Analysis of symmetricity in the three different (sagittal, transverse and frontal) planes in generalized nonsegmental vitiligo

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Abstract

Background: Nonsegmental vitiligo is defined as being "*often symmetrical*", however, no work has tackled the point as to how valid it is to depend upon the concept of symmetricity in generalized nonsegmental vitiligo.

Aims: To investigate vitiligo symmetry, taking into account sites of predilection, the clinical characteristics of patients were studied.

Methods: This multicentric study included 712 nonsegmental vitiligo patients with 2876 examined lesions. Three models were drawn for each patient. Sagittal, transverse and frontal planes were drawn to divide the body into right/left, upper/lower and anterior/posterior halves respectively. Patients were examined by Wood's light and analyzed for symmetry.

Results: Bilateral involvement was present in 78% ($P < 0.001$). Studying the similarity of clinical involvement in the upper and lower body parts revealed that such similarity was present in 38%, with a significant positive association in some areas. Studying clinical similarity in the anteroposterior distribution pattern revealed a significant positive association in 11%.

Limitations: Relatively low number of patients.

Conclusions: We found significant bilateral symmetry in the lesions of 78% of vitiligo patients. Our work could aid in drawing the anticipated vitiligo map in patients with active disease, helping in increasing our understanding of the clinical behaviour of this disease.

Key words: Distribution, predilection, symmetry, vitiligo

Introduction

Vitiligo is a chronic and highly recognizable skin disease that often leads to a decrease in quality of life.[1] Even though many efforts have been made to acquire a deeper understanding of the pathophysiology of vitiligo, it remains enigmatic in many aspects. Its precise cause is unknown with multiple theories being proposed: chiefly those based on autoimmune, neural and autocytotoxic phenomena.[2]

The course and distribution pattern of generalized nonsegmental vitiligo is unpredictable.[3] The determination of the anticipated clinical phenotype and evolution pattern of vitiligo in the individual patient is a dream, which if fulfilled, might aid in predicting the site of the next attack. Prophylaxis can be then integrated into the treatment plans for each patient.

Nonsegmental vitiligo has been described to mainly involve the face (periorificial), dorsal surface of the

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hands, nipples, axillae, umbilicus, sacrum and inguinal/anogenital regions. On extremities, it has been shown to favor the elbows, knees, digits and flexor wrists.[4] Taieb and Picardo,[5] described sites of predilection of generalized nonsegmental vitiligo to coincide with areas more prone to the occurrence of the Koebner phenomenon.[5] A recent work highlighted the fact that the distribution pattern might depend on several clinical characteristics such as age (age of patient and age of disease onset), gender and duration of disease.[6]

Furthermore, the Vitiligo European Task Force (VETF) defines nonsegmental vitiligo as being "*often symmetrical*"; however, no work has tackled the point as to how valid it is to depend upon the concept of symmetricity in generalized nonsegmental vitiligo to draw the individualized map of vitiligo in each patient.[7] Therefore, in this study we aimed to investigate this concept of "symmetry" of vitiligo lesions, taking into account previously described sites of predilection. Furthermore, we studied other clinical characteristics of the included generalized nonsegmental vitiligo patients in relation to this concept, in an attempt to de-mystify this intriguing disease.

Methods

This multicentric study was approved by the local Dermatology Research Ethics Committee Office. Generalized nonsegmental vitiligo patients were collected consecutively from the dermatology outpatient clinics of Kasralainy teaching hospitals, Ain Shams University, Hod El Marsoud Hospital, Al Minya University and Al Fayoum University.

All patients were examined by dermatologists and patients were included if they satisfied the definition of generalized nonsegmental vitiligo.[7]

A detailed history was retrieved from each patient through a questionnaire to document their age and sex, the presence of a positive family history in a first-degree relative, as well as the duration and course of the disease based on the Vitiligo Disease Activity Score.[8] Personal and family history of autoimmune diseases (thyroid disease, diabetes mellitus type 1, alopecia areata, psoriasis, pernicious anemia, rheumatoid arthritis and systemic lupus erythematosus and Addison disease) were also assessed.[6]

Three models were drawn for each patient, in which sagittal, transverse and frontal (coronal) planes were drawn to divide the body into right/left, upper/lower and anterior/posterior halves, respectively. Included patients were thoroughly examined by Wood's light and the lesions drawn in the three models were analyzed for symmetricity.

