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Study of Thyroid Dysfunction in Vitiligo Patients

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ABSTRACT

Background: Vitiligo is an autoimmune depigmentation skin disease resulting from melanocyte damage with an estimated global prevalence of 0.5–2%. It most often begins before age of 30 and may be linked with autoimmune, genetic, and environmental issues, and has a significant association with thyroid illnesses. Thyroid dysfunction early detection in vitiligo patients especially symptomatic or with family history can improve clinical outcome and disease course.
Aim: We aimed to study thyroid dysfunction in a group of Egyptian patients with vitiligo.
Patients and methods: A cross-sectional study included 200 patients clinically diagnosed with vitiligo by two expert dermatologists and confirmed through Wood's light examination. The study was conducted at Dermatology Department of Menoufia University Hospital, Vitiligo Unit in Kafr El-Sheikh General Hospital, Kafr El-Sheikh Dermatology Hospital, Mabaret El Asafra Labs. **Results:** The mean age of vitiligo patients was 36.5 years with slight female predominance (55.5%), and the most common clinical types were vitiligo vulgaris (43%) and acro-facial vitiligo (41.5%). Thyroid disorders were detected in 7.5% of patients, most commonly sub-clinical hypothyroidism, with no significant gender difference. However, patients with thyroid dysfunction had a significantly longer disease duration. FT3 levels showed a significant gender difference and varied with clinical types, particularly elevated in focal vitiligo, while thyroid dysfunction was most frequent in vitiligo vulgaris and absent in focal cases. **Conclusion:** Thyroid dysfunction, particularly hypothyroidism, may be associated with certain vitiligo types and disease duration, emphasizing importance of routine thyroid function screening in vitiligo patients to ensure early detection and management of potential thyroid abnormalities.
Keywords: Autoimmune, Thyroid dysfunction, Vitiligo, Vitiligo types, Wood's light examination.

INTRODUCTION

Vitiligo represents a dermatological condition characterized by progressive melanocytic abnormalities, leading to focal or widespread depigmentation of the skin, mucous membranes, and hair [(1)]. The global estimated prevalence of this disorder ranges from 0.5% to 2% [(2)]. The comprehensive pathophysiological mechanisms underlying vitiligo have not yet been fully elucidated, a deficit that contributes to the current lack of highly specific and consistently effective treatments. This often has profound repercussions on the quality of life for patients affected by this type of pathology [(3)]. Furthermore, the emotional and psychological impact on the affected population can be considerably high, necessitating holistic patient care [(4)]. Vitiligo demonstrates the capacity to manifest at any age and across all ethnic groups. However, in the majority of documented cases, the onset of the disease typically occurs during a younger age, specifically before 30 years of age [(5)]. Regarding its etiological factors, evidence suggests a multifactorial interplay involving the immune system, as well as the nervous and endocrine systems, operating within a specific genetic predisposition following exposure to particular environmental triggers, all contributing to the occurrence of this condition [(6)].

Vitiligo can be significantly associated with various autoimmune diseases, reflecting a shared immunological dysregulation. Nevertheless, it is important to note that not all instances of depigmentation will invariably present with coexisting autoimmune pathologies [(7)]. Thyroid damage, in particular, has been frequently and consistently described in association with vitiligo [(8)].

A notably higher prevalence of autoimmune thyroid pathologies has been observed among patients diagnosed with vitiligo when compared to the general population [(9)]. These autoimmune thyroid conditions most commonly present as either thyrotoxicosis, encompassing Graves' disease and hashitoxicosis indicating both hypo- and hyper-functional states [(9)]. In light of these associations, professional guidelines have offered recommendations for screening. Specifically, the British guidelines have suggested the routine checking of thyroid function for adult patients with vitiligo, while the Dutch guidelines recommend that thyroid function testing should be performed when patients with vitiligo exhibit overt clinical symptoms indicative of thyroid disease [(10)].

