

Thyroid dysfunction and autoantibodies among patients infected with Covid 19 in Erbil city /IRAQ

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Abstract

Background and objectives: Autoimmune thyroid diseases or specifically Anti-thyroid peroxidase antibodies increasing after corona virus infection pandemic. This study investigating Anti-thyroperoxidase, anti-thyroid stimulating receptor antibodies in conjunction with traditional thyroid markers after corona virus infection hoping that this would aid in reduction of enduring morbidity and associated health concerns.

Methods: This cross sectional study was conducted in Rizgary Teaching Hospital and Erbil Teaching Hospital in Erbil, Iraq, within the period of February to September 2022. The study comprised hundred patients; 80 females and 20 males, these patients had clinical symptoms suspecting thyroid abnormalities and were suspected for having a sort of thyroid disease. They had abnormal thyroid function tests, with investigating thyroid autoantibodies and corona virus infection. Investigations include thyroid function test and antithyroid antibodies.

Results: The level of Anti-thyroid peroxidase antibodies was positive among 75 hypothyroidism patients than among hyperthyroidism cases 2, p value 0.012. Positive Anti-thyroperoxidase antibodies and hypothyroidism were significantly more common among corona virus infected cases, p value 0.012 and 0.0109 respectively. However; anti-thyroid stimulating hormone receptor antibody was positive only among hyperthyroidism group (18%); p value was significant 0.019.

Conclusions: This study confirmed the correlation between thyroid function test, Anti-thyroperoxidase antibodies values and corona virus infection. Autoimmune thyroid diseases are more common among female cases, in addition; antithyroid antibodies especially Anti-thyroperoxidase antibodies were more common among female patients. There was high prevalence of both hypothyroidism and positive anti TPO Ab in Covid 19 cases.

Key words: Corona virus; Thyroid autoantibodies; Thyroid peroxidase.

Introduction

Thyroid gland has one of the most important functions in human body as it regulates common physiological actions of the body. Thyroid hormones thyroxine (T4) and triiodothyronine (T3) are hormones produced from thyroid and they have numerous actions including metabolism, development, protein

synthesis, and the regulation of many other important hormones. Dysfunction of the thyroid gland can affect the production of thyroid hormones (T3 and T4) which can be linked to several pathologies throughout the body.¹ Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was firstly recorded in

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Wuhan/China at December, 2019 with unknown etiology and declared as a pandemic coronavirus disease 2019 (COVID-19) disease by World Health Organization (WHO) affecting hundreds of millions and more than four million deaths globally.² The first confirmed COVID-19 patient in Kurdistan region/Iraq was reported at February 2020 followed by outbreak causing many comorbidities and mortalities in the region.³ Thyroid dysfunction, which is defined as a broad spectrum of sicknesses related to the thyroid gland, has a massive effect on human wellbeing. Approximately 20 million people are suffering from any form of thyroid disease in the United States.⁴ Functional thyroid disease is generally classified into hypothyroidism and hyperthyroidism that is further subdivided into overt and subclinical diseases.⁵ Many people with thyroid disease go undiagnosed because symptoms progress gradually and are not very specific. Although screening for thyroid disease looks appropriate, universal screening has not been recommended totally due to lack of clinical trials that establish the benefits of subsequent therapy.⁶ Anti-thyroid peroxidase (Anti TPO Ab) antibodies develop against a transmembrane protein

