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"A COMPREHENSIVE REVIEW OF THE INCREASE IN THYROID DISEASE CASES DUE TO THE COVID-19 PANDEMIC"

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ABSTRACT:
COVID-19is the pandemic of the new millennium, SARS-CoV-2, the virus responsible for COVID-19, has been associated with numerous post-infection complications.COVID-19 may result in systemic and pulmonary inflammation, which may have an impact on the function of multiple organs. Information about how COVID-19 and thyroid have emerged and are growing more quickly since March 2020.The virus that infects the thyroid gland and its function is well known to interact intricately with linked inflammatory-immune responses.SARS-CoV-2 combines ACE2 with Trans membrane protease 2 (TMPRSS2) is the essential molecular complex that infects host cells. Remarkably, ACE2 and the thyroid gland expresses TMPRSS2 at higher levels than the lungs do. Our review of the literature revealed more evidence that the entire hypothalamic-pituitary-thyroid (HPT) axis and the thyroid gland may be relevant targets of damage by SARS-CoV-2.To be more precise, thyroid disorders associated with COVID-19 include thyroid toxicosis, hypothyroidism, and nonthyroidal illness syndrome.

KEYWORD: SARS-CoV-2, COVID-19, Overactive thyroid functioning, Grave's illness syndrome, subacute thyroiditis, hypothyroidism, and nonthyroidal illness syndrome, hyperthyroidism.

INTRODUCTION:

The thyroid gland is shaped like a butterfly and is situated under the voice box on the front of the neck. Its two lobes are joined by a thin tissue known as the isthmus and are located on opposite sides of the trachea.[1] The production of thyroid hormones and preservation of the body's iodine balance depend on this gland, which weighs around 25 grams and has dimensions of roughly 5 cm in length, 3 cm in width, and 2 cm in thickness, with the isthmus measuring about 1.25 cm in height and width.[2] Follicular and parafollicular cells line the functional units of the thyroid gland under a microscope. The two main hormones produced by the gland are triiodothyronine (T3), which makes up approximately 10% and is active, and thyroxine (T4), which makes up approximately 90% and is inactive, and triiodothyronine (T3), which constitutes about 10% and is active. Additionally, it secretes the peptide hormone calcitonin. Thyroid hormones regulate metabolic rate and protein synthesis, while calcitonin is involved in calcium homeostasis.[3]

The secretion of T4 and T3 is regulated by thyroid-stimulating hormone (TSH), which in turn is controlled by thyrotropin-releasing hormone (TRH) produced by the hypothalamus, located in the brain above the pituitary gland and below the third ventricle as shown below.[4]

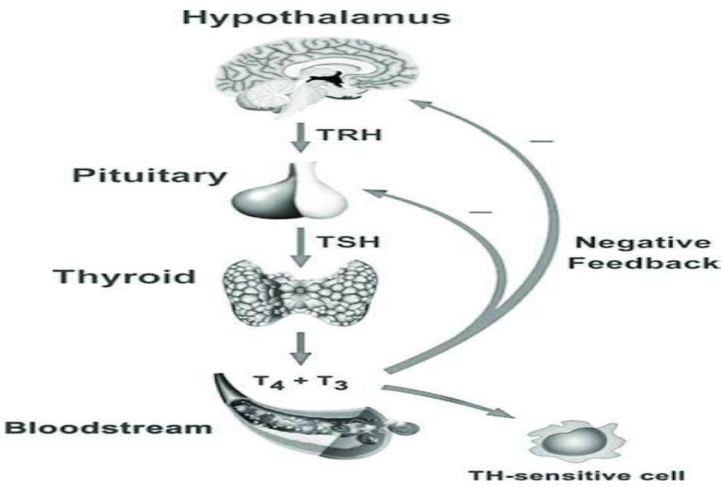

Figure:2:Hypothalemic-pituitary-thyroid axis

SARS-CoV-2, a new enveloped RNA beta coronavirus, is responsible for the infection.[5]Ever since it was initially discovered in Wuhan, COVID-19 is rapidly expanding, and the number of outbreaks is increasing exponentially.GloballyCOVID-19 has now claimed the lives of 761,700 people.[6]SARS-CoV-2 enters human tissues through the angiotensin converting enzyme 2 (ACE2) receptor, just like SARS-CoV-1 does.[7,8]

The discovery of SARS-CoV-2 in the thyroid tissues of COVID-19 patients who passed away has reinforced the link between thyroid dysfunction and the virus.[9]
The most recent research on SARS-CoV2 infection and thyroid is what we will examine next. First, we will review the association between COVID-19 and the thyroid gland, followed by an examination of COVID-19-related thyroid issues that have surfaced thus far; finally, we shall discuss the information about the clinical experiences with treating patients with thyroid complications during the COVID-19 pandemic.

