Dermatology Practical & Conceptual

Dermatoscopic Patterns in Childhood Vitiligo and Their Association With Reflectance Confocal Microscopy Findings

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ABSTRACT

Introduction: The diagnosis of vitiligo is mainly based on clinical findings. However, dermoscopy or reflectance confocal microscopy (RCM) could be useful for assessing its progression (stability, pigmentation, or depigmentation).

Objectives: To evaluate the correlation of dermatological findings by dermoscopy and RCM in pediatric vitiligo.

Methods: We conducted a cross-sectional, descriptive, and analytical clinical study. Pediatric patients with vitiligo of both sexes, aged > 1 year and < 18 years, with all spectrums of the disease were included. Vitiligo lesions were evaluated clinically, by dermoscopy, and microscopy.

Results: A total of 40 patients with vitiligo were included. Eight dermoscopic patterns were found: reduced/absent pigment network, perifollicular pigmentation, trichromic, tapioca *sago*, perifollicular

depigmentation, starburst, leukotrichia, and erythema. Skin with a normal pigment network showed complete dermal papillary rings and half-rings. Skin with reduced/absent pigment network also had an absence of papillary rings or only showed half-rings and was more common in unstable vitiligo. The trichrome pattern only showed half-rings. The Tapioca sago pattern showed complete papillary rings and appeared in younger patients. Perifollicular pigmentation showed half-rings and complete rings and did not show associations. The diffuse borders did not present complete papillary structures. It was found that vitiligo duration time of fewer than 24 months (Odds Ratio 4.56, CI 1.09-18.99) and absent papillary rings (OR 2.75, CI 1.01-7.51) are associated with unstable prognosis.

Conclusions: Certain dermatoscopic and microscopic findings, such as the reduction/absence of the pigment network, tapioca sago pattern, and absence of papillary rings, can be used to assess the stability of the disease and provide insight into the clinical behaviour of vitiligo.

Introduction

Vitiligo is a chronic and acquired disorder of pigmentation. It is characterized by the loss of function and/or destruction of epidermal melanocytes and, occasionally, of the hair follicle, causing achromatic macules or spots that increase in size over the years [1]. It is the most frequent disorder of pigmentation and has a worldwide incidence of 0.38% to 1% [2]. Vitiligo affects both sexes equally and in 37% of cases it appears during infancy [2,3]. Since children have thinner skin, greater regenerative capacity, and a lower frequency of vitiligo associated with other autoimmune diseases, vitiligo has a distinct clinical prognosis and expression compared with the adult population [4-6].

Under its evolution, vitiligo can change and exhibit three distinct behaviours: stability, progression, or regression. Vitiligo is considered stable or inactive when no new lesions have developed in the last 12 months and existing lesions show no signs of progression. On the other hand, it is referred to as progressive or unstable vitiligo when there is formation and/or development of new lesions within 12 months, or when pre-existing lesions grow larger. Finally, regressive or pigmentary vitiligo occurs when spontaneous re-pigmentation of existing lesions takes place [3,4].

The diagnosis of vitiligo is clinical and usually does not require laboratory tests or extension studies. Skin biopsy is reserved for cases of diagnostic doubt or when other pigmentary disorders need to be excluded [7]. Clinical evaluation of the different evolutionary stages of this disease (stability, pigmentation, or depigmentation) remains inconclusive. To date, there is no standardized method for determining the stability of vitiligo. The lack of standardization is due to the high variability in vitiligo assessment. Because of these issues, objective and non-invasive methods are needed to assess the behaviour and extent of depigmented skin in comparison to the surrounding normal skin.

Dermoscopy (also known as epiluminescence microscopy or dermatoscopy) is an in vivo diagnostic technique that allows visualizing sub-macroscopic morphological structures that are invisible to the naked eye and correspond to specific histological structures [8]. Initially, dermoscopy was used for the study and screening of pigmented lesions, but nowadays, it has different applications, including disorders of pigmentation such as vitiligo. This diagnostic tool detects subtle changes in the pigmentary pattern that help in the non-invasive confirmation of vitiligo, evaluates its activity, and differentiates it from other hypo-pigmentary disorders in the early stages of the disease (eg, piebaldism, tuberous sclerosis, hypomelanosis of Ito, Waardenburg syndrome, achromic nevus, post-inflammatory hypomelanosis, etc) [9]. The application of this technique to hypopigmented lesions is recent; therefore, there have been only a few studies conducted on vitiligo. The majority of these studies has been conducted in adults and is limited to describing dermatoscopic patterns. So far, there has been no successful correlation between the microscopic structures beneath these dermatoscopic images.

RCM is a non-invasive study that allows for the instant capture of black- and -white images of the skin, ranging from the epidermis to the upper reticular dermis, with an imaging depth of up to 250-300 μm. This provides a resolution similar to that of skin histology and is particularly well-suited for pigmentary disorders due to the contrast provided by melanin. In vitiligo lesions, RCM reveals the absence of dermal papillary rings (non-edged papillae), and bright keratinocytes are not detected in the epidermis [10]. Currently, there are no studies that establish a connection between dermatoscopic patterns, and the microscopic findings observed through RCM.

