

IN THE NAME OF GOD



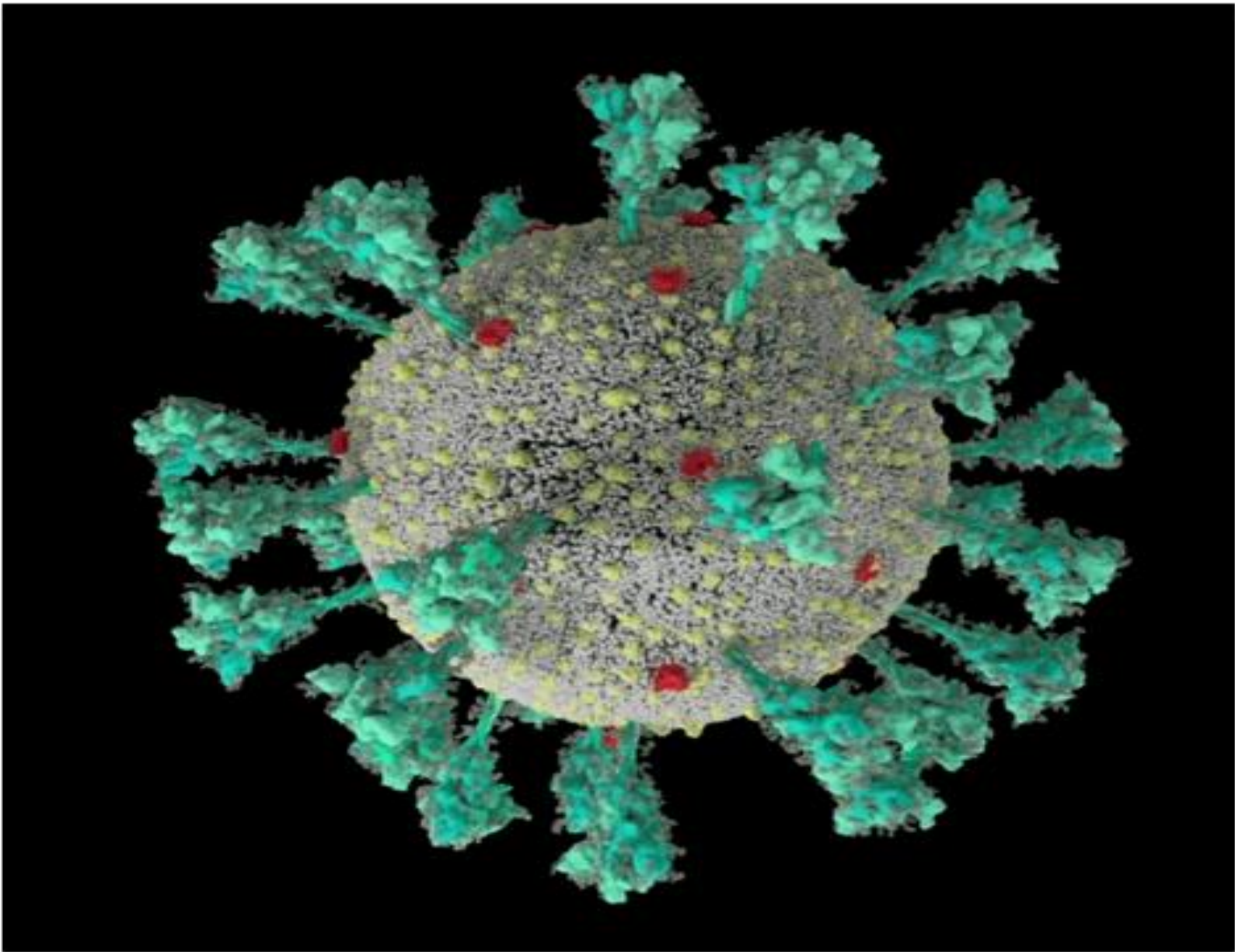


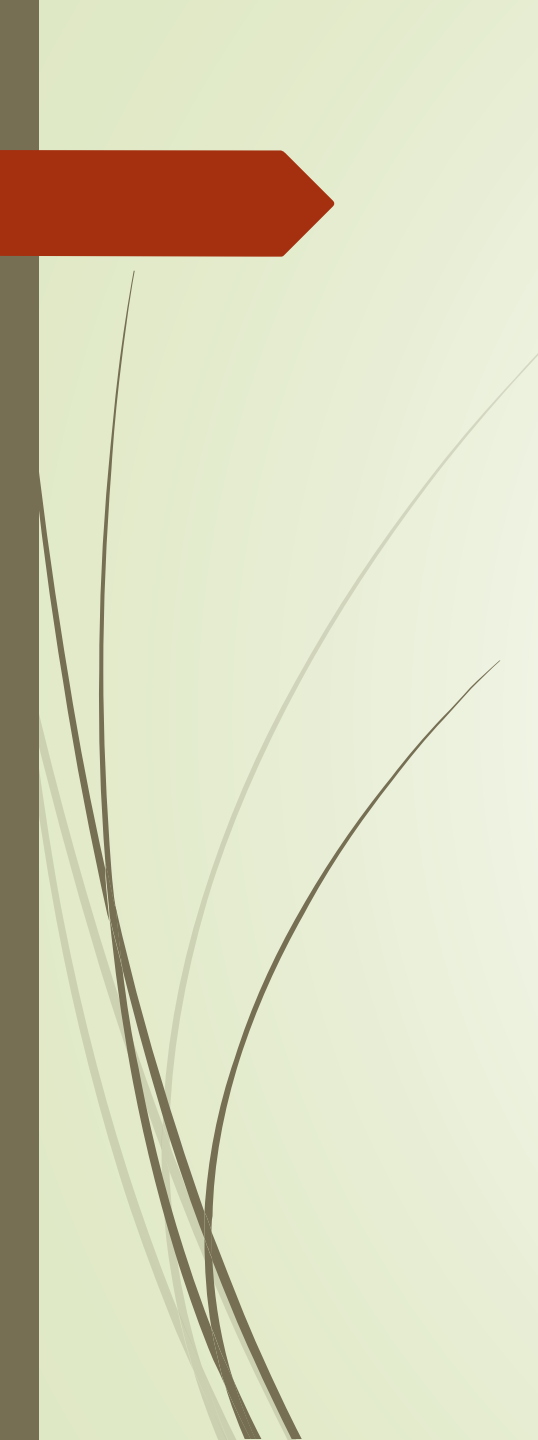
Endocrine Follow-up During Post-Acute COVID-19:

Practical Recommendations Based on Available Clinical Evidence


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The novel COVID-19 is now recognized as a multiorgan disease with several clinical manifestations. The sequelae of COVID-19, often referred to as **post-acute COVID-19**, are **defined** as persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms.



