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Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

# Evaluation of thyroid abnormalities in childhood vitiligo from a tertiary care centre: A case-control study

**Senthil Kumar AL[1], K Sridevi[1], DVSB Ramamurthy[1], Akshay Jain Salecha[1,*], Leepika Annamreddy[1]**

[1] *Dept. of DVL, Katuri Medical College & Hospital, Guntur, Andhra Pradesh, India*

ARTICLE INFO

*Article history:*
Received 11-02-2022
Accepted 28-03-2022
Available online 07-04-2023

*Keywords:*
Childhood vitiligo
Thyroid
Autoantibody

ABSTRACT

**Background:** Vitiligo is an usual acquired pigmentary disorder of the skin characterized by well-circumscribed depigmented macules and patches. Though the association between vitiligo and thyroid disorders has been suggested, only a few studies from India and overseas have paid attention to describe the association between vitiligo and thyroid abnormalities, particularly in children. Hence, this study was taken up for evaluating thyroid disease in childhood vitiligo compared to controls in a tertiary care centre.

**Materials and Methods:** This was a hospital-based case-control study conducted at a tertiary teaching hospital over 18 months which included 50 new patients of vitiligo and 50 age and sex-matched controls. Blood samples were garnered from cases and controls to access the levels of free triiodothyronine (fT3), free thyroxine (fT4), Thyroid-stimulating hormone ( TSH), anti-thyroid peroxidase (anti-TPO), and anti-thyroglobulin (anti –Tg).

**Results:** In our study, females outnumbered males in both groups. The frequencies of thyroid function and thyroid autoantibody abnormalities among vitiligo patients and control were 32% and 6%, respectively. The difference between case and controls for thyroid function abnormality was significant with a p-value of 0.001.

**Conclusion:** Our study found a significant association betwixt thyroid disease and childhood vitiligo. Thus, evaluating vitiligo patients for thyroid abnormalities help to detect thyroid diseases or determine the possibility of eventual onset.



## 1. Introduction

Vitiligo is a common acquired pigmentary disorder of the skin characterized by well-circumscribed depigmented macules and patches.[1] It affects 0.1-2% of the world population, and both genders are affected equitably.[2]

Presently, the precise pathogenesis of vitiligo hovers recondite. The largely endorsed theory is autoimmune, endured by multiple epidemiological, clinical, and investigational findings.[3–5]

Various studies have described an association of vitiligo with autoimmune disorders such as thyroid disease (Hashimoto's thyroiditis and Graves' disease), insulin-dependent diabetes mellitus, Addison's disease, pernicious anaemia, and alopecia areata.[6–8] A genetic co-localization between vitiligo and thyroid autoantibodies have also been proposed.[9] As vitiligo usually occurs prior to the onset of thyroid disease, screening for thyroid function and anti-thyroid antibodies in all patients of vitiligo may be advantageous.[10]

Only a few studies from India and other parts of the world have paid attention to describe the association of vitiligo and

* *Corresponding author*.
*E-mail address*: akshaysalecha92@gmail.com (A. J. Salecha).

https://doi.org/10.18231/j.pjms.2023.043

thyroid abnormalities, particularly in children, and there is a paucity of data. Hence, this study was taken up to evaluate thyroid disease in children with vitiligo when compared to controls in a tertiary care centre.

## 2. Material and Methods

This was a hospital-based case-control study conducted at a tertiary care centre in South India over 18 months after obtaining institutional ethics committee clearance. 50 children of age less than or equal to 15 years with a clinical diagnosis of vitiligo were recruited as cases after taking informed consent from parents/guardians. Children with other depigmenting disorders, known thyroid disease, and antithyroid medications were excluded. Age and gender-matched 50 healthy children were recruited as controls.

A detailed history and clinical examination were undertaken among cases and controls regarding the onset of disease, type of vitiligo, familial incidence of vitiligo and thyroid disease, and any other associations.

Blood samples were collected from both groups, and sent to the central lab to assess the levels of free triiodothyronine (normal range: fT3 2.3 – 4.2pg/ml), free thyroxine (normal range: fT4 0.8 – 2.2ng/dL), thyroid-stimulating hormone (normal range: TSH 0.7 – 6.4 $\mu$IU/ml), anti-thyroidperoxidase (positive anti-TPO > 60 IU/ml), and anti-thyroglobulin (positive anti-Tg > 60 IU/ml).

