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ORIGINAL ARTICLE

Study of COVID-19 Effect on Thyroid Gland Functions in Sharkia Governorate

Khaled Ahmed El-Banna, Fawzy Abdel-Fattah El-Messallamy, Basant Hani Mohamed Al-Jamal *, Arafa Mousa El-Shabrawy
Internal Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt.

Corresponding author:
Basant H. Al-Jamal

Email:
passantaljamal@gmail.com

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ABSTRACT

Background: The COVID-19 pneumonia outbreak has had a significant impact on society at large and has tested the capacity of global healthcare systems.

Aim: The aim of the present study was to detect the incidence of thyroid hormonal disturbance in COVID-19 patients.
Methods: This retrospective cross-sectional study included 177 positive Covid-19 patients were enrolled at Internal Medicine Department, Al-Ahrar Teaching Hospitals. TSH, FT4, FT3 and TPO antibody were estimated. Follow up of the patients who revealed abnormal lab results during covid-19 infection 1 month after discharge from hospital.
Results: The current study showed age was distributed as 57.83±12.9. Females are significantly associated with abnormal thyroid functions. Leucocytes are significantly high in all groups. Granulocytes were significantly higher among thyrotoxicosis than other groups while lymphopenia and mild elevation in monocytes can be seen in all groups. ESR and CRP are significantly high in all groups**.** TSH is slightly elevated in Sick Euthyroid group while Free T3 and Free T4 are Low. Free T4 was significantly lower among hypothyroid group and significantly higher among Thyrotoxicosis group and TSH was significantly higher among hypothyroid group and significantly lower among Thyrotoxicosis group.
Conclusions: Thyroid function abnormalities were common in COVID-19 patients seems to dynamically change within the course of disease and recover gradually and spontaneously. While this may be partially explained by non-thyroidal illness syndrome or thyroiditis, it is also possible that the thyroid gland is a direct target of the SARS CoV-2 virus.

Keywords: COVID-19; TSH, FT4, FT3 and TPO antibody; Thyroid abnormalities

INTRODUCTION

The 2019 pandemic coronavirus illness (COVID-19), an infectious disease caused by the severe acute respiratory syndrome coronavirus 2, has been declared a public health emergency by the World Health Organization (WHO) (SARS-CoV-2). By 2020, there will have been 80 million confirmed cases worldwide, with 1.8 million of those cases ending in death **[1].** Similar to pneumonic symptoms including fever, coughing, and shortness of breath, COVID-19 confirmed patients frequently present with extrapulmonary symptoms like poor appetite, nausea, diarrhea, abdominal pain, and eventually vomiting **[2].**

COVID-19 has rapidly become a multi-system. The interaction between the endocrine system and the severe acute respiratory syndrome corona virus-2 (SARS CoV-2)

happens on a variety of levels, thus it should not be excluded **[3].**

The endocrine system and SARS CoV-2 are thought to interact through three different mechanisms. through ACE-2 Receptors, direct viral invasion of the gland inflammation-mediated hypothalamo-pituitary axis (HPA) stimulation and immune-mediated glandular injury brought on by the production of antibodies or cell-mediated damage **[4].** Thyroid impairment has been recorded in SARS patients who were suffering from another coronavirus strain, despite the fact that the impact of COVID-19 on thyroid function is yet unknown. This suggests that the thyroid gland may be a target organ for the SARS-CoV-2 virus **[5].**

Therefore, this study aimed to detect the incidence of thyroid hormonal disturbance in Covid-19 patients.

METHODS

This prospective cohort study was performed at Internal Medicine Department, Al-Ahrar Teaching Hospital from July to October 2020. The study was approved by the Zagazig University institutional review board (IRB), official permission from study setting departments and an informed written consent was obtained from all patients before they joined the study. One hundred and seventy-seven positive Covid-19 patients were enrolled in this study.

Inclusion criteria:

Hospitalized Adult patient with confirmed Covid-19 by swab of males and females.