One of the most critical considerations when advocating for screening for thyroid dysfunction in individuals with vitiligo is the potential for improved clinical outcomes. Screening asymptomatic individuals and initiating early treatment for any underlying thyroid pathology can lead to significantly better outcomes in terms of the prognosis and progression of the cutaneous pathology, compared to subjects who were not screened and presented to a physician with already clinically manifested skin pathologies and concurrent thyroid dysfunction [(11)]. Research has indicated that the onset of vitiligo often precedes the clinical manifestation of thyroid dysfunction [(9)]. Furthermore, it has been demonstrated that thyroid dysfunction with an underlying autoimmune

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etiology is more commonly observed in patients over 30 years of age [12]. An additional association has been identified between thyroid dysfunction and a positive family history of thyroid pathology, as well as a higher incidence among older women [13].

The percentage of total body surface area (TBSA) affected by vitiligo is significantly higher in the presence of coexisting thyroid pathology. This, in turn, is a phenomenon more commonly encountered among women. Additionally, patients presenting with coexisting thyroid pathologies have demonstrated a particular predisposition to develop acral vitiligo and depigmentation specifically affecting the joints, suggesting a distinct clinical phenotype [10].

The aim of this work was to systematically study the prevalence and characteristics of thyroid dysfunction within a defined group of Egyptian patients diagnosed with vitiligo.

PATIENTS AND METHODS

This cross-sectional study was conducted on 200 clinically diagnosed vitiligo patients. The patients were diagnosed by two senior dermatologists and confirmed by Wood's light examination, which highlights depigmented characteristic lesions. Some of the dermatology centers were involved in the research: Menoufia University Hospital Dermatology Department, Kafr El-Sheikh General Hospital Vitiligo Unit, Kafr El-Sheikh Dermatology Hospital, and Mabaret El Asafra Labs. Data collection was conducted from February 2024 to January 2025.

Inclusion criteria: Male and female patients between 20 and 60 years of age with a confirmed clinical diagnosis of vitiligo.

Exclusion criteria: Individuals with coexisting autoimmune conditions, except for those with thyroid disease, were excluded from the study.

Data collection involved several steps. Firstly, complete medical history was taken from each participant including personal, family, and clinical histories, especially those related to vitiligo and thyroid malfunction. A general physical examination was then performed, noting for clinical findings suggestive of thyroid dysfunction. Features assessed for hyperthyroidism were fine hair, thinning of skin, weakness of muscles, tachycardia, tremors, stare, and lid lag. The reverse, dryness and thickening of skin and bradycardia, was considered indicative of hypothyroidism. A local examination of the thyroid was also carried out to check for enlargement, nodules, or tenderness. Full dermatological assessment of all patients was then carried out, and diagnosis of vitiligo was further confirmed by Wood's lamp examination. This was performed by two experienced dermatologists to achieve greater accuracy of diagnosis. For laboratory examination, venous blood samples were drawn under aseptic conditions by venipuncture. Approximately 5 mL venous blood from each individual was drawn into plain vacutainer tubes. The blood samples were left to clot at room temperature and, after that, were spun at 3000 rpm for 10 minutes for separation of the serum. The obtained serum was aliquoted and stored at −20 °C until quantitation. Thyroid function was ascertained by radioimmunoassay techniques. Triiodothyronine (T3) levels were measured by the Coat-A-Count Total T3 kit by solid-phase radioimmunoassay. Serum TSH was measured by the Immunocorp-coated tube assay, a two-site immunoradiometric (sandwich) assay designed for quantitative measurement. Laboratory tests were performed according to standard operating procedures to assure accurate and reproducible results.

Ethical approval: This study was formally granted by The Ethical Committee of the Faculty of Medicine, Menoufia University, operating under the designated approval code: 11/2023DERMA4. Prior to their inclusion in the investigation, all prospective participants were comprehensively and transparently informed regarding the precise purpose, intricate procedures, and any foreseeable risks associated with their involvement. A stringent process of written informed consent was meticulously adhered to, ensuring that each participant voluntarily assented to their participation. Furthermore, it was explicitly communicated and assured that all personal data collected during the study would be maintained with the utmost confidentiality, safeguarding participant privacy. The entirety of this study's execution rigorously conformed to the ethical principles outlined in the Helsinki Declaration, underscoring a steadfast commitment to the highest standards of human research ethics.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS) version 24. Qualitative data were presented as frequencies and percentages, while quantitative data were expressed as mean ± standard deviation (SD) for normally distributed variables, or as median and interquartile range (IQR) for non-normally distributed data. Statistical comparisons were made using the Mann-Whitney U test for two-group comparisons involving non-normally distributed data, and the Kruskal-Wallis test for comparisons among more than two groups. The Chi-square test was used for analyzing categorical data. A p-value ≤ 0.05 was considered statistically significant, a p-value ≤ 0.001 was considered highly significant, and a p-value > 0.05 was considered not significant.

