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Research Paper

Detection of Thyroid Antibodies in Non-Segmental Vitiligo Patients

Maryam Khalid Abd-Alhussien[1], Nahla Ghanim Abdul Majeed[2]

ABSTRACT:

BACKGROUND:

Vitiligo is chronic autoimmune disease characterized by pale white patches developing on the skin caused by lack of melanin pigment which produced by melanocytes. Most common autoimmune disease association with vitiligo is autoimmune thyroid disease that characterized by presence of autoantibody (anti-thyroperoxidase, anti-thyroglobulin) in serum of vitiligo patients.

OBJECTIVE:

Detection of serum anti-thyroperoxidase and anti-thyroglobulin antibodies in patients with non-segmental vitiligo.

PATIENTS AND METHODS:

Serum level of Anti-thyroperoxidase and anti-thyroglobulin antibodies were assessed in 50 non segmental vitiligo patients in the dermatology Consultation Clinic of IMAM ALSADIQ Teaching Hospital / Babil Health Directorate compare with 30 apparently healthy control, their age and sex matched to the patients' group, number of males in this study was 46 (57.5%) and female were 34 (42.5%)., using enzyme linked immunosorbent assay (ELISA) technique in the medical city\teaching laboratories\immunity unit.

RESULTS:

A significant association is found between positive anti –thyroperoxidase antibody and vitiligo patients p value 0.036, the rate of anti-TPO positive in males (80 %) more than females (20%) p value=0.058 and no significant association between positive anti – thyroglobulin antibody and vitiligo patients p value 0.0596. Both antibodies were elevated in same patient.

CONCLUSION:

Both antibodies could be used as screening test to autoimmune thyroid diseases in vitiligo patients.

KEYWORDS: Non-segmental vitiligo, Autoimmune thyroid disease, Anti-thyroperoxidase antibody, Anti-thyroglobulin antibody, Enzyme linked immunosorbent assay.

1 M.B. Ch.B./permanent of path /Microbiology and Clinical Immunology, Medical city, The National Centre for Teaching Laboratories, Baghdad Iraq.

2 Consultant, Medical city, The National Centre for Teaching Laboratories, Baghdad Iraq.

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INTRODUCTION:

The most prevalent acquired depigmenting illness is vitiligo, which affects 0.5–2% of people globally, according to estimates [(1)]. There are three main types of vitiligo: segmental vitiligo, mixed vitiligo, and non-segmental vitiligo (NSV), which is the most prevalent type of the illness [(2)]. In fact, autoimmune diseases—of which autoimmune thyroid disorders are the most prevalent and more likely in vitiligo /NSV patients [(3)]. Autoantibodies against thyroglobulin (TG) and thyroperoxidase (TPO), two essential thyroid-specific components required to produce thyroid hormones, are a typical characteristic of AITD [(4)].

PATIENTS AND METHODS:

This research was carried out at the Dermatology Consultation of IMAM ALSADIQ teaching hospital at Babil Health Directorate from January 2023 to May 2023.Ethical approval and an informed consent were obtained from each participant after describing to them the purpose of the investigation. Every patient had their complete medical history obtained. A questionnaire was used for this purpose and excluded any patient with immunosuppressants and thyroid disease. Samples of total of 50 vitiligo patients 29 males and 21 females' patients have non segmental vitiligo and

on ultraviolet B (UVB) compared with 30 apparently healthy17males and 13 females were selected as control group in the current study, their age and sex matched to the patients group. Samples were worked at the medical city\teaching laboratories\immunity unit by enzyme –link immunosorbent assay (ELISA).

Blood sample collection and preparation

Each participant had five milliliters of blood drawn using a septic method. Following the evacuation of the blood samples into gel tubes and centrifugation to extract serum, the supernatant was carefully moved to an Eppendorf container and kept there at -20°C until the anti-thyroperoxidase and anti-thyroglobulin antibodies ELISA tests was conducted.