Statistical analysis

Data were statistically described in terms of range, mean ± standard deviation, or frequencies (number of cases) and percentages when appropriate. For comparing categorical data, Chi-square ($\chi 2$) test was performed. The exact test was used when the expected frequency was less than 5. Correlation between various variables was found using the Spearman rank correlation equation for non-linear relation. *P* values of less than 0.05 were considered statistically significant. All statistical calculations were done using computer program Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

Results

This multicentric study included 712 nonsegmental vitiligo patients in whom 2876 lesions were examined. Their age ranged from 5 to 65 years with mean ± standard deviation 31.54 ± 15.437 years. There were 271 (38%) males and 441 (62%) females. The duration of disease ranged from 0.08 to 12 years with mean ± standard deviation 9.61 ± 19.243 years. The clinical and demographic data of patients is included in Table 1.

Bilateral distribution across the sagittal plane

Studying the clinical symmetry of the affected lesions revealed that bilateral involvement was present in 78% (n = 555) of patients. This figure was statistically significant (P < 0.001). All studied areas, apart from the shoulders, revealed the statistically significant positive occurrence of bilateral symmetry [Table 2]. The prevalence of bilateral distribution in different body sites is demonstrated in Table 2 and Figures 1-4.

Bilateral clinical involvement (n = 555/712) showed no statistically significant difference (P = 0.396). in males (n = 204/271, 75%) versus females (n = 351/441, 79%).

Table 1: Clinical and demographic data of all patients

Data	Results
Age/years, range (mean±SD)	5-65 (31.54±15.44)
Sex (male/female), *n* (%)	271 (38)/441 (62)
Disease duration/years, range (mean±SD)	0.08-12 (9.61±19.24)
Course of the disease (VIDA score), *n* (%)	
0	75 (10.6)
+1	106 (14.8)
+2	126 (17.7)
+3	120 (16.9)
+4	285 (40)
Family history of vitiligo, *n* (%)	
Present	252 (35.4)
Absent	460 (64.6)
Associated autoimmune disease, *n* (%)	
Present	70 (9.8)
Absent	642 (90.2)
Family history of autoimmune disease, *n* (%)	
Present	48 (6.7)
Absent	664 (93.3)

SD: Standard deviation, VIDA: Vitiligo disease activity

Upper versus lower part distribution across the transverse plane

Involvement of both upper and lower parts of the body was present in 38% (n = 270) of patients [Table 3 and Figure 5].

In addition, studying the clinical similarity in vitiligo distribution comparing upper and lower parts of body affection revealed a statistically significant positive association only between some areas e.g., upper and lower lips, upper and lower lip mucosa, nasal tip and chin, chin and neck [Table 4].

Involvement of both upper and lower body parts (n = 270/712) was not significantly different (P = 0.241). in males (n = 109/271, 40%) versus females (n = 161/441, 37%).

Anteroposterior distribution across the frontal plane

The anteroposterior distribution pattern among vitiligo patients revealed a significant positive association in 11% (n = 80/712). This was detected between the periauricular and postauricular areas (n = 40), and also between the abdomen and the back (n = 40) [Table 5 and Figures 6, 7].

Anteroposterior clinical was not significantly different (P = 0.387) involvement (n = 80/712) in males (n = 35/271, 12.9%) versus females (n = 45/441, 10.2%).

A significant positive correlation was detected between longer disease duration and symmetry in all the 3 studied

Table 2: The association of clinical similarity in bilateral distribution pattern in the studied vitiligo patients, shaded areas are the sites of predilection