Objectives

The objective of this study was to evaluate the association of different dermatoscopic patterns with findings observed with RCM as a diagnostic alternative to help evaluate the evolution of vitiligo in children.

Methods

Study Type and Location

We conducted a cross-sectional, descriptive, analytical, prospective, and observational study at the Dermato-Oncology Clinic, Experimental Medicine Unit, Faculty of Medicine, National Autonomous University of Mexico from March 27th to November 30th, 2022. This study adhered to the guidelines outlined in the Helsinki Declaration, Belmont Report, and the General Health Law regarding health research, including information regarding internal ethics committees in health institutions (Articles 100, 103, and 105) and the Mexican Official Standard NOM012-SSA3-2012, the internal registration number is ODFM/059/22 [11,12].

Study Protocol

Pediatric patients with vitiligo who spontaneously attended the Clinic, of both sexes, >1 year and <18 years old, with all spectra of the disease and regardless of associated diseases were included. Those who withdrew informed consent were eliminated.

A vitiligo patch was evaluated clinically, dermoscopically, and with RCM. The most recent lesion was evaluated. The extent of vitiligo was calculated using the online application Vitiligo Extend Score (VES). A panoramic image of the dermatosis was taken with the Fotofinder ATBM MASTER equipment, and then polarized dermoscopic evaluation of the healthy skin (10 cm away from the lesion), center, and edge of the lesion was performed with 20x magnification. The same areas were evaluated with the Vivascope 3000 RCM (Caliber I.D.) to assess microscopic findings, and photographs of both techniques were taken. All three evaluations were performed on the same day. The selection of participants and clinical, dermoscopic, and microscopic results were evaluated by 1 pediatric dermatologist and 1 dermatologist specialized in dermoscopy and RCM .

Statistical Analysis

The sample size was calculated using the statistical program Open Epi version 3 based on a population proportion with a hypothetical disease frequency of 2.8%, the prevalence was derived from information described in other populations. Kolmogorov-Smirnov hypothesis tests were conducted to assess normality. Variables meeting this criterion were summarized as means and standard deviation as a measure of dispersion. Variables with non-normal distributions were summarized as means and interquartile range (IQR). Nominal variables such as dermoscopic patterns were summarized with frequencies and percentages. A comparison of dermoscopic findings between the center and edge of the lesion was made using a Chi-Square (Xi^2) test. Multivariate analysis logistic regression analyses were stratified according to the type of vitiligo and its prognosis. The SPSS program version 26 IBM was used, and a bilateral P value of <0.05 was assumed to be statistically significant.

Results

Forty patients with vitiligo were enrolled, including 27 men (67.5%) and 13 women (32.5%). All participants underwent clinical, dermatoscopic, and reflectance confocal microscopy evaluations. Table 1 shows the characteristics of the population. Only 13 patients had any associated comorbidity: 4 had atopic dermatitis, 3 had diabetes mellitus, 2 had hypothyroidism, 2 had epilepsy, and there was one case each of psoriasis and cyclic neutropenia.

Tables 2 and 3 summarize the characteristics of patients with vitiligo stratified by type of vitiligo (segmental, non-segmental, and indeterminate) and by behavior (unstable, stable, and pigmented).

Regarding dermatoscopy, 8 different dermatoscopic patterns were found in vitiligo lesions: 1) reduced/absent pigment network, 2) perifollicular pigmentation, 3) trichromy, 4) tapioca sago, 5) perifollicular depigmentation, 6) starburst, 7) leukotrichia, and 8) erythema (Figure 1). The most common pattern was reduced or absent pigment network, followed by leukotrichia, tapioca sago, and trichromy. When comparing dermatoscopic patterns with clinical characteristics, we found that reduced/absent pigment network pattern was associated with unstable vitiligo (P = 0.05). A tapioca sago pattern appeared in younger patients (6.5 ± 5.1 versus 10.8 ± 3.9 years, P = 0.05) and leukotrichia was more common in segmental vitiligo (100% of cases, P < 0.05). The rest of the dermatoscopic patterns showed no association with the other study variables.

In Table 4 and Figure 2, the results of dermatoscopic patterns contrasted with the microscopic findings seen on the reflectance confocal microscope are summarized; normal skin, the center, and the edge of the lesion were analyzed (see Table 4). Table 5 summarizes the unadjusted logistic regression model to predict vitiligo instability with the main variables of interest; only evolution time less than 24 months, reduced/absent pigment network, and RCM of the lesion edge were risk factors associated with vitiligo instability. Finally, in Table 6, an adjusted logistic regression model is presented with the variables of time of evolution and absent papillary rings.

Conclusions

In our study, the most relevant epidemiological characteristics were a) vitiligo was more common in men (67.5%), this result differs from what has been reported in the literature but did not show a statistically significant, b) the onset age of vitiligo occurred in middle childhood (7.3 years +3.8) and was similar

Table 1. Characteristics of the pediatric population with vitiligo.

