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SARS-COV2 VIRUS AND THYROID GLAND DISORDERS; A REVIEW

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SARS-COV2 ვირუსი და ფარისებრი ჯირკვლის დაავადებები

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რეზიუმე

კვლევა მიზნად ისახავდა SARS-COV2 ვირუსის გავლენის შესწავლას ფარისებრ ჯირკვალზე. მიუხედავად კონტრასტული შედეგებისა, მზარდი მტკიცებულებების მიხედვით, SARS-COV2 ვირუსი ფარისებრი ჯირკვლის ფუნქციის დარღვევებს იწვევს, რაც, ძირითადად, ქვემწვავე თირეოიდიტის, არაფარისებრი ჯირკვლის დაავადების სინდრომისა და ჰიპოთირეოზის სახით ვლინდება. თავის მხრივ, ფარისებრი ჯირკვლის დარღვევები გავლენას ახდენენ SARS-COV2 ვირუსით გამოწვეული ინფექციური დაავადების COVID-19-ის მიმდინარეობის სიმძიმესა და გამოსავალზე. ეს ურთიერთქმედება კომპლექსურ ხასიათს ატარებს. ქვემწვავე თირეოიდიტი ფარისებრი ჯირკვლის ყველაზე გავრცელებული დარღვევაა და, შესაძლოა, COVID-19-ის პოტენციურ გრძელვადიან გართულებად ჩამოყალიბდეს.

Background: The recent respiratory infection pandemics showed that they are a great public health problem worldwide and a serious disease and economic burden to all populations. A newly emerged disease – COVID-19, caused by SARS-CoV2 virus, rapidly acquired pandemic patterns in 2020. Viral infections are frequently cited as a major environmental factor implicated in subacute thyroiditis and autoimmune thyroid diseases [1,8]. Clusters of the disease have been reported during outbreaks of viral infection. Onset of the disease are observed between June and September and this seasonal distribution is almost identical to that of established infections due to some enteroviruses (Echovirus, Coxsackievirus A and B), suggesting that enterovirus infections might be responsible for a large proportion of cases [2,3]. Subacute thyroiditis has occurred in epidemic form: patients with subacute thyroiditis diagnosed during a mumps epidemic were found to have circulating anti-mumps antibodies even without clinical evidence of mumps [4]. Patients with subacute thyroiditis, who had no clinical evidence of viral disease, demonstrated increases by at least four times in viral antibodies. These viral antibodies included antibodies to mumps virus, but also coxsackie, adenovirus and influenzae. Coxsackie viral antibodies were the most commonly found, and the changes in their titers most closely approximated the course of the disease [5]. Thyroid disorders in patients with congenital rubella were first reported in 1975 [6]. A substantial number of patients with SARS have shown abnormalities in thyroid function. As SARS is a disease known to cause multiple organ injury, it has been supposed that SARS could have a harmful effect on the thyroid gland [7]. However, low serum triiodothyronine and thyroxine levels associated with decreased TSH concentration are in favor of central hypothyroidism assumed to be of viral origin [8]. In a recent study Weider T. et al. investigated the presence of enteroviruses, parvovirus B19, HHV-6, EBV, CMV and HCV in addition to five gastroenteric viruses (adenovirus, astrovirus, norovirus, rotavirus and sapovirus) in thyroid tissue from AITD (autoimmune thyroid disease) patients and controls and concluded that viruses may represent environmental triggers of thyroid autoimmunity. Actually, the findings may add evidence to this possibility proving that multiple viral agents are capable of producing unapparent infection of the gland [9].

Aim: The study aimed to identify whether COVID-19 infection impact on thyroid gland function based on the literature review.

Methods: Thyroid gland disorders were selected in accordance with ICD-10: E00-E04 – Subclinical iodine deficiency hypothyreosis and other forms of hypothyreosis, E06 – Thyroiditis, presented by: EO6.0Acute thyroiditis, E06.1Subacute thyroiditis, EO6.2Chronic thyroiditis with transient thyrotoxicosis and E06.3Autoimmune thyroiditis, E0-05 – Thyrotoxicosis, C73 – Thyroid cancer. References were searched in PubMed and ResearchGate for articles published during COVID-19 pandemic. Preference was given to studies, published in 2021and 2022. The MeSH terms were based on the thyroid gland pathology in accordance with ICD-10.

