DERMOSCOPIC FINDINGS OF VITILIGO AND THEIR RELATIONSHIP WITH DISEASE IN THE SOUTHWEST OF IRAN

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Abstract

Objective: Vitiligo is an autoimmune skin pigment disease characterized by the absence of epidermal melanocytes. Dermoscopy is fast becoming an important adjunctive tool for assessing disease activity. The present study was conducted with the aim of determining the relationship between dermoscopic findings of vitiligo disease and disease activity in patients referred to Dermatology clinic of Imam Hospital in Ahvaz in 2021.

Materials and Methods: The present cross-sectional study was conducted on 45 patients with a clinical diagnosis of vitiligo. Patients were divided into active and stable groups based on disease activity. A total of 113 lesions were examined to evaluate the association between dermoscopic findings and disease activity.

Results: In this study 113 lesions was examined, 84 lesions (74.33%) were in active stage patients and 29 lesions (25.67%) were in stable stage patients. Dermoscopic findings such as perifollicular pigmentation, marginal/perilesional hyperpigmentation, intra/perilesional erythema with telangiectasia, leukotrichia, and perifollicular depigmentation were observed significantly more frequently in stable lesions than in active lesions, which was statistically significant ($p<0.05$). Other dermoscopic findings, including trichrome pattern, comet tail, starburst appearance, polka dot, and salt & pepper patterns were more common in active lesions than in stable lesions, but no statistically significant association was found ($p > 0.05$).

Conclusion: Dermatoscopy can be an effective tool for diagnosing vitiligo, assessing disease activity, response to treatment, and prognosis. In addition, dermoscopy can detect disease activity earlier than the clinical onset of disease instability and thus be effective in determining the most appropriate treatment.

Keywords: Dermoscopy, stable, active, vitiligo

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Introduction

Vitiligo is a common acquired skin disease with an overall prevalence of 0.5-2%. Its incidence varies from 0.1 to 8.8% in different parts of the world (1). The disease is characterized by white macules due to autoimmune destruction of melanocytes and depigmented patches, sharp borders with or without leukotrichia, which may be associated with psychological effects due to social stress (2, 3). The normal reticular pigment pattern along distant rete ridges with pale areas associated with the papillary dermis is a feature of normal skin that changes in various pigment disorders, including vitiligo (4). Differentiating primary vitiligo findings from other causes of hypopigmentation and depigmentation is challenging (5). Dermascopy facilitates the diagnosis of changed reticular pigmentation and can be valuable to evaluate the progression of the disease stage (stable, progressive, repgimented) as well as the response to treatment (6). Dermascopy helps in the early diagnosis of vitiligo by identifying subtle changes in the pigment pattern (7). Dermascopy of normal skin is characterized by the natural reticular pattern of the pigment network, which includes homogeneous pigmented lines related to associated with the rete network and pale bright areas between these lines which this normal reticular pigment network is altered in some cases of developing vitiligo findings (8). Dermascopy has been widely used for examining melanoma and other pigmented findings and for early diagnosis of localized vitiligo (9). This study was conducted with the aim of determining the dermoscopic features of vitiligo in order to assess the stage of the disease in patients referred to our dermatology clinic in Southwest of Iran.

Materials and Methods

The present cross-sectional analytical epidemiological study included all patients referred with skin problems and clinical diagnosis of vitiligo in 2021 to a dermatology clinic in Southwest of Iran. The sample size was based on a simple random sampling and on the information from the study by Badad et al. from 2019 that 73% of skin complications with progressive clinical status and considering the probability of a type 1 error of 0.05 and an accuracy of 0.082, 113 findings were estimated (10). The inclusion criteria for the study included outpatients referred to the our dermatology clinic with skin problems, a definitive clinical diagnosis of vitiligo by a dermatologist, and the patient's consent to participate in the study. Exclusion criteria were unwillingness to participate in the study or other causes of hypopigmented or depigmented findings. A detailed medical history was then taken from the patients and a clinical and dermoscopic examination was performed while maintaining the confidentiality of the information to the patients. The criteria used to confirm persistence of vitiligo included the absence of progression of old lesions over the past year, the absence of new lesions over the same period, and the absence of Kobner's phenomenon over the same period. Dermoscopic findings was evaluated with a dermoscope (FotoFinder handyscope,Germany) attached to a One Plus 6 iphone with magnification (10x).

