COVID-19 И ЩИТОВИДНАЯ ЖЕЛЕЗА:РАСПРОСТРАНЁННОСТЬ ВО ВСЁМ МИРЕ
ОБЗОР ЛИТЕРАТУРЫ

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Аннотация: по информации Всемирной организации здравоохранения в 2020 году новая коронавирусная инфекция Covid-19 очень быстро распространилась во многих странах и достигла уровня пандемии. В свою очередь, эта проблема стала одной из глобальных проблем всего мира, в том числе и ВОЗ. В этом обзоре обобщены последние достижения в области знаний о дисфункции щитовидной железы, вызванной коронавирусной инфекцией (SARS CoV-2).Дисфункция щитовидной железы при SARS-CoV-2, включая аутоиммунный тиреоидит, болезнь Грейвса, нетиреоидные состояния, тиреотоксикоз, болезнь Хашимото. Обсуждение результатов относительно роли тиреоидита во время и после развития короновирусной болезни в 2019 г.
Ключевые слова: *коронавирусная болезнь 2019, щитовидная железа, гипертиреоз, тиреоидит, гипотиреоз, рак щитовидной железы.*

COVID-19 ВА ҚАЛҚОНСИМОН БЕЗ: ДУНЁ БЎЙИЧА ТАРҚАЛГАНЛИГИ АДАБИЁТЛАРИ ШАРҲИ

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Аннотация: Жаҳон соғлиқни сақлаш ташкилотининг 2020 йилдаги маълумотлаотга кўра, янги коронавирус инфекцияси Covid-19 кўплаб мамлакатларда жуда тез тарқалди ва пандемия даражасига етди. Ўз навбатида бу муаммо бутун дунёнинг, қолаверса ЖССТ нинг глобал муаммоларидан бўлиб келмоқда. Ушбу шарҳда кронавирус (SARS CoV-2) инфекцияси туфайли қалқонсимон без дисфункцияси хақидаги билимлардан сўнгги ютуқлар хақида тўлиқ маълумот берилган.SARS-CoV-2 ning қалқонсимон без дисфункцияси,шужумладанаутоиммунтиреоидит,Грейвскасаллиги,қалқонсимонбезкасаллигибўлмаганхолатлар,тиреотоксикоз,Хашимототиреоидити2019йилдакороновирускасаллигидавридаваундан кейингиривожланишидагиролигаоиднатижалармухокамасикелтирилган.
Калит сўзлар: *коронавирус касаллиги 2019, қалқонсимон без, гипертиреоз, тиреоидит, гипотиреоз, қалқонсимон без саратони.*

THE THYROID AND COVID-19: WORLDWIDE PREVALENCE REVIEW OF LITERATURE

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Annotation: According to the World Health organization in 2020, a new coronavirus infection Covid-19 spread very quickly in many countries and reached the level of a pandemic. In turn, this problem has become one of the global problems of the whole world, including the WHO. This review summarizes the latest advances in knowledge about coronavirus-associated thyroid dysfunction (SARS CoV-2). Thyroid dysfunction in SARS-CoV-2, including autoimmune thyroiditis, Graves' disease, non-thyroid conditions, thyrotoxicosis, Hashimoto's disease. Discussion of the results regarding the role of thyroiditis during and after the development of coronovirus disease in 2019.
Keywords: *coronavirus disease 2019, thyroid, hyperthyroidism, thyroiditis, hypothyroidism, thyroid cancer.*

