



Clinical Features of COVID-19 Patients with Preexisting Hypothyroidism: A Retrospective Study

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ABSTRACT

Background and objectives: Coronavirus disease 2019 (COVID-19) has been reported to be more severe and highly fatal in patients with co-morbidities. Thyroid dysfunction leads to multisystem derangements, as thyroid hormones have major role in the development and functioning of all the human cells. The present study evaluated the variation in the clinical and biochemical parameters of COVID-19 patients with preexisting hypothyroidism.

Methods: This retrospective cohort study was carried out on eight COVID-19 patients with hypothyroidism who were admitted to a tertiary care hospital in Mangalore, India. Various clinical and biochemical parameters of the patients were recorded.

Results: Out of eight patients, three were men and five were women. With respect to other co-morbidities, six patients had associated type-2 diabetes mellitus and the remaining two patients had no other co-morbidities apart from hypothyroidism. Regarding the severity of COVID-19, one patient had mild symptoms, two had moderate symptoms, and the remaining five patients had severe COVID-19 symptoms. Most biochemical and hematological parameters in all patients were deranged from normal values. Moreover, only 25% of the patients recovered from the disease.

Conclusion: Most COVID-19 patients with hypothyroidism had low oxygen saturation and high level of inflammatory markers. In addition, the risk of mortality in COVID-19 patients with hypothyroidism and type 2 diabetes mellitus was higher compared to patients with hypothyroidism alone. It is recommended to closely monitor COVID-19 patients with hypothyroidism and limit the use of steroids during the course of treatment.

Keywords: [Hypothyroidism](#), [COVID-19](#), [Biomarkers](#).

INTRODUCTION

The world is in the state of coronavirus disease 2019 (COVID-19) pandemic which has brought it to stand still. Every sector has been affected immensely, bringing the economy to its lowest during recent decades. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spreading around the world and the emergency care services are of utmost important now. The World Health Organization (WHO) declared the COVID-19 as a pandemic on 11th March 2020. The clinical manifestations of COVID-19 have been broadly defined by the WHO with most of the confirmed COVID-19 cases having mild to moderate clinical presentations (1). In the initial phases of the infection, symptoms such as fever, cough, and dyspnea can occur (2). Few patients rapidly develop acute respiratory distress syndrome (ARDS) and additional severe complications, which finally result in multiple organ failure (3).

In addition, COVID-19 is more severe in patients with co-morbidities. Thyroid dysfunction may lead to multisystem derangements, as thyroid hormones have major impact on the development and functioning of all the human cells (4). Hypothyroidism is one of the apparently neglected co-morbidities which may be overshadowed by other co-morbidities such as diabetes and hypertension. A meta-analysis published in July 2020 concluded that people with thyroid disorders are at higher risk of developing severe COVID-19 (5).

Recent studies have reported onset of thyroid dysfunction in previously thyroid healthy patients diagnosed with COVID-19 as well as the potential negative impact of COVID-19 on preexisting thyroid diseases. The SARS-CoV-2 virus enters the human cells through the angiotensin-converting enzyme-2 (ACE-2) receptor. Expression of ACE-2 receptor has been demonstrated in thyroid follicular cells, making them a potential target for SARS-CoV-2 entry.

Currently, the WHO has not recommended systematic thyroid function testing for hospitalized COVID-19 patients, and routine assessment of thyroid function in COVID-19 patients requiring intensive care is to be considered for the frequent co-occurrence of thyrotoxicosis due to SARS-CoV-2 infection (6). It is also thought that preexisting or new-onset thyroid hormone imbalance, such as low

T3 syndrome, could be associated with the disease severity in COVID-19. Since healthcare services have been reorganized and access to healthcare facilities is restricted, thyroid disease management is potentially affected (7). Given the lack of enough studies on the severity of COVID-19 in Indian patients with hypothyroidism, the present study was carried to study the variations in the clinical and biochemical parameters of COVID-19 patients with hypothyroidism admitted to a tertiary care hospital in Mangalore, India.

MATERIALS AND METHODS

This retrospective cohort study was started after obtaining approval from the Yenepoya Medical College Ethics Committee (ethical code: YEC-1/2020/063). The study has been registered in the Clinical Trial Registry-India (CTRI/2021/06/034303) and complied with the guidelines of institutional ethics committee and Indian Council of Medical Research. The study was carried out on all COVID-19 patients with hypothyroidism who were admitted to a tertiary care hospital in Mangalore, India, between 22nd June 2020 and 22nd July 2020. Demographic information as well as clinical and biochemical parameters of the patients were retrieved from the central laboratory and medical record departments of our institution. All the biochemical investigations were carried out using the VITROS® 5600 Integrated System of NABL accredited laboratory.

Data were described using descriptive statistics including frequency and percentage. Mean values were calculated to summarize all laboratory parameters. statistical analysis were performed using SPSS (version 23).

