International Journal of Research in Dermatology
Alnemari R et al. Int J Res Dermatol. 2024 Mar;10(2):60-65
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20240323

Original Research Article

The prevalence of thyroid function test abnormalities and serum thyroid autoantibodies in vitiligo and alopecia areata patients in Saudi Arabian population

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Received: 18 January 2024
Revised: 02 February 2024
Accepted: 08 February 2024

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ABSTRACT

Background: Alopecia areata (AA) and vitiligo are immune-mediated inflammatory diseases characterized by hair loss and depigmented macules, respectively. It is often associated with other autoimmune conditions especially with autoimmune thyroid disorders indicating a potential role of autoimmunity in its development.
Methods: A 222 patients, 113 AA and 109 vitiligo diagnosed, were retrospectively reviewed. We analyzed TG-Ab, TPO-Ab, Thyroid function tests (free T3, free T4, and TSH) in all patients.
Results: In vitiligo patients, 11% (n=12) had elevated levels of anti-TG levels and 26.6% (n=29) had elevated levels of anti-TPO, Thyroid hormonal abnormalities were found in 15.6% (n=17) of vitiligo patients, and fT4 was elevated in 1.83% (n=2) patients. Within AA patients, 15.9% (n=18) had anti-TG elevation and 23.9% (n=27) had anti-TPO elevation, thyroid hormonal abnormalities were found in 16.8% (n=19), and fT4 was high in 0.88% (n=1) patient. No significant difference was found between the two groups for all measured parameters. No statistically significant correlation between the gender of the patients and the diagnosis, thyroid hormonal test, and thyroid autoantibody levels could be detected ($p>0.05$)
Conclusions: In our study, impaired thyroid functions and thyroid autoantibodies in vitiligo and AA patients were identified at similar rates of the previous studies. Moreover, we could not find differences in comparison to other ethnicities

Keywords: Vitiligo, AA, Thyroid disease, Thyroid autoantibody, Saudi Arabia

INTRODUCTION

Alopecia areata (AA) is an immune-mediated inflammatory disease characterized by a nonscarring circumscribed loss of hair follicles in the anagen phase.[1] It is expected to have an incidence rate of 0.1-0.2% in the general population and 7-30 instances per 1000 dermatology patients with a lifetime risk of 1.7%.[2] AA is a heterogeneous variant of alopecia it may affect the entire scalp (alopecia totalis) or the entire body (alopecia universalis).[3]

Although its etiology is minimally understood AA has been widely reported with other autoimmune processes, such as autoimmune celiac disease, diabetes mellitus, psoriasis, and lupus erythematosus, but hypothyroidism and Vitiligo have the strongest association, and this is considered a potent indicator of the contribution of autoimmunity in the pathogenesis of AA.[4,5]

Vitiligo is an idiopathic disease characterized by the destruction of epidermal melanocytes resulting in depigmented macules.[6] With a prevalence of 0.5-2% of the population in both adults and children worldwide.[7,8] There is international consensus on the classification of nonsegmental and segmental vitiligo. Nonsegmental vitiligo often is symmetrically distributed and includes the generalized, acrofacial, or acral, mucosal, and universal subtypes. Segmental vitiligo appears to be a different disease, characterized by a unilateral distribution of the lesions that occurs in a dermatomal or quasi-dermatomal pattern.[9] The etiology is unknown but hypothesized to be of genetic susceptibility, autoimmunity, neural, biochemical, oxidative stress, and melanocyte detachment mechanisms.[10]

Even though etiology of these 2 diseases is still unclear, Many studies demonstrated that AA and vitiligo are commonly associated with autoimmune thyroid diseases, therefore, in addition to free T3, free T4, and thyroid stimulating hormone (TSH), serum thyroid autoantibody, anti-thyroglobulin (anti-TG), and anti-thyroid peroxidase (anti-TPO) are important to investigate.