Ethics

The study was accepted by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences.
(IR.AJUMS.HGOLESTAN.REC.1400.085).
Written, informed consent was achieved from each patient.

Statistical analysis

For quantitative variables, mean and standard deviation were used to describe quantitative data, and frequency distribution and percentage were used to describe qualitative data. The chi-square test was also used for data analysis. All analyzes were performed using SPSS version 26 software and at a significance level of less than 0.05

Results

The mean and standard deviation of the age variable was 33.78± 11.32, the lowest age was 6 years and the highest age was 55 years. In the current study, 28 patients were women and 17 patients were men. 33 patients have no family history of the disease and 12 patients have a family history of the disease. In terms of the clinical pattern, the most common pattern was related to vulgaris pattern (46.7%) and the least frequent was segmental at 6.7%, while no case was observed in the universal pattern. The

highest frequency of the underlying disease was related to atopy disease (20%) and the lowest frequency was insulin-dependent diabetes and alopecia areata (2.2%). The frequency of anatomical regions involved 41 patients in the head and neck, 23 patients in the trunk, 34 patients in the upper extremities, and 12 patients in the lower extremities. It should be noted that in some patients the extent of involvement involved more than one region. In terms of disease stage, 31 patients were in the active stage and 14 patients were in the stable stage. 113 skin lesions from 45 patients were examined with dermoscope. Lesions selection was as follows: 3 lesions were examined from patients with vulgaris and acrofacial clinical patterns, and one lesion was examined from patients with focal and segmental clinical pattern. 84 and 29 lesions were in the active and stable stages of the disease, respectively. Demographic and clinical information of patients listed in table 1.

Table 1- Demographic and clinical information of patients

Variables		Frequency (Percent)
Gender	**Male**	17 (37.8)
	Female	28 (62.2)
Familial history	**Yes**	12 (26.7)
	No	33 (73.3)
Underlying disease	**No**	30 (66.7)
	atopic dermatitis	9 (20)
	Thyroid disorders	4 (8.9)
	Insulin-dependent diabetes	1 (2.2)
	Alopecia areata	1 (2.2)
Clinical pattern	**Vulgaris**	21 (46.7)
	Acrofacial	12 (26.7)
	Focal	9 (20)
	Segmental	3 (6.6)
	Universal	0 (0)
Anatomical region	**Head and Neck**	41 (91.1)
	Trunk	23 (51.1)
	Upper Extremities	34 (86.6)
	Lower Extremities	12 (26.6)
Stage of disease according to number of patients	**Active**	31 (68.9)
	Stable	14 (31.1)
Stage of disease according to number of lesions	**Active**	84 (74.33)
	Stable	29 (25.67)

Ten dermoscopic findings were examined in 113 lesions. It should be noted that more than one dermoscopic finding was observed in a number of lesions. In terms of the frequency of features observed, the most common finding was perifollicular pigmentation with a frequency of 47 (41.5%), followed by a salt & pepper pattern and perifollicular depigmentation with a

frequency of 42 (37.1%). and 41 (36.2%), while the lowest frequency was associated with a comet tail with a frequency of 12 (10.6%) and a polka dot with a frequency of 9 (7.9%) (Table 2).