RESULTS

Table (1) showed the description of demographic data in all studied patients. As regards age, the mean age of all studied patients was 36.5 ± 13.5 years with minimum age

of 20 years and maximum age of 60 years. As regards gender, there were 89 males (44.5%) and 111 females (55.5%) in the studied patients. As regards duration of vitiligo, the mean duration of all studied patients was 3.4 ± 4.4 years with a minimum duration of 0.1 years and maximum duration of 35 years. As regards family history of vitiligo, positive family history was reported in 12 of vitiligo patients (6%). As regards drug history, all studied patients received treatment for their condition the most frequently tried line of treatment was phototherapy (140 patients, 70%) followed by excimer laser (60 patients, 30%). As regards chronic diseases, 20 vitiligo patients suffered from one or more chronic diseases, DM in 9 patients (4.5%), HTN in 7 patients (3.5%), cardiac disease in 2 patients (1%) and thyroid disease in 2 patients (1%).

Table (1): Description of demographic data in all studied patients

		Studied patients (N = 200)	
Gender	**Male**	89	44.5%
	Female	111	55.5%
Age (years)	**Mean ±SD**	36.5 ± 13.5	
	Min - Max	20 – 60	
Duration of vitiligo (years)	**Mean ±SD**	3.4 ± 4.4	
	Min - Max	0.1 – 35	
Family history of vitiligo	**Negative**	188	94%
	Positive	12	6%
Drug history	**Phototherapy**	140	70%
	Excimer laser	60	30%
Chronic diseases	**Non**	180	90%
	DM	9	4.5%
	HTN	7	3.5%
	Cardiac	2	1%
	Thyroid disease	2	1%

This table showed the description of clinical types of vitiligo in all studied patients. The most common clinical types were vitiligo vulgaris (86 patients, 43%) and acro-facial vitiligo (83 patients, 41.5%), while the least common types were focal vitiligo (30 patients, 15%) and segmental vitiligo (1 patient, 0.5%) (Table 2).

Table (2): Description of clinical types of vitiligo in all studied patients

		Studied patients (N = 200)	
Clinical types of vitiligo	**Acro-facial vitiligo**	83	41.5%
	Vitiligo vulgaris	86	43%
	Focal vitiligo	30	15%
	Segmental vitiligo	1	0.5%

Regarding TSH, the mean TSH of all studied patients was 3.02 ± 8.8, median TSH was 1.53 (1.13 – 2.47) and TSH ranged from 0.01 to 106.9. As regards FT3, the mean FT3 of all studied patients was 3.3 ± 0.58, median FT3 was 3.24 (2.9 – 3.6) and ranged from 2.13 to 6.25. Concerning FT4, the mean FT4 of all studied patients was 1.23 ± 0.22, median FT4 was 1.21 (1.12 – 1.37) and range from 0.45 to 2.07. Accordingly, there was thyroid disorder in 15 patients (7.5%) of the studied patients, 2 patients (1%) showed sub-clinical hyperthyroidism, 6 patients (3%) showed sub-clinical hypothyroidism, 3 patients (1.5%) showed overt hyperthyroidism and 4 patients (2%) showed overt hypothyroidism (Table 3).

