

## ORIGINAL ARTICLE

# Childhood- and later-onset vitiligo have diverse epidemiologic and clinical characteristics

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**Background:** Vitiligo onset during childhood is common. There are limited data regarding childhood-onset vitiligo.

**Objective:** We sought to provide an epidemiologic and clinical comparison between childhood- and later-onset vitiligo.

**Methods:** Two groups of patients were included in this cross-sectional study. Consecutive patients examined at the Vitiligo Clinic of Andreas Sygros Hospital for Skin and Venereal Diseases, Athens, Greece, from January 2005 to December 2009 with a disease onset before the age of 12 years were included in the childhood-onset group. The later-onset group included randomly selected patients who were examined at the same period and had a disease onset after the age of 12 years. After clinical examination, a standardized questionnaire was completed for each patient.

**Results:** In all, 126 patients were included in the childhood-onset and 107 patients in the later-onset group. Childhood-onset vitiligo: (1) involved different sites at initial presentation, (2) included more cases of segmental type, and (3) was characterized by a higher prevalence of allergic diseases and a lower prevalence of thyroid diseases. Longer duration of disease and a positive family history of thyroid disease were associated with the presence of thyroid disease only in the childhood-onset group. In the later-onset group, only female sex was associated with the presence of thyroid disease.

**Limitations:** The study was conducted in a hospital specializing in skin diseases and a selection bias toward more severe vitiligo cases is possible.

**Conclusions:** Childhood-onset vitiligo had distinct epidemiologic and clinical characteristics, compared with later-onset disease. (J Am Acad Dermatol 10.1016/j.jaad.2011.07.010.)

**Key words:** childhood vitiligo; clinical presentation; epidemiology; thyroid disease.

Vitiligo quite often appears early in life. Disease onset before the age of 20 years has been reported in 29%<sup>1</sup> and 50%<sup>2</sup> of patients with vitiligo. However, few reports<sup>1,3-13</sup> have addressed clinically and epidemiologically the issue of childhood vitiligo, that is vitiligo occurring before the age of 12 years. Even fewer have compared childhood- with later-onset vitiligo on clinical and epidemiologic grounds.<sup>1,3,4,8</sup>

In this study, we provide an epidemiologic and clinical comparison between childhood- and later-onset vitiligo.

## METHODS

Two groups of patients were included in the study. Consecutive patients examined at the Vitiligo Clinic of Andreas Sygros Hospital for Skin and Venereal Diseases, Athens, Greece, during the

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5-year period from January 2005 to December 2009 with a disease onset before the age of 12 years were included in the childhood-onset group. The later-onset group included randomly selected patients who were examined at the same period and had a disease onset after the age of 12 years.

A detailed history was obtained from each patient.

Vitiligo was classified as focal ( $\geq 1$  macules in one area, but not clearly in a dermatomal configuration), acral (several macules on the extremities on different areas), acrofacial (several macules on the extremities and face), vulgaris (scattered macules widely distributed), universal ( $>80\%$  of body surface area affected), or segmental ( $\geq 1$  macules in a dermatomal configuration or unilateral segment of the body).

### Statistical analysis

The comparison of quantitative variables between different groups was performed using the independent samples *t* test and Mann-Whitney test in case of violation of normality. The comparison of qualitative variables between different groups was performed using the  $\chi^2$  test or the Fisher exact test. All tests were two-sided; statistical significance was set at *P* less than .05.

A logistic regression model was used to detect which of several independent variables affected the probability of presence of thyroid disease in our patients.

All analyses were carried out using the statistical package SPSS, Version 13.00 (Statistical Package for the Social Sciences, SPSS Inc, Chicago, IL).

## RESULTS

In all, 394 patients were examined during the 5-year period of the study and 126 of them had a disease onset during childhood (32%). Among the rest of the patients with later-onset disease, we randomly selected 107 patients to be included in the study.

### Demographic features of patients

Table I shows the demographic characteristics of patients. Female patients were similarly overrepresented in both groups. Patients with later-onset vitiligo had darker skin phototypes ( $P < .002$ ).

### Disease presentation

Sites of initial disease presentation were statistically significantly different between the two groups (Table II). Childhood-onset (vs later-onset) vitiligo had a predilection for the eyelids (21% vs 6.5%) and lower extremities (20.3% vs 3.7%), whereas the main site of presentation for later-onset vitiligo were the upper extremities (47.7% vs 16.3%) and particularly the hands (40.2% vs 12.2%).

The type of vitiligo upon initial presentation of the disease is shown in Table III. Segmental vitiligo was more common in the childhood vitiligo group (6.6% vs 1%,  $P < .05$ ).

Patients with later-onset vitiligo recalled a stressful event at disease presentation with greater frequency, compared with the childhood-onset group (37% vs 24%,  $P < .02$ ).

