The Egyptian Journal of Hospital Medicine (January 2024) Vol. 94, Page 799-804

Anti-Thyroid Peroxidase Antibody and Segmental Vitiligo

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ABSTRACT

Background: Vitiligo is an autoimmune disease (AID) of the skin, which affects pigment-producing melanocytes and results in depigmented patches. It has been demonstrated that; anti-thyroid hormones autoantibodies may have a role in the process of depigmentation among cases with vitiligo.

Objective: To evaluate auto-immunity role in segmental vitiligo (SV) by comparing anti-thyroid peroxidase (anti-TPO) antibody (Ab) in vitiligo and healthy subjects. To compare anti-TPO Ab in segmental vitiligo and non-segmental vitiligo (NSV) patients. **Patients and Methods:** This was a case-control study that comprised 3 groups, 20 patients with SV, 20 patients with NSV and 40 healthy individuals with age and sex-matched controls. Thyroid stimulating hormone (TSH) and thyroid peroxidase antibody (antiTPO) were measured by enzyme linked immunosorbent assay (ELISA) technique in each group.

Results: Anti-TPO positivity was demonstrated to be significantly more common in non-segmental vitiligo (NSV) than segmental vitiligo patients. While TSH level did not differ significantly between groups.

Conclusions: This result suggests that AIDs are more common among cases with NSV than SV. Anti-TPO Ab positivity is more common among females and among cases with a long duration of vitiligo.

Keywords: Segmental vitiligo, Non-segmental, Thyroid stimulating hormone, Thyroid peroxidase antibody.

INTRODUCTION

Vitiligo is a depigmented dermal lesion developed owing to the extensive loss of melanocytes [(1).] The distinctive lesion is a totally amelanotic, nonscaly, chalky-white macule with well-circumscribed outlines [(2).] In recent years, it is classified, based on the manifestations of macules, into 3 main types, called NSV, SV, and undetermined/unclassified vitiligo [(3).]

Vitiligo is now classified as an AID, accompanied by genetic and environmental factors in association with metabolic, free radicals generations and cell detachment alterations [(2).] The degrees of AID are greater in NSV in comparison with SV, especially concerning thyroid disease [(4).] Different thyroid autoantibodies such as thyroid stimulating Ab, anti-thyroglobulin (Tg) Ab and antiTPO were noticeable in autoimmune thyroid diseases (AITD) [(5).]

Till now, the actual mechanism of anti-thyroid hormone autoantibodies-mediated depigmentation remains controversial. These comprised the reactions of anti-thyroid hormone autoantibodies with melanogenic enzymes or enzymes comprised in regulation of free radical generation, which ultimately ends in inhibition of their activity and consequent affection of melanin production [(6)].

Cases with NSV were demonstrated to be accompanied by increased anti-TPO Ab, which is of great sensitivity in terms of AITD diagnosis and supervision. Moreover, AIDs are frequently associated with NSV cases, while cases with SV are not. Such outcomes are reinforcing the hypotheses of SV pathogenesis and NSV is different [(7)].

This study carried out to evaluate auto-immunity role in SV by comparing anti-TPO Ab in vitiligo and healthy subjects. Also, comparing anti-TPO Ab in SV and NSV patients was conducted.

PATIENTS AND METHODS:

This case-control study enrolled 20 patients with NSV, 20 patients with SV. Additionally, forty healthy subjects were comprised as a control group. Cases with manifestations of thyroid dysfunctions were excluded.

Methods:

All patients were subjected to history taking and general and dermatological examination. Vitiligo lesions were described according to site, symmetry, type, activity and stability. Then, venous samples were withdrawn from all subjects to measure thyroid stimulating hormone (TSH) and thyroid peroxidase antibody (antiTPO) were measured by enzyme linked immunosorbent Assay (ELISA) technique in each group.

Ethical approval:

The Mansoura Medical Ethics Committee of the Mansoura Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis: Data were analysed by IBM SPSS Corp, V22.0. Armonk, NY. Qualitative data were represented as numbers and percent. Quantitative data were represented as medians and range for non-normal distribution of data and means ±standard deviation (SD), for normally distributed data after testing normality by Kolmogrov-Smirnov test. P value was considered significant when its value was less than 0.05.