Exclusion criteria:

Patients receiving drugs for hypothyroidism or hyperthyroidism, severely ill patients on mechanical ventilators, patients on drugs affecting Thyroid functions as amiodarone, patients with evidence of malignancy and patient refusal.

Ethical Consideration:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee (IRB Approval Number #6672-17-1-2021 and Date 17-1-2021). Written informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All patients were subjected to:

A- Full history: detailed history was taken, with special considerations for age, sex, comorbidities, and medications. Special comment on symptoms of thyrotoxicosis such as (heat intolerance, palpitation, weight loss, insomnia, irritability, tremors, neck swelling).

B-General and local examination: under Full Personal Protective Equipment (PPE), we examined the patients for weight, height, body mass index, chest infection such as

(fever, cough and dyspnea), abdominal pain, tenderness. Signs of hyperthyroidism such as (starring look, tachycardia, hyperreflexia, flushing, wide pulse pressure) were observed. Examination of thyroid gland for presence of goiter, thyroid thrill and bruit. Signs of Graves' disease such as thyroid ophthalmopathy and dermopathy

C-Laboratory investigations included complete Blood Count (CBC), erythrocyte sedimentation rate (ESR), TSH, free T3 and free T4 and TPO antibody **[6]**. Polymerase Chain Reaction (PCR) of SARS-CoV-2 in quantitative reverse transcriptase polymerase chain reaction of samples from the respiratory tract.

All the confirmed cases tested positive for SARS-CoV-2 in quantitative reverse transcriptase polymerase chain reaction of samples from the respiratory tract. All the cases were non-mild and divided into three clinical classifications: moderate, severe, and critical, based on clinical symptoms, laboratory results, and chest computed tomography scans, in accordance with the diagnosis and treatment plan for COVID- 19 (Trial Version 7) issued by National Health Commission of China **[7]**.

- **Estimation of TSH:**

The TSH enzyme immunoassay test is based on the principle of a solid phase enzyme-linked immunosorbent assay. The mean TSH values based on 160 random normal adult blood samples are 0.4-4.2 μIU/mL.

- **Estimation of FT4:**

The fT4 ELISA kit is used for the quantitative measurement of free Thyroxine (fT4) in human serum. Normal levels of free T4 range from 0.8–1.8 nanograms per deciliter (ng/dl) of blood.

- **Estimation of FT3:**

The fT3 ELISA kit is used for the quantitative measurement of free Thyroxine (fT3) in human serum. Normal levels of free T4 range from 0.2–0.5 ng/dl of blood.

- **Estimation of TPO antibody:**

The Thyroid Peroxidase (TPO) ELISA Kit is intended for the detection of IgG antibody to Thyroid Peroxidase in human serum or plasma. The following was intended as a guide to interpretation of TPO antibody test results:

(a) Antibody Index Interpretation: <0.9 No detectable TPO antibody by ELISA, 0.9-1.1 Borderline positive. Follow-up testing is recommended if clinically indicated;

>1.1 detectable TPO antibody by ELISA.

(b) Converting of Ab Index to IU/mL: as an option, TPO Ab index may beconverted to IU/mL by multiplying Ab index value by 50. International units may then be interpreted as follows: <45 IU/mL: Negative; 45-55 IU/mL: Borderline positive; > 55IU/mL positive.

Follow up:

Follow up of the patients who revealed abnormal lab results during covid-19 infection 1 month after discharge from hospital by:

- Thyroid U/S for patients with abnormal clinical examination in follow up appointment.
- Repeat Thyroid Function Tests and TPO antibody for patients with abnormal lab studies during Covid-19 infection.
- Technetium Isotopic scanning on selected cases with high Thyroid Hormone and low TSH to differentiate between thyroiditis and hyperthyroidism.

Statistical analysis:

Data analyzed using Microsoft Excel software then imported into Statistical Package for the Social Sciences (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X2) paired by Mac Nemar. Differences between quantitative independent groups by t test paired by paired t. P value was set at <0.05 for significant results & <0.001 for high significant result.

