

## Vitiligo epidemiological profile and the association with thyroid disease \*

### Perfil epidemiológico dos pacientes com vitiligo e sua associação com doenças da tireoide

Daniel Holthausen Nunes <sup>1</sup>

Ligia Maria Hademann Esser <sup>2</sup>

**Abstract:** BACKGROUND: Vitiligo is considered the most frequent acquired hypomelanosis. Although its pathogenesis is uncertain, it is believed that autoimmune etiology is the most plausible. This theory is based on the coexistence of vitiligo with autoimmune diseases. Objectives: To describe the epidemiological profile of vitiligo patients and to estimate the prevalence of the association of vitiligo with autoimmune thyroid diseases. Methods: A cross-sectional study was conducted through analysis of the medical records of patients diagnosed with vitiligo in the AME-UNISUL Outpatient Clinic of Dermatology and at HU-UFSC. The clinical and laboratorial characteristics of these patients were assessed. Results: 85 medical records were evaluated; 56 patients were female, with a mean age of 37.14 years and mean onset age of 25.25 years. Vitiligo vulgaris occurred in 70.6%. Autoimmune thyroid diseases were found in 22.4%. Other autoimmune diseases were identified in 5.9%. Patients with positive thyroid autoantibodies showed a probability of extension of vitiligo greater than 25%. There was no statistical difference with regard to the clinical characteristics of vitiligo in patients with or without autoimmune thyroiditis with hormonal change. Conclusion: The findings of this study are similar to those obtained by other authors, showing that autoimmune thyroid diseases are more common in patients with vitiligo.

**Keywords:** Autoimmunity; Thyroid diseases; Vitiligo

**Resumo:** FUNDAMENTO: O vitiligo é considerado a hipomelanose adquirida mais frequente. Apesar de sua etiopatogenia ser incerta, acredita-se que a etiologia autoimune seja a mais plausível, teoria que se fundamenta na concomitância de vitiligo com doenças autoimunes.

OBJETIVOS: Traçar o perfil epidemiológico dos pacientes com vitiligo e estimar a prevalência da associação de vitiligo com doenças autoimunes da tireoide.

MÉTODOS: Efetuou-se um estudo transversal, analisando-se prontuários dos pacientes com diagnóstico de vitiligo atendidos no Ambulatório de Dermatologia AME-Unisul e do HU-UFSC. Avaliaram-se as características clínicas e laboratoriais desses pacientes.

RESULTADOS: Foram avaliados 85 prontuários, sendo 56 do sexo feminino, com idade média de 37,14 anos e idade média de início de 25,25 anos. O vitiligo vulgar ocorreu em 70,6% dos casos. As doenças autoimunes da tireoide foram encontradas em 22,4% dos casos. Outras doenças autoimunes foram identificadas em 5,9% dos casos. Os pacientes com anticorpos antitireoidianos positivos revelaram uma probabilidade elevada de extensão do vitiligo maior que 25%. Não houve diferença estatística quanto às características clínicas do vitiligo em portadores ou não de tireoidite autoimune com alteração hormonal.

CONCLUSÃO: Os resultados deste estudo são similares aos de outros autores, mostrando que as doenças autoimunes da tireoide são mais frequentes nos pacientes com vitiligo.

Palavras-chave: Autoimunidade; Doenças da glândula tireoide; Vitiligo

Received on 08.02.2010.

Approved by the Advisory Board and accepted for publication on 07.07.10.

\* Work conducted at the Outpatient Clinic of Medical Specialties, University of Southern Santa Catarina (AME-UNISUL) and Polydoro Ernani de São Thiago University Hospital, Federal University of Santa Catarina (HU-UFSC) - Santa Catarina (SC), Brazil.

Conflict of interest: None / *Conflito de interesse: Nenhum*

Financial funding: None / *Suporte financeiro: Nenhum*

<sup>1</sup> PhD in Medical Sciences - Dermatologist - Head of the Dermatology Service, Polydoro Ernani de São Thiago University Hospital - Federal University of Santa Catarina (HU-UFSC). Professor of Dermatology, University of Southern Santa Catarina (UNISUL). Preceptor of the Medical Internship at the University of Southern Santa Catarina (ISAAC) - Federal University of Santa Catarina (UFSC) Outpatient Clinic of Psoriasis, Skin Cancer, STD/HIV - HNR - Santa Catarina (SC), Brazil.

<sup>2</sup> Medical student at the University of Southern Santa Catarina (ISAAC) - Santa Catarina (SC), Brazil.