The common symptoms observed in post acute COVID-19 include fatigue, poor quality of life, muscle weakness, joint pain dyspnea, cough, decreased exercise capacity, and persistent oxygen requirement. In a cohort of individuals with COVID-19 who were followed up for 9 months after illness, approximately 30% reported persistent symptoms. One third of outpatients with mild disease also reported persistent symptoms. Fatigue was the most commonly reported symptom in the cohort.



Other long-term sequelae of COVID-19 include **neuropsychiatric** (headache, dysautonomia, cognitive impairment, anxiety, depression, sleep disturbances, and posttraumatic stress disorder), **cardiovascular** (palpitations, chest pain, myocardial fibrosis or scarring, arrhythmias), **renal** (declining renal function), **hematologic** (thromboembolic events), and **dermatologic** (hair loss) manifestations.




Like other organ systems, COVID-19 exerts several effects on the human endocrine system. The well-described endocrine manifestations of COVID-19 mainly reported during the acute phase of the disease include **dysglycemia, new-onset diabetes mellitus, euthyroid sick syndrome, subacute thyroiditis (SAT), and pituitary apoplexy**. However, data on long-term sequelae of COVID-19 on endocrine functions are limited.




COVID-19 and Diabetes Mellitus


Ample data suggest that diabetes mellitus portends a poor prognosis in patients with COVID-19. Moreover, COVID-19, directly and/or indirectly, predisposes to hyperglycemia (in patients without preexisting diabetes mellitus) and worsening of **dys glycemia** (in patients with preexisting diabetes mellitus). SARS-CoV-2 has been demonstrated to cause pancreatic b-cell damage ex vivo and in vivo, resulting in **reduced numbers of insulin-secretory granules** in b-cells and impaired glucose stimulated insulin secretion. Furthermore, altered secretion persists in patients even after recovery from COVID-19 and contributes to insulin resistance in the post-COVID-19 period.




In addition, drugs used in managing COVID-19, namely, steroids, remdesivir, and lopinavir-ritonavir, can lead to dysglycemia. The landmark Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial showed that oral or intravenous dexamethasone administered at a dose of 6 mg once daily for up to 10 days in patients with COVID-19 receiving either invasive mechanical ventilation or oxygen alone reduced the 28-day mortality by 18% to 32%.



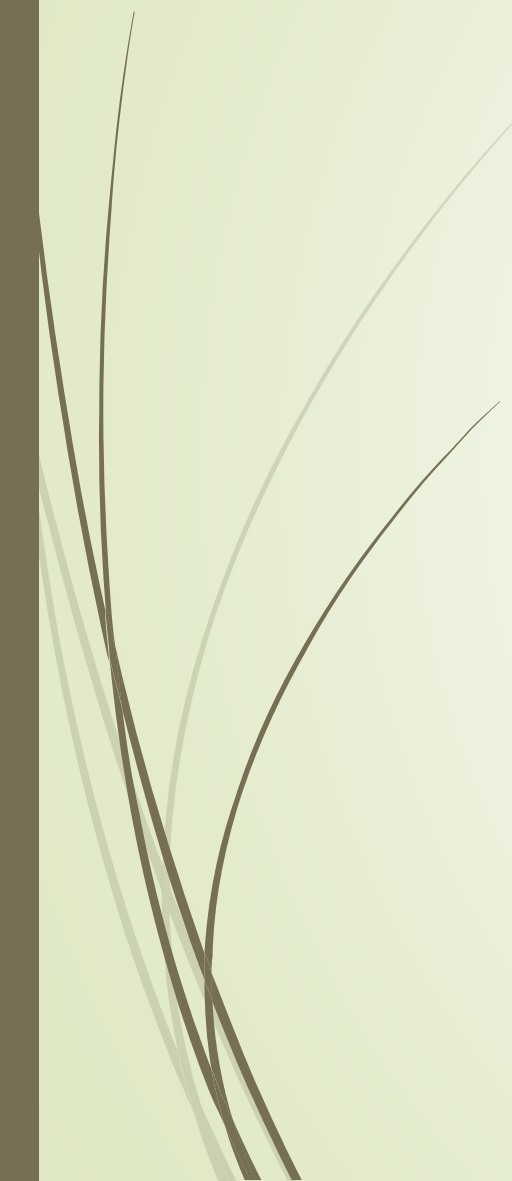
Of note, the use of steroids in patients with COVID-19, often at an irrationally high dose, has predisposed to the development of in hospital **glucocorticoid-induced hyperglycemia (GIH)**. Although GIH is suggested to be a transient problem resolving after discontinuing glucocorticoids, data indicate that diabetes can persist, and glucocorticoids may unmask a preexisting disorder of glucose metabolism.