### Disease progression

Vitiligo vulgaris was the predominant type of the disease upon consultation for both groups (Table IV).

The vast majority of patients in both groups reported a progressive course of their disease. No progression among patients with a disease duration of more than 4 years was reported by 4.8% and 2.4% of patients in the childhood- and later-onset group, respectively. An immediate progression of the disease was reported by 10.5% and 35.5% of patients in the childhood- and later-onset group, respectively ( $P < .001$ ). Among patients whose disease did not progress immediately, the mean number of years from disease appearance until progression to other sites was  $4.14 \pm 6.13$  and  $2.7 \pm 4.1$  for the childhood- and later-onset group, respectively ( $P < .06$ ).

### Personal history of autoimmune and/or endocrine diseases

Allergic diseases had a higher prevalence within the childhood-onset group (5.7% vs 0%,  $P < .01$ ) (Table V). On the contrary, thyroid diseases were reported with a greater frequency from patients with later-onset vitiligo (42% vs 18%,  $P < .01$ ).

Several variables, such as patients' sex, skin phototype, age of vitiligo onset, duration of disease, presence of a stressful event at disease presentation, progression or not of the disease, years before disease's progression, body surface area affected by

### CAPSULE SUMMARY

- Childhood-onset vitiligo may differ from later-onset disease.
- Childhood-onset vitiligo affected different sites at initial presentation and it was characterized by a higher prevalence of allergic diseases and a lower prevalence of thyroid diseases.
- In childhood-onset vitiligo, the presence of thyroid disease was associated with duration of vitiligo and a positive family history of thyroid disease and not with female sex, as in later-onset vitiligo.

**Table I.** Demographic features of patients

|                          | Childhood vitiligo | Later-onset vitiligo |
|--------------------------|--------------------|----------------------|
| Sex                      |                    |                      |
| Female                   | 81 (65.9%)         | 65 (60.7%)           |
| Male                     | 42 (34.1%)         | 42 (39.3%)           |
| Age on consultation, y   |                    |                      |
| Mean $\pm$ SD            | 25.4 $\pm$ 11.6    | 43.3 $\pm$ 13.8      |
| Range                    | 6-62               | 16-75                |
| Age of vitiligo onset, y |                    |                      |
| Mean $\pm$ SD            | 8 $\pm$ 3.1        | 30.3 $\pm$ 13.6      |
| Range                    | 1-12               | 14-73                |
|                          | 0-4 y: 14 (11.4%)  | 13-18 y: 23 (21.5%)  |
|                          | 5-8 y: 59 (48%)    |                      |
|                          | 9-12 y: 50 (40.6%) |                      |
| Duration of disease, y   | 16.3 $\pm$ 11      | 13 $\pm$ 10.4        |
| Skin phototype*          |                    |                      |
| II                       | 22 (18.5%)         | 24 (22.4%)           |
| III                      | 67 (56.3%)         | 36 (33.7%)           |
| IV                       | 30 (25.2%)         | 44 (41.1%)           |
| V                        | 0 (0%)             | 3 (2.8%)             |

\* $P < .002$ .

the disease, family history of vitiligo, and family history of thyroid disease were assessed for their association with the presence or not of thyroid disease in the patients. Within the childhood-onset group, the multivariable analysis revealed that the two variables associated with the presence of thyroid disease were family history of thyroid disease (odds ratio 4.3 [CI 1.343-13.799],  $P < .014$ ) and duration of vitiligo (odds ratio 1.080 [1.033-1.130],  $P < .001$ ).

In the later-onset group, the only variable that could predict the presence of thyroid disease in multivariable analysis was patient's sex (odds ratio 2.578 [1.127-5.897] for females,  $P < .025$ ).

### Family history

Family history of vitiligo was reported by 35% and 33% of patients with childhood- and later-onset vitiligo, respectively (Table VI). A high number of patients reported a family history of thyroid diseases (59% and 48% for childhood- and later-onset vitiligo, respectively). No statistically significant difference was revealed between the two groups in the above rates.

Within the childhood vitiligo group, there was no difference in the percentage of patients who reported a positive family history of vitiligo between patients with disease onset before and after 7 years of age (33.3% and 36.2%, respectively). Furthermore, there was no difference in the number of relatives with vitiligo between these two groups.