Subjects and methods

This study was a prospective cross-sectional study carried out in Rizgary Teaching Hospital and Erbil Teaching Hospital in Erbil city-Kurdistan region/Iraq over a period of seven months from February 1st to September 18th, 2022. The study included one hundred cases; 80 females and 20 males with abnormal thyroid function test, either hypothyroidism or hyperthyroidism, underwent anti thyroperoxidase antibodies (anti-TPO Ab) and anti-thyroid stimulating hormone receptor antibodies (anti TSH receptor Ab). Also; demographic data were taken through special questionnaires from all patients by the researchers (specialist

of thyrocytes. Anti TPO Ab (previously known as anti-thyroid microsomal antibodies) are considered diagnostic of autoimmune thyroid disorders AITDs since these are present in over 90% cases of Hashimoto's thyroiditis. Anti-TPO Ab had been detected, from those patients had been recovered from COVID-19.⁷ Also; anti thyroid stimulation hormone receptor antibodies Anti-TSH receptor Ab can be detected in over 80% cases of Graves' disease.⁸ Anti-TPO and anti-TSH receptor antibodies are correlated to levels of thyroid stimulating hormone (TSH) and both alone or in combination have been used to expect development of hypo-/hyperthyroidism.⁹ Establishing association of anti-thyroid antibodies with thyroid profile testing could recognize such group of patients who have disturbed thyroid profile and consequently also need screening for thyroid autoantibodies to rule out underlying autoimmune process.¹⁰ Keeping in view, it is hypothesized that anti-thyroid antibodies are more often positive in patients with unbalanced thyroid profile.¹¹ The aim of this study is to investigating for thyroid dysfunctions and autoantibodies in patients after corona virus infection hoping that this would aid in reduction of enduring morbidity and associated health concerns.

physicians). Patient's past medical history, and treatment history with thyroxine tablet prescription was recorded. History of corona virus infections (COVID-19) during last two years to be proved by PCR-COVID19 test positivity was obtained from all patients. Also; ultrasound examination for thyroid gland were done by specialist radiologist. We studied the prevalence of thyroid hormone dysfunction through testing the level of TSH, free T3, free T4, anti-TSH receptor Ab, anti-TPO Ab titers in patients suspected for thyroid-related disorders. These have been measured by using the (cobas e 411 analyzer), which is a fully automated

analyzer that uses a patented electrochemiluminescence (ECL) technology for immunoassay analysis. TSH, free T3 and free T4 were estimated by the electrochemiluminescence immunoassay “ECLIA” is intended for use on (Elecys) and (cobas) immunoassay analyzers by Roche. The normal levels for TSH, freeT3, free T4 is 0.3–4.5 IU/ml, 2.0 to 7.0 pmol/L and 12-30 pmol/L respectively. Elecys Anti-TSHR (TRAK) is a fully automated test for detection of autoantibodies to the TSH receptor, the electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecys and cobas e immunoassay analyzers by Roche. Measuring range:0.8 - 40 (results below the LoD are reported as <0.8 IU/L). Cut-off for normal rang was:1.75 IU/L. Immunoassay for the in vitro quantitative determination of antibodies to thyroid peroxidase in human serum and plasma (anti- TPO Ab), the electrochemiluminescence immunoassay “ECLIA” is intended for use on (Elecys) and (cobase) immunoassay analyzers by Roche. Measuring range 5.00-600 IU/mL (defined by the lower detection limit and

the maximum of the master curve). The upper limit of the normal range for anti-TPO Ab is >30 IU/ml. Inclusion criteria include all patients with abnormal thyroid function tests. Exclusion criteria include children less than 12 years old and malignant disease of thyroid gland. Statistical analysis; Data were analyzed using Statistical Package for Social Sciences version 26 (SPSS Inc., IBM Company, Chicago, Illinois, USA). Descriptive analyses were expressed as frequencies and percentages and the inferential results were compared between the subjects with different variables using a statistical significance level of ≤ 0.05 and analyzed using Pearson Chi square or Fisher’s exact tests if necessary. This study was explained for each patient and a verbal consent was obtained from each patient or his/her guardian. Confidentiality and anonymity of data were ensured. Ethical approval was taken from ethical committee from Kurdistan Higher council of Medical Specialties by ordered issue number 1469 date 24-8-2022. And in agreement with the ethical standards set out at the Helsinki Declaration

Results

The total number of the studied sample was one hundred. The mean age (+ SD) of the studied sample was 42.12 ± 15.41 years, minimum age was thirteen years old and

the maximum age was eighty two years old. Our cases involved eighty female and twenty males, Figure (1).