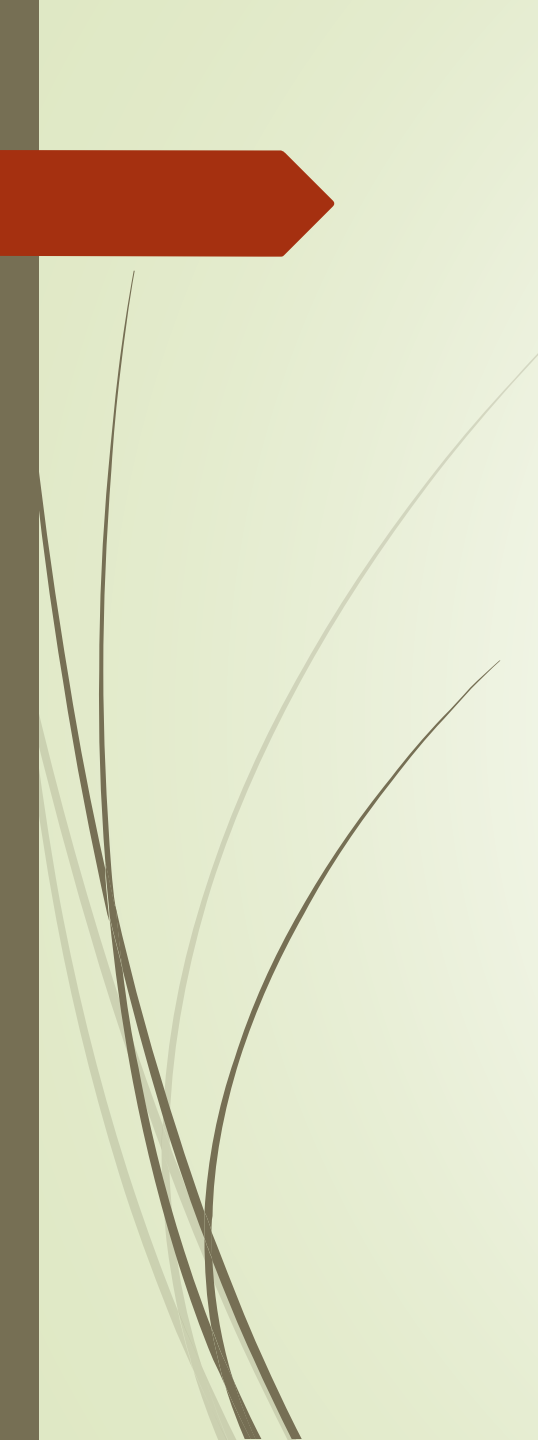


In a recently published retrospective cohort study from England, 47 780 individuals with COVID-19 who were admitted to the hospital and subsequently discharged by August 31, 2020 were included. After discharge, diabetes was diagnosed in 4.9% of COVID-19 survivors, amounting to a rate of 127 per 1000 person-years. Individuals who needed to be admitted to the intensive care unit (ICU) had higher rates of diabetes (8.8%) after discharge than those who did not require ICU admission (4.6%). The rate ratio was higher for individuals aged <70 years than for those aged 70.



Apart from diabetes mellitus, **metabolic syndrome** is also independently associated with poor outcomes in COVID-19. Metabolic syndrome increases the risk of severe disease, complications, hospitalization, and mortality with COVID-19.





In the wake of the COVID-19 pandemic, there has been an upsurge in the number of cases of **mucor mycosis**, an entity being referred to as COVID-19-associated mucor mycosis (CAM). Most of the cases of CAM have been reported from **India**.

Uncontrolled hyperglycemia and the use of steroids in the context of COVID-19 have been implicated in the pathogenesis of CAM.




Recommendations Based on Available Evidence

a. Patients with preexisting diabetes mellitus should be more vigilant about optimum glycemic control in the post-COVID-19 . In patients without preexisting diabetes: i. Routine evaluation of glycemic status in patients with COVID-19 without documented in-hospital hyperglycemia or new-onset diabetes mellitus is not recommended.

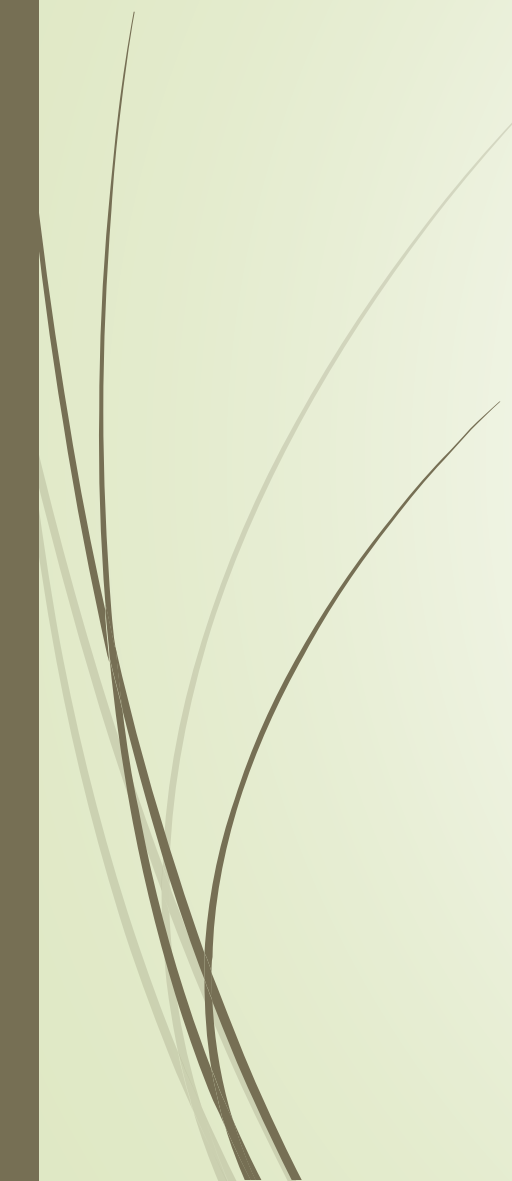


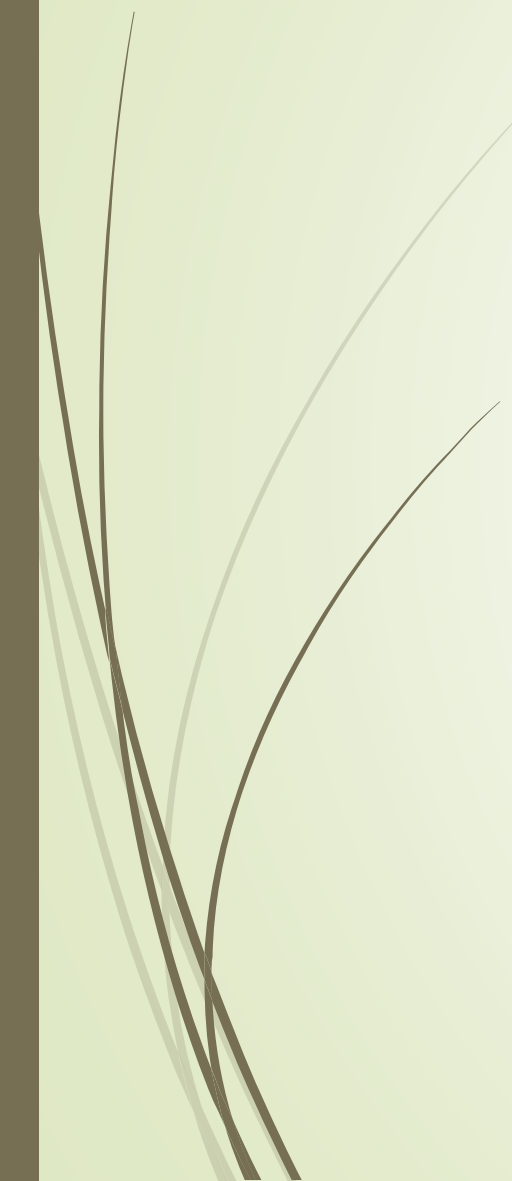

b. In patients without preexisting diabetes:

i. Routine evaluation of glycemic status in patients with COVID-19 without documented in-hospital hyperglycemia or new-onset diabetes mellitus is not recommended. Patients with COVID-19 admitted to the ICU and those aged <70 years are at high risk of new-onset diabetes post-COVID19 and, thus, may be screened for new-onset diabetes at 3 months after discharge with a fasting plasma glucose or 2- hour plasma glucose during oral glucose tolerance test or glycated hemoglobin (HbA1C) as per the American Diabetes Association (ADA) Standards of Medical Care in Diabetes.




