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Original Research Article

Prevalence of thyroid dysfunction and anti-thyroid peroxidase antibodies in vitiligo patients

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ABSTRACT

Background: Vitiligo is associated with various autoimmune diseases, including autoimmune thyroid disease. The objectives of the present study was to determine the prevalence of thyroid dysfunction and anti-thyroid peroxidase antibodies in patients with vitiligo, and to compare the clinical profile of anti-thyroid peroxidase positive and anti-thyroid peroxidase negative patients.
Methods: A cross-sectional comparative study was conducted in 100 patients with vitiligo and 100 controls. After dermatologic and systemic evaluation, serum thyroid hormones and anti-thyroid peroxidase antibody levels were measured in all the subjects.
Results: Thyroid dysfunction was more common in the vitiligo group (27%) than in the controls. Serum thyroid stimulating hormone abnormalities were more common in the vitiligo group (27%) than in the controls (6%). The most common thyroid dysfunction was subclinical hypothyroidism. Anti-thyroid peroxidase antibody positivity was higher in the vitiligo group (36%) when compared to the controls (24%), and the most common type of vitiligo was vitiligo vulgaris (18%) in this group. Thyroid dysfunction and anti-thyroid peroxidase positivity were more common in women (58%) when compared to men (42%). There was a significantly higher prevalence of other autoimmune diseases in the vitiligo group (20%) compared to the controls (6%).
Conclusions: This study shows a significant association between vitiligo and thyroid dysfunction, anti-thyroid peroxidase antibodies and other autoimmune diseases. We recommend that thyroid evaluation and regular follow-up should be done in patients with vitiligo for prompt detection of thyroid dysfunction.

Keywords: Vitiligo, Thyroid dysfunction, Autoimmune thyroid diseases

INTRODUCTION

Vitiligo is an autoimmune disease which is often associated with other autoimmune diseases, of which the most common is thyroid dysfunction. Conversely, the prevalence of vitiligo among patients with hypo-thyroidism is significantly higher when compared to the general population.[1,2] This study was planned to compare the prevalence of thyroid disease and the presence of anti-thyroid peroxidase (anti-TPO) antibodies in patients with vitiligo and in controls, and to study the clinical profile of anti-TPO positive patients with vitiligo.

METHODS

This cross sectional comparative study was conducted in our tertiary care centre from March 2014 to April 2015. The study population comprised of 100 consecutive patients with vitiligo attending the outpatient department of the department of dermatology and venereology, government medical college, Kozhikode and an equal number of age and sex matched individuals without vitiligo. Patients on thyroid replacement therapy or anti-thyroid drugs, those with a history of thyroid surgery or thyroid irradiation, or patients under the age of one year

(as the presence of maternal antibodies would interfere with the antibody levels of the infant), were excluded from the study.

After obtaining approval from the institutional ethics committee, written informed consent was obtained from the subjects. The diagnosis of vitiligo was done on clinical grounds. A detailed history was taken including age of the patient, age of onset and extent of the vitiligo, associated systemic disease, any history of auto immune disease, drug history, family history of vitiligo and thyroid diseases, and past history of thyroid disease. General, dermatological, thyroid and systemic examinations were done in all the patients and controls.

Serum levels of triiodothyronine (T3), thyroxine (T4), thyroid-stimulating hormone (TSH) and anti-TPO antibodies were measured and entered in a preset proforma. Total T4 (normal range: 55–135 nmol/L) and total T3 (normal range 0.7– 2 nmol/L) were measured by radioimmuno assay. TSH levels (normal range: 0.2–4 micro IU/L) were determined by the use of immunoradiometric assay. Serum levels of anti-TPO antibodies were measured by electrochemiluminescence immuno assay. The upper limit of anti-TPO autoantibody was taken as 30 IU/ml. The data were analysed using predictive analysis software.

RESULTS

The age of the vitiligo patients ranged from 9 to 82 years with a mean of 34.91 years (Standard Deviation (SD) = 16.595), and that of the control group from 9 to 82 years with a mean of 35.37 years (SD= 16.151). There were two peaks, in the 31 to 40 age group and in the 11 to 20 age group. In both groups, 88 patients were above 12 years of age and 12 were equal to or below 12 years of age.

The age of onset of vitiligo varied from 1 year to 51 years. Mean age of onset of vitiligo was 26.06 years with a SD of 12.411. A positive family history of vitiligo was present in 5 (5%) of the vitiligo patients and only one (1%) in the controls. The difference was not statistically significant (p =0.097). The demographic details of the study group are shown in Table 1.

In the vitiligo group 18 (31%) women and 9 (21.4%) men had thyroid dysfunction, but it was not statistically significant (p= 0.286). In the control group 6 (10%) women and 1 (2%) man had thyroid dysfunction. Overall, altered thyroid function was seen in 27% of the vitiligo patients and 7% of the controls and the difference was statistically significant (p <0.001).