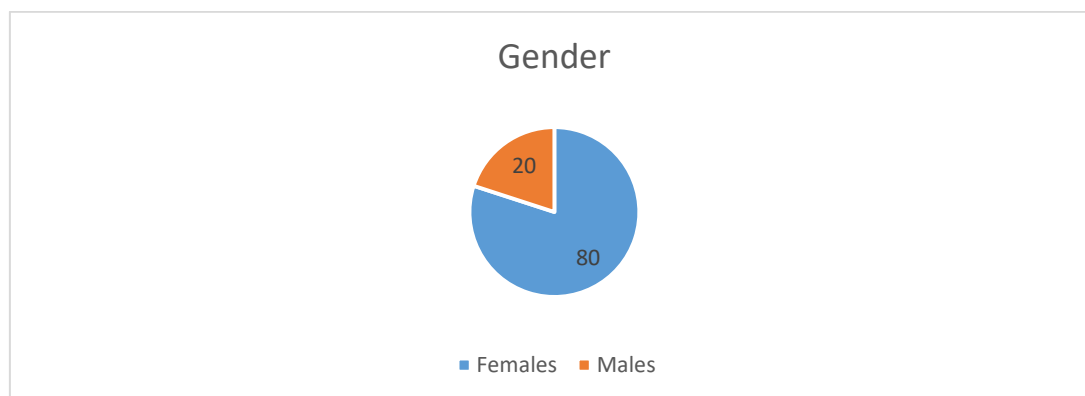


Figure (1): showed gender distribution

As for demographic data of collected cases, there were eighty two married cases,

fifty eight were housewives, and eighty two of them were from urban areas.

Table (1): Demographic data of the involved cases

Variable	Subtype	Frequency
Marital state	Married	82
	No	18
Occupation	Housewife	58
	Teacher	7
	Employee	29
	Student	6
Residence	Urban	82
	Rural	18

We found that seventy nine cases were hypothyroid and twenty one cases were hyperthyroid state. Sixty eight cases were infected with corona virus infection within last two years, and auto antibodies; Anti TSH receptor Ab were positive in only eighteen cases but Anti TPO Ab was positive in seventy seven cases. Table (2)

Table (2): Thyroid function test status

Variable	Subtype	No.
Thyroid function test	Hypothyroid	79
	Hyperthyroid	21
COVID19	Positive	68
	Negative	32
Anti TSH receptor Ab	Positive	18
	Negative	82
Anti TPO Ab	Positive	77
	Negative	23

We found that sixty five females were hypothyroid, while only fourteen males were hypothyroid and the p value is significant 0.046, regarding hyperthyroidism fifteen females they had hyperthyroidism and only six male patients complaining of hyperthyroidism and the p value was 0.09 insignificant. Anti-TPO Ab

were positive in seventy one females and in six males so the Chi square test was done p value was significant 0.032, regarding Anti TSH receptor Ab were positive among thirteen females and only five males p value was insignificant 0.096, Table (3).

Table (3): Gender distribution among thyroid variables

Thyroid status and thyroid autoantibodies	Gender		Total	p value
	female	Male		
Hypothyroid	65	14	79	0.046
Hyperthyroid	15	6	21	0.09
Positive Anti-TPO Ab	71	6	77	0.032
Positive Anti-TSH receptor Ab	13	5	18	0.096

The level of Anti-TSH receptor Ab was positive in only eighteen cases whom diagnosed with hyperthyroidism and negative in three cases with

hyperthyroidism. But no any case was tested positive for Anti-TSH receptor Ab in hypothyroid group, this association was significant; p value was 0.019, Table (4).