Table 2- Frequency of dermoscopic findings

Dermoscopic findings	**Frequency (Percent) N=113***
Perifollicular pigmentation	47 (41.5)
Marginal/perilesional hyperpigmentation	32 (28.3)
Intra/perilesional erythema with telangiectasia	28 (24.7)
Trichrome pattern	13 (11.5)
Leukotrichia	38 (33.6)
Perifollicular depigmentation	41 (36.2)
Comet tail appearance	12 (10.6)
Starburst appearance	25 (22.1)
Polka dot	9 (7.9)
Salt & pepper pattern	42 (37.1)
*** More than one dermoscopic finding was observed in a number of lesions, bringing the overall frequency to 113 more.**	

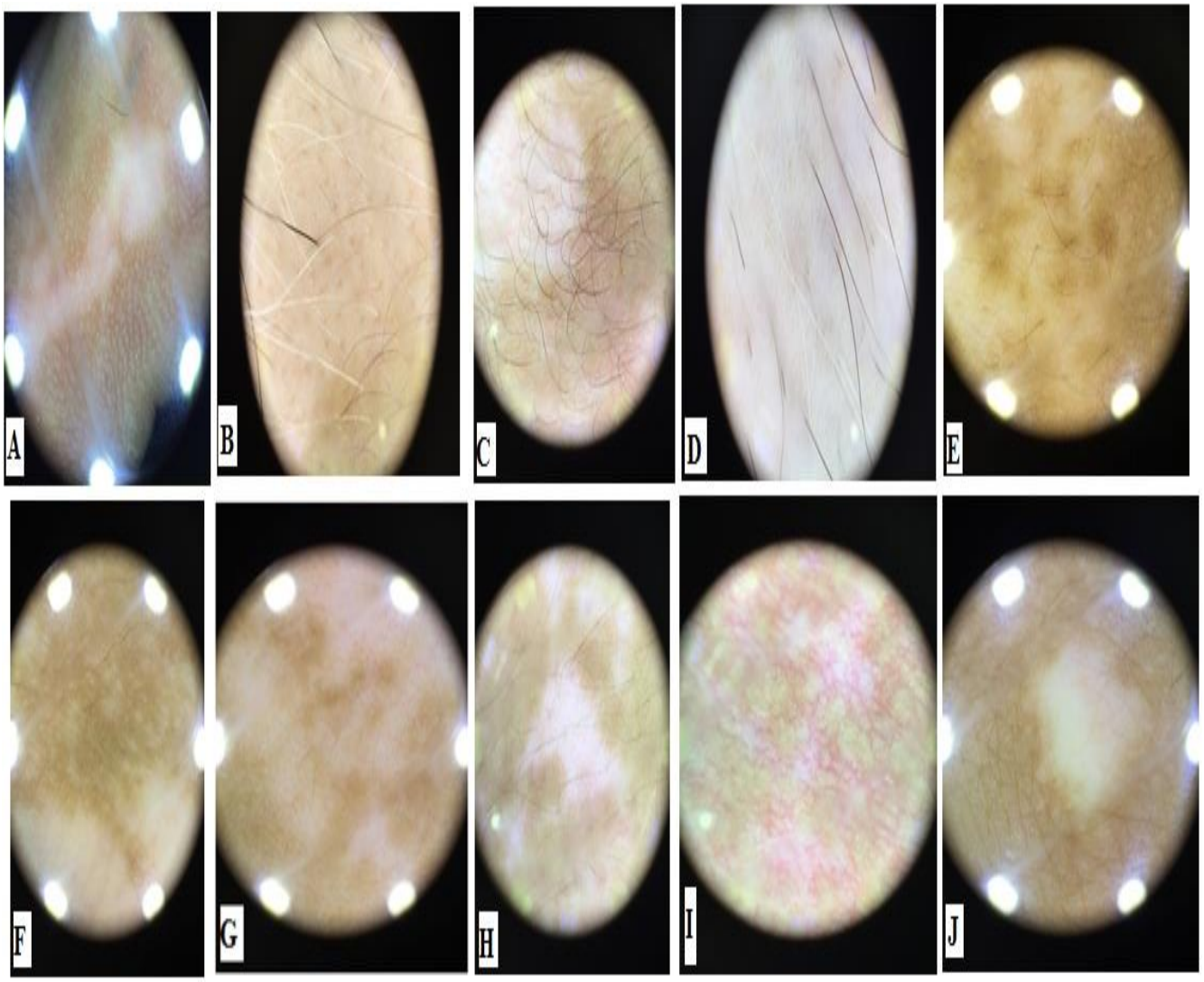

Figure 1- Dermoscopic findings.(A)Comet tail appearance. (B)Leukotrichia. (C)Marginal/perilesional hyperpigmentation. (D)Perifollicular depigmentation. (E)Perifollicular pigmentation. (F)Polka dot. (G)Salt & pepper pattern. (H)Starburst appearance. (I)Intra/perilesional erythema with telangiectasia. (J)Trichrome pattern.