### *2.1. Statistical analysis*

The results were shown as mean ± SD. The unpaired t-test was used for normally distributed data. The difference between classified variables was tested using the Chi-square test. The P-value of <0.05 was considered significant.

## 3. Results

A total of 100 paediatric patients, 50 cases and 50 controls of age less than 15 years with similar baseline findings were enrolled in the study. Patients with vitiligo had a significantly higher positive family history of vitiligo when compared to controls (Table 1). The mean age of onset of the disease among cases was 7.04±3.49. Among the 50 patients, 23 had generalized vitiligo (vitiligo vulgaris-19, acrofacial-4) and 27 had localized vitiligo (mucosal-10, focal-11, segmental -6). The most common site involved was the lower limbs (54%), followed by head and neck (28%) among the cases.

Among the cases, thyroid function and thyroid autoantibody abnormalities were found in a total of 16 (32%) patients; seven (14%) males and nine (18%) females. Out of 16 patients, 11 (22%) patients had thyroid profile abnormality with seven (14%) subclinical hypothyroidism most frequent, followed by three (6%) hypothyroidism and the thyroid autoantibody abnormality was found in a total of five (10%) patients as shown in Table 2. Among the controls, two had subclinical hypothyroidism, and one had hypothyroidism.

There was no statistically significant difference in thyroid function abnormality concerning age (P=0.401) and between male and female cases (P=0.585.) in our study. However, the difference between cases and controls for thyroid function and thyroid autoantibodies was significant with p-value of 0.021 and 0.049, respectively. The overall difference between cases and controls for thyroid function abnormality was significant with a p-value of 0.001, as shown in Table 3.

## 4. Discussion

Vitiligo is a depigmenting disorder characterized by asymptomatic, well defined, round-oval, ivory-white macules and patches.[11] Its aetiology is unknown, with autoimmunity being considered the major etiological factor. Its association with different autoimmune diseases has been shown previously. The association betwixt vitiligo and thyroid disorders has also been suggested.[12,13]

Vitiligo affects both genders equally, but women often visit doctors most frequently due to cosmetic reasons. In our study, females were more than males with a ratio of 1.5:1. Many studies have also reported females outnumbering males, as vitiligo is an autoimmune disease and also due to aesthetic concern.[14,15]

In the present research, the mean age of disease onset was 7.04±3.49, which was almost similar to 7.85±2.94 years noted by Kayal A et al.[16] Vitiligo has been reported to start between 8 to 12 years of age in 51% of the children.[17] We encountered maximum cases between the age group of 6 to 10 years with 40%, whereas it was 45.5% in the study by Afsar FS et al.[15]

In our study, a family history of vitiligo was seen in 14% of cases. It is similar to Indian studies by Hafi et al.[18] 12%, Murugaiyan et al.[19] 12.5%, PK Sheth et al.[20] 14% and SM Kambil et al.[21] 15%, but much lesser than the findings of Nicolaidou et al.[22] 35% respectively. Positive familial incidence indicate that genetic influences have a role in the pathogenesis of vitiligo.

Genome-wide association analysis suggest that the correlation betwixt vitiligo and thyroid disease may be described by portioning a subgroup of susceptibility genes.[23–31] For example, in families, genome-wide linkage analysis found an autoimmunity susceptibility locus on chromosome 1 in cases with both Hashimoto's thyroiditis and vitiligo.[30–32]

A systemic review conducted by Vrijman C et al.,[33] involving 48 studies, emphasizes us one should be cognizant of the likelihood of thyroid abnormalities in patients with vitiligo. The systemic review involving about 77 studies with 3,643 vitiligo patients by Yuan J et al.[34] supports a significant association between vitiligo and atleast one thyroid disorder.