ii. Patients with COVID-19 with documented in-hospital hyperglycemia (including steroid-induced hyperglycemia) but normoglycemia and off all antidiabetic drugs at the time of discharge should be reevaluated at 3 months after discharge with a fasting plasma glucose or 2-hour plasma glucose during oral glucose tolerance test or HbA1C as per the ADA Standards of Medical Care in Diabetes.





iii. Patients with COVID-19 with documented in-hospital hyperglycemia (including glucocorticoid-induced hyperglycemia) and discharged on antidiabetic medications should maintain glycemic control based on the standard of care. The dose and number of antihyperglycemic medications should be adjusted as per the glycemic profile. Antidiabetic medications may need to be stopped based on the blood glucose profile. It may be possible to discontinue antihyperglycemic medications in those with confirmed stress-induced hyperglycemia, that is, an HbA1C level of <6.5% in the presence of hyperglycemia at the time of discharge.




c. Patients with COVID-19 with diabetes mellitus/hyperglycemia are at high risk of mucormycosis even after recovery from COVID-19, and the caregivers need to be vigilant about the same.

d. Screening for other diabetes-related complications should be undertaken as per routine standard of care.

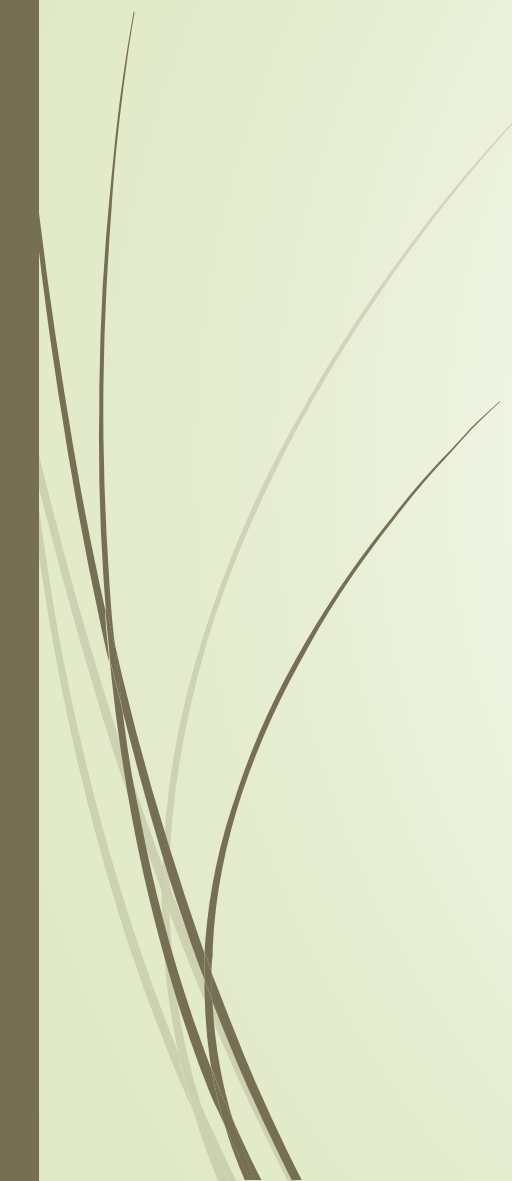



COVID-19 and Thyroid Function

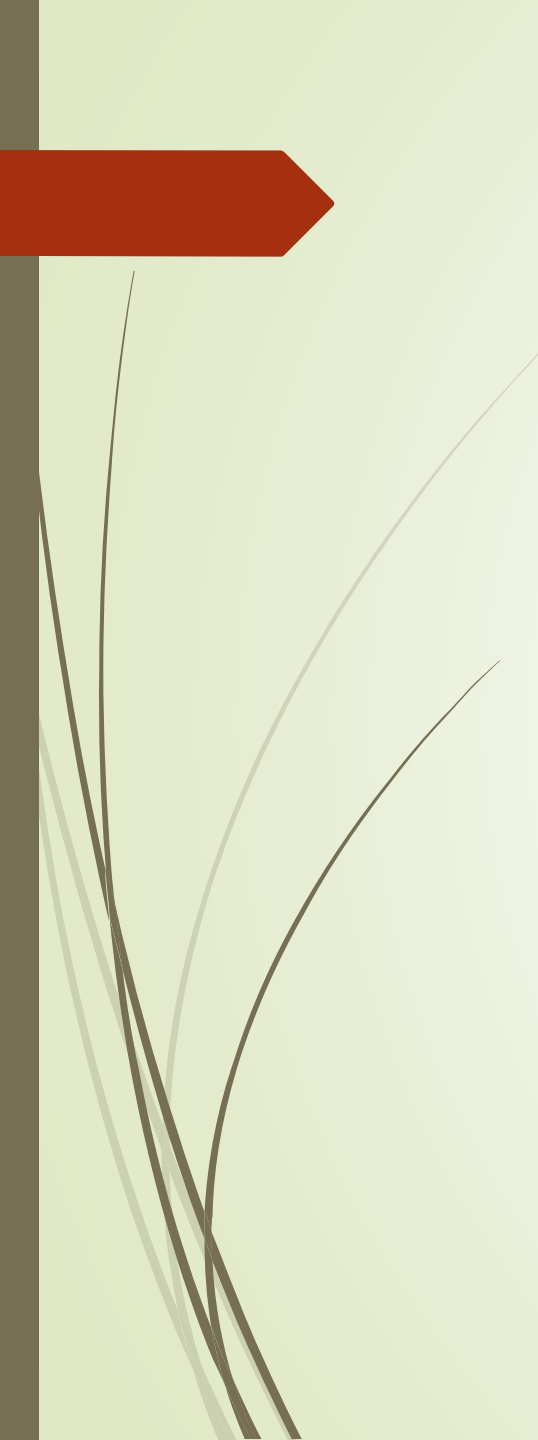
There exists ample literature about thyroid function in active COVID-19. The majority of the patients presenting with COVID-19 tend to be biochemically euthyroid. The most common thyroid dysfunction observed in patients with active COVID-19 is euthyroid sick syndrome/nonthyroidal illness syndrome, the magnitude of the decrease in thyroid-stimulating hormone (TSH) and triiodothyronine (T3)/thyroxine (T4) levels correlating positively with the severity of the disease.



While overt hypothyroidism is rare in patients with COVID-19, thyrotoxicosis without hyperthyroidism, due to destructive SAT, is more commonly reported. COVID-19-associated SAT is biochemically characterized by low TSH and free T3 levels and normal or elevated free T4 levels. In the context of COVID-19, such an entity is often referred to as **atypical thyroiditis** and should be considered a differential diagnosis when acutely infected patients present with tachycardia without evidence of progression of COVID-19 illness. Although follow-up data are limited, most of the available data suggest that thyroid function returns to normal without any specific treatment.