Variable	N = 40
Male gender, No. (%)	27 (67.5)
Age, mean (SD), years. Onset of dermatosis	10.4 (4.2) 7.3 (3.8)
Skin phototypes, No. (%) - III - IV	 27 (67.5) 13 (32.5)
Type of vitiligo, No. (%) - Segmental - Non-segmental - Indeterminate	 10 (25.0) 23 (57.5) 7 (17.5)
Non-segmental subtype, No. (%) N = 23 1. Acrofacial 2. Generalized 3. Universal 4. Mucosal 5. Mixed 6. Rare variants (Follicular/Menor vitiligo/Punctate)	 4 (10.0) 16 (40.0) - - 2 (5.0) 1 (2.5)
Segmental subtype, No. (%) N = 10 1. Unsegmented 2. Bisegmental 3. Multisegmental	 8 (20.0) 2 (5.0) -
Indeterminate subtype, No. (%) N = 7 1. Focal 2. Mucosal	 7 (17.5) 0
Asymmetric distribution No. (%)	20 (50.0)
Duration time, median (IQR), months	24 (12.0, 57.0)
Evolution, N° (%) 1. Pigmentary 2. Stable 3. Unstable	 11 (27.5) 7 (17.5) 22 (55.0)
VES (Vitiligo Extent Score), median (IQR)	0.59 (0.16,1.36)
Patients with treatment, No. (%)	31 (77.5)
Type of treatment, No. (%) 1. None 2. Topical steroid 3. Topical calcineurin inhibitor 4. Topical steroid + Topical calcineurin inhibitor 5. Psoralens 6. Phototherapy	 9 (22.5) 3 (7.5) 10 (25.0) 12 (30.0) 2 (5.0) 4 (10.0)
Comorbidity, No. (%) 1. No 2. Yes	 27 (67.5) 13 (32.5)

IQR = interquartile ranges; SD = standard deviation.

to the French and Brazilian pediatric populations, c) Skin phototype III was the most common and did not show any epidemiological association, d) Non-segmental vitiligo was the most common, followed by segmental and indeterminate, with a frequency similar to other populations [13-16], d) Segmental vitiligo appeared in younger patients, and early onset has been reported in other pediatric populations [15]. Additionally, it usually does not have a re-pigmentation treatment ($P < 0.05$); this situation may occur because, at the beginning, the lesion is single, small, and non-specific, therefore, it does not receive management and continues the natural history of the disease. e) The Vitiligo Extent Score (VES), which measures the extent of dermatosis, showed that the condition in children is less than 10% [17]. On the other hand, the non-segmental type had the highest extent (0.78) followed by the segmental (0.49) and the indeterminate (0.16). The differences were statistically significant and can be explained because indeterminate vitiligo precedes any of the other types by months or years, thus, its extent stops and/or occurs slowly, making its final classification difficult.

There are different ways to diagnose vitiligo without the need for invasive procedures. These methods serve to assess size, stability, severity, and treatment response. These methods can be divided into subjective, semi-objective, and objective categories. Subjective methods include clinical evaluation by a dermatologist, as well as visual comparisons of the skin before and after treatment using photos that can be digital or non-digital, taken under visible or ultraviolet light, and the Vitiligo Disease Activity Score to assess vitiligo stability over time. This last method relies on information provided by the patient about the activity of their disease. Semi-objective methods include the Vitiligo Area Scoring Index (VASI) and point counting. Objective methods include image analysis using software, tristimulus colorimetry, spectrophotometry, reflectance confocal microscopy, and more recently, dermatoscopy [10].

This study described the dermatoscopy of vitiligo in children. Eight different patterns were found: reduced/absent pigment network, perifollicular pigmentation, trichrome, tapioca *sago*, perifollicular depigmentation, starburst, leukotrichia, and erythema. The border of the lesion showed more dermatoscopic findings. Analyzing the patterns individually, we found that the reduced/absent pigment network was more common in unstable vitiligo. The tapioca *sago* appeared in younger patients, and some authors associate it with instability and early stages of the disease [18,19]. The perifollicular depigmentation showed no associations; however, in two publications by Kumar Jha et al, it was related to stable vitiligo [18,19]. Leukotrichia appeared in segmental and asymmetric vitiligo ($P = 0.05$), and this pattern has also been associated with stable or pigmentary vitiligo [18,19]. Perifollicular pigmentation had no association in our study; however, some studies link it to pigmentary vitiligo [20-22]. The starburst and erythema patterns showed no associations in our study, but the number of cases collected is limited to assert the presence or absence of possible clinical associations.

Table 2. Characteristics of pediatric patients with vitiligo stratified by type of vitiligo.