According to a study involving 87 vitiligo patients, 23% of the patients had positive anti-TG titers, and 24.1% of the patients had positive TPO-Ab. The results were found to be significantly higher when compared to healthy controls. in additions higher frequency was found in females between the ages of 11 and 20.[11] Uncu study, the evaluation of 50 vitiligo children did not demonstrate hypo- or hyperthyroidism, but similarly they found a significant association between autoimmune thyroiditis and sex, as of patients with autoimmune thyroiditis were girls.[12] Unlike Saylam Kurtipek's study had concluded that there was no statistically significant association between the levels of thyroid autoantibodies and sex.[13]

In an Egyptian study conducted in 50 AA patients reported that subclinical hypothyroidism was found in 16% with significant differences between cases and controls regarding levels of TSH, free T3 and free T4. Also had concluded that there statistically significant differences were found between cases and controls regarding the levels of both anti-TG ($p<0.05$) and TPO-Ab ($p<0.05$). Anti-TG were positive in 23 patients (46%) and TPO-Ab were positive in 24 (48%) cases and both were negative in all control subjects.[14] Another study from the Middle East, this one from Iran, found that 8.9% of patients had abnormal thyroid function tests, given that the prevalence of thyroid disease in the Iranian general population is 2.97%.[15,16] additionally It was discovered that the frequency of thyroid autoantibodies was 51.4% of cases, which is higher in this community than in other populations, and that these variations were considered to be partially linked to racial and genetic factors.[5,17] However, Cunliffe and Puavilai reported that there no significant difference between patients with AA and control population regarding the presence of Anti-TG and TPO-Ab.[4,18]

Due to the paucity of regional research and the lack of research of this matter in Saudi Arabia taking into consideration the genetic factors differences, we aimed in this study to Investigate the relation between thyroid dysfunction and autoimmunity to vitiligo and AA.

METHOD

Patients who visited our dermatological clinic between June 2016 to June 2023 and had AA or vitiligo were evaluated retrospectively. Questionnaires are used to capture demographic information, clinical characteristics, and laboratory results. All patients have their thyroid function tests (free T3, free T4, and TSH) and serum thyroid autoantibody (Anti-TG, anti-TPO) levels analyzed. All information was taken from the NGH system, hence there is no intervention to be done on patients, no need for consent.

This is a retrospective study from our dermatological department at national guard hospital (NGH) in Jeddah. All Patients who visited our dermatological clinic between June 2016 to June 2023 and were diagnosed with either AA or vitiligo were randomly selected and included in the study. Demographic information, clinical characteristics, and laboratory results of the patients were extracted from the NGH system. Thyroid function tests (free T3, free T4, and TSH) and serum thyroid autoantibody (Anti-TG, anti-TPO) levels were analyzed for all patients. This study was conducted in accordance with the ethical guidelines and was approved by the ethics committee of NGH.

Mean±SD was used for descriptive analysis, and for significantly chi-square test was used. A $p<0.05$ was considered significant. The statistical analysis was conducted using SPSS version 11.

RESULTS

A total of 222 participants were included in the study, with 109 individuals diagnosed with vitiligo. Among the vitiligo cases, 64 were females (58.7%) and 45 were males (41.3%), with an average age of 24.12±15.94 years. The peak age at the onset of the disease for vitiligo was 6-15 constituting 35.8% of the patients. Additionally, 113 AA cases, including 46 females (40.7%) and 67 males (59.3%), and a mean age of 26.48±11.41. The peak age at the onset of the disease for AA was between 26-35 comprising 44.2% of the patients.

Table 1 shows that vitiligo cases had a significant higher percent of females. While AA cases had a significant higher percent of patient with an age at diagnosis between 26-35 years (44.2% vs. 21.1%), ($p\leq0.05$).

In 84.4% (n=92) of vitiligo patients TSH levels were within normal limits, and in 15.6% (n=17) of vitiligo patients had thyroid hormonal abnormalities. While for AA cases, TSH measurements were evaluated as within

the normal levels in 83.2% (n=94) and in thyroid hormonal abnormalities were found in 16.8% (n=19).

fT4 levels were within normal limits in 95.41% (n=104) of patients with vitiligo and were high in 1.83% (n=2). fT4 measurement was normal in 96.46% (n=109) of the patients with alopecia and it was high in 0.88% (n=1). Hypothyroidisms for both vitiligo as well as AA was found in three cases, (n=3) 2.8% and the (n=3) 2.7% respectively.

The mean of TSH levels was 2.23±1.63 mIU/l in vitiligo patients, and was 3.99±9.38 in alopecia patients. The mean of free T4 levels were 13.48±2.44 ng/dl in the patients with vitiligo, and were 13.24±1.98 ng/dl in the patients with alopecia. The mean of free T3 levels were 6.89±8.35 pg/ml in the patients with vitiligo (n=18), and were 4.13±0.86 pg/ml in patients with alopecia (n=25).