Transmembrane protease serine 2 (TMPRSS2), in conjunction with ACE2, is the essential molecular complex that allows SARS-CoV-1 and SARS-CoV-2 to enter and infect host cells, as previously stated. Remarkably, the thyroid gland expresses ACE2 and TMPRSS2 at greater concentrations than the lungs do.[9,10]
However, very few studies have looked closely at the part COVID-19 plays in the development of autoimmune thyroid disease (ATD).thyroiditis is a general term for inflammation of the thyroid gland.[11] When compared to pre-pandemic, healthy controls, Anaya et al.[12]found an increase in the frequency of thyroperoxides antibody (TPOAb) in 120 COVID-19 hospital patients, suggesting an activation of SARS-CoV-2 driven thyroid autoimmunity. Lui et al [13]reported a consistent increase in TPOAb concentration, after being hospitalized for a duration of three months. However, the majority of the patients in this cohort were treated with interferon beta (IFN-beta). Because IFN-beta has been linked to thyroid induction autoimmunity, the authors have reconsidered treating a larger group of patients in order to provide a conclusive response.

Low TSH levels, attributed either to a destructive thyroiditis associated with thyrotoxicosis or to a non-thyroidal illness (NTI), were reported in several studies.[14-20]According to most studies TFTs usually normalize after COVID-19 recovery, but this finding has not been established in a large population.[16-20]

An additional longitudinal cohort study with 240 expectant mothers monitored for postpartum glycaemic condition revealed that SARS patient's Comparable thyroid risks were associated with CoV-2 infection.[21] impairment or recently developed thyroid autoimmunity within one to others who don't have it. However, more information from a broad band of survivors from primarily non-Serious COVID-19 is not present. These details are crucial because the majority of COVID-19 survivors only have minor symptoms, and recommendations for endocrine surveillance based on evidence There aren't enough lance in this population right now.[22]

CAUSES:

- Autoimmune Reactions
- Inflammation and Cytokine Storm
- Stress and Lifestyle Changes
- Delayed Healthcare
- Impact on Immune System
- Medication Effects
- Post-viral Syndrome

PATHOPHYSIOLOGY:

Hypothyroidism is the most frequent clinical thyroid malfunction,[23] affecting women and the elderly.[24] In adult women, it affects about 2% of them. and 0.2% in men who are adults, rising to 0.5% by the age of 75.[25] two types of hypothyroidism can be distinguished: primary hypothyroidism as well as its secondary. Principal Hypothyroidism is characterized by a lack of thyroid hormones. inadequate levels of thyroid hormone. Secondary hypothyroidism (central) happens far less frequently and is brought on by a diminished thyroid stimulation by TSH due to Hypothalamic or Hypopituitarism illness. The primary cause of hypothyroidism worldwide is a lack of iodine, particularly among areas where sufficient amounts of Iodine is available, Hashimoto's (autoimmune) thyroiditis is the disease's most frequent cause.[26]Iodine is necessary in order to produce THs**.** Almost 2 billion people, or one-third of the global population, were deficient in iodine in 2005 and at risk of getting iodine-related illnesses (IDDs).[27]
Women of reproductive age face the greatest risk of IDD because of its impact on fertility, pregnancy, and ovulation.[28]

An example of an autoimmune thyroiditis is Hashimoto's thyroiditis. This involves lymphocytic infiltration into the gland and generation of autoantibodies against Thyroid and thyroglobulin peroxidase. Thus, the structural component and the enzyme accountable for the hormone's synthesis are inhibited.[29]
Increased thyroid function brought on by an excessive amount of TH production and secretion is known as hyperthyroidism.[30]The incidence of hyperthyroidism is0.2–0.5% in women, which is around ten times greater compared to males. The primary reason for hyperthyroidism Graves' illness is prevalent in areas with high iodine levels. It causes the generation of antibodies directed against the TSH receptor causes the thyroid gland to become overactive and produces too much of TH.[31]Where iodine deficiency is prevalent, increased TH production brought on by toxic goitre and neoplasia is a significant contributor to hyperthyroidism.[32,33]
When the concentration of FT4 is within the reference range,[34,35] It is linked to low TSH levels (lower than the reference range). Elevations of TSH in the serum are used to diagnose hyperthyroidism. Simultaneous measurement of T4 improves the diagnostic accuracy. Free T3 levels might be helpful in confirming the diagnosis, particularly in cases when a diagnosis of T3 toxicity is suspected.[36]Antibodies directed against the TR confirm the Graves' disease diagnosis. Fatigue, irritability, anxiety, rage, sleeplessness, palpitations, weight loss, increased appetite, heat intolerance, sweating, menstruation dysfunction, tachycardia, anaemia, osteoporosis, and vision issues are some of the signs and symptoms of the illness.[37,38]