Variable	Type of vitiligo								
	Segmental (SV) N = 10	Other types (NSV and IV) N = 30	P-value	Non-segmental (NSV) N = 23	Other types (SV and IV) N = 17	P-value	Indeterminate (IV) N = 7	Other types (SV y NSV) N = 33	P-value
Sex Male N = 27 Female, No. (%) N = 13	 5 (18.5) 5 (38.5)	 22 (81.5) 8 (61.5)	0.24[a]	 7 (63.0) 6 (46.2)	 10 (37.0) 7 (53.8)	0.49[a]	 5 (18.5) 2 (15.4)	 22 (81.5) 11 (84.6)	0.99[a]
Age, mead (SD), years	8.3 (±4.1)	11.1 (±4.0)	0.05[b]	11.0 (±4.4)	9.6 (±3.9)	0.03[b]	11.5 (±2.8)	10.1 (±4.4)	0.43[b]
Skin phototypes, No. (%) - III N = 27 - IV N = 13	 6 (22.2) 4 (30.8)	 21 (77.8) 9 (62.9)	0.70[a]	 15 (55.6) 8 (61.5)	 12 (44.4) 5 (38.5)	0.99[a]	 6 (22.2) 1 (7.7)	 21 (77.8) 12 (92.3)	0.39[a]
Distribution - Symmetrical, No. (%) N = 20 - Asymmetrical No. (%)N = 20	 1 (5.0) 9 (45.0)	 19 (95.0) 11 (55.0)	0.01[a]	 17 (85.5) 6 (30.0)	 3 (15.0) 14 (70.0)	0.01[a]	 2 (10.0) 5 (25.0)	 18 (90.0) 15 (75.0)	0.40[a]
Duration time, median (IQR), months	24.0 (5.0, 45.0)	27.0 (16.5, 60.0)	0.34[c]	30.0 (22.0, 60.0)	24.0 (6.5, 42.0)	0.21[c]	24.0 (7.0, 48.0)	24.0 (15.0, 60.0)	0.60[c]
VES (Vitiligo Extent Score), median (IQR)	0.49 (0.20, 1.63)	0.60 (0.14, 1.40)	0.98***	0.78 (0.19, 1.51)	0.22 (0.13, 0.63)	0.04[c]	0.16 (0.08, 0.24)	0.70 (0.20, 1.46)	0.01[c]
Evolution, No. (%) - Pigmentary N = 11 - Stable N = 7 - Unstable N = 22	 2 (18.2) 2 (28.6) 6 (28.3)	 9 (81.8) 5 (71.4) 16 (72.7)	0.89[a]	 7 (63.6) 2 (28.6) 14 (63.6)	 4 (36.4) 5 /71.4) 8 (36.4)	0.29[a]	 2 (18.2) 3 (42.9) 2 (9.1)	 9 (81.8) 4 (57.1) 20 (90.9)	0.08[a]
Patients with treatment, No. (%) - No N = 9 - Yes N = 31	 5 (55.6) 5 (16.1)	 4 (44.4) 26 (86.9)	0.02[a]	 3 (33.3) 20 (63.5)	 6 (66.7) 11 (35.5)	0.13[a]	 1 (11.1) 6 (19.4)	 8 (88.9) 25 (80.6)	0.99[a]

[a]Fisher exact test, [b]Student t-test, [c]Mann-Whitney U test.

Table 3. Characteristics of pediatric patients with vitiligo by clinical stability.

Variable	Vitiligo stability								
	Unstable N = 22	Others: stable and pigmentary N = 18	P-value	Stable N = 7	Others: unstable and pigmentary N = 33	P-value	Pigmentary N =11	Others: stable and unstable N = 29	P-value
Sex Male, No. (%) N = 27 Female, No. (%) N = 13	 14 (51.9) 8 (61.5)	 13 (48.1) 5 (38.5)	0.73[a]	 4 (14.8) 3 (23.1)	 23 (85.2) 10 (76.9)	0.66[a]	 9 (33.3) 2 (15.4)	 18 (66.7) 11 (84.6)	0.28[a]
Age, mead (SD), years	9.6 (±4.0)	11.3 (±4.4)	0.19 [b]	11.8 (±3.1)	10.1 (±4.4)	0.33[a]	11.0 (±5.1)	10.1 (±3.9)	0.54[b]
Skin phototypes, No. (%) - III N = 27 - IV N = 13	 17 (63.0) 5 (38.5)	 10 (37.0) 8 (61.5)	0.18[a]	 5 (18.5) 2 (15.4)	 22 (81.5) 11 (84.6)	0.99[a]	 5 (18.5) 6 (46.2)	 22 (81.5) 7 (53.8)	0.12[a]
Distribution - Symmetrical, No. (%) N = 20 - Asymmetrical No. (%) N = 20	 10 (50.0) 12 (60.0)	 10 (50.0) 8 (40.0)	0.75[a]	 2 (10.0) 5 (25.0)	 18 (90.0) 15 (75.0)	0.40[a]	 8 (40.0) 3 (15.0)	 12 (60.0) 17 (85.0)	0.15[a]
Duration time, median (IQR), months	24 (7.5, 31.5)	48 (24.0, 72.0)	0.01[c]	72 (48.0, 84.0)	24 (8.5, 36.0)	<0.01[c]	24 (22.0, 72.0)	24 (8.5, 48.0)	0.45 [c]
VES (Vitiligo Extent Score), median (IQR)	0.63 (0.10, 1.10)	0.45 (0.18, 2.30)	0.63[a]	0.25 (0.11, 0.78)	0.63 (0.17, 1.41)	0.42 [c]	0.70 (0.19, 3.38)	0.35 (0.11, 1.05)	0.22 [c]
Type of vitiligo, No. (%) - Segmental N = 10 - Non-segmental N = 23 - Indeterminate N = 7	 6 (60.0) 14 (60.9) 2 (28.6)	 4 (40.0) 9 (39.1) 5 (71.4)	0.37[a]	 2 (20.0) 2 (8.7) 3 (42.9)	 8 (80.0) 21 (91.3) 4 (57.1)	0.11[a]	 2 (20.0) 7 (30.4) 2 (28.6)	 8 (80.0) 16 (69.6) 5 (71.4)	0.89[a]
Comorbidity, No. (%) - No N = 27 - Si N = 13	 18 (66.7) 4 (30.8)	 9 (33.3) 9 (69.2)	0.04[a]	 2 (7.4) 5 (38.5)	 25 (92.6) 8 (61.5)	0.02[a]	 7 (25.9) 4 (30.8)	 20 (74.1) 9 (69.2)	0.99[a]
Patients with treatment, No. (%) - No N = 9 - Yes N = 31	 6 (66.7) 16 (51.6)	 3 (33.3) 15 (48.4)	0.47[a]	 2 (22.2) 5 (16.1)	 7 (77.8) 26 (83.9)	0.64[a]	 1 (11.1) 10 (32.3)	 8 (88.9) 21 (67.7)	0.39[a]

