Evaluation of nail characteristics in patients with vitiligo

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Background: Vitiligo is an acquired skin discoloration with melanocytic destruction. Vitiligo is associated with other autoimmune disorders; hence, an autoimmune etiology is among the most important theories for this disorder. The nails can be involved in numerous cutaneous or systemic non-cutaneous disorders. We have taken into consideration previous studies on nail abnormalities in vitiligo and alopecia areata (AA), which are ethologically closely-related, in addition to the few, not well designed studies on nail changes in vitiligo, and lack of similar studies in Iran. This case-control study was conducted to evaluate the autoimmune etiology of vitiligo with a larger number of participants.

Methods: In this case-control study, we assessed the nail characteristics of 303 participants at Razi Hospital, Tehran, Iran from 2013-2014. These changes were also assessed in terms of diseases properties of the case group and included distribution, duration, and presence of other concomitant cutaneous disorders.

Results: There was a statistically significant odd's ratio (OR) for leukonychia in the case and control groups. The relationship between the prevalence of leukonychia and disease duration was meaningful ($P<0.05$). The risk of longitudinal ridging was approximately 1.5 times higher in vitiligo patients, which was not statistically significant ($P>0.05$). There was no other significant difference between each type of nail abnormality in the case and control groups. We observed no association between these abnormalities and disease duration. None of the nail abnormalities, including leukonychia, had an association with distribution pattern of the disorder.

Conclusion: Leukonychia was the most common abnormality in nails of vitiligo patients that had a relation to disease duration.

Keywords: vitiligo, nail, leukonychia, abnormality, case-control

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INTRODUCTION

Vitiligo is usually an acquired chronic disorder with slowly progressive cutaneous de-pigmentation. This disorder involves about 1% of the world's population and has probable spontaneous re-pigmentation in approximately 10% to 20% of patients. Vitiligo has a tremendous psychological burden, particularly in people with dark skin [1]. The exact cause of vitiligo is unknown; however, genetic factors appear to have a leading role in its developmental course as 20% to 30% of patients report a positive familial history. Vitiligo can manifest at any age and any distribution pattern, but usually begins in the second-third decades of life as the generalized form [2-6].

Vitiligo is an autoimmune process against melanocytes; its association with other autoimmune

disorders could be suggestive of autoimmunity in its pathogenesis. Although cellular and humoral immunity have been reported in its etiology, in terms of the incidence of vitiligo, cellular immunity plays the most important role. $CD8^+$ T cells infiltrate skin lesions and result in melanocyte destruction. In patients with vitiligo, reduced serum levels of transforming growth factor beta have been observed. Low levels of this substance could increase CD8+ T lymphocyte response and reduce regulatory T cell maturation [7-13].

A higher prevalence of other autoimmune disorders such as thyroid diseases, pernicious anemia, lupus, and Addison's disease have been reported in patients with vitiligo in addition to numerous genetic factors [14-20].

Diagnosis of vitiligo is basically clinical; Wood' s lamp examination helps in uncertain cases. A complete cutaneous physical exam should be done with patients that have a recent onset of this disorder in order to rule out melanoma-associated de-pigmentation [21-24]. It is logical to screen patients for other autoimmune disorders, particularly younger women or children with assessments of thyroid function and blood glucose levels [5,25-27]. Treatments used for re-pigmentation include corticosteroids, calcineurin inhibitors, ultraviolet light, and surgery. There is moderate evidence on short-term topical corticosteroids, in addition to ultraviolet light therapy alone or in combination with ertopical or oral agents [28]. The nails could be involved in numerous conditions such as kidney, hepatic, pulmonary, autoimmune, and collagen vascular disorders [29,30]. Vitiligo and alopecia areata (AA) are related disorders. Both are immune-mediated and related to other auto-immune disorders and psychological stresses [31-34]. A study has reported that the nails could be targets in AA by the same inflammatory process as hair follicles [34]. Nail pitting is the most common nail disorder in AA [35]. Trachyonychia, punctate leukonychia, spotting of the lunula, and onycholysis are other nail changes in AA [29-30,35,36]. There are few studies in this field, particularly in Iran. Hence, we have evaluated the nail characteristics of vitiligo patients in a case-control study. We enrolled a larger sample size than previous studies that assessed these nail changes based on disease properties of distribution pattern and duration. In this study, we attempted to obtain a new point of view and focus on the nail problems of vitiligo patients as well as perform clinical examinations for probable concomitant vitiligo on those patients who presented with special nail changes.

PARTICIPANTS AND METHODS

We conducted this case-control study on 303 patients at Razi Hospital, Tehran, Iran from 2013-2014. In this study, we evaluated the nail characteristics of patients with vitiligo and those from a healthy control group. These changes were also assessed in terms of disease properties in the case group that included distribution, duration, and presence of other concomitant cutaneous disorders like AA, lichen planus, and psoriasis. Both the case and control groups did not have any systemic disorders such as systemic autoimmunity. The eligibility criteria for the case group consisted of a definitive diagnosis of vitiligo and lack of any systemic non-immune or auto-immune disorders. In the control group, inclusion criteria consisted of the lack of vitiligo lack of any non-immune or auto-immune systemic disorders. Eligible participants who consented to enter the study signed an informed consent form and enrolled in the study.