## INTRODUCTION

Vitiligo is a relatively common dermatologic finding observed since ancient times.<sup>1</sup> It presents as an idiopathic acquired skin disease, characterized by pearly-white macules of different shapes and sizes, with a tendency to increase in size centrifugally. For this reason, diagnosis is mainly clinically established.<sup>2</sup>

This dermatosis has a variable frequency ranging from 0.38% to 2.9% of the world population and it changes according to the region studied.<sup>3,4</sup> Average age of onset occurs around the second to the third decade of life.<sup>5</sup> Adults and children of both genders are equally affected, but some studies indicate a slight prevalence of cases among females, possibly due to greater psychosocial consequences caused by this skin condition; however, this<sup>2,6</sup> is not considered statistically significant because some studies show similar rates for both genders.<sup>7</sup> The site of onset and distribution of lesions differ according to age and region of the study population, but the most affected sites are, respectively, the head, limbs and trunk; the less affected sites are mucous membranes.<sup>8,9</sup>

This pigmentation disorder follows a suggested classification because not all cases behave in the same way. The classification is based on the distribution and size of the depigmented area. It is divided into localized, generalized and universal. The localized form consists of the following types: focal, which is characterized by the presence of one or more macules in a specific area, without a particular distribution; segmental, which is characterized by the presence of one or more macules following the distribution of a dermatome, and mucosal, in which only the mucous membrane is affected. Generalized vitiligo involves the following types: acrofacial, which is characterized by the presence of typical lesions in the distal extremities and face; vitiligo vulgaris, constituted by achromatic macules with variable distribution, and mixed, when there is a combination of two or more types. The universal form corresponds to 50% depigmentation of the skin and/or mucous membranes.<sup>2,6,10</sup>

Vitiligo is caused by a pigmentation disorder due to the destruction of melanocytes. However, its etiopathogenesis has not yet been fully understood.<sup>11</sup> Therefore, there are many theories about its etiology, including autoimmune, genetic, autotoxic (melanocyte), neural and biochemical explanations.<sup>10</sup> The autoimmune etiology seems most plausible, in which the destruction of melanocytes is secondary to autoantibodies, which are related to the extent and activity of the disease.<sup>10</sup> This theory is based on observation of the simultaneous occurrence of vitiligo and autoimmune diseases such as pernicious anemia, rheumatoid arthritis (RA), Addison's disease, diabetes

mellitus, thyroiditis and alopecia areata.<sup>3,12</sup> Vitiligo is most commonly associated with autoimmune thyroid diseases.<sup>12,13</sup> Autoimmune diseases typically involve interactions between genetic risk factors and environmental triggering factors. In vitiligo, the main environmental triggering factors are poor nutrition, emotional stress, trauma, drugs, infections, exposure to the sun and chemicals, toxins and sepsis. All these factors are cited in the natural history of vitiligo, but it is very difficult to define which of these predominates in the pathogenesis of the disease.<sup>6,14</sup>

Thyroid disorders and autoimmune thyroid diseases have been associated with vitiligo, and the incidence of clinical or subclinical involvement of the thyroid is more common in patients with vitiligo as compared to healthy subjects.<sup>5,11</sup> Studies have reported the prevalence of this association to be between 4.4% and 21%,<sup>12,15</sup> and cases of hypothyroidism were found in 12%.<sup>16</sup> The prevalence of this association is also common in children, in whom thyroid parameters can be altered in up to 16% of the cases, especially in non-segmental types.<sup>17</sup>

Autoimmune thyroid disease is a common disease. In the U.S. it is estimated that 10% of the population has antibodies to thyroid antigens.<sup>18</sup> Hashimoto thyroiditis and Graves disease are the most important and prevalent thyroid diseases associated with vitiligo. The main antithyroid autoantibodies detected in autoimmune diseases are thyroid stimulating antibody, antithyroglobulin antibody (anti-TG) and antithyroid peroxidase antibody (anti-TPO). These are sensitive for the diagnosis and follow-up of this disease.<sup>11,19</sup> Anti-TPO antibodies are the ones most associated with clinical thyroid dysfunction. The presence of this antibody is strongly linked to lymphocytic inflammation and glandular lesion.<sup>18,20</sup> Vitiligo often precedes the clinical manifestations of thyroid gland dysfunction.<sup>12,15</sup> Thus, screening of patients with vitiligo for thyroid function and antithyroid antibodies to diagnose early changes in the function of this gland becomes relevant and necessary.<sup>1,11</sup>

Vitiligo is considered the most frequent acquired hypomelanosis.<sup>1</sup> Currently in our literature, there is a paucity of studies that demonstrate the epidemiological profile of this skin disease, as well as the association of vitiligo with autoimmune diseases. This study will evaluate the association of these two diseases to raise the awareness of physicians about the need for a more careful evaluation of patients with vitiligo and to trace their epidemiological profile in order to estimate the prevalence of the association between vitiligo and thyroid diseases.