Serum T3 values were abnormal in 3 (3%) vitiligo patients and only 1 (1%) in the control group. The difference was not statistically significant (p= 0.364). Serum T4 values were abnormal in 4 (4%) vitiligo patients and only 1 (1%) patient in the control group. The difference was not statistically significant (p= 0.218). TSH values were abnormal in 27 (27%) vitiligo patients and 6 (6%) controls. The difference was statistically significant (p <0.001).

Table 1: Demographic characteristics of the study group.

Characteristics	Number (n=100)
Age (years)	
0-10	4
11-20	21
21- 30	14
31- 40	25
41- 50	18
51- 60	14
61-70	3
7 1- 80	0
81- 90	1
Sex	
Male	42
Female	58
Type of vitiligo	
Generalised	59
Acrofacial	31
Segmental	6
Mucosal	3
Liptip	1

In the vitiligo patients with thyroid dysfunction, the most common type of vitiligo was vitiligo vulgaris in 15 (55.6%) followed by acrofacial vitiligo in 12 (44.4%). The details of thyroid status of the study group and controls are shown in Table 2.

Table 2: Thyroid status.

	Study group (n=100)	%	Control group (n=100)	%
Euthyroid	73	73	93	93
Hypothyroid				
Subclinical	17	17	5	5
Clinical	7	7	2	2
Hyperthyroidism				
Subclinical	2	2	0	0
Clinical	1	1	0	0
Serum TSH				
Increased	11	11	0	0
Decreased	16	16	6	6
Anti TPO antibody				
Present	36	36	24	24
Absent	64	64	76	76

TSH: Thyroid stimulating hormone TPO: thyroid peroxidase antibody

Autoimmune diseases other than vitiligo (alopecia areata, Addison's disease, type one diabetes mellitus, pernicious anaemia and rheumatoid arthritis) were present in 20 (20%) vitiligo patients and in 6 (6%) controls. The difference was statistically significant (p= 0.003). Associated systemic diseases (hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, cerebral vascular disease, multiple sclerosis) were present in 30 (30%) vitiligo patients and in 15 (15%) the controls. The difference was statistically significant (p= 0.011).

Anti-TPO antibody was present in 36 (36%) vitiligo patients and 24 (24%) controls. The difference was statistically significant (p= 0.046). Anti-TPO antibody positivity was higher in women than in men in the vitiligo group (53.1%) as well as in the controls (66.7%). The result was statistically significant (p= 0.118). The risk of developing vitiligo (odds ratio) was found to be 1.765 times higher in women than in men. In the vitiligo group with anti-TPO antibody positivity, 30 (83.3%) patients were above the age of 12 years and 6 (16.7%) were at or below the age of 12 years. Mean age of vitiligo patients with anti-TPO positivity was 35.69 years with a SD of 15.458. All the controls with anti-TPO positivity were above the age of 12 years (100%). None of the children below 12 years had anti-TPO positivity. But the difference was not statistically significant (p= 0.281).

The age of onset of vitiligo in 39.1% of the anti-TPO positive patients and 36.1% of the anti-TPO negative patients was 12 years or earlier. Anti-TPO antibody positive group had an earlier age of onset of vitiligo when compared to the anti-TPO negative group. But the difference were not statistically significant (p= 0.770).

Table 3: Details of anti-TPO antibody positivity.

Anti-TPO antibodies	Vitiligo group	Control group
Present	36 (36%)	24 (24%)
Absent	64 (64%)	76 (76%)
Women	24 (66.7%)	19 (79%)
Men	12 (%)	5 (5%)
Children below 12 years	6 (16.67%)	0
Other autoimmune diseases	10 (27.8%)	3 (12.5%)

Table 4: Sex distribution and thyroid status.

Thyroid status	Study group		Controls	
	Male (n=42)	Female (n=58)	Male (n=42)	Female (n=58)
Euthyroid	33 (78.6%)	40 (68.96%)	41 (97.6%)	52 (89.7%)
Thyroid dysfunction	9 (21.4%)	18 (31.03%)	1 (2.4%)	6 (10.35%)
Anti-TPO antibodies	12 (33.33%)	24 (6.67%)	5 (20.83%)	19 (79.17%)

In the vitiligo group with anti-TPO positivity, 18 (50%) had vitiligo vulgaris, 16 (44.4%) had acrofacial vitiligo, 1 (2.8%) had segmental vitiligo, and one (2.8%) had mucosal vitiligo. No patient with lip tip vitiligo had anti-TPO positivity. In this group, 10 (27.8%), and in the anti-TPO negative group 10 (15.6%) had autoimmune diseases other than vitiligo. The details of anti-TPO positivity are shown in Table 3, and sex distribution in Table 4.

DISCUSSION

In the present study, the mean age of onset of vitiligo was 26 years, similar to other studies from India.[3] Studies conducted in Turkey and in Brazil report the mean age of onset of vitiligo in the fourth decade of life.[4,5] However, another study from India found a later onset of the disease, with a mean age of 55 years.[6] These data indicate that vitiligo can occur at any age.

