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Original Research Article

Status of thyroid autoantibodies among Nigerian vitiligo patients

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ABSTRACT

Background: The prevalence of thyroid autoantibodies among vitiligo patients is higher than the general population. This study was therefore aimed to evaluate the status of thyroid autoantibodies in Nigerian patients with vitiligo.
Methods: A retrospective study of thyroid autoantibody test parameters of vitiligo patients who visited the Department of Chemical Pathology and Metabolic Medicine of the University of Port Harcourt Teaching Hospital between 1st January 2012 and 31st December 2016 was undertaken to evaluate the status of thyroid autoantibody. Data collected irrespective of vitiligo variant were age, sex, serum thyroid stimulating hormone (TSH), thyroid peroxidase antibody (anti-TPO) titers and thyroglobulin antibody (anti-Tg) titers. The analysis was done using Shapiro-Wilk, descriptive statistics, chi-square, and Fisher's exact, two-sample t-test. The level of $p<0.05$ was considered significant.
Results: There were a total of 102 subjects with 40 (39.2%) males and 62 (60.8%) females. Subjects' age ranged from 4–61 with a median value of 23 years. The mean serum TSH, anti-TPO and anti-Tg were 2.6 IU/ml, 64.6 IU/ml, and 55.2 IU/ml respectively. Positive thyroid autoantibodies titers was documented in 35 (34.3%; <0.001) subjects. Anti-TPO and anti-Tg positive titers were detected in 34 (33.3%) and 19 (18.6%) subjects respectively, while autoimmune thyroid disease was observed in 20 (19.6%) of the vitiligo subjects.
Conclusions: Thyroid autoantibodies are more prevalent among vitiligo patients than the general population. Regular screening for these thyroid autoantibodies should be made compulsory in the management of patients with vitiligo.

Keywords: Nigeria, Age, Sex, Vitiligo, Thyroid autoantibodies

INTRODUCTION

Vitiligo is the most common acquired hypomelanotic condition occasioned by the selective destruction of melanocytes in the epidermis and mucous membranes resulting in the macular whitish appearance of the skin, hair and the mucous membranes.[1] It has a distribution between 0.5% to 2% of the world's population.[1,2] While in Nigeria, its distribution in the population varies between 0.96% to 4.96% in various studies.[3,4] Its etiology is unknown, however, theories of autoimmunity, genetics, auto-cytotoxicity, oxidative stress, neural, abnormalities of the melanocytic cells, inflammatory and environmental factors have all been proposed as factors in the evolution and progression of vitiligo.[5-8] The theory of autoimmunity is the most accepted as the vitiligo is frequently associated with various organ-specific autoantibodies in addition to autoantibodies against melanocytes.[9] The most common of these autoantibodies frequently associated with vitiligo in various studies is thyroid autoantibodies of which autoantibodies to thyroid peroxidase enzyme (anti-TPO) and thyroglobulin molecule (anti-Tg) is paramount.[9,10] These thyroid autoantibodies in vitiligo patients are responsible for the high frequency of thyroid dysfunction and autoimmune thyroid diseases reported among vitiligo patients in various studies.[11,12] The prevalence of anti-TPO and anti-Tg among healthy Nigerians without thyroid disease is

7% and 4% respectively.[14] However, there is a scarcity of data regarding the status of these autoantibodies among vitiligo patients in Nigeria. Hence, this study is aimed to assess the thyroid autoantibodies among patients with vitiligo in Port Harcourt, South-South Nigeria, and compare the findings here with the literature.

Objectives

- To determine the prevalence of thyroid autoantibodies among vitiligo patients.
- To compare the findings from this study with the literature.

METHODS

This study was conducted retrospectively among all vitiligo patients irrespective of vitiligo variant who had presented to the Department of Chemical Pathology and Metabolic Medicine of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria between 1st of January 2012 to December 2016 for routine screening for thyroid disorders using thyroid stimulating hormone (TSH) and thyroid autoantibodies (anti-TPO and anti-Tg). The diagnosis of vitiligo was all done by the specialist dermatologist in UPTH. Being a retrospective study, ethical approval and informed consent were not required.

Criteria for inclusion were records of TSH and thyroid autoantibodies of patients with any variants of vitiligo who presented for routine screening for thyroid disorders. Criteria for exclusion were records of vitiligo patients who are either diagnosed or on treatment for thyroid disorders, and also including those with incomplete data.

Fasting serum samples were used for all laboratory analysis. Serum TSH, anti-TPO and anti-Tg analysis were done via enzyme immunoassay methods with same brands of laboratory reagents sourced from Monoblind Incorporated, California, United States of America. All records from laboratory result sheets and case notes of each vitiligo patient were collected, reviewed and entered into Statistical Package for Social Sciences (SPSS) version 20.