Table (4): level of Anti-TSH receptor Ab;

Anti-TSH receptor Ab	Groups		Total	p value
	Hypothyroidism	Hyperthyroidism		
positive	0	18	18	0.019
negative	79	3	82	
Total	79	21	100	

The level of Anti-TPO Ab level was positive among seventy five patients of the hypothyroidism group. Regarding those with hyperthyroidism only two cases

tested positive for Anti TPO Ab, this association was statistically significant. P value was 0.012, Table (5)

Table (5): level of Anti-TPO Ab

Anti-TPO Ab	Groups		Total	p value
	Hypothyroidism	Hyperthyroidism		
positive	75	2	77	0.012
negative	4	19	23	
Total	79	21	100	

Among COVID 19 positive cases; sixty seven of them developed hypothyroid which was statistically significant, p value was 0.0109. Anti-TPO Ab was positive in sixty six cases, which was statistically

significant, p value was 0.05, but both hyperthyroidism and Anti-TSH receptor Ab were only one case which was statistically insignificant, Table (6).

Table (6): COVID 19 associations with thyroid variables

Thyroid status and thyroid autoantibodies	COVID 19		Total	p value
	Positive	Negative		
Hypothyroidism	67	12	79	0.0109
Hyperthyroidism	1	20	21	0.802
Anti-TPO Ab	66	11	77	0.012
Anti-TSH receptor Ab	1	17	18	0.72

Discussion

Autoimmune thyroid diseases are a group of organ-specific autoimmune diseases, the most common of which include Hashimoto's thyroiditis and Graves' disease.¹² Although autoimmune thyroid diseases occur in only 1% of population, subclinical and focal thyroiditis and circulating antithyroid antibodies may be found in 15% of euthyroid subject.¹³ Thyroid stimulating hormone (TSH) and direct measurement of serum thyroxine concentration T3 and T4 has been used widely to found the presence of primary hypothyroidism and hyperthyroid states.¹⁴ Patients recovered from (COVID19) found

to become positive for anti-thyroid antibodies, whither affecting thyroid function or not.¹⁵ In current study eighty percent of the sample were females and the mean age (+ SD) of the studied sample was 42.12±15.41 years and these findings are in agreement with study by(Meng, et al 2021) in which females had significantly higher overall incidence of hypothyroidism found in (65%) female cases with significant differences (p value 0.046). and also, hyperthyroidism than males.¹⁶ The percentage of females who have thyroid dysfunction (80%) is greater than that of males (20%) which is

statistically significant (p value 0.019), similar finding was elucidated in other studies, Al-Geffari M et al.¹⁷ In addition, the percentage of patients with abnormal Anti TPO Ab who have thyroid dysfunction (77%) is greater than the percentage of patients with normal Anti TPO Ab who have thyroid dysfunction (23%) which is statistically significant (p value 0.012). This observation was also declared by Hajieh S, et al.¹⁸ In the current study the level of Anti TPO Ab level was higher among those with hypothyroidism (75) cases, compared to those with hyperthyroidism which was only two cases with significant differences (p value 0.012). Regarding gender association Anti TPO Ab was found among (71) females while only six male cases found to be Anti

TPO Ab positive with significant differences (p value 0.032). and this were in agreement with a study done by Bromińska, et al.¹⁹ In our study; we found that Anti-TSH receptor Ab was higher among hyperthyroid cases which was positive in (18 from a total 21 cases 86%) with significant differences (p value 0.019). and this result was agreed by (Mistry et al).²⁰ But it has no relation with COVID19 infection. This study found that among COVID 19 positive cases; sixty seven of them developed hypothyroid which was statistically significant (p value 0.0109). Anti-TPO Ab was positive in sixty six cases, which was statistically significant (p value 0.012) and these results were similar found by Whiting A. ET al.²¹

Conclusions

This study confirmed the correlation between thyroid function test, anti-TPO Ab values and COVID19. Autoimmune thyroid diseases; antithyroid antibodies especially Anti TPO Ab were more

common among female patients; these antibodies increase the incidence of hypothyroidism. There was high prevalence of both hypothyroidism and positive anti TPO Ab in COVID19 cases.

Conflicts of interest

The author reports no conflicts of interest.

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