RESULTS

The current study showed age was distributed as 57.83±12.9 with minimum 22 and maximum 85, female was majority with 59.9% and male 40.1%. Females are significantly associated with abnormal thyroid functions **(Table 1).** Regarding Lab results, leucocytes are significantly high in all groups. Granulocytes were significantly higher among thyrotoxicosis than other groups while lymphopenia and mild elevation in monocytes can be seen in all groups. ESR and CRP are significantly high in all groups **(Table 2)**.

TSH is in high normal range in the Sick Euthyroid group while Free T3 is low and Free T4 is in low normal range. Free T4 was significantly lower among hypothyroid group and significantly higher among Thyrotoxicosis group and TSH was significantly higher among hypothyroid group and significantly lower among Thyrotoxicosis group **(Table 3)**. Change assessment of TSH, fT3 and fT4 of the 3 groups B1, B2 and B3 during the infection (Base) and in the (follow-up) as TSH is decreasing to normal levels in follow-up and Free T4 and Free T3 are increasing to normal levels **(Table 4)**.

Regarding TPO ELISA in follow up cases, no significant change was found **(Table 5)**. Ultrasonography follow up in our study revealed that thyrotoxicosis group was associated with high vascularity of the thyroid gland while the hypothyroid groups showed low vascularity and sick euthyroid group was mainly normal gland but with a slight hypervascularity. Normal gland with slight hypervascularity is highly significant in sick

euthyroid group **(Table 6)**. Regarding isotopic scan among thyrotoxicosis, low uptake was 71.5% suggesting thyroiditis **(Table 7)**.

Table 1: Demographic data distribution among studied group (n=177)

			Thyrotoxicosis group (Group B1)	Hypothyroid group (Group B2)	Sick Euthyroid group (Group B3)	Normal Group	F	P
Age			52.46±14.55	65.87±12.87	59.21±11.49	57.93±12.43	2.681	0.071
Sex	**Female**	**N**	5	3	20	87		
		%	71.5%	100.0%	66.6%	63.5%		
	Male	**N**	2	0	10	50	14.6	0.0007**
		%	28.5%	0.0%	33.4%	46.5%		
Total			7	3	30	137		

Table 2: LAB distribution among studied groups

	Thyrotoxicosis group (Group B1)	Hypothyroid group (Group B2)	Sick Euthyroid group (Group B3)	F	P
WBC	18.26±8.63	8.86±3.21	13.08±5.63	2.153	0.119
RBC	4.79±0.91	4.46±0.27	4.53±0.89	0.276	0.759
HB	12.58±1.76	11.38±1.55	11.38±2.38	0.756	0.471
Platelet	252.66±85.6	216.87±53.9	253.17±124.54	0.339	0.713
Granulocyte	15.76±6.96*	6.21±2.13#	9.91±3.03	12.440	0.00**
Lymphocytes	1.75±0.68	1.47±0.42	1.60±0.56	0.171	0.843
Monocytes	0.75±0.35	0.60±0.22	0.66±0.28	0.036	0.965
ESR	68.66±20.2	64.87±21.8	64.82±21.69	0.085	0.918
CRP	35.42±10.7	30.04±12.2	31.14±14.23	0.082	0.942

Table 3: Thyroid profile distribution among studied groups

	Thyrotoxicosis group (Group B1)	Hypothyroid group (Group B2)	Sick Euthyroid group (Group B3)	F	P
TSH (MIU/L)	0.1±0.05#	10.35±1.84*	1.1±0.45	54.575	0.00**
Free T4 (ng/dl)	2.32±0.30*	0.39±0.32#	1.33±0.54	15.623	0.00**
Free T3 (pg/ml)	3.15±1.22	2.11±0.51	1.5±0.51	34.214	0.00**

Table 4: Change assessment regard TSH, Free T4 and Free T3 between base and follow up cases (n=40)