RESULTS

There was no significant difference among the 3 groups, regarding gender. Regarding age and body mass index (BMI), there was a statistically significant difference between SV group and NSV group (Table 1).

Received: 17/10/2023
Accepted: 17/12/2023

Table (1): Comparison among the different studied groups based on sociodemographic data:

Parameter		Control group (n=40)	Non-segmental vitiligo (n=20)	Segmental vitiligo (n=20)	P value
Gender	**Male**	**17 (42.5%)**	**6 (30.0%)**	**7 (35.0%)**	0.619
	Female	**23 (57.5%)**	**14 (70.0%)**	**13 (65.0%)**	
Age (years)	**Median (Min-Max)**	**26.0 (9-60)**	**36.5 (16-60)**	**19.0 (9-60)**	**P=0.021*** P^1=0.132 P^2=0.055 **P^3=0.010***
BMI	**Mean ± SD**	**24.8 ± 4.20**	**28.4 ± 5.64**	**22.7 ± 3.75**	**P=0.001*** **P^1=0.012*** P^2=0.295 **P^3=<0.001***
Marital status	**Single**	**26 (65.0%)**	**10 (50.0%)**	**15 (75.0%)**	0.252
	Married	**14 (35.0%)**	**10 (50.0%)**	**5 (25.0%)**	
Smoking	**Non-smoker**	**35 (87.5%)**	**18 (90.0%)**	**18 (90.0%)**	0.939
	Smoker	**5 (12.5%)**	**2 (10.0%)**	**2 (10.0%)**	
Occupation	**Professional person**	**14 (35.0%)**	**6 (30.0%)**	**3 (15.0%)**	**P=0.015*** P^1=0.852 **P^2=0.007*** **P^3=0.016***
	Housewife	**15 (37.5%)**	**9 (45.0%)**	**3 (15.0%)**	
	Student	**11 (27.5%)**	**5 (25.0%)**	**14 (70.0%)**	

P^1, between group1 and group2, **P^2**, between group1 and group3, **P^3**, between group2 and group3, *Significant

Regarding duration of the disease, there was a statistically significant difference between SV group and NSV group (Table 2).

Table (2): Comparison of clinical data among studied groups

Parameter		Non-segmental vitiligo (n=20)	Segmental vitiligo (n=20)	P value
Duration of disease	**Median (Min-Max)**	**7.0 (1-20)**	**2.0 (1-10)**	**0.007***
Stability	**Stable**	**11 (55.0%)**	**15 (75.0%)**	0.185
	Non stable	**9 (45.0%)**	**5 (25.0%)**	
Medical history	**Negative**	**18 (90.0%)**	**20 (100.0%)**	0.487
	Positive	**2 (10.0%)**	**0 (0.0%)**	
Family history of vitiligo	**Negative**	**15 (75.0%)**	**18 (90.0%)**	0.407
	Positive	**5 (25.0%)**	**2 (10.0%)**	

*Significant

The most common Subtype of non-segmental vitiligo patients is generalized subtype (40%) while most common in segmental vitiligo is unisegmental subtype (85%) (Table 3).

Table (3): Subtypes of included vitiligo patients.

Parameters		Vitiligo patients	
		N	%
Non-segmental vitiligo subtypes	**Generalized**	8	40.0%
	Focal	5	25.0%
	Acrofacial	7	35.0%
Segmental vitiligo subtypes	**Unisegmental**	17	85.0%
	Bisegmental	1	5.0%
	Multisegmental	2	10.0%

The analysis revealed that facial patches (60%) and leukotrichia (55%) were very common among cases with SV, while in cases with NSV, patches were more frequently limited to the trunk (40%) and exposed sites (face and limbs) (45%), and leukotrichia occurred less frequently (10 %) (Table 4 and figures 1 and 2).