Foreword: The coronavirus disease, COVID-19, is a highly infectious disease caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), and this virus causes severe acute respiratory syndrome (SARS). Like SARS-CoV-2, SARS-CoV-1 enters human tissues through the angiotensin-converting enzyme 2 (ATF2) receptor [2]. Histopathology of the thyroid gland shows that during the SARS CoV-1 epidemic, para follicular and epithelial follicular cells in the thyroid gland are severely damaged. saw In turn, the virus caused the destruction of the epithelium in the thyroid gland and their rupture. However, there was no inflammatory infiltration or cell necrosis, consistent with the hypothesis that SARS-CoV-1 infection causes thyroid damage and apoptosis. Overall, the thyroid pathology induced by SARS-CoV-1 and SARS-CoV-2 infection may suggest that although SARS-CoV-2 is more causative, its effect on the thyroid gland is relatively less severe than that of SARS-CoV-1.3 Most patients with COVID-19 are asymptomatic or present with mild flu-like symptoms. But about 14% of patients have severe symptoms, and 5% of patients have severe symptoms.3,4 COVID-19 is caused by SARS-CoV-2 infection of the lung parenchyma. Viral RNA is present in the blood, stool, and urine of patients with COVID-19. This suggests that it is SARS-COV-2 and can bind and interact with ATF2, allowing it to spread to organs other than the lungs. SARS-CoV-2 can cause inflammation of the lungs and systemic diseases. As a result, the risk of developing organ failure is high [2,7,8]. The diversity of clinical manifestations and multi organ failure of COVID-19, both direct (due to viral infection of target cells) and indirect (resulting from anomalous immune-inflammatory responses against the virus, involving the coagulation, cytokine, and complement systems) is connected [2,9–13]. The most common critical complications of COVID-19 are acute respiratory distress syndrome (ARDS), respiratory failure, sepsis, acute cardiac injury, and heart failure [7].The tissue tropisms of SARS-CoV-2 are cardiovascular, coagulative, gastrointestinal, and nervous systems [3]. In addition, among numerous endocrine glands, the pancreas, testes, ovaries, adrenal glands, thyroid gland, and pituitary gland were found to express ATF, which are considered target tissues of SARS-CoV-2 [14,15]. Infection with SARS-CoV-2 can aggravate existing diseases in endocrine organs or cause new anomalies. In turn, endocrine diseases worsen the prognosis of SOVID-19 [3,5,16]. Because ATF2 receptors are abundant in the thyroid parenchyma, the thyroid gland may be vulnerable to SARS-COV-2 infection [17 ,3]. In addition, Rotondi and colleagues18 thyroid follicular detected ATF2 receptor mRNA expression in their cells. This suggests that the thyroid gland may be a potential target of SARS-CoV-2 [3].Thyroid hormones and immunomodulatory signaling molecules are involved in the complex interaction between the thyroid gland and viral infection. Viruses can significantly affect thyroid function when linked to inflammation and immune responses [2]. Because thyroid hormones affect multiple organ systems, including the cardiovascular and respiratory systems, thyroid status has a direct impact on the course of COVID-19. can do. In addition, given the association of thyroid abnormalities with diseases such as diabetes, obesity, kidney dysfunction, and liver disease, patients with these conditions are at increased risk of contracting COVID-19.19 SARS-CoV-2 infection may exacerbate poorly controlled thyroid disorders [17,20]. In addition, viral infections are considered an important factor for the development of autoimmune thyroiditis. It should also be noted that T4 has been shown to activate existing human platelets, which may contribute to the pathological coagulation that occurs during COVID-19 infection [2]. Thus, a better understanding thyroid pathophysiology may help during SARS CoV-2 infection Correct and accurate interpretation of thyroid function test abnormalities Assessment of thyroid function facilitates more appropriate management, especially in patients with severe forms of infection. COVID-19 and the hypothalamus - relationship between the pituitary-thyroid axis. It has been mentioned that the infection produced by SARS-CoV-2 causes loss of smell and taste as a result of disrupting the existing nervous system and damaging the cranial nerves [21]. When 5 patients were dissected, the SARS genome was detected in the cytoplasm of many neurons of the hypothalamus and in the immune histochemical analysis of the adenohypophysis, and the amount of TTG hormones decreased. departure is determined. SARS-CoV-2 can spread through nerve axons because high levels of ATF2 trigger a cytokine storm. (IL)-6, IL-7, high circulating concentrations of interleukin (FNO)-α, tumor necrosis factor-α, a soluble version of IL-2, receptors and inflammatory chemokines have been identified during the cytokine storm induced by SARS-CoV-2 [23]. The -2 virus significantly affects TTG-producing cells, as a result of which the concentration of TTG in the

blood decreases and the reconnection of the pituitary endocrine axis is disturbed. These effects may involve four different mechanisms affecting TTG-producing cells:

1. Direct damage to the pituitary gland caused by SARS-CoV-2 (central TTG abnormality caused by viral hypo physitis)

2. Direct damage caused by anti-inflammatory cytokines and cytokine storm.

3. Chronic stress caused by hypoxia. 4. Effects of specific classes of drugs such as glucocorticoids [21].

Chenetal. and others. Patients with COVID-19 had lower serum TTG and um T3 compared to control patients [24].