	Base			Follow-up			Paired t	P
	B1	**B2**	**B3**	**B1**	**B2**	**B3**		
TSH	0.3±0.02	10.51±1.32	4.21±0.54	0.1±0.05	10.35±1.84	1.1±0.45	0.217	0.721
Free T4	2.14±0.45	0.34±.41	0.7±0.42	2.32±0.30	0.39±0.32	1.33±0.54	0.128	0.877
Free T3	3.32±1.38	2.27±0.43	2.11±0.51	3.15±1.22	2.11±0.51	1.5±0.51	0.134	0.842

Table 5: Change assessment regard Anti TPO ELISA in follow up cases (Group B) (n=40)

		Base			Follow up			Mac Nemar	P
		B1	B2	B3	B1	B2	B3		
Anti TPO ELISA	Negative	5	0	29	5	0	29	0.66	0.25
	Positive	2	3	1	2	3	1		

Table 6: US distribution among studied groups

			Group			X^2	P
			Thyrotoxicosis group	Hypothyroid group	Sick Euthyroid		
US	Normal gland with slight hypervascularity	N	1	0	14	3.19	0.52
		%	14%	0%	46%		
	Enlarged diffuse homogenous thyroid gland with high vascularity	N	3	0	7		
		%	44%	0%	24%		
	Mildly enlarged hypoechoic gland with normal / low vascularity	N	0	2	3		
		%	0%	66.7%	10%		
	Enlarged thyroid gland, with heterogenous echotexture, showing hypervascularity on color doppler.	N	2	0	3		
		%	28%	0.0%	10%		
	Enlarged thyroid gland showing normal vascularity and some nodules	N	1	1	3		
		%	14%	33.3%	10%		
Total		N	7	3	30		

Table 7: Tech. Isotopic scan among thyrotoxicosis to differentiate between hyperthyroid and thyroiditis.

		N	%
Isotopic scan	High homogenous uptake of tracer	2	28.5
	Low uptake	5	71.5
Total		7	100.0

DISCUSSION

The worldwide community has been substantially impacted by the COVID-19 pneumonia outbreak, and the capacity of the health care systems in every nation has faced significant difficulties. Numerous investigations showed that SARS-COV-2 could influence lipid, glucose, and systemic blood pressure levels via endocrine and metabolic pathways in which angiotensin-converting enzyme 2 plays a significant role. Because ACE2 is highly expressed in the thyroid gland in humans and was discovered to be a functional receptor for the SARS coronavirus in 2003, it is clear why COVID-19 causes thyroid dysfunction **[8,9]**.

Thyrotropin-releasing hormone, thyroid stimulating hormone, free triiodothyronine, and free thyroxine are among the hormones

that are part of the hypothalamus-pituitary-thyroid axis. The link between COVID-19 and thyroid function is still unknown at this time. **Zou et al. [10]** discovered that thyroid illness was present in 27.52% of COVID-19 individuals. According to a study on severe instances in the UK, 22.2% of thyroid follicular epithelial cells were destroyed **[11,12]**.

In this study, the aim was to detect the incidence of Thyroid hormonal disturbance in Covid-19 patients. Our study was prospective cohort study performed at internal medicine department, Al-Ahrar teaching hospital, conducted on 177 hospitalized adult patients with confirmed COVID-19 by swab of males and females. Patients receiving drugs for hypothyroidism or hyperthyroidism, severely ill patients on mechanical ventilators, patients on drugs affecting Thyroid functions as amiodarone and patients with evidence of malignancy were excluded from the study.

As the regard of demographic data of the included patients, the admitted 177 patients aged between 22 to 85 with the median age of 60, with female sex was predominant (59.3%) compared to males (40.7%). In our study, among the included subject, there were 40 cases with abnormal thyroid functions (Group B) in comparison to 137 normal cases (Group A). It was worthy to mention that the female gender was significantly higher among the follow-up cases with abnormal lab results (Group B) with (55%) than male this could be explained due to higher expression of angiotensin- converting enzyme-2 (ACE 2; receptors for coronavirus) in female than male **[13,14]**.