In the current study, the frequency of stable stage dermoscopic features included marginal/perilesionalhyperpigmentation (86.2 %). perifollicular pigmentation (72.4%), telangiectasia (72.4%), leukotrichia (75.8%), perifollicular depigmentation (93.1%), and starburst appearance (27.5%). Dermoscopic findings most frequently observed in the active stage of the disease included trichrome pattern (13%), comet tail appearance (13%), salt & pepper pattern (40.4%), and Polka dot (10 .7%). Dermoscopic features perifollicular pigmentation, marginal/perilesionalhyperpigmentation, intra/perilesionalerythema with telangiectasia, leukotrichia, and perifollicular depigmentation were observed significantly more frequently in stable than in active lesions, which was statistically significant($p<0.05$). Other dermoscopic findings, including trichrome pattern, comet tail appearance, starburst appearance, polka dot and salt & pepper patterns, were more likely to appear in active lesions than in stable lesions, however, no statistically significant association was found ($p>0.05$, Table 3).

Table 3- Relationship between the dermoscopic findings of the lesions between the active and stable stages of the disease

Dermoscopic findings		Stage disease		p-value
		Active(84)	Stable(29)	
Perifollicular pigmentation	Present	26 (30.9)	21 (72.4)	P<0.001 *
	Absent	58 (69.1)	8 (27.6)	
Marginal/perilesional hyperpigmentation	Present	7 (8.3)	25 (86.3)	P<0.001 *
	Absent	77 (91.7)	4 (13.7)	
Intra/perilesional erythema with telangiectasia	Present	7 (8.3)	21 (72.4)	P<0.001 *
	Absent	77 (91.7)	8 (27.6)	
Trichrome pattern	Present	11 (13)	2 (6.8)	0.367
	Absent	73 (87)	27 (93.2)	
Leukotrichia	Present	16 (19)	22 (75.8)	P<0.001 *
	Absent	68 (81)	7 (24.2)	
Perifollicular depigmentation	Present	14 (16.6)	27 (93.1)	P<0.001 *
	Absent	70 (83.4)	2 (6.9)	
Comet tail appearance	Present	11 (13)	1 (3.4)	0.146
	Absent	73 (87)	28 (96.6)	
Starburst appearance	Present	17 (20.2)	8 (27.5)	0.411
	Absent	67 (79.8)	21(72.5)	
Polka dot	Present	9 (10.7)	0 (0)	0.066
	Absent	75 (89.3)	29 (100)	
Salt & pepper pattern	Present	34 (40.4)	8 (27.5)	0.216
	Absent	50 (59.6)	21 (72.5)	
*: *Significant at a level of 0.001*				

Discussion

In the present study, 12 patients (26.7%) had a family history of this disease. In the study by Pajvani et al, The relationship between family history and childhood vitiligo, it was concluded that family members of affected children are more susceptible to vitiligo. A positive family history was observed in 18 patients (22.5%), consistent with the results of the present study. Various studies have reported a similar association between 11% and 46% (11).

Regarding comorbidities, studies have shown that vitiligo can be associated with other autoimmune diseases such as alopecia areata, diabetes mellitus, pernicious anemia, Addison's disease and thyroid disorders (12). In the current study, the most common comorbidities was atopic dermatitis 9 patients (20%), followed by thyroid disorders with a frequency of 4 patients (8.9%), and lowest frequency was related to insulin-dependent diabetes and alopecia areata one case each (2.2%) . Also, no comorbidities were observed in 30 patients (66.7%). In the study of Sneha Gandhi in India (2017) presented that in relation to the underlying disease, 32 patients had a history of atopic dermatitis, which similar to the present study, atopic dermatitis was the most frequently observed disease in vitiligo patients (13).