Table (4): Localization of lesion and incidence of poliosis in vitiligo patients:

Patches location	Segmental type (n=20)		Nonsegmental type (n=20)	
	Number patches	%	Number patches	%
Scalp	**2**	**10%**	**2**	**10%**
Face	**12**	**60%**	**6**	**30%**
Neck	**1**	**5%**	**1**	**55%**
Upper limb	**1**	**5%**	**2**	**10%**
Lower limb	**1**	**55%**	**1**	**5%**
Trunk	**3**	**15%**	**8**	**40%**
Poliosis	**11**	**55%**	**2**	**10%**

No significant difference was found between the studied groups as regard TSH level. On the other hand, there was statistically significant difference in TPO Ab level between studied groups. TPO antibody concentration was significantly higher in NSV group as compared to the control and SV groups. TPO antibody concentration was elevated in 30% in NSV patients, while it was not elevated in patients with SV (Table 5).

Table (5): Comparison of TSH and TPO antibody among the studied groups

Parameter		Control group (n=40)	Non-segmental vitiligo (n=20)	Segmental vitiligo (n=20)	P value
TSH	**Median (Min-Max)**	**1.16±0.28**	**1.56 ±0.37**	**1.42 ±0.34**	0.438
TSH	**Normal**	**39 (97.5%)**	**15 (75.0%)**	**19 (95.0%)**	0.051
	Decreased	**1 (2.5%)**	**4 (20.0%)**	**1 (5.0%)**	
	Elevated	**0 (0.0%)**	**1 (5.0%)**	**0 (0.0%)**	
TPOab	**Median (Min-Max)**	**12.85 (7.6-76.5)**	**21.7 (9.1-114.4)**	**11.85 (9.3-51.9)**	**P=0.040*** **P^1=0.016*** P^2=0.851 **P^3=0.043***
TPOab	**Normal**	**39 (97.5%)**	**13 (65.0%)**	**18 (90.0%)**	**P=0.001*** **P^1=0.002*** P^2=0.101 **P^3=0.028***
	Borderline	**0 (0.0%)**	**1 (5.0%)**	**2 (10.0%)**	
	Elevated	**1 (2.5%)**	**6 (30.0%)**	**0 (0.0%)**	

P, between 3 groups; **P^1**, between group1 and group2, **P^2**, between group1 and group3, **P^3**, between group2 and group3, *Significant

There was significant positive correlation between TPO antibody with duration of disease in non-segmental vitiligo cases (Table 6).

Table (6): Correlation between TSH and TPO antibody with basic characters in cases of segmental and non segmenal vitiligo.

Non-segmental vitiligo cases			
		TSH	**TPOab**
TSH	**r**	1.000	
	P	0	
TPOab	**r**	0.406	1.000
	P	0.076	0
Age	**r**	0.093	-0.023
	P	0.697	0.922
Duration of disease	**r**	0.295	**0.549**
	P	0.207	**0.012***
Segmental vitiligo cases			
		TSH	TPOab
TSH	**r**	1.000	
	P	0	
TPOab	**r**	-0.408	1.000
	P	0.074	0
Age	**r**	-0.024	0.369
	P	0.920	0.109
Duration of disease	**r**	0.043	0.277
	P	0.857	0.237

*Significant

Duration of disease was significantly increased in cases with TPO antibodies in comparison with patients without TPO antibodies. Most cases of positive anti-thyroid anti bodies were females (77.8%) (Table 7).

Table (7): Comparison of demographic and clinical data among vitiligo patients with and without anti-thyroid peroxidase antibody.

Parameter		Without autoantibodies (n=31)	With autoantibodies (n=9)	P value
Gender	**Male**	**11 (35.5%)**	**2 (22.2%)**	0.690
	Female	**20 (64.5%)**	**7 (77.8%)**	
Age (years)	**Median (Min-Max)**	**22.0 (9-60)**	**35.0 (10-60)**	0.321
Duration of disease	**Median (Min-Max)**	**3.0 (1.0-12.0)**	**8.0 (1.5-20)**	**0.020***
Stability	**Stable**	**22 (71.0%)**	**4 (44.4%)**	0.234
	Non-stable	**9 (29.0%)**	**5 (55.6%)**	
Medical history	**Negative**	**29 (93.5%)**	**9 (100.0%)**	1.00
	Positive	**2 (6.5%)**	**0 (0.0%)**	
Family history of vitiligo	**Negative**	**25 (80.6%)**	**8 (88.9%)**	1.00
	Positive	**6 (19.4%)**	**1 (11.1%)**	
Types of vitiligo	**Non-segmental**	**13 (41.9%)**	**7 (77.8%)**	0.127
	Segmental	**18 (58.1%)**	**2 (22.2%)**	

