
Vitiligo and overt thyroid diseases: A nationwide population-based study in Korea



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Background: Associations between vitiligo and thyroid diseases have been reported repeatedly.

Objective: We investigated the associations between vitiligo and overt autoimmune thyroid diseases and thyroid cancer using the Korean National Health Insurance claims database.

Methods: We defined patients with vitiligo as those whose records showed ≥ 4 physician contacts between 2009 and 2013 in which vitiligo was the principal diagnosis. We also established an age- and sex-matched control group without vitiligo (2 per 1 vitiligo patient). The outcomes of interest were concurrent Graves disease and Hashimoto thyroiditis (the patients were taking relevant thyroid medications) and thyroid cancer.

Results: The study enrolled 73,336 vitiligo patients and 146,672 controls. Patients with vitiligo were at increased risks of Graves disease (odds ratio [OR] 2.610 [95% confidence interval [CI] 2.319-02.938]), Hashimoto thyroiditis (OR 1.609 [95% CI 1.437-1.802]), and thyroid cancer (OR 1.127 [95% CI 1.022-1.242]), compared with the controls. The associations were consistently stronger in males and younger patients.

Limitations: Individual clinical information was not available, and the homogeneous population may limit the generalizability of the results.

Conclusion: Vitiligo was significantly associated with overt autoimmune thyroid diseases and overt thyroid cancer. (J Am Acad Dermatol 2017;76:871-8.)

Key words: autoimmune thyroiditis; Graves disease; Hashimoto thyroiditis; hyperthyroidism; hypothyroidism; thyroid cancer; vitiligo.

INTRODUCTION

Vitiligo is a common acquired depigmentation disorder characterized by the loss of functional skin and mucosal melanocytes; the reported incidence is 0.5% to 2% worldwide.^{1,2} Although the etiology has not been fully established, autoimmunity is considered the principal contributor to pathogenesis. Several reports have suggested associations between vitiligo and a variety of other autoimmune diseases,

including thyroid conditions, alopecia areata, type 1 diabetes mellitus, pernicious anemia, and rheumatoid arthritis. Of these, autoimmune thyroid diseases are common in patients with vitiligo.¹ Studies have reported that the incidence of thyroid disease is 0% to 52% in patients with vitiligo, and that 3% to 90% of vitiligo patients have antithyroid antibodies.³⁻²³ Therefore, routine screening for thyroid dysfunction is recommended for patients with vitiligo. However,

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the results of thyroid function tests often do not reflect actual thyroid disease status.

South Korea has one of the largest National Health Insurance (NHI) systems worldwide, which is mandated by law. The Korean NHI covers up to 98% of the 50 million people in Korea, and the NHI claims database has been used to provide reliable estimates of the prevalence of certain diseases in the country.²⁴ In this study, we investigated the risks of overt thyroid diseases in patients with vitiligo using the Korean NHI claims database to identify patients on relevant thyroid medications. We also evaluated the association between vitiligo and thyroid cancer.

METHODS

Study design and database

This nationwide population-based cross-sectional study used the Korea NHI claims database (which records diagnoses based on *International Classification of Diseases, 10th revision* [ICD-10] codes) containing all claims information from the NHI program and the Korean Medical Aid program from 2009 until 2013.

Study population

To minimize misclassification, we defined patients with vitiligo as those who had ≥ 4 documented physician contacts between 2009 and 2013 at which vitiligo (ICD-10 code L80) was the principal diagnosis (the vitiligo group). The control group was drawn from all individuals who had undergone hemorrhoidectomy or appendectomy and had not visited a physician with a diagnosis of vitiligo during the same period. Next, we randomly selected controls (2 per 1 vitiligo patient) after frequency matching for age and sex with the vitiligo group (the control group).

Definition of overt or active thyroid diseases

The outcomes of interest were concurrent Graves disease, Hashimoto thyroiditis, and thyroid cancer. Patients with Graves disease were defined as those with hyperthyroidism (ICD-10 codes E05, E050, E058, or E059) as the principal diagnosis and who took antithyroid medications (eg, methimazole, propylthiouracil, or carbimazole) for ≥ 60 days between 2009 and 2013. Patients with Hashimoto disease were defined as those with thyroiditis (ICD-10 codes E063 or E069) as the principal

diagnosis who took thyroid hormone replacements (ie, levothyroxine sodium or liothyronine sodium) for ≥ 60 days between 2009 and 2013. Patients with thyroid cancer were defined as those with ≥ 4 documented physician contacts attributable to thyroid cancer (ICD-10 code C73) during the same period.

CAPSULE SUMMARY

- Vitiligo is associated with thyroid disease.
- The association between vitiligo and overt thyroid diseases including Graves disease, Hashimoto thyroiditis, and thyroid cancer was confirmed using the Korean National Health Insurance claims database.
- Vitiligo patients, especially males and younger patients, should be screened for thyroid disease.

Subgroup analyses

Subgroup analyses were carried out by sex and age groups (<20, 20-39, 40-59, and ≥ 60 years).

Statistical analysis

Categorical variables were expressed as percentages and were compared using the χ^2 test. We used multi-variable logistic regression analyses to examine the associations between vitiligo and each thyroid disease

after adjusting for age and sex. Sensitive analyses were performed after additional adjustment for insurance type to assess the robustness of our results. All data were analyzed using SAS software (v 9.4; SAS Institute, Cary, NC).

RESULTS

Characteristics of the study population

We identified 73,336 patients with vitiligo and 146,672 controls without vitiligo (Table I). In both groups, 55.7% were females, and the peak age of incidence of vitiligo was 40 to 59 years of age (31.5%), followed by <20 years of age (24.7%).

Prevalence rates of overt or active thyroid diseases

Patients with vitiligo had higher prevalence rates of thyroid diseases than did the controls without vitiligo (Table II). The prevalence rates of overt or active Graves disease, Hashimoto thyroiditis, and thyroid cancer in patients with vitiligo were 0.86%, 0.75%, and 0.87%, respectively. In the control group, the prevalence rates were 0.33%, 0.47%, and 0.78%, respectively.

Association of vitiligo with overt or active thyroid diseases

After adjusting for age and sex, patients with vitiligo were at significantly increased risk for Graves disease (odds ratio [OR] 2.610 [95% confidence interval {CI} 2.319-2.938]) and Hashimoto thyroiditis (OR 1.609 [95% CI 1.437-1.802]). We also

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