In our Study, the abnormal 40 cases were divided into 3 groups: Thyrotoxicosis (group B1) (7 cases) 4%, Hypothyroid (group B2) (3 cases) 1.7%, and Sick Euthyroid (group B3) (30 cases) 17%. The largest cohort of patients to date was done by **Khoo et al. [15]** which investigated the acute effects of COVID-19 on thyroid function. Most of the patients were euthyroid at admission with COVID-19.

In agreement with our study, **Muller et al. [16]** revealed that cases of primary hypothyroidism linked to COVID-19. Only 5.2% of 287 patients hospitalised in a non-intensive care environment had hypothyroidism, according to the THYRCOV research. Muller and colleagues discovered thyrotoxicosis in 15.3% of COVID-19 patients as opposed to just 1.3% of controls in their investigation.

Lania et al. [17] conducted another study on 287 non-critical COVID-19 patients which revealed that 20.2% had thyrotoxicosis, and that thyroid function assessed during hospitalization was associated with the concentrations of different inflammatory markers **[18].**

In our study, there was a decrease in mean lymphocyte count in all groups (1.35±0.45 10^9/L). Lymphopenia is a common hematological abnormality in SARS- CoV-2 infection which may reduce the lympho-plasmacytic infiltration of the thyroid gland thus causing pain in the anterior cervical region that occurs in some patients**[16]**.

The thyrotoxicosis group (Group B1) contained 7 patients which represents 4% of all examined patients. They were 5 females and 2 males with a mean age of 52±14. There was a marked increase in ESR (68±20 mm/hr), CRP (35±10 mg/L) and WBCs (18±8 10^9/L). TSH level is low in group B1 (0.1±0.05 uIU/ml) while Free T3 (3.15±1.2 pg/ml) and Free T4 (2.3±.3 ng/dl) are high. 3 patients out of 7 (44%) showed enlarged diffuse homogenous glands with high vascularity in ultrasonography follow- up. Technetium isotopic scan was done among this group to differentiate between hyperthyroid (Grave's) and sub-acute thyroiditis. 5 patients out of 7 (71.5%) were lowuptake denoting thyroiditis.

Liu et al. [19] reported 125 cases of mild COVID-19 pneumonia were compared to 125 cases of severe COVID-19 pneumonia, it was discovered that 13% of the severe pneumonia patients had hyperthyroidism (6.4% overt and 5.6% subclinical), while the prevalence was lower in the mild pneumonia group (1.6% overt and 4.8% subclinical). 14 (7%) of the 191 COVID-19 cases had thyrotoxicosis-related symptoms, such as low TSH and/or high FT4 levels. The incidence of atrial fibrillation and thromboembolic events in COVID-19 individuals with overt thyrotoxicosis is 32% and 16%, respectively. Additionally, people with COVID-19 who also have thyrotoxicosis are more likely to die

in hospitals and require longer hospital stays than those who only have COVID-19. Thus, it appears that thyrotoxicosis is clinically relevant to COVID-19 infection and has significant consequences. **Pizzocaro et al. [20]** reported that thyrotoxicosis caused by SARS-CoV-2 typically spontaneously returned to normal. Future research is necessary to determine whether or whether this ultrasonographic abnormality may lead to late-onset thyroid dysfunction, as thyroid hypoecogenicity was discovered in a significant number of instances.

The hypothyroid group (B2) contained 3 cases which represents 1.5% of all examined patients. They were all females. There was an elevation in ESR (64.8±21) and CRP (30±12). Their lab results in both base and follow up showed high TSH (10.3±1.8), low Free T3 (2.1±.5) and Free T4 (.39±.32), Positive anti-TPO. 2 out of 3 patients (66.7%) showed mildly enlarged hypoechoic gland with normal vascularity in their ultrasonography follow-up. **Guven et al. [21]** reported cases of mild COVID-19 pneumonia were compared to cases of severe pneumonia, none of the mild pneumonia patients who were hospitalised had hypothyroidism, although 3.2% of the patients with severe chest symptoms did (2.4% overt and 0.8% subclinical).