Studies conducted in Surat and Culcutta showed an equal sex distribution of vitiligo.[7,8] In the present study, there were more women (58%) than men (42%). A similar finding has been noted in studies conducted in Brazil and China.[5,9] This may be due to an increased cosmetic concern of female patients leading to increased hospital attendance.[10]

The most common type of vitiligo was vitiligo vulgaris (51%), similar to other studies, followed by acrofacial vitiligo (39%).[9,11,12] In children, focal vitiligo was found to be the most common type.[13] This is probably due to seeking early medical treatment, immediately after the appearance of the first vitiligo lesion in children. Mucosal vitiligo has been found to be the most common in patients with thyroid dysfunction.[14] But in our study, the most common type associated with thyroid dysfunction was vitiligo vulgaris, followed by acrofacial vitiligo,

The present study showed a positive family history of vitiligo in 5% of patients. A higher incidence of positive family history has been found in other studies, varying from 9% to 38.7%.[5,3,16-18]

An increased occurrence of various thyroid antibodies including thyroid stimulating antibodies, anti-thyroglobulin antibodies and antithyroid peroxidase antibodies have been detected in patients with vitiligo.[19] Of these, antithyroid peroxidase antibodies are the most

sensitive for diagnosis and follow up of thyroid disorders, as well as being a sensitive tool for detection of early subclinical autoimmune thyroid disorders.[20]

In the present study, 27% of the vitiligo patients had statistically significant thyroid dysfunction, similar to other studies with a frequency of 21.4%, 21%, 24.1%, 17%.[17,21-23] An Iranian study found a prevalence of autoimmune thyroid disorders of up to 30% in patients with vitiligo.[24] However, a lower prevalence of 1.36%, 3% and 8.4% have been reported from China, Romania, and Japan respectively.[9,16,25]

In the present study, hypothyroidism was more common than hyperthyroidism. Subclinical hypothyroidism was more common than clinical hypothyroidism. Subclinical hyperthyroidism was present in 2 patients (2%) and clinical hyperthyroidism in one (1%). In India, significant biochemical but no clinical thyroid dysfunction was found in 51.7% of patients with vitiligo, with subclinical hyperthyroidism being more common in one study, while hypothyroidism was present in 12% vitiligo cases and in none of the controls in another study.[12,15] Autoimmune thyroid diseases often present with initial transient hyperthyroidism which may be missed and later progress to subclinical or overt hypothyroidism. Often, there is a delay in seeking medical advice and thyroid evaluation in our population which may explain the higher prevalence of hypothyroidism in our study.

Statistically significant elevation of TSH values was observed in our study (27%). The results were similar to other studies where TSH abnormalities were found in 22.4% and 17.4% of the cases.[5,24]

A statistically significant higher prevalence of anti TPO antibodies in 36% was observed in the present study in the vitiligo group. This may be attributed to the greater seafood consumption in coastal areas of Kerala leading to a high iodine intake which may predispose to auto-immune thyroid diseases, and an increased prevalence of anti TPO antibody positivity.[26]

Organ specific antibodies such as anti-microsomal and anti-thyroglobulin (anti-Tg) antibodies have been demonstrated in 50% and 40% of patients with vitiligo, as well as anti-thyroid antibodies in the relatives of these patients.[27] Dave et al showed antibody positivity (anti-Tg, anti-TPO) in 31.4% of their cases in India against 10% of their controls.[15]

In our study the anti TPO antibody positivity was more common in women in both the vitiligo and the control groups, though not statistically significant. A higher prevalence was also seen in other studies.[5,22,28] Estrogen may play a possible role in the pathogenesis of autoimmune thyroid disorders, and other auto immune diseases like systemic lupus erythematosis and systemic sclerosis are also more common in women.

In our study hypothyroidism, especially subclinical hypothyroidism was more common in the anti TPO positive group, consistent with other reports.[29] The presence of TPO antibodies is significantly associated with thyroid failure as age increases, and women with elevated anti-TPO antibodies are at increased risk for progression to hypothyroidism.[30,31]

Our study revealed a statistically significant co-existence of other autoimmune diseases in the study group. The relative risks for other coexisting autoimmune disorders are markedly increased in vitiligo cases, and this may be due to a common aetiologic factor.[9,14,17,23,31,32] A 30% incidence of systemic diseases such as hypertension, coronary artery disease and cerebral vascular disease was noted in the study group, and it was statistically significant (p= 0.01). None of our patients had deafness or visual defects.

Limitation of the study

Since this was a cross-sectional study, the patients were not followed up.

CONCLUSION

Our findings indicate that the prevalence of subclinical hypothyroidism, altered serum TSH levels and anti TPO antibodies in the serum are significantly higher in vitiligo patients than in controls. Patients with vitiligo, especially if female, or with vitiligo vulgaris, or early onset of vitiligo, or with other auto immune diseases, should undergo clinical and serological thyroid screening. Patients with anti-TPO antibodies should be followed-up annually, because thyroid dysfunction can develop much later. Both vitiligo and thyroid disorders are fairly common in south India, and early screening and diagnosis help to reduce the morbidity associated with thyroid dysfunction.

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