Human Anti-thyroperoxidase and Anti-thyroglobulin Antibodies Enzyme-linked Immunosorbent Assay (ELISA) (Anti-TPO and Anti-TG) (same technique for both), serum level was measured in accordance to the manufacturer's instructions using the of antibodies against TG and TPO, ELISA kit (AESKULISA/Germany).

Analysis of statistics

The collected data of antibodies against TG and TPO, was introduced into Social Science statistical program (IBM SPSS statistics Version 26). The chi square test was employed to find out the significances correlation between related categorical data. The correlation test was used to find out significance of correlation between related variables. ROC curve was used to find out significance of anti-TPO and anti-TG antibodies as a screening test to detect AITD. P value(P) less than 0.05 was considered as a discrimination point for significance.

RESULTS:

Within this research, the average age of study team were 32±16 year which divided into 29 (36.25%) cases aged less than 18 years 31 (38.75%) of cases between 18-40 year and 20 (25%) of cases more than 40 years. No significant association noticed between vitiligo age group and control group. P value=0. 911. The number of males in this study was 46 (57.5%), and females were 34 (42.5%), no significant association noticed between sex of the patient and control group. P value=0. 907.Fifteen (18.75%) studied subjects had family history of Vitiligo all of them were in the vitiligo group, there is a strong correlation between the vitiligo group and a favorable family history of the condition. P value is 0.049 in Figure 1 and Table 1.

Table 1: Association between studied groups and independent studied variables.

Characteristics	Variables	Total 80		Vitiligo 50		Control 30		P value
		N	%	N	%	N	%	
	Mean ± SD	32±16 years						
Age	< 18 years	29	36.25	19	38	10	33	0.911
	18-40 years	31	38.75	19	38	12	40	
	> 40 years	20	25	12	24	8	27	
sex	Male	46	57.5	29	58	17	57	0.907
	Female	34	42.5	21	42	13	43	
Family history of vitiligo	Yes	15	18.75	15	30	0	0	0.049

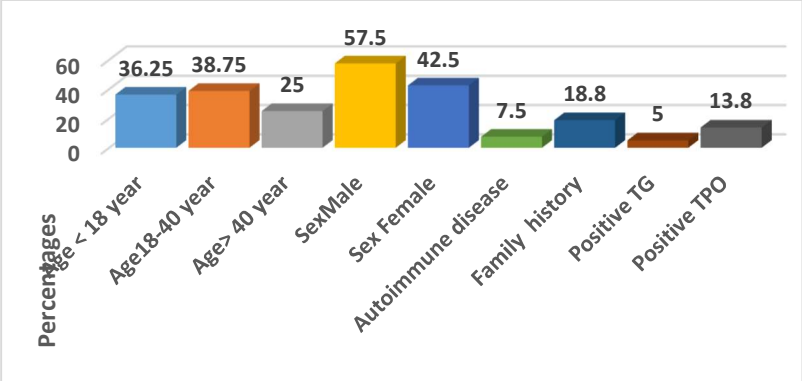

Figure 1: Distribution of all studied cases according to essential studied variables.

There was significant Anti-TPO antibody correlation with studied group p. value 0.036 and no significant association between Anti-TG antibody as well studied group p. value 0.596 table 2.

Table 2: Relationship between the group under study and anti-TG and anti-TPO antibodies.

Group	TPO positive		TPO negative		TG positive		TG negative	
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %
Vitiligo	10	20.0%	40	80.0%	3	6.0%	47	94.0%
Control	1	3.3%	29	96.7%	1	3.3%	29	96.7%
Value of p	0.036				0.596			

There was nothing noteworthy association between gender, age, duration of disease, history of vitiligo in the family and anti-TPO test results. p value> 0.05 in all conditions**.** Interesting result was found that 80% of positive anti-TPO were males while found only in 20% in females Table 3.

Table 3: Association between anti- TPO test results and independent studied variables.