Results: Studies showed that the prevalence of thyroid dysfunction in patients positive for COVID-19 virus varied widely between 13-64% [10] and SARS-CoV2 can contribute to increased rates and severity of thyroid dysfunction in COVID-19 patients. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can lead to multiorgan dysfunction through pulmonary and systemic inflammation. Infection also affects the thyroid gland directly via cytopathological effects of the virus or indirectly through cytokines, complement systems and coagulation mechanisms. The direct cytopathological damage of host cells and the dysregulated immune response caused by the severe acute respiratory syndrome coronavirus 2 is assumed to be the primary underlying mechanisms of COVID-19 [11]. Though cases of subacute thyroiditis developing secondarily to SARS-CoV-2 virus infection has been described in literature during the pandemic induced by hypophysitis or by hypothalamic dysfunction [7], growing evidences suggest that subacute thyroiditis is a prevalent disease during COVID-19 epidemic years [12-15]. Furthermore, independent of any other underlying causes, patients with hyperthyroidism are likely to be at risk for poor outcomes, such as long hospital stay and mortality, as well as higher risks of severe and fatal COVID-19 disease [16]. Given that thyroid abnormalities have been linked to disorders such as diabetes, obesity, kidney dysfunction and liver disease, and that patients with these conditions are more likely to contract COVID-19 [17], an underlying poorly-controlled thyroid disorder might exacerbate SARS-CoV-2 infection [18,19], however contrasting results have been reported in the reviewed literature across the thyroid disorders. In a study with 50 patients confirmed with moderate to critical COVID-19 with no history of thyroid disease, Chen et al. reported altered thyroid function in more than 60% of patients [20]. A Chinese cohort of 367 patients with predominantly mild to moderate COVID-19 detected abnormal thyroid function in 62 patients (16,9%). Twenty-seven patients (7,4%) had non-thyroidal illness syndrome (NTIS) and 30 patients (8,2%) had biochemical alterations that were suggestive of distinct phases of thyroiditis such as: isolated low TSH and high-normal fT4, isolated slightly elevated fT_3, high-normal Ft4 or isolated low fT4. None had overt thyrotoxicosis. Of these 30 patients with subnormal TSH, 5 presented anti-TPO or anti-TSHR autoantibodies, suggesting an autoimmune component in these cases. Pre-existing autoimmune thyroid disorder was present in 5 patients [21]. In contrast with the previous studies, Khoo and collaborators, did not found any case of overt thyrotoxicosis in a cohort of 334 patients admitted with COVID-19 in intensive therapy unit [22]. Most COVID-19 patients (86.6%) were euthyroid but 5.7% present subclinical hyperthyroidism and a small proportion present overt hypothyroidism (0,6%), which did not differ from non-COVID patients. A small significant reduction in TSH and fT_4 was observed in patients with COVID-19 when compared with non-COVID-19 patients which might be compatible with a nonthyroidal illness syndrome and did not justify any treatment. A retrospective study conducted in the New York City health system evaluated a cohort of 3703 COVID-19 patients, of which 251 patients (6.8%) had pre-existing hypothyroidism. The authors found that hypothyroidism was not associated with increased risk of hospitalization or an increased risk of mechanical ventilation or death [23]. Other studies have also shown that the prevalence of hypothyroidism appears similar in COVID-19 patients compared to the general population, which indicates that hypothyroidism does not increase the chance of COVID-19 infection, and also that hypothyroidism is not associated with a greater COVID-19 death risk [24,25]. Little is known regarding the effect of COVID-19 on the development or progression on thyroid cancer, or the development or progression of thyroid cancer, or susceptibility of people with thyroid cancer to Cancer or COVID-19-related complications [17,41]. Early data suggests that COVID-19 per se does not worsen the outcome of cancer, but as the pandemic

continues, with investigations and treatment delay, morbidity and mortality from thyroid cancer may increase [26-28], controversial results were presented by Guan WJ et al. Based on the study on 1590 hospitalized patients across mainland China between 11 December 2019 and 31 January 2020, Guan WJ et al. concluded that malignancy predisposed to adverse clinical outcomes in patients with COVID-19 [29]. Relatively more consistent results in the reviewed literature were found on thyroiditis. Subacute thyroiditis (SAT; also known as de Quervain thyroiditis) is a self-limiting disorder consisting of three phases: painful swelling of the thyroid, hypothyroidism and euthyroidism. In May of 2020 an Italian case-report provided the first case of subacute thyroiditis (SAT) potentially associated with a prior mild COVID-19 infection [30]. Subsequent studies also reported additional isolated cases of painful symptomatic SAT, developing secondarily to SARS-CoV-2 infection and reinforcing a possible association between SARS-CoV-2 infection and SAT [31-38,13,14]. Studies regarding thyroid function and COVID-19 in adults and children suggest that the virus can contribute to increased rates and severity of thyroid dysfunction [10,38-40]. One systematic review incorporating 1,237 adult patients, identified a positive correlation between thyroid dysfunction and clinical severity of COVID-19, with prevalence of thyroid dysfunction in patients positive for COVID-19 varying between 13-64% [10]. The study on the effect of COVID-19 on the presentation of thyroid disease in children showed that the distribution of thyroid presentation by year increased over the study period; the greatest number of thyroid presentations occurred in 2021 (n=60, 25% of total over time period) and the fewest in 2020 (n=10, 4% of total over time period). There were no statistically significant differences in biochemistry, antibody status or other clinical characteristics between those who presented with hyperthyroidism prior to the pandemic or after [40]. SAT could be a potential long-term complication of COVID-19 [40]. Though prevalence of manifestations of thyroid dysfunction differs by its type across studies, thyroid dysfunction is common [17,16,31,35,43] and SAT could be potential long-term complication of COVID-19. Interestingly, it's of note that several studies have emphasized a relationship/bidirectional impact or interaction between COVID-19 infection and SAT [16-18,31,38]. According to these studies the interaction between the thyroid gland and COVID-19 is complex and bidirectional: on one hand, similarly to other respiratory viruses, thyroid dysfunction is also common in patients with COVID-19 infection.

Conclusion: SARS-Cov2 virus effects functioning of thyroid gland and aggravates existing thyroiditis, there also might be a complex and bidirectional interaction between COVID-19 and thyroiditis.

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SARS-COV2 VIRUS AND THYROID GLAND DISORDERS; A REVIEW

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SUMMARY

The study aimed to identify whether COVID-19 infection impact on thyroid gland function. SAR-CoV-2 virus impacts on thyroid gland function. Thyroid dysfunction is common and subacute thyroiditis is a prevalent thyroid gland disorder tend to be a potential long-term complication of COVID-19. The interaction between the thyroid gland and COVID-19 is complex and bidirectional.

Keywords: SAR-CoV-2 virus, thyroid gland, thyroiditis, relationship