SAT has also been described after recovery from COVID-19. Such patients tend to present with neck pain, fever resurgence, weight loss, and/or palpitations. In addition, occasional cases of **Graves'** disease have been described following COVID-19. In a prospective observational study, 70 patients aged 18 years were included at least 3 months after the diagnosis of COVID-19. Of the 68 patients who were not known to have any thyroid disease, thyroid function (TSH, free T4, and free T3) was all within the normal range.




Moreover, there was no difference in the frequency of hypothyroidism or hyperthyroidism in patients complaining of fatigue compared with those without. In another study where 204 patients with COVID-19 were reassessed at a median of 89 days, most abnormal thyroid function test (TFT) results in acute COVID-19 resolved (81.4%), and incident thyroid dysfunction was rare (1.9%)

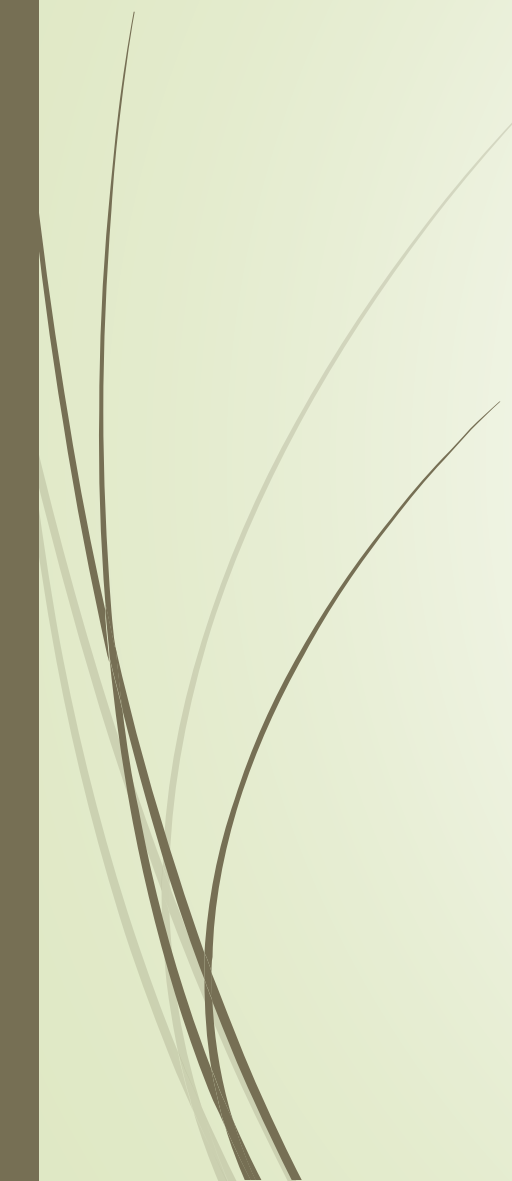



Recommendations Based on Available Evidence

a. Patients with COVID-19 with biochemically documented euthyroid sick syndrome during the acute phase of the disease may undergo a TFT performed at 6 weeks after discharge.

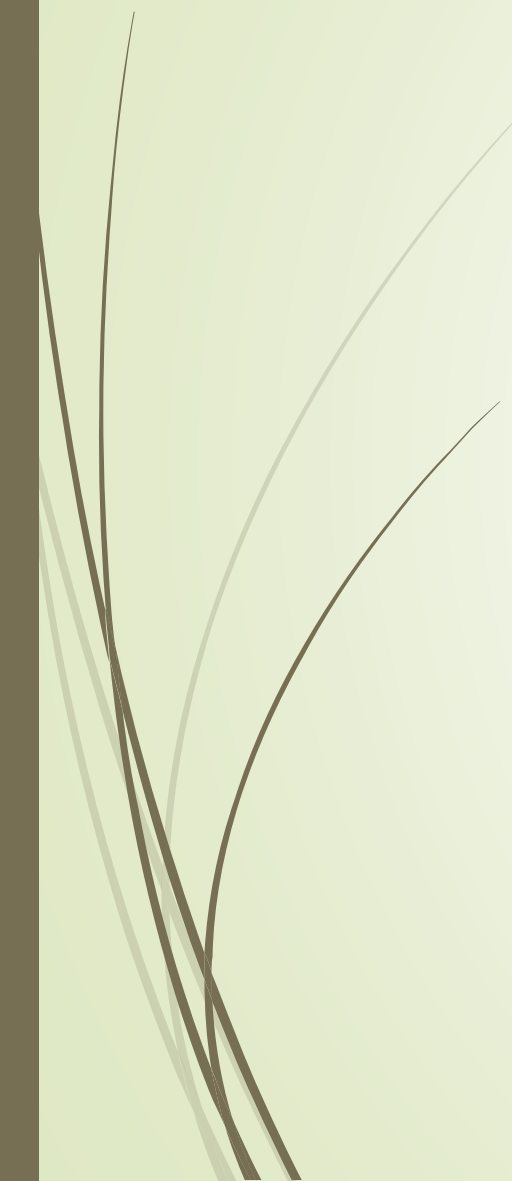



b. Patients with COVID-19 with biochemically documented subclinical hypothyroidism during the acute phase of the disease should undergo a TFT 3 months after discharge. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19.






c. Patients with COVID-19 with biochemically documented overt hypothyroidism during the acute phase of the disease should undergo a TFT performed at 6 weeks after discharge while on levothyroxine supplementation. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19.