In the present study, the clinical patterns of vulgaris and acrofacial were the most commonly observed in vitiligo, with frequencies of 22 cases

(48.8%) and 12 cases (26.7%), respectively. In addition, 9 cases (20%) had a focal clinical pattern and 2 cases (4.5%) had a segmental pattern. No case of a universal clinical pattern was observed during this study.

Similar to the present study, in other studies identified the clinical pattern vulgaris was the most common of the clinical pattern (14-20). The order of frequency of other clinical patterns of vitiligo disease is diverse in different studies (21, 22). Also, a recent study in a large population of 571 patients with vitiligo disease showed that the clinical pattern of this disease, especially in non-segmental forms, the most common type of clinical pattern, differs by age group, such as children and adolescents. The focal type (41.4 %) was common, while the vulgaris type (48 %) was more common in adults and the elderly, indicating that the pattern of vitiligo disease is diverse in different populations (23).

In order to determine the possible course of the disease, clinical, histological and biological methods are used that each of them has certain limitations. However, in most cases, vitiligo stability assessment was a prerequisite (24).

In this study, of 113 selected skin lesions, 84 lesions (74.33%) and 29 lesions (25.67%) were in active and stable stages of disease, respectively. In the study by Ambresh S. Badad et al (2019), similar to the present study, out of the 120 lesions examined, 88 lesions (73.3%) were in the active stage of the disease and 32 lesions (26.7%) were in the active stage disease (10). Also in the present study, based on the number of patients, 31 (68.9%) patients were in the active stage and 14 (31.1%) patients were in the stable stage. Consistent with the results of the study, the Suman Singh et al (2011) showed that the number of patients with the active stage of the disease (59.5%) was higher than the number of patients with the stable stage of the vitiligo disease (40.5%), (25). In the similar study by Krishnendra Varma et al (2020), 17 out of 50 patients (34%) were in the stable stage and 33 (66%) were in the active stage (26).

The diagnosis of vitiligo is primarily clinical, but confirmation may be needed in some cases (27, 28). In cases of doubt, especially when the patient or their caregiver refuses a skin biopsy, dermatoscopy serves as a complementary tool for diagnostic confirmation and additionally helps to assess disease activity. It has recently been applied for early detection of localized vitiligo. Also utilized to diagnosing and distinguishing hypopigmented lesions from other diseases (29).

According to the present study,the most frequently observed finding was perifollicular pigmentation with a frequency of 47 (41.5%), followed by salt & pepper pattern and perifollicular depigmentation with a frequency of 42 (37.1%) and 41 (36, 2%). While the lowest frequency is related to the comet tail with a frequency of 12 (10.6%) and polka dot with a frequency of 9 (7.9%). In the study conducted by Ambresh S. Badad et al in 2019, the most frequently reported feature was marginal pigmentation (48%), followed by perifollicular pigmentation (32%), which is relatively similar to the present study (10). While in the Krishnendra Varma study et al (2020), the most common dermoscopic finding in patients was telangiectasia (86%), and the frequency perifollicular depigmentation was 64% and perifindingal/marginal hyperpigmentation was 50%, which was contradictory with the results of the present study (26).

Based on the results of the present study and other studies, it showed that the frequency of dermoscopic findings varies across studies, however, among the most common dermoscopic findings in studies was perifollicular pigmentation, marginal hyperpigmentation and telangiectasia. On the other hand the lowest dermoscopic findings in different studies were comet tail patterns, polka dots, and starburst appearances. One of the reasons for the different frequency of dermoscopic findings in diverse studies is that the patients are treated and untreated and the disease stage is not correctly separated and some features can be seen in both active and stable stages of the disease (30).