**Table II.** Sites of initial disease presentation

|                               | Childhood vitiligo | Later-onset vitiligo |
|-------------------------------|--------------------|----------------------|
| Head                          | 38 (31%)           | 29 (27%)             |
| Eyelids*                      | 26 (21%)           | 7 (6.5%)             |
| Upper extremities*            | 20 (16.3%)         | 51 (47.7%)           |
| Hands*                        | 15 (12.2%)         | 43 (40.2%)           |
| Fingers*                      | 10 (8%)            | 22 (20.6%)           |
| Lower extremities*            | 25 (20.3%)         | 4 (3.7%)             |
| Neck and trunk                | 29 (23.6%)         | 22 (20.6%)           |
| Multiple (>2 different sites) | 20 (16.3%)         | 12 (11.2%)           |

\* $P < .008$ .**Table III.** Type of vitiligo on initial presentation

|            | Childhood vitiligo | Later-onset vitiligo |
|------------|--------------------|----------------------|
| Focal      | 85 (69.6%)         | 83 (78.3%)           |
| Vulgaris   | 14 (11.5%)         | 11 (10.4%)           |
| Acrofacial | 11 (9%)            | 8 (7.5%)             |
| Acral      | 4 (3.3%)           | 4 (3.8%)             |
| Segmental* | 8 (6.6%)           | 0 (0%)               |

\* $P < .05$ .

### DISCUSSION

The purpose of this study was to compare childhood- and later-onset vitiligo in clinical and epidemiologic grounds. In contrast to other studies on childhood vitiligo, we included in the childhood vitiligo group not only children but also adults with childhood-onset disease. This enabled us to gather data on the progression of childhood vitiligo and on the risk for development of other diseases later in life in these patients.

Our study revealed several differences between childhood- and later-onset vitiligo. Childhood-onset vitiligo: (1) involved different sites at initial presentation, (2) included more cases of segmental type, (3) had a lower connection to stressful events at initial presentation, (4) demonstrated a slower rate of progression, (5) was characterized by a higher prevalence of allergic diseases and a lower prevalence of thyroid diseases, and (6) was characterized by different risk factors for the presence of thyroid disease (longer duration of disease and positive family history of thyroid disease), compared with later-onset vitiligo (female sex).

The limitations of the study include possible recall errors, especially in patients whose disease started many years before presentation to our clinic and a selection bias toward more severe vitiligo cases, because the study was conducted in a hospital specializing in skin diseases.

Vitiligo onset during childhood (<12 years old) is common. Most studies<sup>3,5,7</sup> report a disease onset

**Table IV.** Type of vitiligo on consultation

|             | Childhood vitiligo | Later-onset vitiligo |
|-------------|--------------------|----------------------|
| Vulgaris    | 84 (68.8%)         | 86 (80.4%)           |
| Acrofacial  | 13 (10.7%)         | 13 (12.1%)           |
| Acral       | 11 (9%)            | 3 (2.8%)             |
| Focal       | 4 (3.3%)           | 4 (3.7%)             |
| Universalis | 2 (1.6%)           | 0 (0%)               |
| Segmental*  | 8 (6.6%)           | 1 (1%)               |

\* $P < .05$ .**Table V.** Personal history of other diseases

|                          | Childhood vitiligo | Later-onset vitiligo |
|--------------------------|--------------------|----------------------|
| Thyroid diseases*        | 22 (18%)           | 45 (42%)             |
| Allergic diseases*       | 7 (5.7%)           | 0 (0%)               |
| Rheumatoid arthritis     | 3 (2.4%)           | 2 (1.8%)             |
| Psoriasis                | 3 (2.4%)           | 2 (1.8%)             |
| IBD                      | 1 (0.8%)           | 1 (0.9%)             |
| Type 1 diabetes mellitus | 0 (0%)             | 2 (1.8%)             |
| Atopic dermatitis        | 1 (0.8%)           | 1 (0.9%)             |
| Alopecia areata          | 1 (0.8%)           | 0 (0%)               |

IBD, Inflammatory bowel disease.

\* $P < .01$ .

before the age of 12 years in about 25% of patients. In the current study, 32% of our 394 consecutive patients noted a disease onset during childhood. In accordance with the results of previous studies,<sup>5,7</sup> the majority of our patients (89%) had a disease onset after the age of 4 years.

No clear sex preference can be established for childhood vitiligo. Some studies report a female predominance of 57%<sup>3,5</sup> to 63%,<sup>6</sup> and, in our study, this percentage was even higher (66%). Other studies describe equal numbers of patients for both sexes.<sup>4,7</sup> Whether girls are overrepresented in childhood, compared with later-onset vitiligo, is also unclear. We found no difference of female:male ratio between childhood- and later-onset vitiligo and this result is in accordance with some other studies.<sup>4,7</sup> However, a female preponderance in childhood-onset, compared with later-onset, vitiligo has also been reported.<sup>5,6</sup>

Regarding the site of initial presentation of childhood vitiligo, our results are in agreement with previous studies that reported the head and neck area as the most common and the upper extremities as the least common site.<sup>4-6</sup> To our knowledge, the site of initial disease presentation has not been compared before between childhood- and later-onset vitiligo. We found a statistically significant difference in the site of initial disease presentation between the two groups, with later-onset vitiligo appearing in almost half the patients in upper

**Table VI.** Family history of patients

|                  | Childhood vitiligo | Later-onset vitiligo |
|------------------|--------------------|----------------------|
| Vitiligo         | 43 (35%)           | 35 (33%)             |
| Thyroid diseases | 72 (59%)           | 51 (48%)             |
| Psoriasis        | 20 (16%)           | 15 (14%)             |

extremities, especially the hands. The reason behind this difference is unclear.