Demographic data (age and sex), clinical diagnosis (vitiligo), serum TSH in mIU/l (normal range: 0.4–6.8), serum ant-TPO in IU/ml (reference threshold is 40 IU/ml), serum anti-Tg in IU/ml (reference threshold is 125 IU/ml) were all collected

A serum ant-TPO titer above 40 IU/ml and an anti-Tg titer above 125 IU/ml were considered positive. While an abnormal TSH level with a positive anti-TPO plus or minus positive ant-Tg was defined as autoimmune thyroid disease (AITD).

The collected data in SPSS version 20 were reviewed, coded and analyzed using descriptive statistics, Shapiro-Wilk test, Chi-square test, Fisher's exact test, and two-sample t-test. A $p<0.05$ was considered statistically significant.

RESULTS

One hundred and ten (110) healthy vitiligo patients presented to the Department of Chemical Pathology of UPTH for routine screening for thyroid disorders and thyroid autoantibodies from 1st January 2012 to 31st December 2016.

Data of 102 of the total 110 vitiligo patients met the selection criteria and were recruited for the study.

There were a total of 40 (39.2%) males and 62 (60.8%) females. Age was not normally distributed and ranged from 4–61 years with a median age of 23 years among the study cohorts.

The sex-specific age of the males ranged from 6–58 years with a median age of 29 years while that of the females ranged from 4–61 years with a median age of 20 years.

Table 1: Age and sex distribution of the vitiligo patients.

Age groups (years)	Male n (%)	Female n (%)	Total n (%)
< 30	24 (35.3)	44 (64.7)	68 (66.7)
31–60	16 (53.3)	14 (46.7)	30 (29.4)
>61	0 (0)	4 (100)	4 (3.9)

Fisher's Exact test: 60.941; $p < 0.001$

In Table 1, most vitiligo patients were below 30 years old (n=68; 66.7%). Females dominated among those below 30 years of age against the males (females n = 44; 64.7% versus males n=24; 35.3%).

In Table 2, no difference was observed in the mean values of TSH, anti-TPO, and anti-Tg between the male and female sex groups.

Table 2: Mean distribution of laboratory parameters in both males and females.

	Mean values ± SD				
Parameters	**Both sexes**	**Males**	**Females**	**t**	**P value**
TSH (IU/ml)	3.6±0.9	3.2±0.7	3.8±1.1	0.571	0.411
Anti-TPO (IU/ml)	64.6±2.4	70.1±2.8	61.0±1.8	0.487	0.627
Anti-Tg (IU/ml)	55.2±4.4	55.7±5.0	55.0±5.4	0.043	0.965

*Statistical significant; t = Two-sample t-test; SD = Standard deviation

Table 3: Comparison of thyroid function laboratory parameters in both sex groups.

Parameter	Male n (%)	Female n (%)	Total n (%)	x^2	P value
TSH (IU/ml)					
< 0.3 (Low)	1 (33.3)	2 (66.7)	3 (2.9)		
>6.8 (high)	7 (30.4)	16 (69.6)	23 (22.5)	1.129[a]	0.657
0.4-6.8 (normal)	32 (42.1)	44 (57.9)	76 (74.5)		
Anti-TPO (IU/ml)					
Negative <40	26 (38.2)	42 (61.8)	68 (66.7)	0.082	0.774
Positive >40	14 (41.2)	20 (58.8)	34 (33.3)		
Anti-Tg (IU/ml)					
Negative <125	32 (38.6)	51 (61.4)	83 (81.4)	0.0082[b]	0.799
Positive >125	8 (42.1)	11(57.9)	19 (18.6)		
Thyroid disease					
NAITD	32 (39)	50 (61)	82 (80.4)	0.06[b]	0.936
AITD	8 (40)	12 (60)	20 (19.6)		

NAITD = Non-autoimmune thyroid disease; AITD = Autoimmune thyroid disease; x^2 = Chi-square test; a = Fisher's exact tests; b = Chi-square test with Yate's continuity correction.

Table 4: Relationship between serum anti-TPO and anti-Tg titers among vitiligo patients.

	Anti-TPO (IU/ml)		Total
	Negative <40	**Positive >40**	
Anti-Tg (IU/ml)	**n (%)**	**n** (%)	**n (%)**
Negative <125	67 (80.7	16 (9.3)	83 (100)
Positive >125	1 (5.3)	18 (94.7)	19 (100)
Total	68 (68.7)	34 (33.3)	102 (100)

Fishers Exact test = 39.616; p<0.001.