[a]Fisher exact test, [b]Student t-test, [c]Mann-Whitney U test.

This study showed that instability is associated with a shorter duration of dermatosis and usually does not have associated comorbidities. On the other hand, stable vitiligo had a longer duration, 6 years after the onset of the dermatosis. Additionally, stability was more associated with the presence of comorbidities.

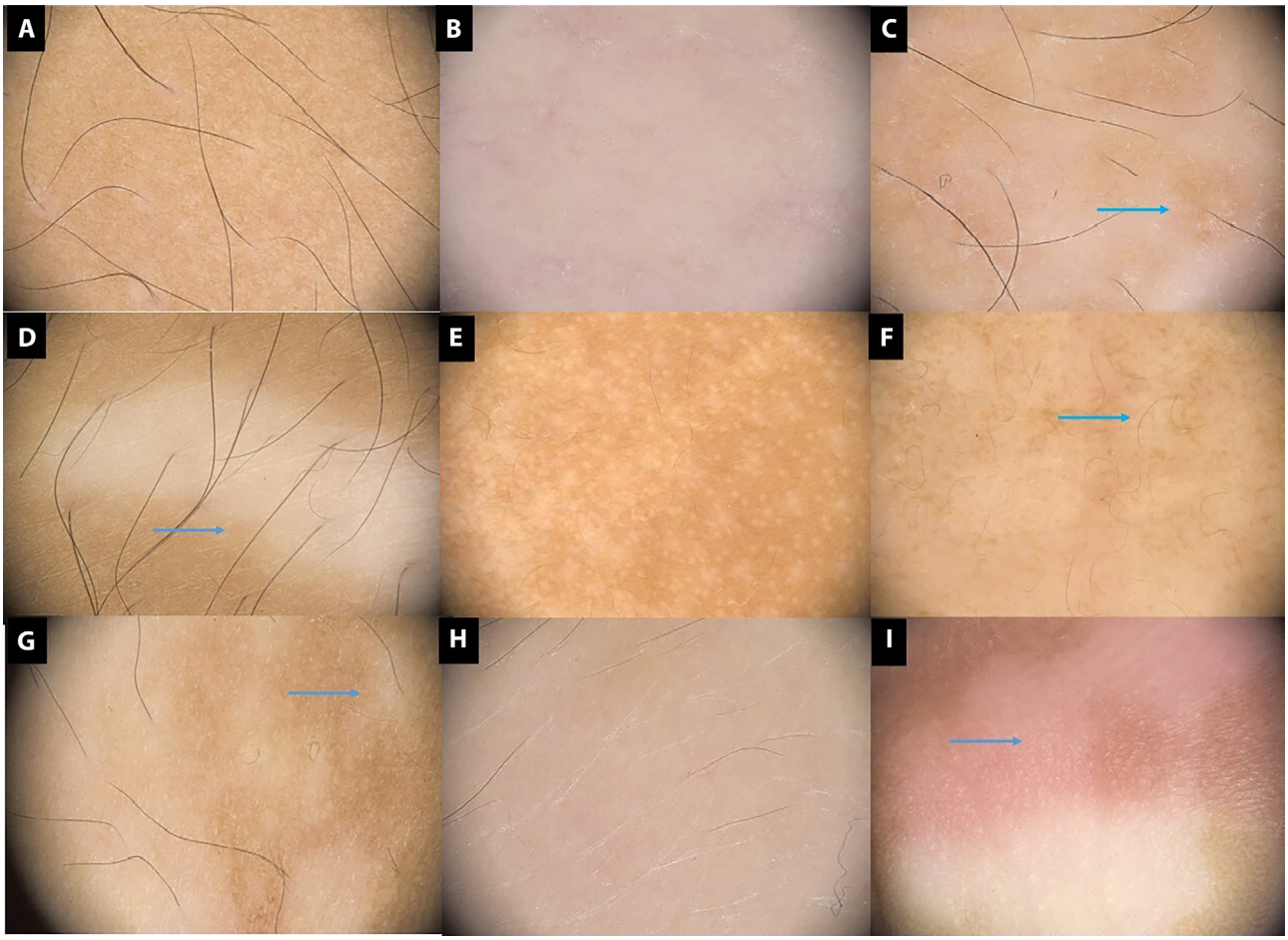

Figure 1. Dermoscopic patterns of vitiligo. (A) Normal pigment network; (B) Absent pigment