Studied association		Positive association, *n* (%)	Negative association, *n* (%)	*P*
Right side forehead	Left side forehead	93/110 (84.5)	17/110 (15.5)	<0.001*
Right side nose	Left side nose	36/36 (100)	0	<0.001*
Right eyelid	Left eyelid	93/160 (58.1)	67/160 (41.2)	<0.001*
Right periauricular	Left periauricular	28/28 (100)	0	<0.001*
Right postauricular	Left postauricular	21/21 (100)	0	<0.001*
Right ear	Left ear	7/7 (100)	0	<0.001*
Right cheek	Left cheek	36/36 (100)	0	<0.001*
Right shoulder	Left shoulder	7/32 (21.8)	25/32 (78.2)	<0.002*
Right axilla	Left axilla	156/178 (87.6)	22/178 (12.3)	<0.001*
Right arm	Left arm	36/53 (67.9)	17/53 (32.1)	<0.001*
Right elbow	Left elbow	185/197 (94)	12/197 (6)	<0.001*
Right cubital fossa	Left cubital fossa	7/14 (50)	7/14 (50)	1
Right forearm/wrist	Left forearm/wrist	150/170 (88)	20/170 (12)	<0.001*
Right dorsum of hand	Left dorsum of hand	142/177 (80)	35/177 (20)	<0.001*
Right fingers	Left fingers	142/154 (92)	12/154 (8)	<0.001*
Right periungual area	Left periungual areas	89/98 (90.8)	9/98 (9.2)	<0.001*
Right palm	Left palm	28/28 (100)	0	<0.001*
Right nipple	Left nipple	14/14 (100)	0	<0.001*
Right areola	Left areola	14/25 (56)	11/25 (44)	<0.001*
Right breast	Left breast	71/71 (100)	0	<0.001*
Right half of the chest	Left half of the chest	57/69 (82.6)	12/69 (17.4)	<0.001*
Right half of the abdomen	Left half of the abdomen	28/28 (100)	0	<0.001*
Right half of the back	Left half of the back	50/50 (100)	0	<0.001*
Right buttock	Left buttock	36/36 (100)	0	<0.001*
Right thigh	Left thigh	71/82 (86.6)	11/82 (13.4)	<0.001*
Right knee	Left knee	157/180 (87)	23/180 (13)	<0.001*
Right popliteal fossa	Left popliteal fossa	43/57 (75.4%)	14/57 (24.6)	<0.001*
Right leg	Left leg	178/190 (94)	12/190 (6)	<0.001*
Right malleolus	Left malleolus	164/173 (95)	9/173 (5)	<0.001*
Right dorsum of foot	Left dorsum of foot	150/178 (84)	28/178 (16)	<0.001*
Right toes	Left toes	50/62 (80.6)	12/63 (19.4)	<0.001*
Right periungual areas (toes)	Left periungual areas (toes)	100/120 (83.3)	20/120 (16.7)	<0.001*
Right side of scrotum	Left side of scrotum	21/21 (100)	0	<0.001*
Right side of labia minora	Left side of labia minora	14/14 (100)	0	<0.001*
Right side of vulva	Left side of vulva	7/7 (100)	0	<0.001*

*P<0.05 is significant

Table 3: The association of clinical similarity in the upper versus lower body parts distribution pattern among the studied vitiligo patients

Studied association		Positive association, *n* (%)	Negative association, *n* (%)	*P*
Right arm	Right thigh	11/61 (18)	50/61 (82)	0.273
Left arm	Left thigh	11/53 (20.8)	42/53 (79.2)	0.138
Right forearm	Right leg	52/169 (30.8)	117/169 (69.2)	0.322
Left forearm	Left leg	32/151 (21.2)	119/151 (78.8)	0.462
Right elbow	Right knee	109/193 (56.5)	84/193 (43.5)	<0.001*
Left elbow	Left knee	109/204 (53.4)	95/204 (46.6)	<0.001*
Right cubital fossa	Right popliteal fossa	0	18/18 (100)	0.453
Left cubital fossa	Left popliteal fossa	0	9/9 (100)	0.552
Right dorsum of hand	Right dorsum of foot	64/180 (35.5)	116/180 (64.5)	0.103
Left dorsum of hand	Left dorsum of foot	71/157 (45.2)	86/157 (54.8)	<0.001*
Right fingers	Right toes	22/144 (15.3)	122/144 (84.7)	0.016*
Left fingers	Left toes	22/156 (14.1)	134/156 (85.9)	0.003*

*P<0.05 is significant

Table 4: The association of clinical similarity in the upper versus lower body parts within different organs among the studied vitiligo patients

Studied association		Positive association, *n* (%)	Negative association, *n* (%)	*P*
Upper lip	Lower lip	79/90 (87.8)	11/90 (12.2)	<0.001*
Upper lip mucosa	Lower lip mucosa	11/11 (100)	0	<0.001*
Right arm	Right forearm	9/63 (14.3)	54/63 (85.7)	0.206
Left arm	Left forearm	9/54 (16.7)	45/54 (83.3)	0.575
Right thigh	Right leg	41/82 (50)	41/82 (50)	1
Left thigh	Left leg	30/83 (36.1)	53/83 (63.9)	0.091

*P<0.05 is significant

planes (P = 0.001, 0.035, 0.047, respectively). No other significant associations were detected with any clinical or demographic variable.