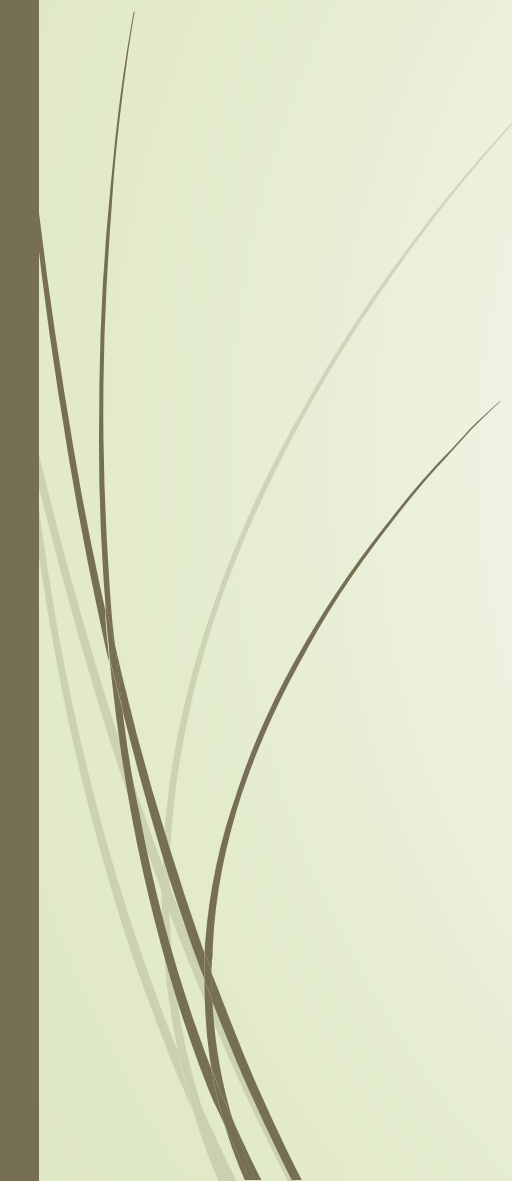





d. Patients with COVID-19 with biochemically documented hyperthyroidism/subclinical hyperthyroidism/SAT during the acute phase of the disease should undergo a TFT performed at 6 weeks after discharge. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19. Even if the thyroid function at 6 weeks is normal, a repeat test should be performed at 12 weeks to rule out the possibility of postthyroiditis hypothyroidism.

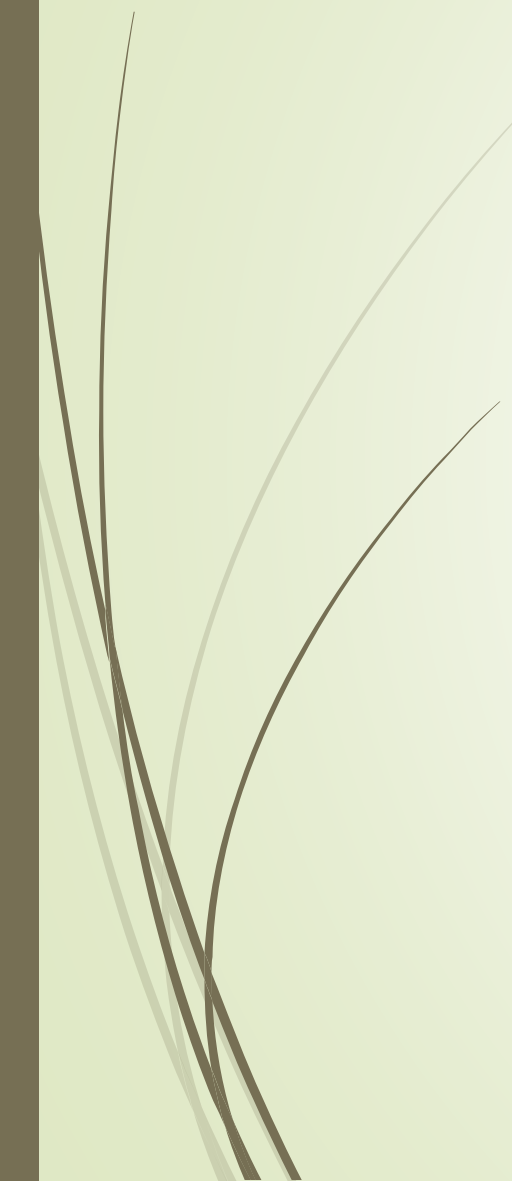



e. Patients with COVID-19 with normal thyroid function assessed during the acute phase of the disease do not need a routine re estimation of thyroid function on follow-up.





f. Patients with COVID-19 in whom thyroid function was not estimated during the acute phase of the disease do not require a routine assessment of thyroid function on follow-up, even in those complaining of persistent fatigue.






g. Patients who have recovered from COVID-19 complaining of neck pain, weight loss, resurgence of fever, and/or palpitations should be suspected of having SAT. A TFT should be immediately performed, and if suggestive of thyrotoxicosis, a radionuclide thyroid uptake scan using technetium-99m may be ordered (if facilities are available). A combination of high erythrocyte sedimentation rate (and/or C-reactive protein levels) and poor radionuclide uptake by the thyroid gland is diagnostic of SAT. A thyroid-stimulating immunoglobulin assay may be ordered when Graves' disease is suspected.



COVID-19 and Adrenal Function

At the inception of the pandemic, there were multiple hypotheses that SARS-CoV-2 may directly damage the adrenocortical cells or induce a state of “molecular mimicry” against adrenocorticotrophic hormone (ACTH). However, adrenal insufficiency (AI) in COVID-19 is not as common as hypothesized.



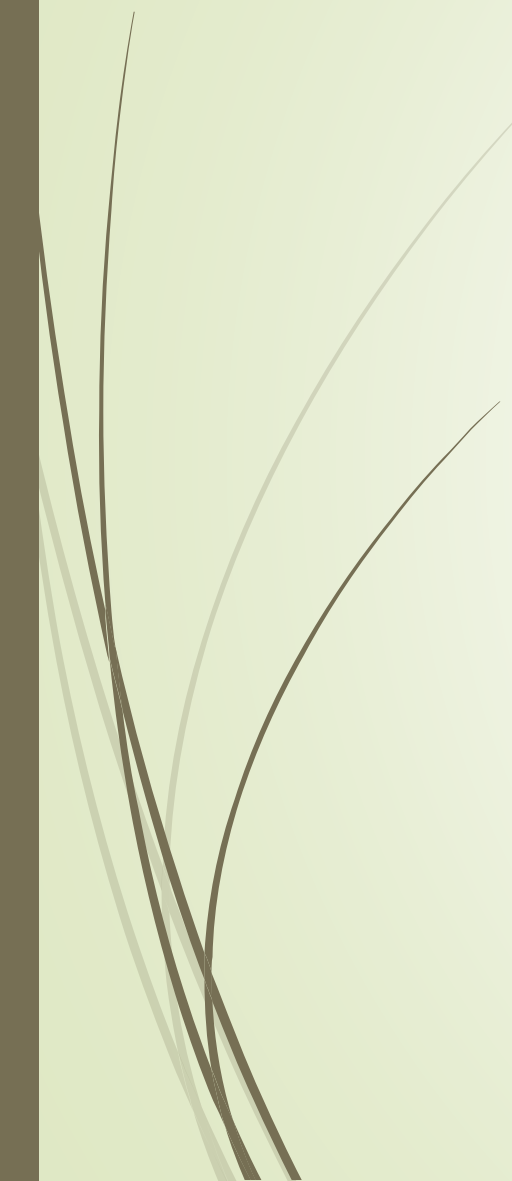

In a cohort of 403 patients with COVID-19, the median plasma cortisol level was 619 nmol/L, which was significantly higher than those without COVID-19. Critical illness-related corticosteroid insufficiency (CIRCI) has been reported to be uncommon in the setting of COVID-19; only 18 (4.5%) of 403 patients with COVID-19 had CIRCI. In another similar study, the median cortisol level of COVID-19-positive patients was higher than that of COVID-19-negative patients (21.84 mg/dL vs. 16.47 mg/dL; $P < .001$).