The Principal Investigator of this study gathered the required data based on a questionnaire administered to participants from both groups. Collected information included demographic characteristics of the patients such as age, sex, and occupation as well as nail characteristics (normal, longitudinal ridging, absent lunula, transverse ridging, flag sign, thinning, thickening, transverse band, pale nails, total nail dystrophy, leukonychia, pitting, distal onycholysis, chronic paronychia, Terry 's sign, pigmentation, transverse groove, proximal onycholysis, clubbing, and koilonychia).

Statistical analysis

Data was entered into the SPSS v. 21 software program. For quantitative variables, the mean and standard deviation were used and percentages for qualitative ones. The chi-square and t-tests were used to compare the groups. *P*-value <0.05 was considered statistically significant. In order to compare the variables between the two groups, we used Fisher's exact test. The odd's ratio (OR) was used to compare the prevalence of variables

in the case and control groups.

We used a similar study which was conducted in Al-minya and Cario University of Egypt [37] to determine the sample size. We took into consideration a type I error of 5% and 90% power of the study, and the assumption of the nail changes in approximately 70% in the case group and 50% in the controls. Therefore, we needed to enroll 63 people in each group. In order to increase the power of this study, we designed a study that had a larger sample size compared to similar studies. We enrolled 101 patients in the case group and 202 individuals in the control group.

Limitations and recommendations

The design of this study could suggest a causal relationship, but could not prove it. It was necessary to have molecular and genetic based studies and a larger statistical population for a better approach and understanding of each type of nail change in vitiligo patients. It would be better to perform histological assessments of the nail changes. This study could be a paradigm for future, larger studies on vitiligo and other immune-mediated dermatological disorders that have probable nail involvement.

The patients enrolled based on their consent to enter the study and data were analyzed with respect to their confidentiality. The Ethical Committee of Tehran University of Medical Sciences approved this study. The authors had no conflict of interests to disclose.

RESULTS

Demographic characteristics of the case and control groups did not statistically differ. In the case group, 44.1% of participants were men and 55.9% were women. In the control group, 51.5% of the participants were men and 48.5% were women. No statistically significant difference existed between the case and control groups in terms of gender ($P>0.05$).

In the case group, 17.8% of the patients were less than 20 years of age, 23.8% were 20-29 years of age, 32.7% were 30-39 years of age, and 25.7% were older than 39 years of age. In the control group, 10.45% were less than 20 years of age, 34.7% were 20-29 years of age, 29.7% were 30-39 years of age, and 25.2% were over the age of 39 years. The stratified age distribution did not show any statistically significant difference between the two groups ($P>0.05$).

Cases and the controls did not differ in the major occupational sub-categories ($P>0.05$).

We observed that 44.7% of the case group and 24.3% of the controls had nail abnormalities. Longitudinal ridging was observed in 11.9% of the patients and 8.4% of the controls. Absent lunula of the thumb/great toe nail was observed in 3% and in 7.9% of the other nails of the case group, whereas only 2% of the control group had absent lunula of thumb/great toe nail and in 3% of the other nails.

Flag sign, thinning and pale nails were observed in 1% of the cases and 0.5% of the controls. There was no thickening of the nail and chronic paronychia in any patient of the case group. In the control group, we observed that 1% of participants had thickening of the nail and 2% had chronic paronychia. Leukonychia was detected in 14.9% of the cases and 5.4% of the controls. Pitting was observed in 3% of the cases and 0.5% of the controls. Koilonychias and clubbing were found in only one patient of the case and control groups, respectively. Based on the analysis of these results, only the prevalence of leukonychia had a statistically significant difference between the case and control groups. Leukonychia also showed a meaningful association with disease duration in the patients. The most prevalent changes in the case group included leukonychia, longitudinal ridging, and absence of lunula. Longitudinal ridging, leukonychia and absence of lunula were the most frequent changes in the controls. Other nail abnormalities were not observed in any of the case or control group participants.

The risk of longitudinal ridging was approximately 1.5 times in vitiligo patients compared with the controls, but this difference was not statistically significant (α 5%; $P>0.05$). The results of Fisher's exact test showed that the OR of leukonychia in the case and control groups was statistically significant and the relationship between prevalence of leukonychia and disease duration was meaningful (α 5%; $P<0.05$).

Fisher's exact test did not show any other significant difference between each type of nail abnormalities in the case and control groups, nor was there any association between the abnormalities

and disease duration. None of the nail abnormalities, including leukonychia, showed an association with distribution pattern of the disorder (generalized, segmental, acrofacial, universal). Table 1 shows the comparison of nail abnormalities between the case and control groups.

DISCUSSION

Vitiligo is an acquired skin discoloration with destruction of epidermal melanocytes. Types of vitiligo include segmental, acrofacial, generalized, and universal. Vitiligo is associated with other autoimmune disorders; therefore, an autoimmune etiology is among the most important theories of this disorder. The nails can be involved in numerous cutaneous or systemic non-cutaneous disorders. In one study, two types of nail changes, nail dystrophy and red lunula, have been demonstrated in vitiligo as a cutaneous autoimmune disorder [38]. In another

Table 1. Comparison of nail abnormalities in the case and control groups.