* Significant P

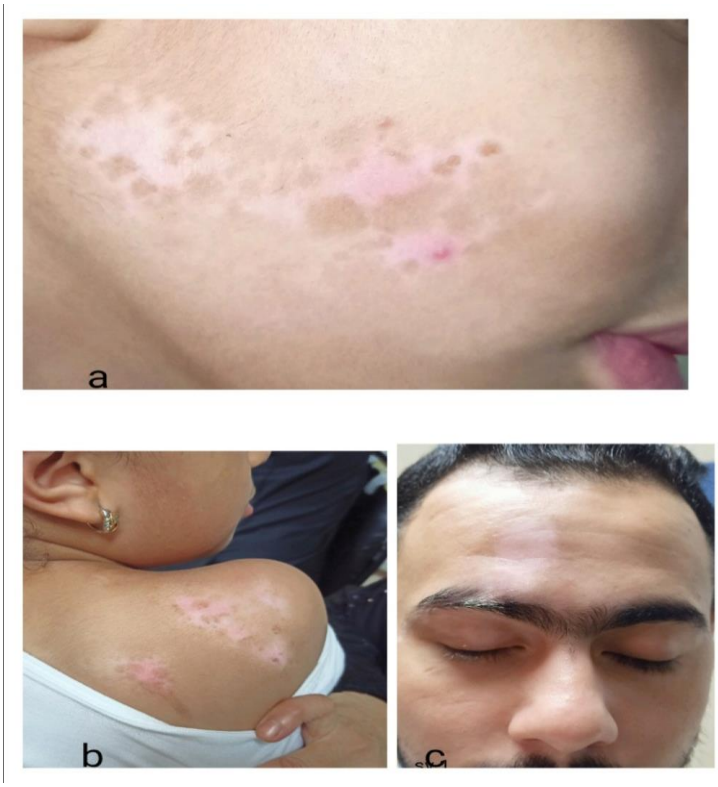

Figure (1): Shows examples of different patients with segmental vitiligo included in the study. (a) segmental vitiligo in lower right side of the face. (b) segmental vitiligo in back of upper right shoulder. (c) segmental vitiligo in upper right side of face with poliosis.