The relationship between COVID-19 and the thyroid gland. Morphological and pathological changes. The pathogenesis of thyroid dysfunction induced by COVID-19 has not been studied but characterized. One theory is that the virus directly affects the thyroid gland. SARS-CoV-2 has the ability to pass through direct infiltration of the thyroid gland from the upper respiratory tract. Post-mortem examinations of individuals who died of COVID-19 revealed pathological abnormalities in various organs, including the thyroid gland. However, surprisingly, morphological abnormalities were not detected, but severe damage to thyroid follicles was discovered. Histological examination revealed the absence of lymphocytic infiltrate of the thyroid gland, but the presence of extensive apoptosis. causes fatal thyroiditis and causes the development of thyrotoxicosis [25,26]. In addition, despite the high expression of ATF2 in the thyroid gland, SARS CoV 2 was not detected in thyroid tissue by PTsR or immunohistochemistry [27–29]. Therefore, it has been hypothesized that the factors that prevent extimol virus infection are the follicular cells of the thyroid gland [3,15]. COVID-19 and hypothyroidism. Some studies worldwide have identified cases of primary hypothyroidism associated with COVID-19 [30–32]. Only 5.2% of 287 patients were admitted to non-intensive care and hypothyroidism was diagnosed [32]. In-hospital mortality was higher in patients with TTG levels above the reference range than in patients with TTG within the normal range, but length of hospitalization was similar in both groups. According to the results of the study of patients in Iran with SOVID-19, 5.4% of hospitalized patients had hypothyroidism, and the age of these patients was above 50. But the death rate was similar to that of patients without hypothyroidism [33].In a study comparing patients with mild or severe COVID-19 pneumonia, none of those hospitalized with mild pneumonia had hypothyroidism. In patients with severe pneumonia, hypothyroidism was found in 3.2% (2.4% manifest and 0.8% subclinical hypothyroidism) [34]. In addition, Tee et al.31 described a case of primary hypothyroidism occurring 7 days after resolution of COVID-19. , and this condition led to the development of chronic autoimmune thyroiditis. Thus, it has been proven that primary hypothyroidism can develop during or after COVID-19.[2]. Central hypothyroidism was diagnosed in several patients with anomalous endocrine disorders in the hypothalamus and pituitary system. Between 2% and 6% of hospitalized patients with COVID-19 had central hypothyroidism. Their serum T4 levels were low and TTG concentrations were low or normal. According to Chen and other authors, these hormonal changes disappeared after recovery from COVID-19. This suggests that COVID-19 may have an acute transient effect on GGS [24]. The results of this study show that the proportion of hypothyroidism was similar in hospitalized patients with or without COVID-19. 8 patients with thyroid dysfunction observed for an average of 55 days, from the hospital after discharge, hypothyroidism was diagnosed.

UTT examination confirmed autoimmune thyroiditis [30]. However, there were insufficient data whether autoimmune hypothyroidism was pre-existing or caused by SARS-COV-2 infection. Nevertheless, there is a clear correlation between the development of the cytokine release syndrome and the induction of autoimmunity by COVID-19, and this is consistent with the hypothesis that, while inducing autoimmune thyroiditis, COVID-19 also develops autoimmune hypothyroidism [26,35]. A prospective study of hospitalized patients with COVID-19 in Hong Kong. Investigations showed that most of them, 13.1% of patients had thyroid dysfunction, that is, low TTG concentration, 0.5% of 191 patients had high levels of TTG and Anti-TPO, and even after leaving the hospital, hypothyroidism remained in this patient [36]. In one study, 43 (9.9%) of 433 hospitalized patients with COVID-19 had hypothyroidism and were treated. This condition has been associated with severe COVID-19 [37]. A recent study demonstrated a higher mortality rate in patients with hypothyroidism and COVID-19 than in euthyroid patients, which is predicted to have a negative impact on the outcome of COVID-19 [32]. Another study found that hypothyroidism did not affect the

course of COVID-19 [17]. In one study, Gerven et al., patients with COVID-19 confirmed by nasopharyngeal swab analysis were registered and collected from an electronic medical database. 251 of 3703 (6.8%) patients with COVID-19 had pre-existing hypothyroidism. Female patients with hypothyroidism accounted for a higher percentage than males. (69% women vs. 43% men, p<0.001), non-Hispanic white ethnicities (45% vs. 26%, p<0.001). They had 2 comorbidities, overweight or obesity, arterial hypertension, and diabetes . (68% vs. 53% p<0.001). However, another study reported that preexisting hypothyroidism had no effect on the prognosis of COVID-19, including hospitalization, mechanical ventilation, and mortality [38].

A retrospective study in New York City further explored the role of hypothyroidism as a putative risk factor for poor prognosis in patients with COVID-19 [38]. There is some evidence for a specific link between lung injury associated with COVID-19 and the thyroid gland. T3 receptors are expressed on alveolar type 2 cells, one of the many cell types that respond to thyroid hormone. T3 increases the size and number of alveolar type 2 cells, stimulates the release of surfactant, and increases the activity of the sodium-potassium ATPase pump, which increases the fluid permeability of these cells. As a result, alveolar type 2 cells are able to absorb alveolar edema fluid and are thought to be involved in recovery from OSRD-induced lung injury. This fluid clearance is improved by administration of liothyronine (LT3) in rats rendered hypothyroid by methimazole therapy [17,39]. Patients with pulmonary fibrosis express significant amounts of deiodinase type 2 in their lungs, which may be related to low concentrations of T3 in lung tissue. Finally, inhaled liothyronine was shown to accelerate recovery from ORDS in two patients hospitalized with COVID-19 in a phase 1 trial at the University of Minnesota. and in a Phase 2 clinical trial (NCT 04115514) liothyronine is being tested as a therapy for O'RDS in humans caused by COVID-19. These findings highlight the importance of thyroid hormones in protecting the lung from injury, including injury associated with COVID-19[17].

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