Pereira et al. [22] stated that patients with hypothyroidism had a tendency toward decreased in-hospital mortality and needed less mechanical breathing. So, it appears that hypothyroidism is not linked to a worse prognosis.

The sick euthyroid group (B3) contained 30 patients representing 17% of all examined patients. They were 20 females and 10 males. TSH was in high normal range (1.1±.4) while Free T4 was in low normal range and Free T3 was extremely low (1.5±.5) and there was significant lymphopenia (1.6±.5). In follow-up, TSH is in normal levels while Free T3 is low and Free T4 is in normal. Ultrasonography follow-up revealed normal gland with slight hypervascularity in 14 out of 30 patients (46% of this group).

Zou et al. [10] conducted a study on a total of 149 COVID-19 cases of whom 41 (27.52%) cases were diagnosed with Sick Euthyroid Syndrome. Compared to non-sick euthyroid syndrome cases, they exhibited lower median T4 and free T4 (FT4) concentrations (106.30 vs. 121.98 nmol/L and 14.47 vs. 16.08 pmol/L, respectively), but no discernible difference was seen for TSH.

Elevated ESR has been reported in our study in almost all cases (97%) with a mean value of 68±20 and CRP was also elevated in almost all cases (96%) with a mean value of 35±10. Several studies revealed increased ESR and CRP in almost all cases (96%) as a subacute thyroiditis specific inflammation marker **[23]**. Therefore, there is a strong correlation between ESR and CRP and abnormal thyroid functions in thyroid patients.

Accordingly, the current theory holds that COVID-19 directly impacts thyroid hormone levels and thyroid function through the hypothalamus-pituitary-thyroid axis and that autoimmune diseases directly affect the thyroid gland through cytokines.

Although we did see a statistically significant difference in FT4 and TSH between baseline and follow-up with COVID-19, the magnitude of the change was small and not likely to justify treatment. These data are limited by the study's single-center design, the absence of rT3 measurement, and characterization of thyroid autoantibody status.

Conclusions:

The results of the current investigation showed that individuals with COVID-19 frequently have aberrant thyroid function; this dysfunction appears to change dynamically as the disease progresses and gradually and spontaneously resolves. While thyroiditis or non-thyroidal sickness syndrome may partially explain for this, it's also plausible that the thyroid is the SARS CoV-2 virus's primary target.

Further longitudinal studies including FT3 and rT3 measurement are now necessary to determine the full impact of COVID-19 on the hypothalamic-pituitary-thyroid axis.

REFERENCES

1- Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. *Clin Chem Lab Med.* 2020;58(7):1063-1069.

2- Choudhary J, Dheeman S, Sharma V. Insights of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) pandemic: a current review. *Biol Proced Online*. 2021;23(1):5.

3- Cabrera Martimbianco AL, Pacheco RL, Bagattini ÂM, Riera R. Frequency, signs and symptoms, and criteria adopted for long COVID-19: A systematic review. *Int J Clin Pract*. 2021;75(10):e14357.

4- Garg MK, Gopalakrishnan M, Yadav P, Misra S. Endocrine Involvement in COVID-19: Mechanisms, Clinical Features, and Implications for Care. *Indian J Endocrinol Metab*. 2020;24(5):381-386.

5- Rossetti CL, Cazarin J, Hecht F, Beltrão FE, Ferreira AC, Fortunato RS, et al. COVID-19 and thyroid function: What do we know so far?. *Front Endocrinol (Lausanne)*. 2022;13:1041676.

6- Al-Tikrity MA, Magdi M, Abou Samra AB, Elzouki AY. Subacute Thyroiditis: An Unusual Presentation of Fever of Unknown Origin Following Upper Respiratory Tract Infection. *Am J Case Rep*. 2020;21:e920515.

