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Wide Spectrum of Thyroid Function Tests in COVID-19: From Nonthyroidal Illness to Isolated Hyperthyroxinemia

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Abstract

Background: Changes in thyroid function test (TFT) in COVID-19 patients have been reported in several studies. However, some features such as thyrotoxicosis are inconsistent in these studies. In addition, some drugs such as heparin interfere with the free T4 assay.

Objectives: This study was designed to examine TFT abnormalities in COVID-19, utilizing direct and indirect methods of free T4 assay.

Methods: This prospective cross-sectional study was conducted on 131 hospitalized COVID-19 patients. Serum levels of total T3, TSH, T3RU, and total T4 were measured. The free T4 assay was performed using direct (free T4) and indirect (free thyroxin index or FT4I) methods. The patients were categorized into different TFT groups. The clinical characteristics, laboratory findings, and outcomes were compared between the groups.

Results: The frequencies of Nonthyroidal Illness (NTI), subclinical/overt hypothyroidism and subclinical/overt thyrotoxicosis were 51.7, 6.9, and 6.9%, respectively. Besides, 6 and 8.1% of the patients had isolated high free T4 and isolated high FT4I without any other TFT abnormality, respectively. The lymphocyte percent was lower in the subclinical/overt group than in other TFT groups ($P = 0.002$). Atrial Fibrillation (AF) was found in 37.5% of subclinical/overt thyrotoxicosis patients versus 1.7% in the NTI and nil in the other three groups ($P < 0.001$).

Conclusions: In addition to the reported TFT abnormalities in COVID-19 in previous studies, some new features like isolated hyperthyroxinemia were found in our study. We found a strong association between subclinical/overt thyrotoxicosis and AF. Regarding the high prevalence of AF in hospitalized COVID-19 patients, the thyroid function test is rational in COVID-19 patients with this arrhythmia.

Keywords: COVID-19, Thyroid Function Test, Isolated Hyperthyroxinemia, Atrial Fibrillation

1. Background

Since the beginning of the COVID-19 pandemic, some clinical manifestations have been reported for the respiratory system and other organ involvement. Angiotensin-converting Enzyme 2 (ACE2) receptors are detected in different organs such as cardiovascular, gastrointestinal, and endocrine systems (1). In the endocrine system, the intensity of these receptors is the highest in the testis, followed by the thyroid, and the least in the hypothalamus (2, 3). These receptors in the thyroid make the thyroid glands a potential target for virus entry (4).

In addition, there are other mechanisms for thyroid function test (TFT) abnormalities in COVID-19. Nonthyroidal illness is a well-known entity as the cause of thyroid test abnormalities in patients with a critical illness (5). During critical illness, the T3 level decreases rapidly mainly because of the decreased activity of deiodinase type-1 (D1), declined thyroid hormones' binding to thyroid-binding globulin and other binding proteins, and decreased TSH secretion in prolonged critical illness (5, 6). Besides, COVID-19-related subacute thyroiditis is another reason for thyroid abnormality during or after the disease course. Clinical manifestations usually occur 2 - 6 weeks after COVID-19 infection, and patients show the typical manifestations of subacute thyroiditis, especially pain, in the thyroid region (7). Moreover, drugs such as corticosteroids and heparin, usually used for treating COVID-19 patients, can interfere