## MATERIAL AND METHODS

A cross-sectional observational study based on analysis of medical records was conducted.

The study population consists of patients seen in the AME-UNISUL outpatient clinic of Dermatology and HU-UFSC outpatient clinic of Dermatology, for six years, from November 2003 to October 2009.

The medical charts of all patients diagnosed with vitiligo in one of these clinics were evaluated from August to September 2009. All the medical records diagnosing vitiligo were included in the study. Medical records that had not been properly filled out or that did not present the data requested in the data record protocol were excluded from the study. Patients who did not give formal consent to participate were also excluded.

The data collected were entered into a Data Record Protocol (Appendix). At the start of follow-up, the following laboratory tests were evaluated: TSH, free T<sub>4</sub>, anti-TPO and anti-TG antibodies. Patients who had elevated antithyroid antibodies were classified as having autoimmune thyroid disease, and patients with altered TSH and/or free T<sub>4</sub> associated with an increase in autoantibodies were classified as having autoimmune thyroid disease with hormonal changes.

The data collected were entered into a database using the Epidata 3.1 software. The SPSS 15.0 software was used for the statistical analysis of the data. Quantitative variables were analyzed for normal distribution by the Kolmogorov-Smirnov test. Gaussian variables are reported as mean and standard deviation and those that did not show normal behavior as median and interquartile range. The chi-square or Fisher's exact test was used for the analysis of associations. Comparisons of quantitative parametric variables were made using analysis of variance (Anova) and those of asymmetric quantitative variables were made with the Mann-Whitney test. P-values < 0.05 were considered statistically significant and the confidence interval was 95%.

This study was approved by the Ethics Committee on Human Research (CEPSH-UFSC) registration number 238/09 FR-277989 and CEP-UNISUL registration number 09.117.4.01.III. Data collection was obtained upon formal consent of the patients.

## RESULTS

Ninety-seven patients with the diagnosis of vitiligo were identified, according to the medical records examined at the Outpatient Clinics of Dermatology. Of these, 85 (87.6%) medical records met the requirements for variables and the patients agreed to participate in the study. Ten (10.4%) medical records were incomplete, and two (2%) patients were

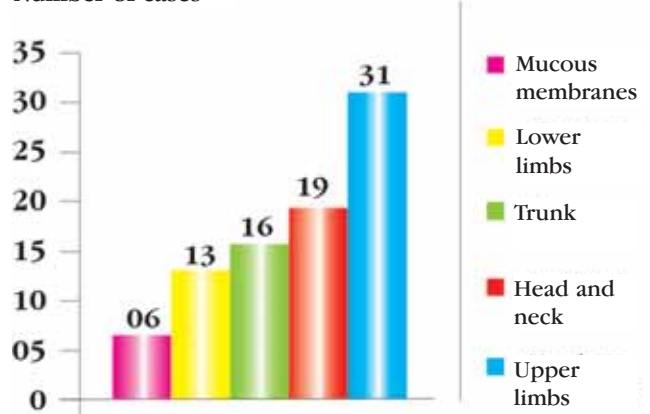
not found due to inconsistent addresses, totaling 12 (12.4%) losses. The sample consisted of 69 (81.2%) patients from the HU-UFSC ambulatory care clinic and 16 (18.8%) from the UNISUL outpatient clinic.

A total of 65.9% (56) patients were women and 34.1% (29), men. The age had a normal distribution with a mean of 37.14 years (SD = 18.64), ranging from 6 to 78 years. However, age at onset showed a skewed distribution, with a median of 19 years (Q<sub>1</sub> = 10.5 and Q<sub>3</sub> = 40), ranging from 1 to 62 years. With regard to skin phototype, according to Fitzpatrick classification, the most common were skin phototype IV with 29.4% (25) and skin phototypes II and III, each with 28.2% (24); only 8.2% (7) had skin phototype V and 5.9% (5), skin phototype I. There were no patients with skin phototype VI.

The sites of onset are shown in Graph 1. The most affected site of onset and current location of lesion were the upper limbs, reported in 36.5% (31) and 63.5% (54) of cases, respectively. Lesion in the face was found in 58.8% (50) of the cases, in the lower limbs in 57.6% (49) and in the trunk in 49.4% (42) of cases.