Table (3): Description of thyroid function tests in all studied patients

		Studied patients (N = 200)	
TSH (µIU/mL**)**	**Mean ±SD**	3.02 ± 0.8	
FT3 (pg/mL**)**	**Mean ±SD**	3.3 ± 0.58	
FT4 (ng/dL**)**	**Mean ±SD**	1.23 ± 0.22	
Thyroid disorder	**No**	185	92.5%
	Yes	15	7.5%
Thyroid disorder pattern	**Sub-clinical hyperthyroidism**	2	1%
	Sub-clinical hypothyroidism	6	3%
	Overt hyperthyroidism	3	1.5%
	Overt hypothyroidism	4	2%

The analysis demonstrated no statistically significant correlation between gender and TSH levels among the studied patients (p = 0.261). Male patients had a higher mean TSH level (4.1 ± 12.9) compared to females (2.1 ± 2.5), though the median values were similar: 1.6 (1.2–2.4) in males and 1.5 (1.07–2.4) in females. However, FT3 levels showed a statistically significant difference between genders (p = 0.024), with males exhibiting higher mean and median FT3 values (mean = 3.3 ± 0.54, median = 3.4) compared to females (mean = 3.2 ± 0.61, median = 3.1). Conversely, no significant correlation was observed between gender and FT4 levels (p = 0.135), as both males and females had comparable FT4 means and medians. Regarding the presence and patterns of thyroid disorders, no statistically significant differences were observed between male and female patients. The prevalence of thyroid disorders was nearly the same across genders 7.9% in males and 7.2% in females (p = 0.861). Additionally, the distribution of thyroid disorder patterns did not differ significantly by gender (p = 0.585). Among male patients with thyroid dysfunction, 14.3% had sub-clinical hyperthyroidism, 28.6% had sub-clinical hypothyroidism, 14.3% had overt hyperthyroidism, and 42.9% had overt hypothyroidism. Female patients showed similar variation: 12.5% had sub-clinical hyperthyroidism, 50% had sub-clinical hypothyroidism, 25% had overt hyperthyroidism, and 12.5% had overt hypothyroidism **(**Table 4).

Table (4): Correlation between gender and thyroid functions in the studied patients

		Gender				Stat. test	P-value
		Male (N = 89)		female (N = 111)			
TSH	**Mean ±SD**	4.1 ± 1.9		2.1 ± 0.5		4482 *	0.261 NS
FT3	**Mean ±SD**	3.3 ± 0.54		3.2 ± 0.61		**4019 ***	**0.024 S**
Ft4	**Mean ±SD**	1.25 ± 0.23		1.21 ± 0.22		4291 *	0.135 NS
Thyroid disorder	**No**	82	92.1%	103	92.8%	0.031 **	0.861 NS
	Yes	7	7.9%	8	7.2%		
Thyroid disorder pattern	**Sub-clinical hyperthyroidism**	1	14.3%	1	12.5%	1.94 **	0.585 NS
	Sub-clinical hypothyroidism	2	28.6%	4	50%		
	Overt hyperthyroidism	1	14.3%	2	25%		
	Overt hypothyroidism	3	42.9%	1	12.5%		

*: Mann Whitney U test. S: p-value < 0.05 is considered significant. **: Chi-square test. NS: p-value > 0.05 is considered non-significant.

There was statistically significant (p-value = 0.013) increase in vitiligo duration in patients with thyroid disorder (mean = 6.7 ± 7.8 & median = 4 (2 – 9)) when compared to patients without thyroid disorder [mean = 3.2 ± 3.9 & median = 2 (1 – 4)] **(Figure 1).**