Variables		Total		Anti-TPO Positive 10		Anti-TPO Negative 40		P Value
		N	%	N	%	N	%	
Age	< 18 years	19	38%	3	30%	16	40%	0.943
	18-40 years	19	38%	4	40%	15	37.50%	
	> 40 years	12	24%	3	30%	9	22.50%	
sex	Male	29	58%	8	80%	21	52.50%	0.16
	Female	21	42%	2	20%	19	47.50%	
Duration	<5 years	16	32%	4	40%	12	30%	0.547
	5-10 years	22	44%	5	50%	17	42.50%	
	>10 years	12	24%	1	10%	11	27.50%	
Family history of vitiligo	Yes	15	30%	4	40%	11	27.50%	0.462
	No	35	70%	6	60%	29	72.50%	

There were no significant association between gender, age, duration of disease, history of vitiligo in the family, and anti-TG test results. p value> 0.05 in all conditions table 4.

Table 4: Association between anti- TG test results among vitiligo group and independent studied variables.

Variables		Total		Anti-TG Positive 3		Anti-TG Negative 47		P Value
		N	%	N	%	N	%	
Age	< 18 years	19	38%	1	33.3%	18	38.3%	0.927
	18-40 years	19	38%	1	33.3%	18	38.3%	
	> 40 years	12	24%	1	33.3%	11	23.4%	
sex	Male	29	58%	2	66.7%	27	57.4%	1
	Female	21	42%	1	33.3%	20	42.6%	
Duration	<5 years	16	32%	1	33.3%	15	31.9%	0.784
	5-10 years	22	44%	2	66.7%	20	42.6%	
	>10 years	12	24%	0	0%	12	25.3%	
Family history of vitiligo	Yes	15	30%	2	66.7%	13	27.7%	0.211
	No	35	70%	1	33.3%	34	72.3%	

ROC curve represents that anti- TG at cutoff value= 19.29 can differentiate correctly 62.1% of studied cases (total area under the curve was (AUC) 0.621, p value was 0.07), with sensitivity

and specificity = 64% and 53% respectively. While TPO at cutoff value= 11.19 can differentiate correctly 60.5% of studied cases (total area under the curve was 0.605, Value of p was 0.116), with sensitivity and specificity = 62% and 53% respectively figure 2 and table 5.

Table 5: **Area under the curve.**

Test Result Variable(s)	Cutoff value	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
					Sensitivity	Specificity
Anti-TG	19.29	0.621	0.063	0.070	64%	53%
Anti-TPO	11.19	0.605	0.062	0.116	62%	53%

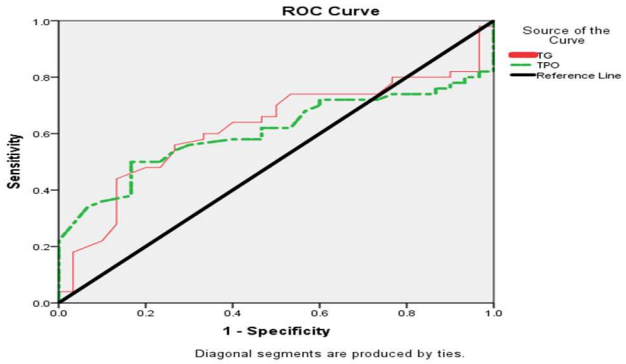

Figure 2: ROC curve showed ability of anti- TG and anti- TPO as a screening test to correctly predict vitiligo cases.

DISCUSSION:

In the current study reported increased prevalence of AITD in vitiligo group compare with control group and was found that the serum anti-thyroperoxidase antibody in patient with non-segmental vitiligo were significantly a p value 0.036. similar to this finding reported by Jishna P et al.,2017 [5], Sara Malik et.al 2021[6] and Wafaa Abd-Elmagid et.al 2023 [7] that reported higher serum levels of anti-thyroperoxidase antibody in vitiligo patients than healthy controls all p value <0.05 showed higher sensitivity and specificity for the disease, as anti- thyroperoxidase antibody a relatively sensitive and specific marker for AITD (The conditions Grave's disease and Hashimoto's thyroiditis).