The most common type of vitiligo according to the distribution of lesions was vitiligo vulgaris, found in 70.6% (60) of the cases, followed by focal in 18.8% (16), acrofacial in 5.9% (5) and segmental in 4.7% (4). The universal form, in which there is involvement of more than 50% of the body, was found in 11.8% (10) of patients. Characteristics such as extension area, activity of the disease, family history and triggering factors are shown in table 1. There was no statistical significance ( $p = 0.281$ ) when family history and age of onset were compared. Patients with skin phototypes I, II and III showed a tendency to report emotional stress as a triggering factor, but this finding

Number of cases



GRAPH 1: Distribution of lesions according to site of onset in vitiligo patients in the AME- UNISUL and HU-UFSC outpatient clinics of Dermatology

is not significant ( $p = 0.056$ ).

Of the 85 participants included, 67 (78.8%) had laboratory diagnosis of autoimmune thyroid disease. Therefore, all the 85 patients were included to evaluate the frequency of the epidemiological profile; however, only the 67 patients who had undergone laboratory testing were considered to calculate the statistical association of thyroid variables .

Autoimmune thyroid diseases with hormonal changes and thyroid laboratory parameters are shown in Graph 2. Thyroid autoimmune disease with hormonal changes was found in 22.4% (15) of the patients. Of the 15 cases, 80% corresponded to hypothyroidism, 13.3% to hyperthyroidism and 6.7% to subclinical hypothyroidism. Five patients presented hypothyroidism prior to the lesions of vitiligo. TSH levels were abnormal in 22.4% (15); anti-TPO antibody was elevated in 32.8% (32) of patients and antithyroglobulin antibodies, in 20.9% (14). All the patients with positive anti-TG also had positive anti-TPO.

There were five (5.9%) cases of other autoimmune diseases, which correspond to pernicious anemia, scleroderma, autoimmune hepatitis, autoimmune parotitis and rheumatoid arthritis.

Table 2 provides data comparing the clinical

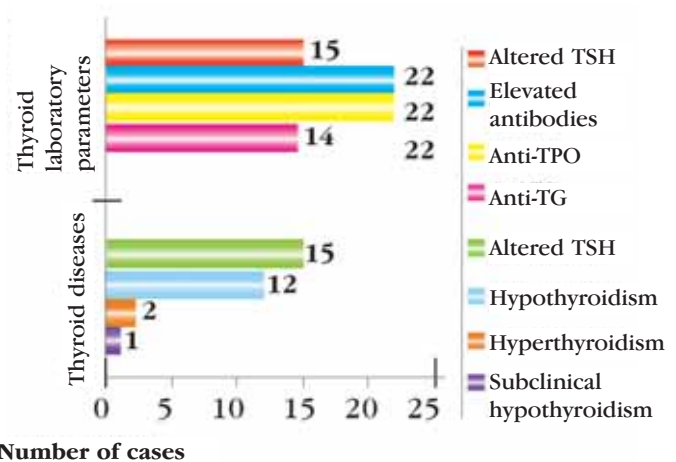
**TABLE 1:** Description of body surface area involvement, disease activity, family history, triggering factors and koebner phenomenon in vitiligo patients in the AME- UNISUL and HU-UFSC outpatient clinics of Dermatology

Clinical feature	Frequency
<b>Extension:</b>	
<25%	80% (68)
25-50%	8.2% (7)
>50%	11.8% (10)
Total	100% (85)
<b>Activity:</b>	
With progression	21.2% (18)
Without progression	78.8% (67)
Total	100% (85)
<b>Family History:</b>	
Present	10.6% (9)
Absent	89.4% (76)
Total	100% (85)
<b>Triggering factor:</b>	
None	55.3% (47)
Emotional stress	31.8% (27)
Physical trauma	12.9% (11)
Total	100% (85)

characteristics of vitiligo patients with and without autoimmune thyroid disease with hormonal changes (DAITAH). According to this analysis, patients with autoimmune thyroid disease with hormonal changes were older compared to those without this diagnosis ( $p = 0.001$ ), and those who were older at the onset of vitiligo were more likely to present thyroid disease ( $p = 0.003$ ).

It is observed in Table 2 that thyroid diseases are more common in women. Family history of vitiligo was present in only 28.6% (2) of the patients with autoimmune thyroiditis. Emotional stress was the triggering factor reported by 13% (3) of the patients, but none of these associations was statistically significant ( $p > 0.05$ ). It was also observed that patients who had more than 25% of their body affected by vitiligo were 2.31 times more likely to develop autoimmune thyroid disease with hormonal changes. This, however, does not have statistical significance ( $p > 0.05$ ). The presence of segmental vitiligo was statistically suggestive of absence of this autoimmune disease ( $p = 0.569$ ).