Table 4. Comparison of dermoscopic findings of lesions based on disease stage between the present study and similar studies

Dermoscopic findings	Stage disease	Present study	Krishnendra Varma (26)	GUNET AWAL (31)	Vishal Wali (32)	Kumar Jha (33)	Sneha Gandhi (12)
Perifollicular	**active**	-	✓	-	-	✓	-

pigmentation	**stable**	✓	-	✓	✓	-	✓
Marginal/perilesional hyperpigmentation	**active**	-	-	-	-	-	-
	stable	✓	✓	✓	✓	✓	✓
Intra/perilesional erythema with telangiectasia	**active**	-	✓	-	-	-	-
	stable	✓	-	✓	✓	✓	✓
Trichrome pattern	**active**	✓	✓	○	✓	○	✓
	stable	-	-	○	-	○	-
Leukotrichia	**active**	-	✓	-	○	-	-
	stable	✓	-	✓	○	✓	✓
Perifollicular depigmentation	**active**	-	✓	○	○	✓	○
	stable	✓	-	○	○	-	○
Comet tail appearance	**active**	✓	✓	✓	✓	✓	✓
	stable	-	-	-	-	-	-
Starburst appearance	**active**	✓	✓	✓	✓	✓	✓
	stable	-	-	-	-	-	-
Polka dot	**active**	✓	✓	✓	○	✓	✓
	stable	-	-	-	○	-	-
Salt & pepper pattern	**active**	✓	○	✓	✓	✓	○
	stable	-	○	-	-	-	○
○ This finding was not investigated in the mentioned study							

Overall, the results of the present study and other similar studies show that the findings of marginal/perilesional hyperpigmentation, intra/perilesional erythema with telangiectasia, and leukotrichia were mainly observed in stable lesions, which were statistically significant in the present study, therefore this findings can be regarded as a suitable criterion for diagnosing the stable stage of the disease using a dermoscope.

In our study, perifollicular pigmentation was observed more frequently in the stable stage which was statistically significant, but in Krishna varma's study, it was seen at both stages that there was no statistically significant association, also in Kumar Jhas study this finding was more found in the active stage. Therefore, perifollicular pigmentation cannot be considered as a definitive finding to determine disease stage.

In this study, perifollicular depigmentation was found as a criterion for stable stage diagnosis, which was statistically confirmed and consistent with the study by Kumar Jhas (33), but in the Varma study, this feature was seen more in active lesions, which is statistically significant (26).

According to the present study and similar studies findings including Salt & pepper, polka dot, Trichrome pattern, Comet tail appearance and starburst appearance were observed in active stage lesions, however, in the study by Krishnendra Varma, starburst appearance was found in both disease stages, but was not statistically significant (26). Considering that the above 5 features in current study are not statistically significant in the active stage compared to the stable stage, this findings generally cannot be considered as a definitive criterion for the diagnosis of disease stage.

The reasons for the inconsistency of some results in the studies can be attributed to the different frequency of the examined lesions in different studies, the lack of separation of treated and untreated patients in some studies, and the lack and comparison between active and stable phase for each finding without statistical analysis,

failure to examine the number of lesions in each patient, the lack compare patients based on the same time period since disease onset and ignoring changes over time, and finally failure to compare lesions based on those involved anatomical areas (34).

Limitations of the current study include small sample size, lack of separation between treated and untreated patients and not comparing dermoscopic findings with histological findings.

Conclusion

Dermascopy can be useful as an effective tool for diagnosing vitiligo, assessing disease activity, and assessing response to treatment and disease prognosis. Also, dermascopy can be effective in the early diagnosis of vitiligo and as a result of determining the stability of the disease for the most appropriate treatment regimen. Dermascopy also helps distinguish vitiligo from other hypopigmentary and pigmentary disorders. Histopathology is the gold standard method for diagnosing vitiligo, but as an invasive procedure it is often not accepted by patients. Therefore, dermascopy is a new tool to diagnose vitiligo, eliminating the need for skin biopsy.

In summary, the results of the present study showed that the dermoscopic findings of perifollicular pigmentation, marginal hyperpigmentation, intra/perilesional erythema with telangiectasia, leukotrichia and perifollicular depigmentation can be used as predictive criteria for the stable stage of vitiligo. Although the findings of trichrome pattern, comet tail, polka dot, starburst appearance, and salt & pepper pattern were more likely to be seen in active stage lesions, but cannot definitely be used as predictive criteria for vitiligo disease stage and studies with higher sample size is needed.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported

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