network; (C) Perifollicular pigmentation (blue arrow); (D) Trichrome (blue arrow); (E) Tapioca-like pattern; (F) Perifollicular depigmentation (blue arrow); (G) Satellite lesion (blue arrow); (H) Leukotrichia; (I) Erythema (blue arrow).

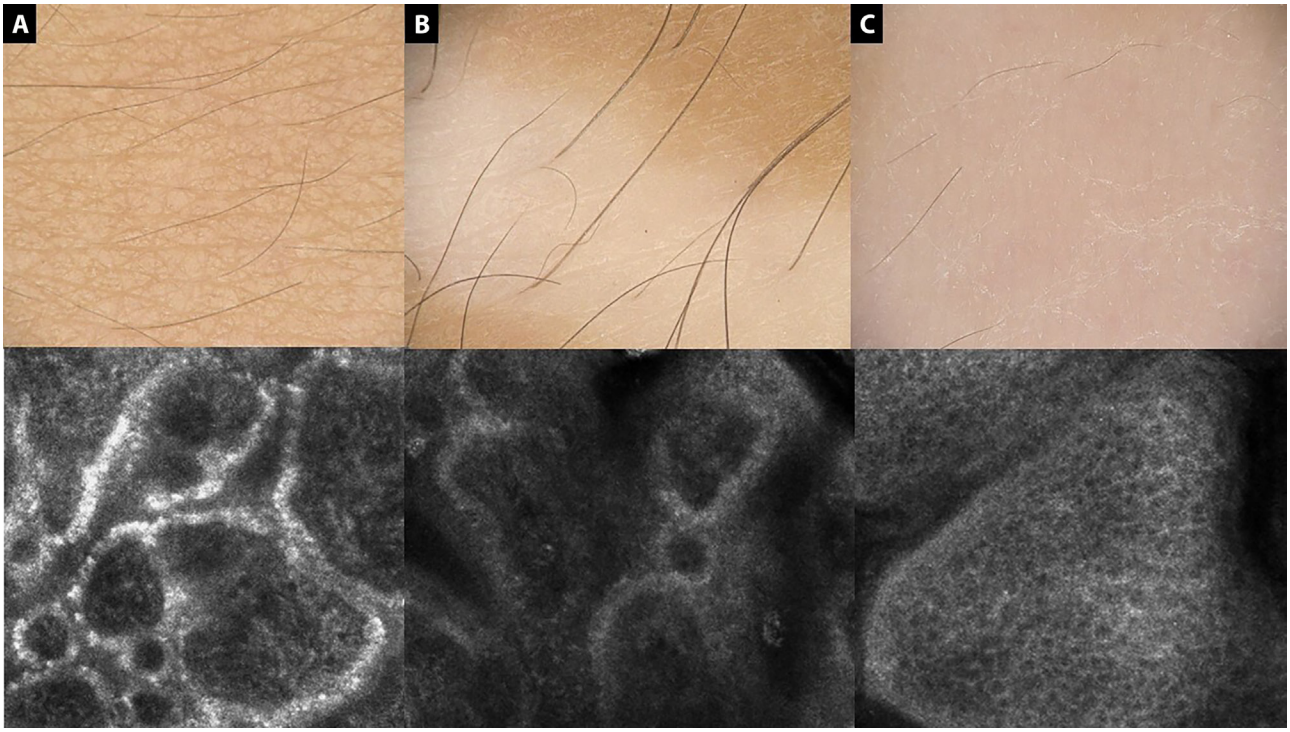

Figure 2. (A) Normal pigment network and complete ringed pattern. (B) Trichrome pattern and half rings. (C) Absent pigment network and lack of rings.

Table 4. Dermoscopic patterns contrasted with findings in reflectance confocal microscopy.