Table 3 shows the analysis of the clinical characteristics of vitiligo patients with positive and negative antithyroid antibodies. According to the table, there is evidence that patients with positive antithyroid antibodies have a higher probability of developing vitiligo in more than 25% ( $p = 0.004$ ) of their bodies. It is also shown that patients with positive antithyroid antibodies were older and had a delayed age of onset of the disease. Positive antibodies were more frequent in women and in the non-segmental type, but without statistical significance ( $p > 0.05$ ).



**GRAPH 2:** Description of autoimmune thyroid diseases and changes in thyroid laboratory parameters associated with vitiligo in the AME- UNISUL and HU-UFSC outpatient clinics of Dermatology

## DISCUSSION

Vitiligo may be a dermatosis that causes many social problems, especially in countries where there is a predominance of dark-skinned individuals, because in this population the depigmented lesions of vitiligo are more noticeable, causing a major impact on these patients' quality of life.

In this sample 65.9% of the participants were women. Similar numbers have been documented in another study, in which the female population accounted for 70.4% of the sample. However, other authors have established that there are no differences between genders.<sup>7,22</sup> It is possible that this predominance could be due to a major concern of women with aesthetics. The mean age and age at onset were 37.14 and 25.25 years, respectively. Similar ages were found in a population in Turkey, with a mean age of 31.3 and mean age at onset of 24.6 years.<sup>15</sup> However, a study in India reported a later onset of

the disease, with a mean age of 55 years.<sup>22</sup> These data reinforce that vitiligo is a disease that can occur at any age.

The prevalence of skin phototypes is similar to that found in Colombia.<sup>5</sup> With regard to the site of onset, the upper limbs were also the most frequently affected. They were also the most commonly affected site (77.9%) in an Indian study. These data confirm that the primary site of involvement are sun-exposed areas. As for the type of lesion distribution, vitiligo vulgaris was reported in several studies,<sup>7,9,11,16</sup> except for one, which was conducted with a child population, in which the focal type was the most common.<sup>24</sup> This is probably due to early medical treatment, immediately after the appearance of the first lesion in the child. Similarly to the results of this study, segmental vitiligo showed a low frequency of 5%.<sup>9</sup> Vitiligo affecting less than 25% of the body surface area was more prevalent in another study

**TABLE 2:** Comparison of the clinical characteristics of vitiligo in patients with and without autoimmune thyroid disease with hormone abnormalities in the dermatology outpatient departments AME-Unisul and HU-UFSC

Clinical characteristic	W/disease n (%)	W/O disease n (%)	PR, CI, F, Z	p
<b>Gender:</b>			RP: 1.12	p <sup>1</sup> = 0.527
Male	3 (15.8%)	16 (84.2%)		
Female	12 (25%)	36 (75%)		
Total	15	52		
<b>Age:</b>	50.7	33.37	F = 11.38	p <sup>2</sup> = 0.001
Age at onset	40,0 (Q1 = 24 e Q3 = 40)	16,0 (Q1 = 9,2 e Q3 = 39,7)	Z = 2.99	p <sup>3</sup> = 0.003
<b>Extent:</b>			RP: 2.31	p <sup>1</sup> = 0.083
<25%	9 (17.3%)	43 (82.7%)		
>25%	6 (40%)	9 (60%)		
Total	15	52		
<b>Type:</b>			RP: 0.76	p <sup>1</sup> = 0.568
Segmental	0	4 (100%)		
Non-segmental	15 (23,8%)	48 (76.2%)		
Total	15	52		
<b>Family history:</b>			RP: 1.31	p <sup>1</sup> = 0.649
Present	2 (28.6%)	5 (71.4%)		
Absent	13 (21.7%)	47 (78.3%)		
Total	15	52		
<b>Triggering factor:</b>			RP: 1.19	p <sup>1</sup> = 0.230
Stress	3 ( 13%)	20 (87%)		
Not stress	12 ( 27.3%)	32 (72.7%)		
Total	15	52		

W/disease – with autoimmune thyroid disease with hormone abnormalities

W/O disease – without autoimmune thyroid disease with hormone abnormalities

p1: Fisher's exact test

p2: ANOVA

p3: Mann-Whitney test

PR: Prevalence ratio

F: Corresponds to the specific unit/function of the Mann-Whitney test

Z: Unit/function of the respective ANOVA test.