Discussion

Pattern recognition is at the heart of clinical dermatology,[9] and several studies have been conducted in recent years to understand the patterns of lesion evolution in vitiligo.[6,10,11] We believe that this study takes us a step closer to understanding the pattern of this unpredictable disease.

Symmetricity is traditionally thought of in terms of the right/left relationship. However, literally it means the quality of being similar in parts facing each other or around an axis,. Accordingly, in our body, we can have horizontal, vertical and anteroposterior symmetry.[12] In this study, 2876 lesions in 712 nonsegmental vitiligo patients were clinically studied for symmetry along those three planes, in an attempt to draw a clearer map for vitiligo.

Bilateral symmetry was the most significant, as it was documented in 78% (n = 555) of patients, followed by upper and lower symmetriy in 53% (n = 376), and anteroposterior symmetry in 11% (n = 80).

Focusing attention on the bilateral symmetry, all examined sites apart from the shoulders exhibited a significant positive bilateral symmetry. All sites exhibited at least 50% positive bilateral symmetry, that reached up to 100% in certain areas (nose, ear with the pre- and postauricular areas, eyelids, cheeks, palms, breasts with nipple, abdomen, back, buttocks, genitalia (scrotum, labia and vulva).

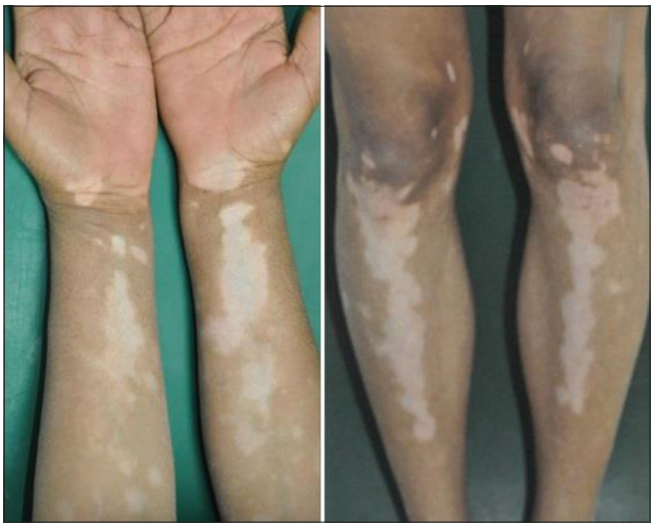

Figure 1: Clinical photo of (patient number 7) showing clinical similarity in vitiligo distribution comparing right and left sides of the body

Furthermore, we noticed that areas of predilection previously described, are also the most prone to exhibit bilateral symmetry.[4] For example, among the 15 sites that exhibited 100% bilateral

Table 5: The association of clinical similarity in the anteroposterior distribution pattern among the studied vitiligo patients

Studied association		Positive association, *n* (%)	Negative association, *n* (%)	*P*
Right periauricular	Right postauricular	20/31 (64.5)	11/31 (35.5)	<0.001*
Left periauricular	Left postauricular	20/31 (64.5)	11/31 (35.5)	<0.001*
Right elbow	Right cubital fossa	9/191 (4.7)	182/191 (95.3)	0.001
Left elbow	Left cubital fossa	0	205/205 (100)	<0.001*
Right dorsum of hand	Right palm	20/186 (11.8)	166/186 (88.2)	<0.001*
Left dorsum of hand	Left palm	20/157 (12.7)	137/157 (87.3)	<0.001*
Right side of chest	Right side of back	22/64 (34.4)	42/64 (65.6)	<0.001*
Left side of chest	Left side of back	22/53 (41.5)	31/53 (58.5)	<0.001*
Right side of abdomen	Right side of back	20/20 (100)	0	<0.001*
Left side of abdomen	Left side of back	20/20 (100)	0	<0.001*
Right knee	Right popliteal fossa	11/172 (6.4)	161/172 (93.6)	<0.001*
Left knee	Left popliteal fossa	34/166 (20.5)	132/166 (79.5)	<0.001*