In AA cases significant lower mean level of T3 compared to vitiligo cases was found (p≤0.05), however, is noted that 179 cases from total had missing values of T3.

Demonstrates that there were no statistically significant differences between vitiligo and AA regarding levels of TSH and free T4, but for AA cases a significant lower mean level of T3 compared to vitiligo cases was found (4.13±0.86 vs. 6.89±8.35) (p≤0.05) (Table 2).

Among the participants, 29 individuals with vitiligo (26.6%) and 27 individuals with AA (23.9%) showed abnormally high titer of TPO-Ab. Additionally, positive titer of anti-TG was observed in 12 cases of vitiligo (11%) and 18 cases of AA (15.9%).

When comparing vitiligo cases as well as the AA cases based on TPO-Ab, anti-TG, TSH, and T4 levels, no significant difference was found between the two groups for the all measured parameters (p>0.05) as shown in the Table 3.

Table 4, illustrates that there is no statistically significant correlation between the gender of the patients and the diagnosis, thyroid function test, and thyroid autoantibody levels could be detected (p>0.05).

Table 1: Comparison between vitiligo cases and AA cases according to demographics, age at diagnosis and disease duration, (n=222).

Variables	Vitiligo (n=109) (%)	AA (n=113) (%)	Mann-Whitney test	P value
Gender				
Female	64 (58.7)	46 (40.7)	7.19*	0.007
Male	45 (41.3)	67 (59.3)		
Age at diagnosis (in years)				
≤5	7 (6.4)	4 (3.5)	23.53	<0.001
6-15	39 (35.8)	17 (15)		
16-25	17 (15.6)	25 (22.1)		
26-35	23 (21.1)	50 (44.2)		
36-45	10 (9.2)	11 (9.7)		
>45	13 (11.9)	6 (5.3)		
Mean±SD	24.12±15.94	26.48±11.41	1.86	0.061

N.B.: *=χ2 test.

Table 2: Comparison between vitiligo cases and AA cases according to the mean values and levels of TSH, T4 and T3.

Variables	Vitiligo (n=109)	AA (n=113)	Kruskal Wallis test	P value
TSH	2.23±1.63	3.99±9.38	1.03	0.302
T4	13.48±2.44	13.24±1.98	0.32	0.749
T3	6.89±8.35	4.13±0.86	2.31	0.021

Table 3: Comparison between Vitiligo cases and AA cases according to categories of TPO and Tg.

Variables	Vitiligo, N (%)	AA, N (%)	χ2	P value
TPO				
Normal	80 (73.4)	86 (76.1)	0.21	0.642
High	29 (26.6)	27 (23.9)		
Tg				
Normal	97 (89)	95 (84.1)	1.14	0.284
High	12 (11)	18 (15.9)		

Table 4: Gender difference according to categories of TPO, Tg, TSH and T4 levels for Vitiligo cases and the AA cases.

Variables	Female, N (%)	Male, N (%)	$\chi 2$	P value
Vitiligo				
TPO				
Normal	47 (73.4)	33 (73.3)	0.001	0.99
High	17 (26.6)	12 (26.7)		
Tg				
Normal	56 (87.5)	41 (91.1)	0.35	0.553
High	8 (12.5)	4 (8.9)		
TSH				
Low	5 (7.8)	5 (11.1)	2.46	0.292
Normal	53 (82.8)	39 (86.7)		
High	6 (9.4)	1 (2.2)		
T4				
Low	1 (1.56)	2 (4.4)	1.37	0.504
Normal	63 (98.44)	41 (91.1)		
High	0 (0)	2 (4.4)		
AA				
TPO				
Normal	35 (76.1)	51 (76.1)	0.001	0.997
High	11 (23.9)	16 (3.9)		
Tg				
Normal	38 (82.6)	57 (85.1)	0.12	0.725
High	8 (17.4)	10 (14.9)		
TSH				
Low	3 (6.5)	4 (6)	0.02	0.99
Normal	38 (82.6)	56 (83.6)		
High	5 (10.9)	7 (10.4)		
T4				
Low	1 (2.2)	2 (3)	3.97	0.197
Normal	44 (95.65)	65 (97.01)		
High	1 (2.17)	0 (0)		