**TABLE 3:** Analysis of clinical characteristics of vitiligo patients with positive and negative antithyroid antibodies (anti-TPO or anti-TG) in the AME- UNISUL and HU-UFSC outpatient clinics of Dermatology

Clinical Feature	Positive Antibody n (%) n=22	Negative Antibody n (%) n=45	PR, CI, F, Z	p
<b>Gender:</b>			RP: 1,026	p1 = 1,000
Male	6 (31,6%)	13 (68,4%)		
Female	16 (33,3%)	32 (66,7%)		
<b>Age:</b>	48,73	31,64	F = 14,56	p2 < 0,0001
Age at onset	40,5 (Q1 = 23,7 e Q3 = 50,2)	13,00 (Q1 = 8,5 e Q3 = 32)	Z = 4,13	p3 < 0,0001
<b>Extension:</b>			PR: 2,88	p1 = 0,004
< 25%	12 (23,1%)	40 (76,9)	CI: 95%	
> 25%	10 (66,7%)	5 (33,3%)	(1,57-5,33)	
<b>Type:</b>			PR: 0,65	p1 = 0,294
Segmental	0 (0,0%)	4 (100%)		
Non-segmental	22 (34,9%)	41(65,1%)		

p<sup>1</sup> = Fisher's exact testp<sup>3</sup> = Mann-Whitney

CI = confidence interval

Z: Unit/function of the respective ANOVA test.

p<sup>2</sup> = ANOVA

PR = prevalence ratio

F: Corresponds to the specific unit/function of the Mann-Whitney test

<sup>21</sup>. However, there was a higher prevalence of vitiligo involving more than 50% of the body surface area in this study as compared with results from previous studies, where this frequency occurred in 5% and 7% of the cases. <sup>11,21</sup> The higher frequency of the universal type in this study may be due to the fact the study population was sought in a referral center of Dermatology, thereby attracting more severe cases of the disease.

It was found that 21.2% had disease progression, in contrast to data presented in other studies in which this figure ranged from 63.9% to 76.9%. <sup>23,24</sup> This is probably due to the cross-sectional nature of this study; the most appropriate study design to assess lesion progression is longitudinal. On the other hand, a Brazilian study found progression in 37.3% of cases. <sup>25</sup> We observed presence of family history in 10.6% of the cases, which amounts to the 9% reported in a Romanian population. <sup>4</sup> However, family history ranged from 34% to 38.7% in studies by other authors. <sup>3,26</sup> One can speculate that there was a higher frequency of this variable, especially in the study by Laberge et al, because it was conducted in a population in which several family members were affected by vitiligo, and there was also a more thorough investigation of these families. A study noted that the higher the number of family members with vitiligo, the early the onset of the disease, <sup>21</sup> but this finding was not statistically significant in this study. The koebner phenomenon, reported in the results of this study as physical trauma, was found in lower rates as compared to those of other studies,

which had rates ranging from 28.6% to 53.3%, <sup>5,25</sup> with the exception of Gopal et al, which showed the presence of the phenomenon in 7.4% of the study cases. <sup>16</sup> The low frequency may have occurred due to lack of questioning about the phenomenon. Emotional stress has been mentioned as a triggering factor in other studies, <sup>6,14</sup> but these data are still limited and there is no established evidence in the literature.

In this sample the prevalence of the association between vitiligo and autoimmune thyroid diseases with hormonal changes was similar to that shown by Laberge et al, who described a frequency of 21.4%. <sup>3</sup> Other studies showed rates of 24.1% <sup>15</sup> 21%, <sup>12</sup> and 17%. <sup>21</sup> However, data from previous studies show low prevalence, such as the values reported in a Chinese study that showed an association of 1.36%, 0.6% in Nigeria, 2.6% in Colombia and 3% in a Romanian population. <sup>4</sup> It is noteworthy that in these studies the lower frequency of these diseases may have occurred due to their methodological characteristic, for laboratory tests were requested only when needed, that is, in the presence of symptoms. According to two studies conducted in Brazil, this association was also low or there was no association, <sup>24,27</sup> but these studies were conducted specifically with pediatric patients. We observed a similar distribution of hypothyroidism (88%) and hyperthyroidism (12%) among the cases of autoimmune thyroiditis in the literature. <sup>21</sup> The literature shows that it is rare for vitiligo to develop after thyroid disease, and <sup>12</sup> when present, it occurred at rates close to 4% in the population. <sup>13</sup> It is assumed

that in most cases vitiligo will develop before autoimmune thyroid diseases. These findings, compared to the rate of 10% of autoimmune thyroid diseases in a study of patients without vitiligo, show the high prevalence of autoimmune diseases and vitiligo.<sup>14</sup>