However, with a percentage of 6% and a p-value of 0.596%, there was no significant correlation found between the anti-thyroglobulin antibody and the vitiligo group, which agrees with Marwa Mahmoud Abdel hameed 2023 that reported 5.9% of vitiligo patients had anti-TG , p value >0.05 and disagrees with previous studies by Sara Malik et.al 2021 [6] who found elevated serum anti-thyroglobulin antibody in 27.27% of vitiligo patients p value<0.05, and by Wafaa Abd-Elmagid et al. 2023 [7] who found (P=0.000) all of them suggest that there was an association between the high level of serum anti-thyroglobulin antibody and vitiligo group this disagree may be due to small sample size and anti-thyroglobulin less sensitive to diagnosis and follow up of AITD [8].

Significant correlation existed between family history with vitiligo (30%) and vitiligo group p value 0.049 as agreed with previous Iraqis' studies by Ronak Ahmed et.al. 2022 [9] revealed that 22.5% of patients with vitiligo had positive family histories from first-degree relatives, whereas 20% of patients had good family histories from second-degree relatives. and by Marwa Mahmoud Abdelhameed 2023 in Egypt Who found statistically significant increase in positive vitiligo family history among anti-peroxidase positive cases (p-value 0.03), which means that vitiligo patients with a family history are more prone to develop anti-TPO in their sera this results will support the genetic role in the inheritance of humoral immunity and due to autosomal dominant inheritance [10].

There were no significant association between age, gender, duration with disease, and Vitiligo in the family history and anti-TPO, anti-TG test results p value> 0.05 in all conditions that agrees with

Daniel Holthausen Nunes2011 [11] that showed no statistical association between autoimmune thyroid disease and vitiligo variables such as age, age at onset, sex, type, and family history of vitiligo and also, with Marwa Mahmoud Abdelhameed 2023 in Egypt who reported the length of the illness was more prolonged in those who have vitiligo with positive anti-thyrogloulin antibody this mean that the prolonged course of vitiligo can develop autoimmune thyroglobulin antibodies (p value=0.01).

Ten patients were diagnosed with positive anti-TPO (8) of them were male (80% of positive cases) and 2 were females p value=0.058 this finding may be due to male participant (57.5%) formed majority and female (42.5%) and explain also by Yi Chen et.al 2017 in china by his study's title (in males autoimmune thyroid disease is linked to a higher ratio of estradiol to testosterone) to 4109 males, the current study shows that men with AITD had considerably higher estradiol/testosterone ratios (E2\T). Through a variety of mechanisms, E2 and T have distinct impacts on the immunological response, both inflammatory and anti-inflammatory. Pathways[12] and agree by Ambreen Ashraf et al. 2021[13] who found Frequency of positive males had thyroid peroxidase antibody levels of 43.6% (n=31) and in females were 18% (n=10) P value 0.003, and contrary to Basman Medhat Fadheel et al. 2022[14] and Jishna P et al. 2017 [5] that found more commonly in female (20.5%), (58%) respectively than male (16%),(42%)respectively this finding due to evidence Sex hormone and X-linked genetic variables may trigger these immunological disorders [15]. Additionally, women's blood contains more CD4 T cells, B cells, and circulating antibodies, and their cytokine production is more robust responses [16].

CONCLUSION:

A noteworthy correlation was observed between Anti–thyroperoxidase antibody in vitiligo patients in comparison to controls p value 0.036 and anti-TPO antibody did not significantly correlate with sex more common in male value of p 0.058. There was no meaningful correlation found between positive Anti-thyroglobulin antibody and vitiligo patients value of p 0.0596. Frequency of positive anti-TG as well as antibodies against TPO could be found Within the same patient and no significant association between both antibodies with age, duration of the disease, family history all p value >0.05. The sensitivity and specificity of serum anti-TG antibody was 64% and 53% respectively with Cutoff value 19.29 while sensitivity and specificity of serum anti-TPO antibody was 62% and 53% respectively with cutoff value of 11.19. A notable correlation was seen between vitiligo in family history and vitiligo group value of p 0.049.

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