ECRONICON OPEN ACCESS

EC ENDOCRINOLOGY AND METABOLIC RESEARCH

Editorial

Thyroid Disease and COVID-19. Any Relationship?

Graciela Cremaschi*

Neuroimmunomodulation and Molecular Oncology Laboratory, Institute for Biomedical Research (BIOMED), National Research Council of Argentina (CONICET), Catholic University of Argentina (UCA), C1107AFB Ciudad Autónoma de Buenos Aires, Argentina

***Corresponding Author:** Graciela Cremaschi, Neuroimmunomodulation and Molecular Oncology Laboratory, Institute for Biomedical Research (BIOMED), National Research Council of Argentina (CONICET), Catholic University of Argentina (UCA), C1107AFB Ciudad Autónoma de Buenos Aires, Argentina.

Received: January 07, 2021; **Published:** January 30, 2021

Since its outbreak in the city of Wuhan, China in December 2019, coronavirus disease 2019 (COVID-19), caused by the new type of coronavirus identified as SARS-CoV-2, has spread all around the world. Since then, the mechanisms involved in the differential progression of the respiratory illness and the body organs that are affected by the virus have been under medical scientific focus. The risk of severe COVID-19 infection is known to be higher in the elderly population and in those with underlying health conditions, including cardiovascular disease, chronic respiratory disease, chronic kidney disease, neurological disorders, hypertension, but also endocrine disorders, among others [1]. Referring to endocrine comorbidities, COVID-19 patients with diabetes are at high risk for serious illness, but people with other endocrine diseases such as obesity, malnutrition, and adrenal insufficiency can also be severely affected if they contract the virus [2]. In high-risk patients, SARS-CoV-2 infection can cause both pulmonary symptoms and systemic inflammation, determining multiorgan dysfunction [3]. Among the multiple organs that can be affected by COVID-19 is the thyroid gland. Since the main causes of thyroid diseases are autoimmune in origin, if the COVID-19 infection causes an overactive immune reaction and generalized inflammation ("cytokine storm"), it could also affect the thyroid.

SARS-CoV-2 virus can lead to direct infection of thyroid cells. In fact, SARS-CoV-2 use angiotensin converting-enzyme 2 (ACE2) receptor to entry and infect host cells, and ACE2 expression levels are high in thyroid glands, even more than in lungs [4-6]. Also, indirect injury of the gland could result from the immunoinflammatory responses to the virus. Viral infections are one of the environmental factors that play a crucial role in autoimmune thyroid disorders (AITD) etiology, through altering immune-endocrine interactions [7]. They could trigger the exposure of thyroid antigens (through cell apoptosis or necrosis) to the immune system, they could form altered antigens with molecular mimicry with thyroid cells and could induce proinflammatory cytokine and chemokine secretion, aberrant HLA-DR expression and Toll-like receptor activation (8). Several studies support that viral infections like Parvovirus B19, Epstein-Barr virus, and mostly Hepatitis C virus are potential involved in triggering AITD (for review see 9) and histopathological studies have shown that previous SARS can cause extensive necrosis and apoptosis of thyroid follicular and parafollicular cells [10].

Abnormal thyroid function was found in COVID-19 patients, with thyrotoxicosis being the most prevalent finding [11,12]. This appears to be associated with higher serum levels of IL-6 (an inflammatory cytokine) [11] or C-reactive protein (a general inflammation marker) [12], thus suggesting that COVID-19 activation of systemic immunity would lead to thyroid inflammation. Although these patients were not found to develop subacute thyroiditis (SAT), their TSH values were compatible with the hyperthyroid phase of SAT. Moreover, there are several reports of SAT cases in patients with COVID-19, that presented with neck pain, fever in most cases and high levels of free T4 (fT4) and free T3 (fT3) together with the low TSH values, although without positive anti-TSH receptor (TRAb) and anti-thyroperoxidase (TPOAb) autoantibodies [13-18].

By the other hand, there is some evidence that primary hypothyroidism could occur during COVID-19 infection, although lower number of hypothyroid patients than those with low levels of TSH or overt hyperthyroidism were reported [11]. Hypothyroidism was found only in 5 of 140 patients with COVID-19, and 4 of them developed severe disease [19]. In these last patients, non-thyroidal illness syndrome (NTIS) was also described [20,21]. NTIS refers to changes in serum thyroid hormone levels observed in seriously ill or starving patients without hypothalamic-pituitary-thyroid dysfunction. The changes include low fT3, usually elevated reverse T3, normal or low TSH, and if prolonged, low fT4 [22]. NTIS would be a predictor of poor outcome in severe and critical patients with COVID-19 and a clinical phase II trial to evaluate the efficacy and safety of T3 administration in critically ill patients requiring respiratory support was recently started [23].