In this study 22 patients showed positive antithyroid antibodies, indicating a frequency of 32.8% of cases of autoimmune thyroiditis. These percentage, compared to those in the literature, which ranged from 3.4% to 25.6%, is higher.<sup>9,11,12,13,24</sup> Antibodies in patients without vitiligo ranged from 13.9% for women to 2.8% for men<sup>19</sup>. Autoimmune diseases mostly associated with vitiligo were pernicious anemia, ranging from 1.8% to 2.3%, and rheumatoid arthritis, varying from 0.38% to 14%, which are higher than the rates found in the study population. Increased frequency of type 1 diabetes mellitus and scleroderma was not found.<sup>3,4,7,21</sup> The presence of autoimmune hepatitis or parotiditis was not cited in the literature. The increased frequency of autoimmune diseases in patients with vitiligo suggests that all these conditions share a common etiologic factor.

Regarding the comparison of the clinical characteristics of vitiligo patients with and without autoimmune thyroid diseases with hormonal changes, studies also report a prevalence of this autoimmune disorder in women - 21.4% against 5.56% in men.<sup>21</sup> This prevalence has also been shown by other authors.<sup>13,17</sup> One explanation may be a possible role of estrogen on the pathogenesis of the disorder. Although in this study age and mean age of onset are higher in patients with autoimmune thyroiditis, with statistical significance, no other study has confirmed these data. A study conducted in Greece showed that there was no statistical association between patients with autoimmune thyroid disease and vitiligo characteristics such as age, age at onset, gender, type and family history.<sup>13</sup> Other works have also indicated that patients with segmental vitiligo hardly ever

manifested this thyroid disease.<sup>14,15,17</sup>

Other studies have reported a variation from 26.1% to 29.6% of positive antibodies in the female population; thus, prevalence in women was statistically significant, which is not in agreement with the data in this study.<sup>11,12</sup> The mean age of 47 years was similar to that found in this work.<sup>12</sup> One study conducted with children described the mean age of onset of vitiligo to be 10.1 years in patients with positive antibodies, but these data were not statistically significant, as opposed to the findings in this study.<sup>17</sup> With regard to the extension of vitiligo, a previous study showed that more severe forms of vitiligo had positive antibodies.<sup>28</sup> In another study there was greater involvement of body surface area in 25% of patients with positive antibodies, but without statistical significance.<sup>11</sup> These data differ from the results found in this study - 66.7% with statistical significance.

These discrepancies may be due to variations in the sample population, small-sized sample, lack of data in medical records and reduced laboratory tests for thyroid parameters.

## CONCLUSION

Research on the presence of autoimmune disease, especially thyroid disease in patients with vitiligo, is remarkable. Data from this study, similar to those found by other authors in the literature, have also shown a high frequency of autoimmune thyroid disease. This disease affected 32.8% of patients with vitiligo. It is also important to note that vitiligo affecting more than 25% of the body area surface was three times more associated with the presence of elevated antibodies.

Therefore, the early diagnosis of autoimmune thyroid diseases is important to foresee changes that may cause a great impact on the development and growth of children as well as changes in the various functions of organs in the human body. □