*P<0.05 is significant

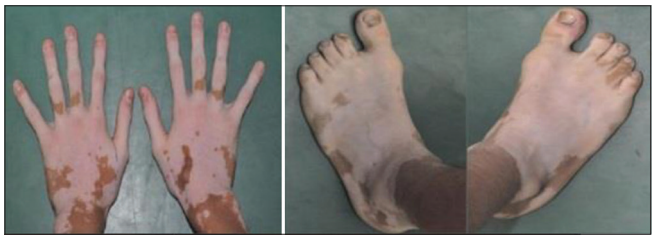

Figure 2: Clinical photo of (patient number 13) showing clinical similarity in vitiligo distribution comparing right and left sides of the body

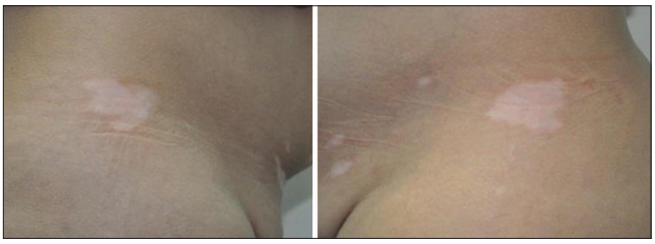

Figure 3: Clinical photo of (patient number 20) showing clinical similarity in vitiligo distribution comparing right and left sides of the body

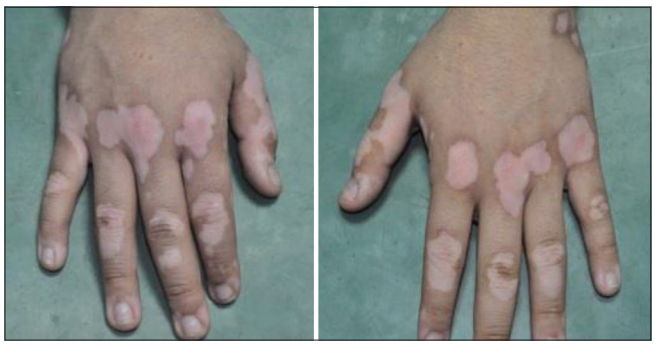

Figure 4: Clinical photo of (patient number 25) showing clinical similarity in vitiligo distribution comparing right and left sides of the body

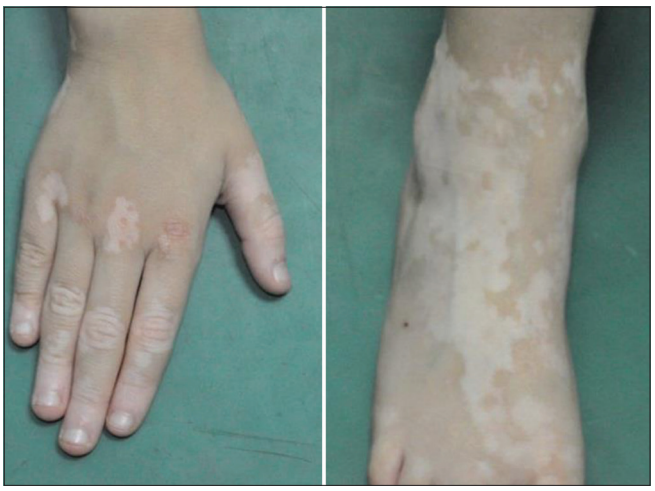

Figure 5: Clinical photo of (patient number 27) showing clinical similarity in vitiligo distribution in both upper and lower parts of the body

symmetry, ten belonged to the previously categorized areas of predilection.[4] Furthermore, areas prone to koebnerization demonstrated high rates of bilateral symmetry, such as the malleolus which is highly prone to trauma owing to the praying and sitting habits in our country (95%), as well as the palms (100%). The high rates of bilateral symmetry exceeding 50%, support the previous notion of *"often"* symmetrical, but our study revealed some areas to be more prone than others.[4]

Analyzing the vertical symmetricity pattern (upper/lower) around the transverse plane, most sites did not show such a pattern. We did not observe lesions occurring on lips or neck and genitalia in any patient. The vertical symmetry rate ranged from 15% (fingers and toes) around 55% (elbows and knees). Even here, positive vertical symmetry was mainly noted in the areas previously described to be sites of predilection (elbows, knees, digits, dorsum of hands/feet).