In Table 3, TSH was abnormally low in 2 (2.9%) and abnormally high in 23 (22.5%) subjects. The females predominated in both groups with abnormal low (females 66.7% versus males 33.3%) and abnormal high (females 69.7% versus males 30.4%) TSH levels. 34 (33.3%) and 19 (18.6%) subjects had positive anti-TPO and anti-Tg titers respectively, with a female preponderance in both the anti-TPO (females 58.8% versus males 41.2%) and anti-Tg (females 57.9% versus 42.1%) positive groups. Autoimmune thyroid disease (AITD) was observed in 20 (19.6%) of the vitiligo patients with a female predominance (females 60% versus males 40%).

In Table 4, 67 of the 102 patients were both negative for anti=TPO and anti-Tg while the remaining 35 (34.3%) were positive for thyroid autoantibodies.

Among these 35 (34.3%) vitiligo patients with positive thyroid autoantibodies, 18 were both anti-TPO positive and anti-Tg positive, 16 were anti-TPO positive but anti-Tg negative and only I was anti-TPO negative but anti-Tg positive.

DISCUSSION

Among the several theories proposed as the possible pathogenesis of vitiligo, the autoimmune theory is widely accepted.[5-8] The theory emphasizes the alteration in both cellular and humoral immunity resulting in the simultaneous destruction of melanocytes and other organ-specific tissues by autoantibodies and cytotoxic T-cells in patients with vitiligo.[9] High on the list of these altered organ-specific tissues in vitiligo is the thyroid gland. This is evidenced by the high frequency of thyroid autoantibodies and autoimmune thyroid diseases documented among vitiligo patients.[9] The prevalence of thyroid autoantibodies in general population is reported to be around 10%, however, the prevalence of could be as high as 50% among the vitiligo patients.[10]

Robert was one of the first authors to report alteration along the thyroid axis in vitiligo patients.[6] He had observed a distinct rise in the metabolic rate in 50% (10 out of 20) patients with vitiligo which he attributed to the alteration in the thyroid function of these patients. Several authors had since corroborated these alterations in thyroid function among vitiligo patients than the normal control subjects without vitiligo.[11-12] These thyroid disorders have been attributed to the shared genetic risk of developing melanocyte-specific autoantibodies and the simultaneous development of thyroid-specific autoantibodies in vitiligo patients resulting in the altered thyroid functions in vitiligo patients.[10] Autoantibodies to the thyroid peroxidase enzyme (Anti-TPO) and the thyroglobulin molecule (Anti-Tg) are the most extensively documented in vitiligo patients.

In this study, 34.3% (35 of 102) of vitiligo patients had documented positive titer for anti-TPO and the anti-Tg. While Anti-TPO positive titer was detected in 34 (33.3%), the ant-Tg positive titer was detected in 20 (19.6%) of the study cohort. This positivity titer rate of thyroid autoantibodies documented among our study cohort is higher than the rate reported among healthy Nigerians.[13] In a case-control study conducted in India, the prevalence of thyroid autoantibody was 31.4% compared to 10% of normal control subjects.[12] In another study from Turkey, the authors reported the prevalence of these thyroid autoantibodies prevalence as 36.0%.[14] The prevalence observed in these Indian and Turkish studies are all in accord with this study. Usually, about 10% of general population has thyroid autoantibodies making the rate observed in this study a reason to warrant screening of all vitiligo patients for thyroid autoantibodies.[12]

Vitiligo has been reported in association with autoimmune thyroid diseases (AITD) in various studies with variable frequencies.[14-18] Narita et al reported a frequency of 12%, Akay et al reported a frequency of 31.0%, Topal et al reported a frequency of 28.0%, Garg et al reported a frequency of 42.5% while Kumar et al reported a frequency of 40% of AITD among vitiligo subjects in their various studies.[14-18] In addition, the prevalence of AITD in Africa is poorly documented but ranges from 1.2% to 9.9% among the general African population without vitiligo.[19] Due to these variable frequencies of AITD among vitiligo subjects, a systematic review of 48 studies pertaining to the prevalence of thyroid diseases in patients with vitiligo was conducted by Vrijman et al in 2012, who reported 14.3% prevalence of AITD among vitiligo patients.[20] In this present study, the prevalence of AITD was 19.6% which is higher than the prevalence documented among healthy African descendants and that reported by Vrijman et al among vitiligo patients.[19,20] This suggests a high prevalence of AITD among our study cohorts compared to the general population.

CONCLUSION

This study highlights the high prevalence of thyroid autoantibodies and AITD among Nigerian subjects with vitiligo and strengthens the autoimmune theory of vitiligo. Since the risk of development of overt thyroid disease is high in the presence of these autoantibodies, we recommend screening of thyroid autoantibodies among all patients with vitiligo.

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