Psychological stress has been associated with vitiligo onset and progression. In one recent study, 54% of patients with vitiligo mentioned stress as the cause of their disease.<sup>14</sup> A significant difference in the mean number of stressful events between patients with vitiligo and control subjects has also been reported.<sup>15</sup> In the pediatric vitiligo population, disease onset has been connected to psychological factors in 57% of patients.<sup>16</sup> In the current study, we specifically asked for the presence of a stressful event (eg, death of a beloved person or divorce) just before the onset of the disease. A great percentage of patients from both groups recalled such an event. Patients with later-onset vitiligo recalled a stressful event with statistically significantly higher frequency. However, we cannot exclude a recall bias in this difference, because patients with childhood vitiligo might be unable to recall the period of disease onset with clarity.

Most patients from both groups reported a progressive course of their disease and, upon consultation, vitiligo vulgaris was the most common disease type for both groups. However, we cannot conclude that most cases of focal vitiligo progress to the vulgaris type, because our hospital is a tertiary health center and a selection bias toward more severe cases is possible. Among the different types of vitiligo, only the segmental type was more prevalent in the childhood group, as it has been reported elsewhere.<sup>1,3,4</sup> The rates of segmental vitiligo in children vary across studies from 4.6%<sup>5</sup> to 32.5%,<sup>4</sup> with more studies reporting a rate above 16%.<sup>1,3,4,6,7,12,13</sup> Later-onset vitiligo seems to progress faster than childhood disease.

Children with vitiligo are reported to have lower rates of associated autoimmune and/or endocrine disorders, compared with adults.<sup>1,4</sup> However, thyroid dysfunction may be subclinical in children.<sup>9,11</sup> Furthermore, an increased incidence of autoantibodies without further evidence of disease has also been reported in children with vitiligo,<sup>3,13</sup> compared with healthy children, which suggests a propensity for autoimmune disease later in life.

In this study, in agreement with the previously mentioned studies, the prevalence of thyroid diseases was statistically significantly lower in patients with childhood vitiligo, compared with patients with

later-onset disease. Another interesting finding that, to our knowledge, has not been reported before is that in the childhood vitiligo group, the presence of thyroid disease was associated with the family history of thyroid disease and with duration of vitiligo, whereas in the later-onset group, the only association was with the female sex. Thus, one may speculate that the prevalence of thyroid disease in the childhood group will increase, as these patients get older.

We found a higher prevalence of allergic diseases in patients with childhood vitiligo, compared with patients with later-onset disease, which has not been reported before. Alopecia areata is frequently reported in studies on children with vitiligo at a rate of 0.32%<sup>5</sup> to 2.4%,<sup>3</sup> which is in agreement with our rate of 0.8%.

Compared with the general population, patients with vitiligo have higher rates of positive family history of the disease.<sup>6,17</sup> In childhood-onset vitiligo, a positive family history has been reported in 11% to 35% of cases.<sup>3-7,9,10</sup> In our study, 35% of patients with childhood-onset vitiligo and 33% of patients with later onset had a positive family history of the disease. No difference was found between the two groups, as it has been reported elsewhere.<sup>3,4</sup>

Age of vitiligo onset has been reported to be lower in Caucasian familial vitiligo cases than in singleton cases.<sup>6,18,19</sup> We did not find a difference in the positive family history rate between patients with early versus late disease onset within the childhood vitiligo group.

Children with vitiligo have been reported to have a positive family history of autoimmune/endocrine diseases more often, compared with both children without vitiligo<sup>6,8</sup> and adults with vitiligo.<sup>1,3</sup> The autoimmune/endocrine disease most frequently found is thyroid disease. A positive family history of thyroid disease has been described in 32% to 43% of children with vitiligo,<sup>6,9</sup> which is lower than the 59% of our study. This difference could be attributed to the very high rate of thyroid disease in Greece. The positive family history rate for thyroid disease was lower in the later-onset vitiligo group, but the difference was not statistically significant. The prevalence of psoriasis in patients with vitiligo has been reported to be 2.6% to 4.8%, which is not statistically significantly higher than in the general population.<sup>20,21</sup> The prevalence of psoriasis in our patients was slightly lower. Interestingly, many of our patients had a family history of psoriasis.

In conclusion, we found several differences between childhood- and later-onset vitiligo. In clinical practice, it is important to keep in mind that children with vitiligo, both boys and girls, can develop

thyroid disease later in life, especially if they have a positive family history of thyroid disease.

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