## REFERENCES

1. Bellet JS, Prose NS. Vitiligo em crianças: uma revisão de classificação, hipóteses sobre patogênese e tratamento. *An Bras Dermatol*. 2005;80:631-6.
2. Steiner D, Villas RT, Bedin V, Steiner T, Moraes MB. Vitiligo. *An Bras Dermatol*. 2004;79:335-51.
3. Laberge G, Mailloux CM, Gowan K, Holland P, Bennett DC, Fain PR, et al. Early disease onset and increased risk of other autoimmune disease in familial generalized vitiligo. *Pigment Cell Res*. 2005;18:300-5.
4. Birlea SA, Fain PR, Spritz RA. A Romanian population isolate with high frequency of vitiligo and associated autoimmune diseases. *Arch Dermatol*. 2008;144:310-6.
5. Barona MI, Arrunátegui A, Falabella R, Alzate A. An epidemiologic case-control study in a population with vitiligo. *J Am Acad Dermatol*. 1995;33:621-5.
6. Sehgal VN, Srivastava G. Vitiligo: compendium of clinico-epidemiological features. *Indian J Dermatol Venereol Leprol*. 2007;73:149-56.
7. Liu JB, Li M, Yang S, Gui JP, Wang HY, Du WH, et al. Clinical profiles of vitiligo in China: an analysis of 3742 patients. *Clin Exp Dermatol*. 2005;30:327-31.
8. Onunu AN, Kubeyinje EP. Vitiligo in the Nigerian African: a study of 351 patients in Benin City, Nigeria. *Int J Dermatol*. 2003;42:800-2.
9. Ingordo V, Gentile C, Iannazzone SS, Cusano F, Naldi L. The 'EpiList' Project: a dermo-epidemiologic study on a representative sample of young Italian males. Prevalence of selected pigmentary lesions. *J Eur Acad Dermatol Venereol*. 2007;21:1091-6.
10. Kovacs SO. Vitiligo. *J Am Acad Dermatol*. 1998;38:647-66.
11. Daneshpazhooh M, Mostofzadeh GM, Behjati J, Akhyani M, Robati RM. Anti-thyroid peroxidase antibody and vitiligo: a controlled study. *BMC Dermatol*. 2006;10:1-5.
12. Zettinig G, Tanew A, Fischer G, Mayr W, Dudczak R, Weissel M. Autoimmune diseases in vitiligo: do anti-nuclear antibodies decrease thyroid volume? *Clin Exp Immunol*. 2003;131:347-54.
13. Kakourou T, Kanaka-Gantenbein C, Papadopoulou A, Kaloumenou E, Chrousos GP. Increased prevalence of chronic autoimmune (Hashimoto's) thyroiditis in children and adolescents with vitiligo. *J Am Acad Dermatol*. 2005;53:220-3.
14. Huggins RH, Schwartz RA, Janniger CK. Vitiligo. *Acta Dermatovenerol Alp Panonica Adriat*. 2005;14:137-45.
15. Ar˘can O, Koç K, Ersoy L. Clinical characteristics in 113 Turkish vitiligo patients. *Acta Dermatovenerol Alp Panonica Adriat*. 2008;17:129-32.
16. Gopal KV, Rama Rao GR, Kumar YH, Appa Rao MV, Vasudev P, Srikanth. Vitiligo: a part of a systemic autoimmune process. *Indian J Dermatol Venereol Leprol*. 2007;73:162-5.
17. Lacovelli P, Sinagra JLM, Vidolin AP, Marenda S, Capitanio B, Leone G, et al. Relevance of thyroiditis and of other autoimmune disease in children with vitiligo. *Dermatology*. 2005;210:26-30.
18. Melo M. Tiroidites autoimunes. *Acta Med Port*. 2006;19:387-94.
19. Bjoro T, Holmen J, Krüger O, Midtjell K, Hunstad K, Schreiner T, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The health study of Nord-Trøndelag(HUNT). *Eur J Endocrinol*. 2000;143:639-47.
20. Ai J, Leonhardt JM, Heymann WR. Autoimmune thyroid disease: etiology, pathogenesis, and dermatologic manifestations. *J Am Acad Dermatol*. 2003;48:641-59.
21. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. *Pigment Cell Res*. 2003;16:208-14.
22. Dogra S, Pasard D, Handa S, Kanwar AJ. Late onset vitiligo: A study of 182 patients. *Int J Dermatol*. 2005;44:193-6.
23. Dave S, Thappa DM, Dsouza M. Clinical predictors of outcome in vitiligo. *Indian J Dermatol Venereol Leprol*. 2002;68:323-5.
24. Silva CMR, Pereira LB, Gontijo B, Ribeiro GB. Vitiligo na infância: características clínicas e epidemiológicas. *An Bras Dermatol*. 2007;82:47-51.
25. Castro CGS. Prevalência de psoríase em estudo de 261 pacientes com vitiligo. *An Bras Dermatol*. 2005;80:489-92.
26. Boisseau-Garsaud AM, Garsaud P, Calés-Quist D, Hélénor R, Quénéhervé C, Claire RC. Epidemiology of vitiligo in the French West Indies (Isle of Martinique). *Int J Dermatol*. 2000;39:18-20.
27. Fernandes NC, Campos MMC. Vitiligo na criança e doença na tireóide. *An Bras Dermatol*. 2009;84:200-2.
28. Kuhl ICP, Weissbluth ML, Bakos L, Wollmann TM. Pesquisa de auto-anticorpos e função tireoideana em pacientes portadores de vitiligo e alopecia areata. *An Bras Dermatol*. 1995;70:421-5.

---

ENDEREÇO PARA CORRESPONDÊNCIA / MAILING ADDRESS:  
 Ligia Maria Hademann Esser  
 Rua Presidente Getúlio Vargas, 879 – Centro  
 88750-000 Braço do Norte - SC, Brazil  
 E-mail: ligia.esser@gmail.com

Como citar este artigo/How to cite this article: Nunes DH, Esser LMH. Epidemiological profile of vitiligo patients and its association with thyroid disease. *An Bras Dermatol*. 2011;86(2):241-8.