Dermatoscopy	Reflectance confocal microscopy			
Dermatoscopic patterns	Papillary rings			
Normal skin adjacent to the lesion	Absence of rings	Half rings	Complete rings	P-value
Normal pigment network No. (%) N = 40	-	7 (17.5)	33 (82.5)	-
Center of the lesion	Absence of rings N =1	Half rings N =28	Complete rings N =11	P-value
Reduced/absent pigment network, No. (%) N = 31 Others (Leukotrichia/Perifollicular depigmentation/ Erythema) N =9	21 (67.7) 7 (77.8)	10(32.7) 2 (22.2)	- -	0.69[a]
Border of the lesion	Absence of rings N =18	Half rings N =15	Complete rings N =7	
Pattern 1, No. (%) - Reduced/absent pigment network N = 17 - All other patterns N = 23	 11 (64.7) 7 (30.4)	 5 (29.4) 10 (43.5)	 1 (5.9) 6 (26.1)	 0.08[a]
Pattern 2, No. (%) - Perifollicular pigmentation N = 3 - All other patterns N = 37	 0 18 (48.6)	 1 (33.3) 14 (37.0)	 2 (66.7) 3 (13.5)	 0.03[a]
Pattern 3, No. (%) - Trichromic´ N = 4 - All other patterns N = 36	 0 18 (50.0)	 4 (100) 11 (30.6)	 0 7 (19.4)	 0.02[a]
Pattern 4, No. (%) - Tapioca sago N = 4 - All other patterns N = 36	 0 18 (50.0)	 1 (25.0) 14 (38.9)	 3 (75.0) 4 (11.1)	 <0.01[a]
Pattern 5, No. (%) - Perifollicular depigmentation N = 3 - All other patterns N = 37	 1 (33.3) 17 (45.9)	 2 (66.7) 13 (35.1)	 0 7 (18.9)	 0.76[a]
Pattern 6, No. (%) - Starburst N = 1 - All other patterns N = 39	 1 (100) 17 (43.6)	 0 15 (38.5)	 0 7 (17.9)	 0.99[a]
Pattern 7, No. (%) - Leukotrichia N = 7 - All other patterns N = 33	 4 (57.1) 14 (42.4)	 2 (28.6) 13 (39.4)	 1 (14.3) 6 (18.2)	 0.86[a]
Pattern 8, No. (%) - Erythema N = 1 - All other patterns N = 39	 1 (100) 17 (43.6)	 0 15 (38.5)	 0 7 (17.9)	 0.99[a]
Types of borders	Absence of rings n=18	Half rings n=15	Complete rings n=7	
1. Defined - Well-defined border N = 20 - All the others N = 20	 9 (45.0) 9 (45.0)	 4 (20.0) 11 (55.0)	 7 (35.0) 0	 <0.01[a]
2. Trichromic - Trichromic border N = 5 - All the others N = 35	 1 (20.0) 17 (48.6)	 4 (80.0) 11 (31.4)	 0 7 (20.0)	 0.17[a]
3. Diffuse - Diffuse border N = 15 - All the others N = 25	 8 (53.3) 10 (40.0)	 7 (46.7) 8 (32.0)	 0 7 (28.0)	 0.06[a]

[a]Fisher exact test.

The results reveal that skin with a normal pigment network displayed complete dermal papillary rings, although in certain cases only half rings were observed. Within the center of the lesion, all four dermatoscopic patterns exhibited a lack of dermal papillary rings or only half rings. At the border, the perifollicular pigmentation demonstrated half-rings as well as complete rings. The trichrome and tapioca sago pattern showcased complete papillary rings. Lastly, some complete papillary rings appeared in well-defined borders.

Table 5. Unadjusted model of clinical factors and dermatological findings associated with unstable childhood vitiligo.

Variable	OR	CI 95% inferior	CI 95% superior	P-value	R squared
Male	1.486	0.386	5.722	0.565	0.011
Age < 6 years	3.000	0.525	17.159	0.217	0.055
Skin phototypes (III)	2.720	0.696	10.633	0.150	0.069
Type of vitiligo - Non-segmental	1.750	0.492	6.230	0.387	0.025
Duration time - < of 24 months	4.286	1.135	16.182	0.032	0.155
Vitiligo extent score (VES) - > 1.5	2.436	0.494	12.014	0.274	0.041
Treatment, yes	1.875	0.396	8.875	0.428	0.022
Dermatoscopy of the center - Reduced/absent pigment network	3.167	0.663	15.115	0.148	0.072
Dermatoscopy Border - Reduced/absent pigment network - Tapioca *sago* - Leukotrichia - Trichromic - Diffuse border	 5.056 0.238 0.533 2.684 1.385	 1.248 0.023 0.106 0.254 0.378	 20.480 2.517 2.873 28.311 5.066	 0.023 0.233 0.481 0.411 0.623	 0.178 0.054 0.017 0.0253 0.008
Reflectance Confocal Microscopy border- absence rings	2.635	1.038	5.687	0.041	0.146

CI = Confidence Interval; OR = Odds Ratio.

In the unadjusted model of logistic regression, it was found that vitiligo duration time <24 months, a reduced or absent pigment network, and the absence of papillary rings are factors associated with vitiligo instability.

Table 6. Adjusted model of clinical factors and dermatological findings associated with unstable vitiligo.