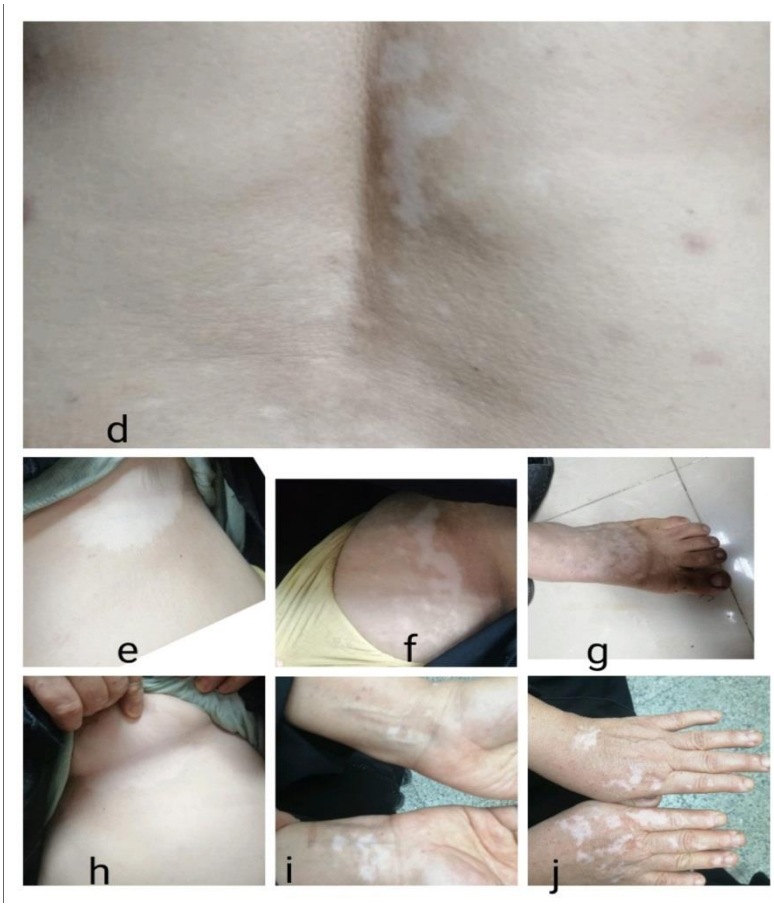

Figure (2): Shows patient with NSV of generalized type comprised in the study. (d, e, h) show patches in back and upper abdomen. (f, g) show patches in inner side of thigh and foot. (i, j) show patches in both sides of hands.

DISCUSSION

Vitiligo has been considered as the commonest cause of depigmentation with estimated prevalence of 0.1%–2% globally **[8].** The prevalence of SV ranges from 5% to 30%, and SV represents 5% to 16% of overall vitiligo cases. SV happens at a younger age; before the age of ten years in 41% of cases, and before the age of thirty years in 87% **[9].** The present results reported that the main age incidence of SV was before 20 years, on the other hand, about 65% of the comprised cases aged less than 20. This is matched with another study **[10].**

The etiopathogenesis of vitiligo could be clarified by autoimmune mechanism as it is occasionally associated with AID and responds to immunosuppressive agents. The immunological meachnism is cell-mediated, humoral, or via the cytokines **[10,11]**.

The rates of auto-immune disorders are higher in non-segmental vitiligo than segmental vitiligo, especially concerning thyroid disease **[4].** AITD are frequently associated with the existence of anti-TPO, anti-Tg, and anti-TSH receptor antibodies **[12-13].**

The present study revealed a significant elevation in the rate of TPO Ab in NSV in comparison to SV, which agreed with **Atallah *et al.*** **[7]** and **Lim *et al.*** **[14]**. It has been demonstrated that; anti-TPO Ab are highly sensitive tests in the context of AITD diagnosis.

This antibody has been confirmed as a sensitive test for the determination of early subclinical AITD; follow-up of the responses to immunotherapy and recognition of at-risk cases for AITD **[6]**. We found a positive association between values of anti-TPO and the disease duration among vitiligo cases, which also agreed with **Atallah *et al.*** **[7]** and **Gey *et al.*** **[15]** who revealed that the risk of cases with vitiligo developing AITD is increased by two-fold every five years, hence cases were frequently screened for anti-thyroid antibodies.

In this study most cases of positive anti-thyroid antibodies were females, such outcomes are in accordance with **Gey *et al.*** **[15]** who reported that AITD reveals a potent female predominance; clarifying that by hormonal hypothesis. Estrogens are believed to be strong stimulators of autoimmunity, on the other hand, androgens appeared to be protective in such context **[16]**. Of note, sex hormones play an essential role in the immune response process, in particular estrogens **[17].**

Endocrine disorders were noted in 8 (20%) vitiligo patients and 1 (2.5%) individual in the control group. Out of 8 vitiligo patients with endocrine disorders, 1 had hypothyroidism, 5 had hyperthyroidism, and 2 had diabetes. The associations

were statistically insignificant, in contrast to **Agarwala and Malkud** [18] who found that out of 40 vitiligo patients (15.32%) with endocrine disorders, 27 had hypothyroidism, 5 had hyperthyroidism, and 8 had diabetes. Also, **Atallah *et al.*** [7] revealed that all the determined hormonal changes in vitiligo cases had hyperthyroidism, with no recorded cases of hypothyroidism.

Current study showed that BMI is significantly increased in NSV cases than SV ones, which is matched with the study of **Tanacan and Atakan** [19] who found that BMI was 26.62±0.39 in NSV while in SV it was 21.90 ± 0.66.

CONCLUSION

We may conclude the following: Anti-TPO positivity was demonstrated to be significantly more common in NSV than SV patients especially in females and patients with long duration, so screening of these cases with NSV for thyroid functions should comprise anti-TPO Ab as its appearance frequently occurs before thyroid dysfunction. In addition, AIDs are very common among cases with NSV compared to SV ones. Such outcomes are reinforcing the hypothesis that the pathogenesis of SV and NSV is different.

Conflict of interest: None.
Source of funding: None.

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