



COVID-19 AND THYROID DISEASE

COVID-19 infection and thyroid function

BACKGROUND

A novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) is responsible for the coronavirus 19 (COVID-19) global pandemic that began in late 2019. COVID-19 infection can range from a very mild or asymptomatic presentation to critical illness and death. Along with multiple organ systems that may be affected by COVID-19 is the thyroid gland. In some patients, infection with COVID-19 may cause a hyper-sensitive immune reaction and widespread inflammation known as a “cytokine storm”. Since the most common causes of thyroid problems result from antibodies attacking the thyroid (autoimmune thyroid disease), this immune system activation may also cause inflammation and dysfunction of the thyroid. The thyroid also can be affected indirectly as a result of the overall severity of the infection. These 2 studies report changes in thyroid function in patients with COVID-19 infection.

Lania et al sought to characterize thyroid function in patients hospitalized with COVID-19 infection. The goal of the study was to assess thyroid function in all patients admitted to the hospital with confirmed COVID-19 to determine if this infection was associated with abnormalities in thyroid function.

Muller et al report the association of subacute thyroiditis and COVID-19. The aim of this study was to evaluate the frequency subacute thyroiditis in COVID-19 patients as compared to non-COVID patients admitted to the intensive care unit in Italy.

THE FULL ARTICLE TITLE

Lania A et al on behalf of Humanitas COVID-19 Task Force. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. *Eur J Endocrinol*. 2020. doi: 10.1530/EJE-20-0335.PMID: 32698147

SUMMARY OF THE STUDY

This study is a medical record review that examines thyroid function in patients hospitalized in one center in Italy with COVID-19 infection. They excluded all

patients who were on treatment for either hyperthyroidism or hypothyroidism. Additionally, patients were not included if they were taking drugs known to alter thyroid function or if they were critically ill requiring ventilator support. TSH was measured routinely and Free T₄ and Free T₃ levels were assessed if the TSH was abnormal. A marker of inflammation (Interleukin-6 (IL-6)) was also measured.

A total of 287 patients were included in the study, of which 214 (74.6%) demonstrated normal thyroid function. Of those with abnormal thyroid tests, 58 (20.2%) showed lab tests consistent with hyperthyroidism (low TSH) and 15 (5.2%) with hypothyroidism (high TSH). Of those with a low TSH, most were mildly low, but 31 of 58 patients (53%) had elevated FreeT₄ levels indicating overt hyperthyroidism. In addition, 10 patients with overt hyperthyroidism had atrial fibrillation, a known heart complication of hyperthyroidism. TSH was lower with increasing age and higher IL-6 levels. Lower death rates were seen in patients with normal TSH levels.

Overall, the results of this study indicated that abnormal thyroid function is common in patients with COVID-19, particularly hyperthyroidism, and that TSH suppression appears to be associated with higher levels of the inflammatory cytokine IL-6. Although more research is needed, these investigators suggest that COVID-19 associated with systemic immune activation may possibly cause thyroid inflammation and result in hyperthyroidism.

THE FULL ARTICLE TITLE

Muller I et al 2020 SARS-CoV-2-related atypical thyroiditis. *Lancet Diabetes Endocrinol*. Epub 2020 Jul 30. PMID: 32738929.

SUMMARY OF THE STUDY

The study evaluated 93 consecutive patients admitted for COVID-19 infection to the ICU at Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico in Milan, Italy, in 2020. The non-COVID group included 101 consecutive ICU patients with thyroid function test



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results available admitted at the same institution in 2019. Patients with pre-existing thyroid disorders were excluded, therefore, data from 78 patients in the COVID-19 group and 85 in the control group was analyzed. Of note, pre-existing thyroid disease was not more frequent in the COVID-19 group, suggesting that thyroid disease does not predispose to COVID-19 infection.

The patients had serum thyroid function tests measured within the first 2 days after their ICU admission. Serum thyroid stimulating hormone (TSH) was measured in all patients, while free thyroxine (FT₄) and free triiodothyronine (FT₃) levels were measured if the TSH was abnormal. Serum C-reactive protein (CRP) was also measured; this is a general marker of inflammation, which increases in subacute thyroiditis. A subset of the COVID-19–infected patients had follow-up tests 1.5 to 2 months after the initial infection when they were COVID-negative, including serum thyroid function tests and thyroid imaging.

The COVID-19 group was younger and included more males than females as compared to the control, non-COVID group (average age, 65 vs. 73 years; males, 69% vs. 56%). In the COVID-19 group, 13 of 85 (15%) patients had thyroid function tests showing hyperthyroidism, as compared with 1 of 78 (1%) in the control group. More men than women had abnormal thyroid function tests (64% vs. 36%). The hyperthyroid patients had low serum TSH levels, while serum free T₄ levels remained within normal range and were similar in both groups.

Serum free T₃ levels were low and similar in both groups. Serum CRP levels were higher in the COVID-19 group than in the controls. No patient reported neck pain, which is usually associated with an episode of subacute thyroiditis.

Among the patients from the COVID-19 group who were followed-up after discharge, 6 patients with initial thyroid tests showing hyperthyroidism had normal thyroid function tests 1.5 to 2 months later. Some of these patients had a thyroid ultrasound and scan, which showed clear evidence of thyroiditis. This supports the idea that the abnormal thyroid function tests noted in COVID-19 patients could be secondary to subacute thyroiditis.

WHAT ARE THE IMPLICATIONS OF THESE STUDIES?

The results of this study indicated that abnormal thyroid function is common in patients with COVID-19, with the most common finding a low TSH. The low TSH levels appear to be associated with higher levels of the inflammatory cytokine IL-6 in the Lania study while the Muller study observed that a substantial proportion of COVID-19 patients requiring intensive care have low TSH levels initially, possibly suggestive of the hyperthyroid phase of subacute thyroiditis. Although more research is needed, these studies suggest that COVID-19 associated with systemic immune activation may possibly cause thyroid inflammation and result in hyperthyroidism or thyroiditis.

— Alina Gavrila, MD, MMSc, and
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ATA THYROID BROCHURE AND WEBSITE LINKS

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

Thyroiditis: <https://www.thyroid.org/thyroiditis/>

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

Novel Coronavirus (COVID-19) and the Thyroid: <https://www.thyroid.org/covid-19/coronavirus-frequently-asked-questions/>



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ABBREVIATIONS & DEFINITIONS

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Subclinical Hyperthyroidism: a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.

Subacute thyroiditis: acute inflammation of the thyroid gland probably caused by a virus that usually follows an upper respiratory infection. Symptoms include fever and thyroid tenderness. This is a self-limited condition with three clinical phases: hyperthyroidism, hypothyroidism and then return to normal function. Alternative Names: deQuervain's thyroiditis; granulomatous giant cell thyroiditis.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Thyroxine (T₄): the major hormone produced by the thyroid gland. T₄ gets converted to the active hormone T₃ in various tissues in the body.

Triiodothyronine (T₃): the active thyroid hormone, usually produced from thyroxine.

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

Thyroid ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize abnormal areas within the thyroid.

Thyroid scan: this imaging test uses a small amount of a radioactive substance, radioactive iodine or technetium-99m, to obtain a picture of the thyroid gland.