7- Lui DT, Li YK, Lee CH, Chow WS, Lee AC, Tam AR, et al. A prospective study of the impact of glycaemic status on clinical outcomes and anti-SARS-CoV-2 antibody responses among patients with predominantly non-severe COVID-19. *Diabetes Res Clin Pract*. 2022;185:109232.

8- Scappaticcio L, Pitoia F, Esposito K, Piccardo A, Trimboli P. Impact of COVID-19 on the thyroid gland: an update. *Rev Endocr Metab Disord*. 2021;22(4):803-815.

9- Malik J, Malik A, Javaid M, Zahid T, Ishaq U, Shoaib M. Thyroid function analysis in COVID-19: A retrospective study from a single center. *PLoS One*. 2021;16(3):e0249421.

10- Zou R, Wu C, Zhang S, Wang G, Zhang Q, Yu B, et al. Euthyroid Sick Syndrome in Patients With COVID-19. *Front Endocrinol (Lausanne)*. 2020;11:566439.

11- Kumari K, Chainy GBN, Subudhi U. Prospective role of thyroid disorders in monitoring COVID-19 pandemic. *Heliyon*. 2020;6(12):e05712.

12- Allam MM, El-Zawawy HT, Ahmed SM, Aly Abdelhamid M. Thyroid disease and covid-19 infection: Case series. *Clin Case Rep*. 2021;9(6):e04225.

13- Clarke SA, Phylactou M, Patel B, et al. Normal Adrenal and Thyroid Function in Patients Who Survive COVID-19 Infection. *J Clin Endocrinol Metab*. 2021;106(8):2208-2220.

14- Gao W, Guo W, Guo Y, Shi M, Dong G, Wang GA, et al. Thyroid hormone concentrations in severely or critically ill patients with COVID-19. *J Endocrinol Invest*. 2021;44(5):1031-1040.

15- Khoo B, Tan T, Clarke SA, Mills EG, Patel B, Modi M, et al. Thyroid Function Before, During, and After COVID-19. *J Clin Endocrinol Metab*. 2021;106(2):e803-e811.

16- Muller I, Cannavaro D, Dazzi D, Covelli D, Mantovani G, Muscatello A, et al. SARS-CoV-2-related atypical thyroiditis. *Lancet Diabetes Endocrinol*. 2020;8(9):739-741.

17- Lania A, Sandri MT, Cellini M, Mirani M, Lavezzi E, Mazziotti G. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. *Eur J Endocrinol*. 2020;183(4):381-387.

18- Naguib R. Potential relationships between COVID-19 and the thyroid gland: an update. *J Int Med Res*. 2022;50(2):3000605221082898.

19- Lui DT, Lee CH, Chow WS, Lee AC, Tam AR, Fong CH et al. Thyroid Dysfunction in Relation to Immune Profile, Disease Status, and Outcome in 191 Patients with COVID-19. *J Clin Endocrinol Metab*. 2021;106(2):e926-e935.

20- Pizzocaro A, Colombo P, Vena W, Ariano S, Magnoni P, Reggiani F, et al. Outcome of Sars-COV-2-related thyrotoxicosis in survivors of Covid-19: a prospective study. *Endocrine*. 2021;73(2):255-260.

21- Güven M, Gültekin H. The prognostic impact of thyroid disorders on the clinical severity of COVID-19: Results of single-centre pandemic hospital. *Int J Clin Pract*. 2021;75(6):e14129.

22- Pereira DN, Silveira LF, Guimarães MM, Polanczyk CA, Nunes AG, de Moura Costa AS, et al. Hypothyroidism does not

lead to worse prognosis in COVID-19: findings from the Brazilian COVID-19 registry. *Int J Infect Dis*. 2022;116:319-327.

23- Trimboli P, Cappelli C, Croce L, Scappaticcio L, Chiovato L, Rotondi M. COVID-19-Associated Subacute Thyroiditis: Evidence-Based Data From a Systematic Review. *Front Endocrinol (Lausanne)*. 2021;12:707726.

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