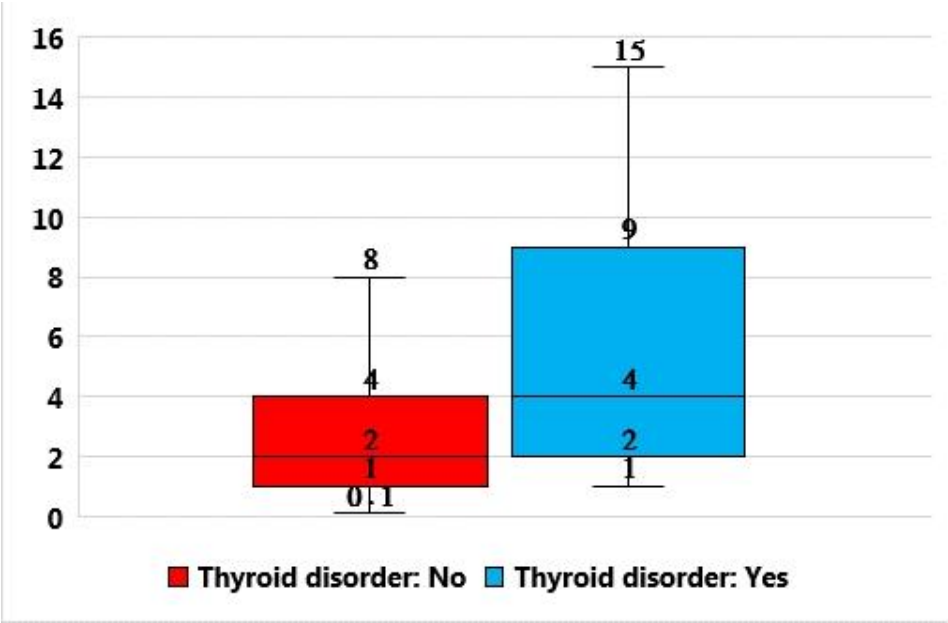

Figure (1): Correlation between thyroid disorder and duration of vitiligo in the studied patients.

Regarding the correlation between different clinical types of vitiligo and thyroid function parameters among the studied patients. There was no statistically significant difference in **TSH** levels across the three clinical types—acro-facial, vitiligo vulgaris, and focal vitiligo—with a p-value of 0.362. The median TSH levels were relatively comparable among the groups: 1.52 C in acro-facial, 1.63 µIU/mL in vulgaris, and 1.47 µIU/mL in focal vitiligo. Similarly, **FT4** levels showed no significant variation (p = 0.698) across the groups, with median values around 1.2 ng/dL for all types. However, a statistically significant difference was noted in **FT3** levels among the groups (p = 0.02). Patients with focal vitiligo had a higher mean FT3 (3.52 ± 0.5 pg/mL) and median FT3 (3.4) compared to those with acro-facial (3.25 ± 0.49 pg/mL) and vulgaris types (3.26 ± 0.67 pg/mL). Regarding the presence of thyroid disorders, although focal vitiligo patients showed no thyroid dysfunction, the difference was not statistically significant among the clinical types (p = 0.173). Patterns of thyroid dysfunction also did not differ significantly between vitiligo types (p = 0.153), though sub-clinical hypothyroidism and overt hypothyroidism were observed across the acro-facial and vulgaris types, with no cases reported in the focal type (Table 5).

Table (5): Correlation between clinical types of vitiligo and thyroid functions in the studied patients

Parameter	Acro-facial (n = 83)	Vitiligo vulgaris (n = 86)	Focal vitiligo (n = 30)	P-value
TSH				0.362
Mean ± SD	2.45 ± 0.8	4.02 ± 1.9	1.81 ± 0.89	
FT3				0.02
Mean ± SD	3.25 ± 0.49	3.26 ± 0.67	3.52 ± 0.5	
FT4				0.698
Mean ± SD	1.2 ± 0.18	1.26 ± 0.26	1.24 ± 0.21	
Thyroid Disorder				0.173
No	77 (92.8%)	77 (89.5%)	30 (100%)	
Yes	6 (7.2%)	9 (10.5%)	0 (0%)	
Thyroid Disorder Pattern				0.153
Sub-clinical hyperthyroidism	2 (33.3%)	0 (0%)	—	
Sub-clinical hypothyroidism	2 (33.3%)	4 (44.4%)	—	
Overt hyperthyroidism	0 (0%)	3 (33.3%)	—	
Overt hypothyroidism	2 (33.3%)	2 (22.2%)	—	

*: Kruskal Willis test. NS: p-value > 0.05 is considered non-significant. **: Chi-square test. S: p-value < 0.05 is considered significant.

DISCUSSION

Vitiligo, a disease of melanocyte dysfunction with loss of skin, hair, and mucous membrane pigment, is still an obscure condition. Despite melanocyte dysfunction being its hallmark, the cause is not known. Theories encompass autoimmune and neurogenic causes along with endocrine and genetic influences possibly with environmental triggers. Vitiligo usually begins under the age of 30 and can have a heavy psychological impact on patients [4, 6].

What has also emerged more clearly in the process, however, is the linkage between vitiligo and other autoimmune disorders namely, autoimmune thyroid diseases such as Hashimoto's thyroiditis and Graves' disease [14, 15]. Some even theorize a shared genetic susceptibility between the two [16].