Nail characteristics in the case and control groups		Case group N=101		Control group N=202		Odd's ratio (OR) (95% confidence interval)	*P*-value
		Number	Percent	Number	Percent		
Longitudinal ridging	Positive	12	11.9	17	8.4	1.47 (0.67-3.2)	0.41
	Negative	89	88.1	185	91.6		
Absent lunula of thumb/great toe nail	Positive	3	3	4	2	1.5 (0.33-6.9)	0.69
	Negative	98	97	198	98		
Absent lunula of the other nails	Positive	8	7.9	6	3	2.8 (0.33-6.9)	0.08
	Negative	93	92.1	196	97		
Transverse ridging	Positive	0	0	0	0		
	Negative	0	0	0	0		
Total nail dystrophy	Positive	0	0	0	0		
	Negative	0	0	0	0		
Flag sign	Positive	1	1	1	0.5	2.01 (0.12-32.47)	1
	Negative	100	99	201	99.5		
Thinning	Positive	1	1	1	0.5	2.01 (0.12-32.47)	1
	Negative	100	99	201	99.5		
Thickening	Positive	0	0	2	1	---	0.55
	Negative	101	100	200	99		
Transverse band	Positive	0	0	0	0		
	Negative	0	0	0	0		
Pale nail	Positive	1	1	1	0.5	2.01 (0.12-32.47)	1
	Negative	100	99	201	99.5		
Chronic paronychia	Positive	0	0	4	2	---	0.21
	Negative	101	100	198	98		
Leukonychia	Positive	15	14.9	11	5.4	3.03 (1.34-6.87)	0.008
	Negative	86	85.1	191	94.6		
Pitting	Positive	3	3	1	0.5	6.15 (0.63-59.92)	0.11
	Negative	98	97	201	99.5		
Distal onycholysis	Positive	0	0	0	0		
	Negative	0	0	0	0		
Koilonychia	Positive	1	1	0	0	---	0.33
	Negative	100	99	202	100		
Terry's sign	Positive	0	0	0	0		
	Negative	0	0	0	0		
Pigmentation	Positive	0	0	0	0		
	Negative	0	0	0	0		
Transverse groove	Positive	0	0	0	0		
	Negative	0	0	0	0		
Proximal onycholysis	Positive	0	0	0	0		
	Negative	0	0	0	0		
Clubbing	Positive	0	0	1	0.5	---	1
	Negative	101	100	201	99.5		

study, longitudinal ridging was the most common nail changes in vitiligo in addition to leukonychia and absent lunula at the next levels [39].

Unfortunately, studies on the nail changes in vitiligo are few and have low levels of evidence. Previous studies on nail abnormalities in vitiligo and AA, one disorder ethologically closely-related to vitiligo, have encouraged us to evaluate this feature of vitiligo in a larger case-control study.

Cohen and colleagues, in 1992, reported a case of long-standing vitiligo in a 54-year-old woman who, during the course of the disease, developed asymptomatic a red lunula in thumbnail [39]. In1999, Peloro and Pride. reported the third case of twenty nail dystrophy (TND) in a10-year-old girl with vitiligo [40]. In 2001 and 2007, Khandpur and colleagues reported two patients with segmental and one patient with acrofacial vitiligo that developed TND [41,42]. Demirsoyand Bilen. reported a patient with vitiligo and TND. All nails showed dystrophy, longitudinal ridging, and pitting. The thumb/great toe nail showed sub-ungual hyperkeratosis [43]. Anbar and colleagues researched nail changes in vitiligo patients at the University of Al-minya and Cario in Egypt. This research was the first case-control study that examined nail changes in vitiligo. They evaluated 91 patients with vitiligo and 91 healthy controls. A total of 68.1% of cases and 50.5% of the controls had nail abnormalities. Longitudinal ridging was the most prevalent, statistically significant abnormality observed between case and control groups (P=0.016), followed by leukonychia (P=0.001), and absent lunula (P=0.037). Longitudinal ridging, leukonychia, and absent lunula were higher in the patient group. Punctate leukonychia, pitting, flag sign, and Terry's sign were the other nail abnormalities observed in this study [37].

The current study design was similar to the study by Anbar and colleagues [37], but with a larger sample size. The results of our study differed with the results of the Anbar study. We found nail changes in 45% of the case group and 24% of the control groups versus 70% of the case group and 50% of the control group in the Anbar study. We observed more leukonychia compared to longitudinal ridging. There was no statistically significant correlation between vitiligo and longitudinal ridging or absence of lunula. In our study, we only observed a correlation between leukonychia and vitiligo, and its duration. It would be beneficial paying more attention to disease burden and its probable associations that makes the better management and compliance with vitiligo [44].

CONCLUSION

Leukonychia is the most prevalent among probable nail abnormalities in patients with vitiligo and could be related to disease duration. It would be of great value to conduct more studies on nail problems of dermatological disorder with probable nail involvement and focus more on etiological and histological features of this entity.

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Conflict of Interest: None declared.

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