PRESENT INVESTIGATION:

Current investigations into the link between COVID-19 and thyroid disease are exploring several key areas:

The global prevalence of thyroid disease is dangerously high and continues to climb, putting a significant strain on healthcare providers. Thyroid nodules (TNs) are the most common thyroid condition, with a prevalence estimated to be as high as 60% based on high-resolution thyroid ultrasonography. It is noteworthy, therefore, that only a small percentage of people with thyroid disease diagnoses also have oncological or clinically severe thyroid abnormalities. For example, only a small percentage of thyroid nodules (TNs), about 5%, will turn out to be cancerous in the end.[39,40] While several studies indicate that environmental risk factors may be involved in a higher diagnosis rate for thyroid cancer, the majority of these diagnoses can be attributed to the increased use of ultrasonography, thyroid gland imaging screening, and greater accessibility to healthcare. [41,42,43]The National Cancer Institute of the United States of America reports that these tumours have tripled in incidence over the past few decades, with a stable and low death rate. Tumours less than 1 cm were actually linked to more than 60% of its incidence. Relying on these suppositions, physicians,and endocrinologists in particular, need to be mindful of the significant developments that have been made in the field of thyroid disease.[44]

The current issue has three papers that discuss imaging methods for thyroid nodule/cancer evaluation. An overview of thyroid ultrasound (US) and its supplementary approaches for the assessment of thyroid nodules can be found in one thorough narrative review by Bojunga et al. To broaden the diagnostic horizons and improve the diagnostic tools, the most pertinent information regarding contrast-enhanced ultrasound, multiparametric ultrasound, elastography, and excellent microvascular imaging is compiled. Furthermore, the possible application of artificial intelligence is a topic of discussion. Dondi et al. also provide an overview of radiomics and machine learning in nuclear medicine. By combining these cutting-edge technologies with nuclear medicine modalities, previously unexplored diagnostic opportunities are starting to become available.[45]

CLINICAL INVESTIGATION:

As indicated in the table, thyroid function tests can assess thyroid regulation, measure serum thyroid hormone concentrations of or measure serum thyroid hormone binding.

Table 1.1 – Clinical Manifestation of Thyroid Gland Functioning.

Measurement of serum thyroid hormone concentration
Serum total thyroxine (TT4)
Serum total triiodothyronine (TT3)
Serum free thyroxine (FT4)
Serum free triiodothyronine (rT3)
Tests of thyroid regulation
Serum thyrotropin (TSH)
TRH test
Measurements of thyroid hormone binding
SerumT4-binding globulin (TBG)
Serum transthyretin (TTR)
Test for autoimmune thyroid disease
Thyroid peroxidase anti body
Thyroglobulin antibody
TSH receptor antibody

Radioimmunoassay is commonly used to measure the amounts of serum total T4 (TT4) and T3 (TT3), with reference values of 4-11 µg/dl for T4 and 100-200 µg/dl for T3 respectively. Serum total thyroid

hormone concentrations, which are higher in hyperthyroid individuals and lower in hypothyroid patients, offer important information on thyroid function. Abnormally high or low concentrations of total thyroid hormones, however, can occur for a number of physiological or pathological reasons, such as changes in protein concentrations, auto-antibodies against iodothyronine in circulation, altered peripheral metabolism of T4, or modifications in thyroid hormone binding.

PRECAUTIONS:

Demographics and major comorbidities should be recorded: COVID-19-related symptoms, must be evaluated with a standard checklist. Respiratory rate, baseline oxygen saturation by pulse oximetry and oxygen requirement on admission compulsorily should be captured. Chest x-ray should be performed on admission. Cycle threshold (Ct) values should be obtained from specimens from NPS/DTS on admission. Studies have shown a good correlation between Ct values and SARS-CoV-2 viral loads

Regular screening:riskfactors or symptoms should be not avoided , such as unexplained weight gain, fatigue,thyroid functioning test should be conducted regularly

Healthy Diet: A healthy diet should include important elements that support thyroid health, such as iodine, selenium, and zinc. Nuts, legumes, dairy, and seafood are examples of foods that may be healthy. If you already have a thyroid disease, though, talk to your doctor about dietary changes.