DISCUSSION

It is possible for AA to start at any age, from infancy to the late seventies.[19,20] Prior reports on the prevalence of AA appearing before the age of 20 years ranged from 27 to 44%, while the majority of patients in our research presented between the ages of 26 and 35 (44.2%).[5]

Our findings concurred with several previous studies, we identified thyroid abnormalities in 19 individuals (16.8%), an Egyptian study by Bakry et al reported hypothyroidism in eight patients (16%) with significant differences between cases and controls.[14]

According to research conducted in India by Thomas et al, 14.1% of the studied AA population had hypothyroidism.[21]

In Croatia conducted by Kasumagić-Halilović, 11.4% of patients with AA had thyroid functioning abnormalities in the form of hypothyroidism.[22] Similarly, Gönül et al a Turkish study retrospectively reviewed, showed abnormal thyroid function tests in 11 out of 110 (10%) of AA patients.[23] However, unlike the previous studies, an Iranian study by Seyrafi et al found hypothyroidism in only 8.9% of the studied AA cases.[15]

In addition, our study found positive TPO-Ab in 27 (23.9%), and anti-TG in 18 (15.9%). Similarly, Croatian study detected frequency of thyroid autoantibodies in AA to be 23.7% that was significantly higher when compared to healthy controls.[22] Moreover, anti-TG was found in 28% of AA patients by Korkij et al.[24]

Few other studies reported higher results of thyroid autoimmunities. According to Kurtev et al, 39.5% of AA patients had thyroid autoantibodies.[25] Additionally, Bakry et al found that anti-TG antibodies were positive in 23 (46%) and TPO-Ab titers positive in 24 (48%) of these patients.[13,14] Furthermore, Iranian study by Syerafi et al discovered thyroid autoantibodies in 51% of the patients. They attributed high ratio to genetic and ethnic factors.[15]

Vitiligo is a systemic autoimmune disease caused by the loss of epidermal melanocytes. Autoimmunity is now recognized as a significant etiological factor. In our study we detected that a total of 17 patients (15.6%) had

thyroid abnormalities, and high levels of TPO-Ab and anti-TG found in 29 (26.6%) and 12 (11%), respectively.

Our findings are compatible with previous studies. In a Chinese study of 87 patients with vitiligo, thyroid abnormalities were observed in 13 (14.9%), and positive anti-TG titers in 23% and TPO-Ab in 24.1% of the patients. The presence of antibodies was significantly more frequent in 11-20 years and 21-40 years subgroups compared to the subgroups of healthy controls.[11]

In a prospective case-control study on 33 vitiligo cases by Kasumagic-Halilovic et al, 6 individuals (18.18%) had abnormal thyroid function tests.[26] Raised anti-TG was found in 9 (27.27%) and raised TPO-Ab in 8 (24.24%) of vitiligo patients, which was significantly higher compared with the control group.

Higher results found in an Iranian study on 109 vitiligo patients, which indicated that TPO-Ab and anti-TG antibodies were positive in 40 (36.7%) and 35 (32.1%) of cases.[27] And also in a study that was carried out in India, 35 cases of vitiligo, thyroid hormonal abnormalities were found in 40% of cases, however significantly increased levels of TPO-Ab and anti-TG were found only in 6 (17.1%), and in 9 (25.7%) respectively.[28]

Our limitation is the retrospective design of this study, which led to the absence of a control group and limited the ability to compare the levels of antibodies with a reference or baseline group. Also, the small sample size, Since the study was conducted at a single tertiary center in Jeddah, the results may not be representative of the whole Saudi population

CONCLUSION

Findings of study regarding impaired thyroid functions and thyroid autoantibodies in patients with vitiligo and AA were consistent with previous data obtained from various ethnic populations. Additionally, study suggests that conducting detailed thyroid autoimmunity tests may not be necessary for all patients with vitiligo and AA who visit clinics, unless they exhibit clinical signs of thyroid disease. Considering the lack of prior studies conducted in Saudi Arabia, it is recommended that future research includes larger populations, and a follow-up period of the patients who tested positive for TG-Ab and TPO-Ab to confirm the presence of autoimmune thyroid disease.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Alnemari R, Alamri A. The prevalence of thyroid function test abnormalities and serum thyroid autoantibodies in vitiligo and alopecia areata patients in Saudi Arabian population. Int J Res Dermatol 2024;10:60-5.