Finally, there are no firm evidences showing that AITD patients have higher risk of COVID-19, but uncontrolled thyrotoxicosis may result in more severe complications including thyroid storm, and a recent meta-analysis showed an enhanced risk of severe COVID-19 infection in thyroid disease patients [24]. In fact, immunocompromised people belong to the risk population for SARS-CoV-2 infection and hypothyroid conditions are associated to immunosuppression [25]. So, it would be advisable to monitor thyroid disease patients with suspected COVID-19, to identify early signs of disease progression. Currently, medical advices for the management of thyroid dysfunction during the COVID-19 pandemic has been well established [26].

Bibliography

1. CDC guidance on individuals at higher risk of severe COVID-19 disease". WHO (2020).

2. Puig M., *et al*. "COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology". *Endocrine* 68 (2020): 2-5.

3. Guo YR., *et al*. "The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak-an update on the status". *Military Medical Research* 7 (2020): 11.

4. Lazartigues E., *et al*. "Endocrine significance of SARS-CoV-2's reliance on ACE2". *Endocrinology* 161 (2020): bqaa108.

5. Ziegler CGK., *et al*. "SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues". *Cell* 181 (2020): 1016-1035.

6. Li MY., *et al*. "Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues". *Infectious Diseases of Poverty* 9 (2020): 1-7.

7. Klecha AJ., *et al*. "Immune-endocrine interactions in autoimmune thyroid diseases". *Neuro Immuno Modulation* 15 (2008): 68-75.

8. Desailloud R and Hober D. "Viruses and thyroiditis: an update". *Virology Journal* 6 (2009):5.

9. Antonelli A., *et al*. "Graves' disease: epidemiology, genetic and environmental risk factors and viruses". *Best Practice and Research: Clinical Endocrinology and Metabolism* 34 (2020): 101387.

10. Wei L., *et al*. "Pathology of the thyroid in severe acute respiratory syndrome". *Human Pathology* 38 (2007): 95-102.

11. Lania A., *et al*. "Thyrotoxicosis in patients with COVID-19: the THYRCOV study". *European Journal of Endocrinology* 183 (2020): 381-387.

12. Muller I., *et al*. "SARS-CoV-2-related atypical thyroiditis". *The Lancet Diabetes and Endocrinology* 8 (2020): 739-741.

13. Asfuroglu Kalkan E and Ates I. "A case of subacute thyroiditis associated with Covid-19 infection". *Journal of Endocrinological Investigation* 43 (2020): 1173-1174.

14. Brancatella A., *et al*. "Subacute thyroiditis after sars-COV-2 infection". *The Journal of Clinical Endocrinology and Metabolism* 105 (2020): dgaa276.

15. Ippolito S., *et al*. "SARS-CoV-2: A potential trigger for subacute thyroiditis? Insights from a case report". *Journal of Endocrinological Investigation* 43 (2020): 1171-1172.

16. Guven M. "Subacute Thyroiditis in the Course of Coronavirus Disease 2019: A Case Report". *Journal of Endocrinology and Metabolism* 10 (2020): 110-112.

17. Ruggeri RM., *et al*. "Subacute thyroiditis in a patient infected with SARS-COV-2: An endocrine complication linked to the COVID-19 pandemic". *Hormones* (2020): 1-3.

18. Mattar SAM., *et al*. "Subacute thyroiditis associated with COVID-19". *BMJ Case Reports* 13 (2020): e237336.

19. Zhang J., *et al*. "Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China". *Allergy* 75 (2020): 1730-1741.

20. Khoo B., *et al*. "Thyroid function before, during and after COVID-19". *The Journal of Clinical Endocrinology and Metabolism* 12 (2020): dgaa830.

21. Chen M., *et al*. "Thyroid function analysis in 50 patients with COVID-19: a retrospective study". *Thyroid* (2020): 1-4.

22. Fliers E., *et al*. "Thyroid function in critically ill patients". *The Lancet Diabetes and Endocrinology* . 3 (2015): 816-825.

23. Pantos C., *et al*. "Triiodothyronine for the treatment of critically ill patients with COVID-19 infection: A structured summary of a study protocol for a randomised controlled trial". *Trials* 21 (2020): 573.

24. Hariyanto TI and Kurniawan A. "Thyroid disease is associated with severe coronavirus disease 2019 (COVID-19) infection". *Diabetes and Metabolic Syndrome* 14 (2020): 1429-1430.

25. Paulazo MA., *et al*. "Hypothyroidism-related zinc deficiency leads to suppression of T lymphocyte activity". *Endocrine* 66 (2019): 266-277.

26. Boelaert K., *et al*. "Endocrinology in the time of COVID-19: Management of hyperthyroidism and hypothyroidism". *European Journal of Endocrinology* 183 (2020): G33-G39.

Volume 6 Issue 2 Febuary 2021