermatologist preferring JAK inhibitors in AA totalis and universalis could be related to the very recent approval of these drugs in this indication and the limited access due to local regulations and high cost.

Limitations

The outcomes of the present survey-based study should be interpreted considering the fact that

responses to the questionnaire reflect what the dermatologists usually do in the certain scenario posed by each question, which may partially differ from their decisions in real daily practice.

CONCLUSION

This survey provides insights concerning the real-life practice in the management of patients with AA, in Greece and Italy. The results highlight that there is a significant diversity and heterogeneity, especially in regards to the treatment of pediatric population, AA of special sites, and recalcitrant and severe forms of the disease, possibly linked to the lack of robust data and uniform, widely accepted guidelines.

ACKNOWLEDGEMENTS

Medical Writing and Editorial Assistance The authors did not use any medical writing or medical assistance for this article.

Author Contributions. Michela Starace, Zoe Apalla: concept and design, drafting the manuscript, revised final manuscript; Bianca Maria Piraccini: revised final manuscript. Francesca Pampaloni: collect and analyze data, drafting the manuscript; Elisabeth Lazaridou, Eirini Kyrmanidou, Alexander Stratigos, Aimilios Lallas, Alexander Katoulis, Dimitrios Sgouros, Federico Quadrelli, Luca Rapparini, Stephano Cedirian, Francesca Bruni, Lorenzo Ala, Alfredo Rossi: read and accepted the final version of the manuscript.

Funding. No funding or sponsorship was received for this study or publication of this article.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Michela Starace, Francesca Pampaloni, Elisabeth Lazaridou, Eirini Kyrmanidou, Alexander Stratigos, Aimilios Lallas, Alexander Katoulis, Dimitrios Sgouros, Federico Quadrelli, Luca Rapparini, Stephano Cedirian, Francesca Bruni, Lorenzo Ala, Alfredo Rossi, Bianca Maria Piraccini, Zoe Apalla. Michela Starace is an Editorial Board member of *Dermatological Therapy*. Michela Starace was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. The questionnaire was created in the English language, with the help of a native English speaker and translated into Greek and Italian languages, by Greek and Italian dermatologists, respectively (native speakers with excellent knowledge of the English language), and it received ethics approval from the Ethics Committee of The Medical School of The Aristotle University of Thessaloniki (protocol number 33/2022). The link to access the questionnaire was sent by email to dermatologists-members of the National Societies of Dermatology (SIDEMAST in Italy and HSDV in Greece). The study was conducted in accordance with the Declaration of Helsinki.

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