Variable	OR	CI 95% inferior	CI 95% superior	P-value	R squared
Absent papillary rings	2.757	1.011	7.513	0.047	0.278
Duration time < de 24 months	4.561	1.095	18.998	0.037	

CI = Confidence Interval; OR = Odds Ratio.

Regarding RCM, in two separate studies conducted by Ardigo et al and Lai et al, the skin of adolescent and adult patients with vitiligo was evaluated, as well as that of patients without the condition. In both studies, at the dermo-epidermal junction of the control group, the presence of bright refractive keratinocytes and melanocytes forming crowns or rings around the dermal papillae (edged papillae) was observed. In the case of vitiligo lesions, the absence of these dermal papillary ring structures was noted, or only remnants of them remained. Additionally, a decrease in brightness, the presence of inflammatory cells (lymphocyte exocytosis), and the absence of melanocytes were observed in the affected areas. In the skin adjacent to vitiligo, complete dermal papillary rings with the same brightness were found, or there was the presence of incomplete melanocytic cells, resulting in an image of partial rings or similar to a "scaly" border-like pattern [23,24]. The results of our study revealed the same microscopic findings in both healthy and affected skin.

Lai et al. also compared the findings observed through RCM with other pigmentation conditions such as nevus depigmentosus and anemic nevus and noted that the dermal papillary rings in both affected skin and adjacent skin maintained their integrity and brightness. Additionally, they described that in areas of re-pigmentation, vitiligo exhibited three distinct patterns: 1) Marginal re-pigmentation with highly refractive melanocytes moving from normal skin to the affected area, 2) Perifollicular re-pigmentation with melanocytes surrounding hair follicles, and 3) Diffuse

re-pigmentation with melanocytes distributed in the affected skin [24]. In our study, being a cross-sectional study, a second measurement of the lesions was not conducted, therefore, it was not possible to compare their microscopic behavior in lesions with re-pigmentation.

The strength of our study was to associate the dermatoscopic and microscopic reflectance confocal findings of childhood vitiligo. This detailed association provides a unique and valuable perspective to understand the nature and evolution of vitiligo within a specific age group. The study revealed that the skin with a normal pigment network showed complete dermal papillary rings, but in some cases (17.5%), only half rings or festooned borders were present. This may be a normal characteristic of infantile skin or there may already be a reduction in melanocytic structures that predisposes to the spread of dermatoses. In the center of the lesion, all 4 dermatoscopic patterns showed the absence of dermal papillary rings or only half rings. The absence of dermal papillary rings was a predictor of the instability of the dermatosis. On the other hand, the border of the lesion showed different characteristics according to the type of dermatoscopic pattern. For example, the trichrome pattern only had half rings. This pattern has been associated by other authors with unstable and stable vitiligo [20,25]. The tapioca sago pattern showed complete papillary rings, and this pattern has been associated with unstable behavior and could be found at the beginning of the disease due to having complete papillary structures [19,21]. Perifollicular pigmentation showed half rings and complete rings, and this pattern has been described in re-pigmentation but other authors such as Pumirna and Wang have associated it with instability of the disease [20-22,26]. Perifollicular areas are key pieces for depigmentation or repigmentation because melanocytic stem cells are at the hair bulb [27]; through various mechanisms of autoimmunity or cutaneous migration, they lose or generate pigment [2].

The lesion border can appear in 3 forms: 1) clear and well-defined, 2) presenting three colors (trichrome) or 3) diffuse (poorly defined borders) [28]. The presence of a clear border has been associated with disease stability [28]. Our study showed the absence of papillary rings in the diffuse border, and in some cases with a clear border, the presence of complete rings (35%). This microscopic finding may be a possible predictor of stability/instability, as diffuse borders lack melanocytic remnants that generate pigment and may lead to lesion extension, while the opposite occurs in clear borders.

The limitations of this study were as follows: a) it was conducted in mixed-race skin phototypes, and further studies are needed to determine if there are differences in other skin phototypes, b) the study only provides an initial overview of the association between dermatoscopic patterns and microscopic findings, c) it is a cross-sectional study that did not have follow-up of the patients, d) due to the number of participants, only 2 predictor variables could be entered into the multivariate model.

This study opens up the possibility for future studies to expand the sample size to improve the generalization and validation of the results, to conduct cohort studies to determine the dermatoscopic and microscopic changes influenced by the disease prognosis or therapeutic regimen, to consider replicating the study in populations with different skin types or in adult populations, and to explore new methodological approaches in data analysis.

The dermatoscopic patterns associated with cutaneous microscopic findings can be used to support the evaluation of the clinical behaviour of vitiligo. The reduced/absent pigment network located in the center of the lesion did not present complete dermal papillary structures or only had partial rings and was associated with instability. The borders of the lesion showed more dermatoscopic and microscopic changes. The tapioca sago presented complete papillary rings and appeared in younger patients. The trichrome pattern only had partial rings, the perifollicular pigmentation showed partial and complete rings, and the diffuse borders did not show papillary structures. However, none of the three patterns showed clinical associations. Further studies with a larger sample size and evaluating concordance are required to determine possible associations and validate the reported results.

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