COVID-19 and Pituitary Function

Occasional cases of pituitary apoplexy in relation to COVID-19 have been reported in the literature. While most cases have been described in association with active COVID-19, some have been reported following recovery from COVID-19 as well. The typical presenting features are headache and visual disturbance, associated with anterior pituitary hormone deficiencies. Whereas most patients were successfully managed with emergent transsphenoidal surgery, postoperative follow-up data are limited.

Cases of post-COVID-19 infundibulo-neurohypophysitis have also been occasionally reported.



a. Patients with COVID-19 complaining of new-onset headache and visual disturbance after recovery should be suspected of having pituitary apoplexy, and a non contrast computed tomography of the head should be performed at the earliest. The possibility of pituitary apoplexy should be kept higher on the cards, especially in those already known to have an underlying pituitary adenoma, pregnant women, and those on antiplatelet medications.




b. Patients with COVID-19 diagnosed with pituitary apoplexy in the acute phase of the disease and not found to have any anterior pituitary hormone deficiency should be reevaluated at 6 weeks for incident hormone deficiencies.

c. Patients with COVID-19 diagnosed with pituitary apoplexy in the acute phase of the disease and found to have 1 or more anterior pituitary hormone deficiencies and supplemented with the respective hormones should be reevaluated at 6 weeks for other incident hormone deficiencies.




COVID-19 and Gonadal System


Hitherto literature suggests that hypogonadism is not uncommon in men affected with COVID-19. In a prospective cohort study involving 221 hospitalized male patients (aged >18 years) with laboratory-confirmed SARS-CoV-2 who had been hospitalized due to COVID-19, 113 (51.1%) had hypogonadism (defined as a serum total testosterone level of <300ng/dL). Men with severe disease tended to have lower testosterone levels. The probable mechanisms involve cytokine-driven gonadotropin suppression nevertheless, elevated luteinizing hormone (LH) and folliclestimulating hormone (FSH) levels have been reported in conjunction with low testosterone levels, pointing toward the possibility of a primary gonadal failure. In fact, testicular samples from autopsies of deceased patients with COVID-19 have shown histopathologic evidence of orchitis. Moreover, SARS-CoV-2 has been detected in the testes of patients with severe disease.



The risk of impaired spermatogenesis has also been observed in patients with moderate infection and convalescents. In an observational study that had involved 43 sexually active men who had recovered from COVID-19, oligo-crypto-azoospermia was observed in 25.6% of the patients. The severity of COVID-19 was related to the occurrence of azoospermia. Azoospermia was observed in 80%, 11.5%, and 8.3% of patients admitted to the ICUs and medicine department and those non hospitalized, respectively. However, gonadal hormones were not estimated in the study. Multivariate analysis revealed that hospitalization (not recovered vs. hospitalized vs. ICU) was the primary determinant of crypto-azoospermia. Nevertheless, there are no robust follow-up data on the effect of COVID-19 on male gonadal function and subsequent fertility



With regard to the female gonadal system, robust clinical data are scarce. Among 177 women of childbearing age with confirmed COVID-19, almost one fifth of patients exhibited a decrease in menstrual volume or cycle prolongation. As part of the same study, the sex hormone and anti-Mullerian hormone levels were estimated in the early follicular phase in 91 patients with COVID-19 and an equal number of controls. There was no significant difference in the FSH, LH, estradiol, progesterone, testosterone, and anti-Mullerian hormone levels between patients with COVID-19 and controls. The authors, thus, concluded that menstrual changes in women with COVID-19 may result from transient sex hormone changes caused by suppression of ovarian function that quickly resume after recovery.




They were divided into 3 study groups:
recovering from confirmed COVID-19 (n = 9),
vaccinated with the BNT162b2 messenger
ribonucleic acid (mRNA) COVID-19
vaccine (n = 9), and uninfected/nonvaccinated
controls (n = 14).

Overall, there was no difference in the surrogate
parameters for ovarian follicle quality between the
3 groups.



COVID-19 and Bone and Mineral Metabolism

Hypocalcemia has been commonly reported in patients with COVID-19. Of 531 patients with COVID-19 admitted to the emergency department, 462 (82%) had hypocalcemia. In univariate and multivariate analyses, hypocalcemia emerged as an independent risk factor predicting hospitalization. In another observational cohort study, 445 patients admitted with COVID-19 were included. Hypocalcemia was observed in 68.8% of the patients.



Hypovitaminosis D has been linked to an increased risk of COVID-19 infection, disease severity, and poor outcomes. In fact, hypocalcemia in the context of COVID-19 is associated with hypovitaminosis D, along with an inadequate compensatory parathyroid hormone response. Vitamin D supplementation, in the form of either cholecalciferol or calcifediol, has also been shown to improve clinical outcomes in COVID-19, although robust and consistent data are lacking.




Recommendations Based on Available Evidence

a. We do not recommend the routine estimation of serum calcium in post-COVID-19 patients.

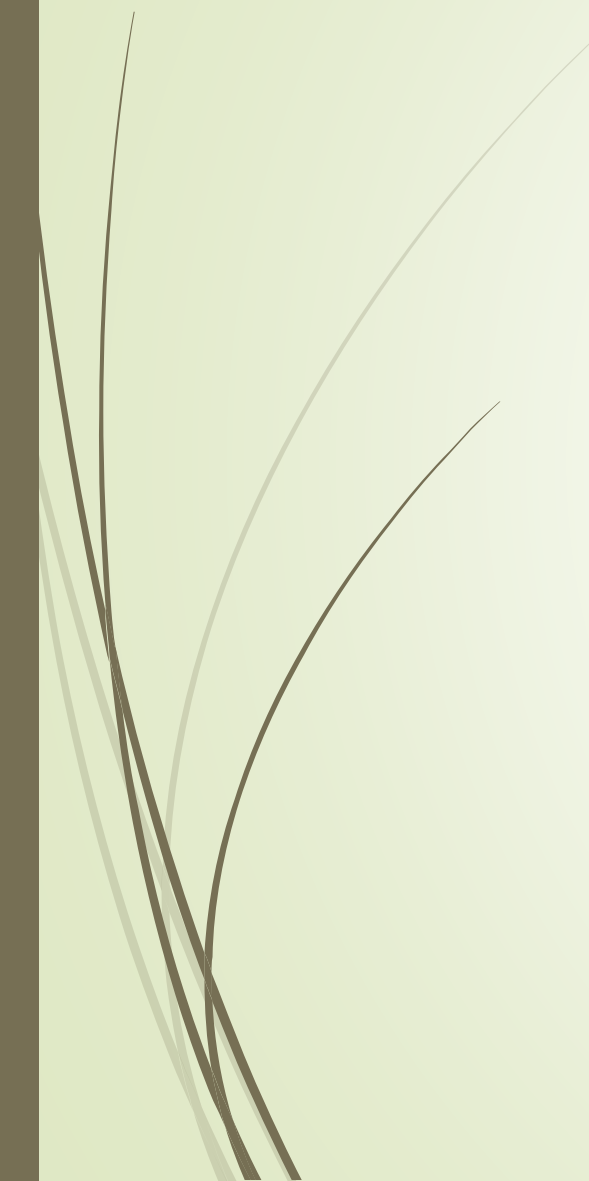

b. Patients with COVID-19 with symptomatic hypocalcemia during the acute stage of the disease should undergo a repeat estimation of serum calcium at 2 weeks after discharge.

c. The 25-hydroxyvitamin D levels may be estimated in post-COVID19 patients, and vitamin D may be supplemented accordingly.




