

POST COVID-19 INFECTION IN SUBCLINICAL HYPERTHYROIDISM AMONG PATIENTS ATTENDING A TERTIARY HOSPITAL IN KATHMANDU

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ABSTRACT

Coronavirus disease 2019 (COVID-19) infection may induce thyroid dysfunction as Coronavirus 2 (SARS-CoV-2) can invade the human tissue cells through the cell receptor of angiotensin-converting enzyme 2 (ACE2), expression of which is high in thyroid tissue. The aim of the present study was to assess the subclinical hyperthyroidism post-COVID-19 effects on thyroid function in patients without history of thyroid disease after complete recovery from mild-to-severe COVID-19 and find the prevalence of subclinical hyperthyroidism. A descriptive cross-sectional study was conducted in the Department of Internal Medicine, of tertiary care center from September 2022 to February 2023 after obtaining ethical approval from the Institutional Review Committee of Nepal Medical College (Ref. No.: 15-079/080). Convenience sampling method was used among patients who met the eligibility criteria. Point estimate at 95.0% confidence interval were calculated along with frequency and proportion for binary data. Out of 38 patients, 34 (89.5%) had thyroid dysfunction. Among them, 7 (20.6%) had subclinical hyperthyroidism, 2 (5.9%) had thyroiditis and 1 (2.9%) had Graves' disease. Those who had thyroid dysfunction, 10 (29.4%) people were diagnosed with hyperthyroidism. The hyperthyroidism among COVID-19 patients is a common finding and subclinical hyperthyroidism was seen in 20.6% of patients post COVID-19. Therefore, while managing COVID-19, patients' thyroid profile should be considered.

KEYWORDS

COVID-19, thyroid dysfunction, hyperthyroidism

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INTRODUCTION

There have been several studies that reported that COVID-19 infection resulted in endocrinopathies.¹⁻⁶ Subclinical hyperthyroidism is characterized by circulating thyrotropin (thyroid-stimulating hormone; TSH) levels below the reference range and normal serum thyroid hormone levels, thus it is a biochemical diagnosis. Clinical manifestations of overt and subclinical thyrotoxicosis are similar but differ in magnitude. Potential complications of untreated subclinical hyperthyroidism are numerous and include weight loss, osteoporosis, atrial fibrillation, embolic events, and altered cognition. Mild subclinical hyperthyroidism is more common than severe subclinical hyperthyroidism. Transient suppression of TSH secretion may occur because of several reasons, one of which may be COVID-19 infection. The aim of the present study was to assess the post-COVID-19 effects on thyroid function in patients without a history of thyroid disease after complete recovery from mild-to-severe COVID-19 and the prevalence of subclinical hyperthyroidism in those with thyroid dysfunction.

MATERIALS AND METHODS

This was a cross-sectional study done in the Department of Internal Medicine at Nepal Medical College Teaching Hospital (NMCTH). The duration of the study was six months from September 2022 to February 2023. Ethical approval for the study was taken from the Institutional Review Committee of the NMCTH (Ref. No.: 15-079/080)

A convenience sampling method was used. A total of 38 participants were included in the study. Patients were included in this study, only after their consent. Basic data including age, gender, occupation, h/o COVID-19, and a family history of thyroid dysfunction were taken from all the participants in the study. Body mass index (BMI) was measured from all participants. Those patients who were treated previously for thyroid dysfunction before COVID-19 were excluded from the study. COVID-19 patients were categorized as per WHO clinical COVID-19 disease severity classification.¹ Venous blood sample was collected and sent for T3, T4, and TSH. For primary hypothyroidism, the T3 and T4 levels lower than the normal range (3.32-7.62 pmol/L) and (8.8-23.6 pmol/L), respectively were taken and primary hyperthyroidism was characterized by the higher level of T3 (more than 7.62) and T4 (more than 23.6) and low level of thyroid stimulation hormones (<0.4

mIU/l). For subclinical hyperthyroidism, T3 and T4 levels are in the normal ranges (3.32-7.62 pmol/L) and (8.8-23.6 pmol/L) respectively but the TSH levels were below the normal range of 0.45 – 5.32 pmol/L.

Data was entered in into Microsoft Excel sheet and analyzed by SPSS-17. Descriptive statistics were presented with frequencies and percentages for categorical variables, and mean along with standard deviation for continuous variables.

RESULTS

Thirty-four patients had thyroid dysfunction among 38 patients included in the study. Ten out of 34 (29.4%) study participants with a history of COVID-19 infections as well as with thyroid dysfunction who participated in the study had hyperthyroidism; seven had subclinical hyperthyroidism, two had thyroiditis and one had Grave's disease. Out of seven, who had subclinical hyperthyroidism four were male and three were female. The median age of them was 55 years (40-72 years). The median BMI among them was 25.5. Regarding COVID severity four had mild and three had moderate severity among the seven subclinical hyperthyroidism.