**Table 1:** Demographic profile of cases and controls

| Age group | Cases | Controls | P-value |
|---|---|---|---|
| 0 – 5 | 11 (22%) | 11 (22%) | |
| 6 –10 | 20 (40%) | 19 (38%) | |
| 11 –15 | 19 (38%) | 20 (40%) | |
| **Age Mean ± S.D** | 9.28 ± 3.76 | 9.32 ± 3.93 | 0.95 |
| **Gender** | | | |
| Male | 20 (40%) | 21(41%) | 0.838 |
| Female | 30 (60%) | 29 (59%) | |
| **Family History of Thyroid** | 5 (10%) | 2 (4%) | 0.239 |
| **Family History of Vitiligo** | 7 (14%) | 1 (2%) | 0.026 |

**Table 2:** Laboratory findings of thyroid abnormalities among cases (fT4: free thyroxine, fT3: free triiodothyronine, TSH: Thyroid Stimulating Hormone, Anti-Tg: Thyroglobulin Antibody, Anti-TPO: Thyro Peroxidase Antibody)

| No. of cases | fT4 | fT3 | TSH | Anti-Tg | Anti- TPO | Clinical Diagnosis |
|---|---|---|---|---|---|---|
| 7 | Normal | Normal | ↑ | Negative | Negative | Subclinical hypothyroidism |
| 3 | ↓ | ↓ | ↑ | Negative | Negative | Hypothyroidism |
| 1 | ↓ | ↓ | ↑ | Negative | Positive | Hypothyroidism + Autoimmune thyroiditis |
| 2 | Normal | Normal | Normal | Positive | Positive | Euthyroidism + Autoimmune thyroiditis |
| 1 | Normal | Normal | ↑ | Positive | Negative | Subclinical hypothyroidism + Autoimmune thyroiditis |
| 1 | ↑ | ↑ | Normal | Negative | Negative | Hyperthyroidism |
| 1 | Normal | Normal | Normal | Negative | Positive | Euthyroidism + Autoimmune thyroiditis |

**Table 3:** Comparision of thyroid abnormalities between cases and controls

| | Cases | Controls | P-value |
|---|---|---|---|
| Thyroid abnormalities (overall) | 16 (32%) | 3 (6%) | 0.001 |
| Abnormal thyroid function tests | 11(22%) | 3 (6%) | 0.021 |
| Thyroid autoantibodies | 5 (10%) | 0 (0%) | 0.049 |

In children with vitiligo, a significant incidence of thyroid disease has been found. In our study, a total of 16 (32%) patients had thyroid function and thyroid autoantibody abnormalities, which was in accordance with a study done by Kumari Neeti et al.[35] 33.3%, and it was a little higher than the study by Afsar FS et al., where 25.3% of children had thyroid abnormalities.[15] Iacovelli et al. showed 10.7% of children, especially females with non-segmental vitiligo having thyroid dysfunction.[36]

Subclinical hypothyroidism is characterized by normal total or free T4 and T3 values and elevated serum TSH levels.[37] In our study, only subclinical hypothyroidism was present in 7 (14%) patients, which were similar to studies by Kumari Neeti et al.[35] 6 (13.33%) and Afsar FS et al. 10 (12.6%).[15]

In our study, one (2%) patient was diagnosed with subclinical hypothyroidism with autoimmune thyroiditis, and it was similar to reports by Kumari Neeti et al.[35] and Afsar FS et al.[15] with 4.44% and 3.79%, respectively. Although subclinical hypothyroidism is a laboratory diagnosis with no significant findings or symptoms in patients, studies have demonstrated the development of overt hypothyroidism at a rate of 5- 20% per year, especially in autoimmune thyroiditis.[38]

Thyroid antibody positivity was present in 5 (10%) cases. In contrast, Afsar et al.[15] have reported in 11.38% of the patients, Kumari Neeti et al.[35] found in 11.11% of patients and Yang Y et al.[39] (11.8%) among children.[17]

The present study had some limitations as it was a single-centre observational study from tertiary hospital. We could not extrapolate our findings to all patients with vitiligo in the general population.

## 5. Conclusion

Our study found a significant association betwixt thyroid disease and childhood vitiligo. Thus, evaluating vitiligo patients for thyroid abnormalities help to detect thyroid diseases or determine the possibility of eventual onset.

## 6. Conflict of Interest

None.

## 7. Source of Funding

None.

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## Author biography

**Senthil Kumar AL,** Associate Professor

**K Sridevi,** Professor

**DVSB Ramamurthy,** Professor and HOD

**Akshay Jain Salecha,** Assistant Professor

**Leepika Annamreddy,** Junior Resident

**Cite this article:** Senthil Kumar AL, Sridevi K, Ramamurthy DVSB, Salecha AJ, Annamreddy L. Evaluation of thyroid abnormalities in childhood vitiligo from a tertiary care centre: A case-control study. *Panacea J Med Sci* 2023;13(1):217-221.