We also studied vertical symmetry among different anatomical areas. We found some interesting data; 90-100% symmetry was detected between the upper and lower lip and its mucosa respectively, drawing attention to the importance of protecting the lips once a lesion starts to appear on one. Lower rates of symmetry were noted in the extremities, with around 15% positive association between arm and forearm,

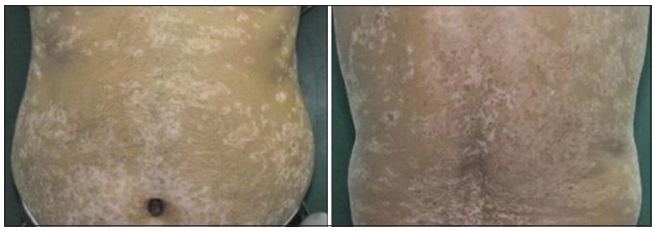

Figure 6: Clinical photo of (patient number 35) showing clinical similarity in the antero-posterior distribution pattern among vitiligo patients

and 36-50% between thigh and leg. Nevertheless, the existence of such associations highlights the importance of taking into account both horizontal and vertical symmetries once lesions emerge on the extremities.

The anteroposterior aspect added further to the vitiligo map. 100% of the cases showed a positive association between the back and abdomen and around 40% between back and chest. Moreover, a positive association between pre- and postauricular areas was detected in around 65% of the cases. The rest of the sites showed strongly negative association (80%-100%). We cannot fully explain this finding. However, several hypotheses can be suggested including different developmental patterns and unlikely exposure to kobnerization in the anteroposterior direction of the body.

It is essential to highlight that negative associations should be considered as important as the positive ones, with both together helping us in drawing the individual map of each case of vitiligo, helping in identifying the areas likely to get affected.

The significant association between the positive symmetry in all studied areas and the duration of the disease is a point of crucial importance. It clarifies the image that vitiligo in each patient follows a preset map, rather than being haphazard. It just takes time to fulfill the picture. It could help us to draw a map for the patient in the first visit itself, so that we can build our therapeutic plan paying attention to areas at higher risk.

Another point of importance is the significance of this symmetry in vitiligo. Still little is known about the biological basis of why any disease has a pattern, despite efforts to categorize pattern inducers.[9] In recent work, cutaneous mosaicism was suggested to be involved in the pattern of segmental vitiligo.[13,14] In general, a pattern formation is claimed to represent the crossroad between three basic elements; genetics, developmental biology and clinical dermatology, a rule that can be applied to nonsegmental vitiligo.[9]

Conclusion

The current work studied the symmetricity along the three different (sagittal, transverse and frontal) planes in generalized nonsegmental vitiligo and found significant bilateral symmetry (78%) was found to be positively correlated with the disease duration. Furthermore, the study sheds light on the positive and negative associations between different body parts which might aid in drawing the anticipated map of vitiligo that in turn could aid treatment and prophylaxis. Still, further work is needed to establish the reliability of this work, and whether it is the same among different ethnic groups. In addition, proper therapeutic plans, based on the prevention concept, need to be established and evaluated regarding long-term outcomes. A relatively small number of participants is a limitation of this study.

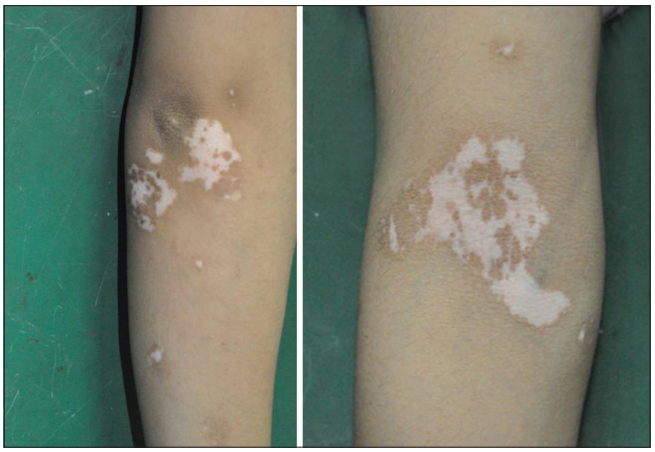

Figure 7: Clinical photo of (patient number 40) showing clinical similarity in the antero-posterior distribution pattern among vitiligo patients

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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