Researchers from a cross-sectional study on 200 Egyptian patients with vitiligo sought to establish the prevalence and pattern of thyroid dysfunction among them. The average age was 36.5 years, which is in line with **Nihalani *et al.*** [17], though marginally younger than the findings of **Gill *et al.*** [12], whose mean was approximately 45. Interestingly, the study found a very minor female majority (55.5%), which is in line with the findings of research by **Khiangte and Lalrindik** [18], **Nihalani *et al.*** [17], and **Alkhateeb *et al.*** [19], though another research has not found a gender imbalance [20].

Vitiligo vulgaris and acro-facial vitiligo were the most common clinical forms encountered—present in 43% and 41.5% of patients respectively. This is consistent with reports from **Zhang *et al.*** [20], **Sushmalatha** [21], **Abdelhameed *et al.*** [22], and **Khiangte and Lalrindik** [18]. Segmental and universal vitiligo were comparatively less common.

Upon assessment of thyroid function, 7.5% of patients were found to be experiencing some dysfunction. Subclinical hypothyroidism was the most common (3%), then overt hypothyroidism (2%), overt hyperthyroidism (1.5%), and subclinical hyperthyroidism (1%). The results are consistent with those of **Yuan *et al.*** [23], **Gill *et al.*** [12], **Ingordo *et al.*** [24], and **Nihalani *et al.*** [19], all of whom observed subclinical hypothyroidism as the most common thyroid abnormality in vitiligo. However, other studies reported much larger prevalence estimates (40% and 15.1% respectively) in **Kumar *et al.*** [25] and **Vrijman *et al.*** [26] studies, possibly because of population genetics, diagnosis strategy, or exposures.

Of particular interest, the mean thyroid hormone concentrations (TSH, FT3, FT4) of patients in the current study were within normal range, which is consistent with the findings of **Vrijman *et al.*** [26] and **Kumar *et al.*** [25].

Gender-specific thyroid dysfunction patterns were also examined. While, overall prevalence did not differ meaningfully between men and women (P = 0.861), there was a subtlety: Subclinical hypothyroidism was more prevalent in women, while overt hypothyroidism was more prevalent in men. These results are partially consistent with those of **Bae *et al.*** [13], **Cappola *et al.*** [27], and **Yuan *et al.*** [23], who also found gender disparities. However, other studies of **Gey *et al.*** [28] and **Sushmalatha** [21] reported a greater predisposition in women, with hormonal and immunological variations likely to influence the expression of the disease.

One of the more fascinating findings was between thyroid dysfunction and disease duration. The patients with thyroid dysfunction had a longer disease duration for vitiligo (mean 6.7 years), which is consistent with findings of **Gey *et al.*** [28]. However **Kakourou *et al.*** [29] didn't see this correlation.

When the researchers looked at the correlation between specific types of vitiligo and thyroid dysfunction, there

was an association. Non-segmental types, particularly vitiligo vulgaris and acro-facial, contained higher prevalences of thyroid disease 10.5% and 7.2% respectively and none in focal vitiligo. Subclinical hypothyroidism was found to be primarily in vitiligo vulgaris, and subclinical hyperthyroidism was found only in the acro-facial type. All these are in good agreement with findings by **Yuan *et al.* [(23)]**, **Chivu *et al.* [(30)]**, and **Sushmalatha [(21)]**, all of them found stronger thyroid associations with generalized or non-segmental vitiligo. On the other hand, **Abdelhameed *et al.* [(22)]** reported acrofacial vitiligo to be more frequently linked with thyroid disease. **Pagovich *et al.* [(31)]** also supports an autoimmune cause in generalized vitiligo. Far from it, though, is the controversy resolved. There are different findings in a study by **Kakourou *et al.* [(29)]** bringing out exactly how complicated and complex the vitiligo-thyroid connection remains.

CONCLUSION

The cumulative findings of this investigation lead to the conclusion that thyroid dysfunction, particularly in the form of hypothyroidism, may exhibit a significant association with specific vitiligo subtypes and the overall duration of the disease. These results underscored the critical importance of implementing routine thyroid function screening protocols in all patients diagnosed with vitiligo, thereby facilitating the early detection and proactive management of potential thyroid abnormalities.

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