RESULTS

Overall, eight COVID-19 patients (three men and five women, age range: 23-75 years) with hypothyroidism were enrolled in the study. The patients had higher mean values of random blood sugar (RBS), serum creatinine, aspartate transaminase (SGOT), C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), and HbA1c compared with the reference range (Table 1).

Table 1- Mean value of biochemical parameters among COVID-19 patients with hypothyroidism

Parameters	Mean value	Reference range
Random Blood sugar (RBS)	171 mg/dl	70-140 mg/dl
Oxygen saturation (SpO ₂)	82%	≥95%
Blood Urea	40.71 mg/dl	19-43 mg/dl
Serum creatinine	1.61 mg/dl	0.62-1.1 mg/dl
Total Bilirubin	0.8 mg/dl	0-2 mg/dl
Direct Bilirubin	0.2 mg/dl	0-0.2 mg/dl
Indirect Bilirubin	0.6 mg/dl	0-1.1 mg/dl
SGOT	142.7U/L	0-31 U/L
SGPT	31.7U/L	0-34 U/L
Alkaline Phosphatase	97.2 U/L	60-170 U/L
CRP	74.36 mg/dl	0-5 mg/L
Ferritin	529.68 µg/L	6.24 – 137 µg/L
TSH	7.1 mIU/ml	0.5-8.9 mIU/ml
D-Dimer	3162 ng/ml	<500 ng/ml
LDH	498.2 U/L	120-246 U/L
HbA1c	8.2%	4.2-6.2%
CK-MB	2.115	0-2.37 ng/ml
Troponin I	0.0205	0.03 ng/ml

Mean value of total protein, albumin, globulin and A/G ratio were found to be 7.8 mg/dl, 4.1 mg/dl, 3.7 mg/dl and 1.12, respectively. Based on the WHO criteria (8) for classifying

severity of COVID-19 infection, one patient had mild symptoms, two had moderate symptoms, and the remaining five patients had severe COVID-19 symptoms (Figure 1).

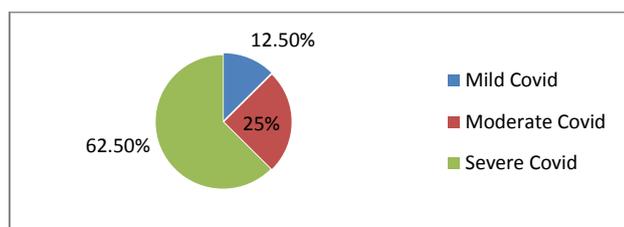


Figure 1- Grading of COVID-19 severity in patients with hypothyroidism

DISCUSSION

The SARS-CoV-2 virus enters the cells via the ACE-2 receptors, which are widely distributed on various organs including the endocrine glands. Infection of the thyroid gland with the SARS-CoV-2 virus can lead to the development of thyroid disorders in the normal individuals or worsen the preexisting thyroid disorders. Moreover, certain medications used in treatment of COVID-19 can also affect the thyroid hormone levels in the blood. For instance, dexamethasone that is given to treat the cytokine storm and control the immune response in COVID-19 patients, can affect triiodothyronine (T3) levels. A low T3 syndrome has been found in some patients treated with dexamethasone, which worsens the patient's condition with thyroid disorders. In our study, the majority of patients with hypothyroidism had altered liver and renal function, low oxygen saturation, and increased inflammatory markers such as ferritin, LDH, CRP, and D-dimer.

Based on the results, the severity of the disease and its outcome was significantly worsened in patients with hypothyroidism and diabetes mellitus. On the contrary, patients with hypothyroidism without any other co-morbidity could recover well without intensive care.

Recent studies have demonstrated that preexisting thyroid disease may be associated with an 2.48 increased risk of severe COVID-19 (9, 10). However, a retrospective study on 3703 hospitalized COVID-19 patients, including 251 patients with preexisting hypothyroidism, did not find any difference between the patients in terms of outcomes, risk of hospitalization, the need for mechanical ventilation, or mortality death (11). Nevertheless, until more is understood regarding the impact of the SARS-CoV-2 virus on the thyroid gland, it is advisable to monitor patients with COVID-19 for new thyroid disease or progression of preexisting thyroid

disease (12). Currently, the American Thyroid Association does not have specific recommendations for patients with hypothyroidism but advises patients with underlying hypothyroidism to continue taking their medication as prescribed and to take appropriate measures to minimize spread of infection.

CONCLUSION

Most COVID-19 patients with hypothyroidism had low SpO₂ and high level of inflammatory markers. In addition, the risk of mortality in COVID-19 patients with hypothyroidism and type 2 diabetes mellitus was higher compared to patients with hypothyroidism alone. It is recommended to closely monitor COVID-19 patients with hypothyroidism and limit the use of steroids during the course of treatment. It is also suggested to conduct further studies using a larger study population to confirm our findings.

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DECLARATIONS

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Ethics approvals and consent to participate

Ethics approval was obtained from the Yenepoya Medical College Ethics Committee (ethical code: YEC-1/2020/063).

Conflict of interest

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