Control Stress: Extended periods of stress might affect thyroid function. Include stress-relieving activities in your daily routine, such as physical activity, meditation, or engaging in a hobby you enjoy.

Avoid Self-Medication: Refrain from self-identifying or treating thyroid-related issues if you possess any indications. Seek advice from a medical expert regarding the proper diagnosis and course of therapy.

Medication: If you take thyroid medication, make sure your dosage is right by paying close attention to your doctor's instructions and scheduling frequent follow-up visits.

Reducing Exposure to Environmental Toxins: Thyroid health may be impacted by some environmental toxins. Minimize your exposure to chemicals and pollution wherever you can.

Frequent Exercise: Maintaining general health through regular physical activity can indirectly boost thyroid function.

Reduce Stress: Stress is one of the major contributors in many health disorders including thyroid disease.

Diet for patients with thyroid disorders: Follow below thyroid diet to avoid or prevent thyroid problem.

Avoid Processed Food: A lot of chemicals can alter the thyroid hormone production. One needs to avoid any kind of processed food; they are on the edge of the thyroid disorder.

Avoid Soy: Limit the soy intake as it alters the hormone production. Stop Smoking: The toxins released during smoking can make the thyroid gland over sensitive which can lead to thyroid disorders.

What to Take: Yogurt, seaweed, nuts, milk, chicken, fish, eggs, berries, cauliflower, and kale.

What to Reduce: Soy and soy products.
What to Avoid: Gluten, processed food, and fast food.
Keep Yourself Hydrated: Enough fluids are necessary for good thyroid function as well as general wellness.

Thyroid disorders are easy to manage. With a little help from the medication and some easy lifestyle changes, you can easily live a normal life. Regular physical activity is very important to stay fit and healthy. Make sure to take a healthy diet and not miss out any medication. Furthermore, regular preventive health checkups can help keep an eye on our body's nutrient levels and health status.

RECENT ADVANCEMENT:

For hyperthyroidism, methimazole and propylthiouracil (PTU) are the usual therapies. The goal of recent research is to optimize treatment plans and reduce adverse effects, like the uncommon but serious agranulocytosis problem.
Advances in the Treatment of Radioactive Iodine: For hyperthyroidism, especially in cases of Graves' disease, this treatment is frequently utilized. Improvements are being made to decrease the frequency of hypothyroidism that follows dosage accuracy.
Recent research has shown that combined thyroid hormone therapy is beneficial for treating hypothyroidism, or an underactive thyroid. These treatments, which combine triiodothyronine (T3) and thyroxine (T4), have been demonstrated to be just as successful as the conventional levothyroxine-only regimen.
Tepezza (teprotumumab), which has been approved for the treatment of thyroid eye disease, is one of the most recent advancements in the treatment of thyroid disease. This ailment, which is frequently connected to Graves' disease, results in eye swelling and enlargement. Tepezza is the first non-surgical treatment for this problem and has proven significant success in lowering eyeprotrusion and other symptoms.
Developments in Personalized Medicine and Biomarker Discovery: Advances in proteomics and genomes have improved the ability to identify biomarkers linked to thyroid disorders. This makes it possible to create individualized treatment plans based on each patient's unique genetic and molecular profile.
Research on Immunomodulatory Therapies: Research is being conducted to assess the possible benefits of monoclonal antibodies and immune checkpoint inhibitors in the management of autoimmune thyroid illnesses, including Hashimoto's thyroiditis and Graves' disease, especially in instances that are not responding to traditionaltreatments.

CONCLUSION:

A serious public health risk is highlighted by the documented increase in cases of thyroid illness after the COVID-19 pandemic. Research points to the possibility that the virus and medications it prescribedcaused or made thyroid disorders worse, including autoimmune thyroiditis, hypothyroidism, and hyperthyroidism. The influence of protracted inflammation, possible direct virus impacts, and the stress of the pandemic all probably play a part in this rise. Sufficient investigation is vital to comprehend the complete extent of these consequences and to formulate efficacious approaches for the individuals impacted. In order to treat and mitigate the long-term thyroid health implications associated with COVID-19, thorough care and continuous monitoring will be essential as the pandemic progresses in case.

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