DISCUSSION

Recent evidence indicates both thyrotoxicosis and suppression of thyroid function in COVID-19. Although the thyroid gland has been depicted as one of the targets for the diverse effects of SARS-CoV-2 infection, the potential relationship between COVID-19 and thyroid function is poorly understood. Thyroid dysfunction during and subsequent to COVID-19 has been documented in clinical studies and multiple pathways have been implicated in the pathogenesis of thyrotoxicosis in the setting of SARS-CoV-2 infection. The initial deviation of thyroid hormones is based on a destructive process caused by SARS-CoV-2 as its expression is more in thyroid tissue. Therefore, low TSH might be a common finding, during and soon after infection in COVID-19 patients.⁸ The most frequently reported abnormality in various research is low TSH levels reported in 15.0% up to 56.0% of patients with COVID-19. In the present study, subclinical hyperthyroidism was seen in 20.6% of cases. Similar study done in mild-to-moderate COVID-19, had found subclinical hyperthyroidism in 13.0% of their cases two months after COVID.⁸ Several authors have reported a decrease in TSH proportional

to the severity of COVID-19 during and soon after infection. In a similar study done by Muller and colleagues⁵ found thyrotoxicosis in 15.3% of patients with COVID-19, compared with only 1.3% of controls in their study, and in another retrospective study of 287 non-critical COVID-19 patients by Lania *et al*¹ showed that 20.2% had thyrotoxicosis. Several other studies have found hyperthyroidism in COVID-19 patients. A similar study had found that the serum concentrations of TSH and total T3 were considerably lower in patients with COVID-19 than in a control group, more consistent with a nonthyroidal disease pattern.³ A prospective study of hospitalized COVID-19 patients conducted in Hong Kong showed that the majority of those with abnormal thyroid function (13.1% of the group) had low TSH concentrations, but only one of 191 participants (0.5%) had a high TSH concentration and a high thyroid peroxidase antibody titre.⁴ Contrary to these findings several studies have identified cases of COVID-19-related primary hypothyroidism to be more common.²

Thyroid hormones play an important role in the functioning of the human body. Any dysregulations in the thyroid hormone levels may have consequences on the immune response and general health.⁶ Factors that increase the mortality risk of COVID-19 patients are not completely known yet. Though hyperthyroidism especially low T3 has been reported to have poor outcomes, such as long hospital stays and mortality, as well as higher risks of severe and fatal COVID-19 disease. Güven *et al*¹² showed that thyrotoxicosis does not have a negative effect on COVID-19 outcomes but if it is left untreated, it can lead to left ventricular hypertrophy and congestive heart failure, which might worsen the outcomes of COVID-19. Pizzocaro *et al*¹³ investigated the outcome of SARS-CoV-2 related thyrotoxicosis in survivors of COVID-19. The study involved 29 cases with primary thyrotoxicosis diagnosed after hospitalization for COVID-19 and then followed up after at least 30 days after discharge, found most cases of SARS-CoV-2-related thyrotoxicosis normalize within a few weeks after resolution. Nakamura *et al*¹⁴ performed an analysis of the thyroid function in Japanese patients with COVID-19 and concluded that the mortality rate of patients with normal and low TSH levels did not differ markedly. In our study, seven of those who had subclinical hyperthyroidism, had either mild or moderately severe COVID infection and among 10 who had hyperthyroidism, only one had severe COVID infection.

A prospective observational study by Lui *et al*.⁴ found abnormal thyroid function tests, with impaired thyroid-stimulating hormone in 25 patients (13.1%), suggesting SARS-CoV-2 could directly induce viral thyroiditis. There have been reports that SARS-CoV-2 may act as a trigger for autoimmune thyroiditis though early in the course of disease.^{1,5} Mateu-Salat *et al*¹⁵ documented two cases of COVID-19-related Graves' disease: one with a history of Graves' disease documented as being in remission for over 30 years, and the other without any documented history of thyroid disease. Muller *et al*,⁵ also report the association of subacute thyroiditis and COVID-19. In our study however we had 1 case of grave disease and two cases of thyroiditis post covid infection. However, in a similar study conducted by Chen *et al*,³ in 50 patients with COVID-19 in China, demonstrated an overall decrease in TSH, total thyroxine (T4), and triiodothyronine (T3), more consistent with a nonthyroidal disease pattern.

Multicentric large prospective studies are needed to validate the findings of current study. However, the findings shed light on the need for vigilance on part of treating physician as new-onset or relapsed hyperthyroidism is possible after COVID-19 infection. These patients are also required to be further assessed for thyroid profile to see if this dysfunction persist or recovers with time.

Overall, subclinical hyperthyroidism was seen in 20.6% post COVID dysthyroid population in this study. Therefore, this indicates that, it still requires further evaluation and should not be underestimated, because thyroid dysfunction should be considered a possible manifestation of COVID-19.

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