COVID-19 Vaccination and Endocrine Systems

The European Society of Endocrinology statement has supported the recommendation that “COVID-19 vaccination should not be handled differently in patients with stable endocrine diseases such as autoimmune thyroiditis, Graves’ disease, Addison’s disease, pituitary adenomas, diabetes type 1 and 2 and obesity as compared to the general population.”⁶⁸ In fact, COVID-19 vaccination should be prioritized in individuals with diabetes mellitus.



The reciprocal effect of COVID-19 vaccination on the endocrine system has not been explored in details. Nevertheless, blood glucose monitoring is required more often than usual for several days after vaccination in individuals with diabetes, and glucocorticoid doses may need to be temporarily hiked up in individuals with AI.



Emerging data suggest that COVID-19 vaccines are associated with thyroid dysfunction. Multiple cases of thyrotoxicosis have been reported following vector-based or mRNA-based SARS-CoV-2 vaccines with a spectrum ranging from SAT and silent thyroiditis to Graves' disease. Thyroid dysfunction could be explained by various mechanisms such as autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome), molecular mimicry between human and viral proteins, mRNA "self-adjuvant" effect, and immune disruption from external stimuli.



Recommendations Based on Available Evidence

Subjects complaining of involuntary weight loss, palpitations, tremors, and/or neck pain after vaccination with vector-based or mRNA-based SARS-CoV-2 vaccines should be suspected of having thyrotoxicosis, and a TFT should be performed.

Diabetes mellitus

- a. Patients with preexisting diabetes mellitus should be more vigilant about optimum glycemic control in the post-COVID period.
- b. In patients without preexisting diabetes:
 - i. Routine evaluation of glycemic status in patients with COVID-19 without documented in-hospital hyperglycemia or new-onset diabetes mellitus is not recommended. Patients with COVID-19 admitted to the ICU and those aged <70 years are at high risk of new-onset diabetes post-COVID and, hence may be screened for new-onset diabetes at 3 months after discharge with a fasting plasma glucose or 2-hour plasma glucose during oral glucose tolerance test or HbA1C as per the ADA Standards of Medical Care in Diabetes.²²
 - ii. Patients with COVID-19 with documented in-hospital hyperglycemia (including steroid-induced hyperglycemia) but normoglycemia and off all antidiabetic drugs at the time of discharge should be reevaluated at 3 months after discharge with a fasting plasma glucose or 2-hour plasma glucose during oral glucose tolerance test or HbA1C as per the ADA Standards of Medical Care in Diabetes.²²
 - iii. Patients with COVID-19 with documented in-hospital hyperglycemia (including steroid-induced hyperglycemia) and discharged on antidiabetic medications should maintain glycemic control based on the standard of care. The dose and number of antihyperglycemic medications should be adjusted as per the glycemic profile. Antidiabetic medications may need to be stopped based on the blood glucose profile. It may be possible to discontinue antihyperglycemic medications in those with confirmed stress-induced hyperglycemia, that is, an HbA1C level of <6.5% in the presence of hyperglycemia at the time of discharge.
- c. Patients with COVID-19 with diabetes mellitus/hyperglycemia are at high risk of mucormycosis even after recovery from COVID-19, and the caregivers need to be vigilant about the same.
- d. Screening for other diabetes-related complications should be undertaken as per standard of care.

Thyroid

- a. Patients with COVID-19 with biochemically documented euthyroid sick syndrome during the acute phase of the disease may undergo a thyroid function test performed at 6 weeks after discharge.
- b. Patients with COVID-19 with biochemically documented subclinical hypothyroidism during the acute phase of the disease should undergo a thyroid function test 3 months after discharge. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19.
- c. Patients with COVID-19 with biochemically documented overt hypothyroidism during the acute phase of the disease should undergo a thyroid function test performed at 6 weeks after discharge while on levothyroxine supplementation. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19.
- d. Patients with COVID-19 with biochemically documented hyperthyroidism/subclinical hyperthyroidism/subacute thyroiditis during the acute phase of the disease should undergo a thyroid function test performed at 6 weeks after discharge. An anti-TPO antibody assay should be performed if not found to be positive during the acute phase of COVID-19. Even if the thyroid function at 6 weeks is normal, a repeat test should be performed at 12 weeks to rule out the possibility of postthyroiditis hypothyroidism.
- e. Patients with COVID-19 with normal thyroid function assessed during the acute phase of the disease do not need a routine reestimation of thyroid function on follow-up.
- f. Patients with COVID-19 in whom thyroid function was not estimated during the acute phase of the disease do not require a routine assessment of thyroid function on follow-up, even in those complaining of persistent fatigue.
- g. Patients who have recovered from COVID-19 complaining of neck pain, weight loss, resurgence of fever, and/or palpitations should be suspected of having subacute thyroiditis. A thyroid function test should be immediately performed, and if suggestive of thyrotoxicosis, a radionuclide thyroid uptake scan using technetium-99 m may be ordered (if facilities are available). A combination of high erythrocyte sedimentation rate (and/or C-reactive protein levels) and poor radionuclide uptake by the thyroid gland is diagnostic of subacute thyroiditis. A thyroid-stimulating immunoglobulin assay may be ordered when Graves disease is suspected.

Aadrenals

- a. We do not recommend the routine estimation of serum cortisol/ACTH in post-COVID patients.
- b. Since patients with COVID-19 treated with dexamethasone as per the RECOVERY trial (6 mg once a day for a maximum of 10 days) do not have impaired adrenal function, they do not require a routine evaluation of adrenal function in the post-COVID setting.
- c. Patients with COVID-19 who have received steroids during the acute phase of the disease for <3 weeks are unlikely to have clinically significant HPA axis suppression and, hence, do not require the evaluation of their HPA function.
- d. Suppression of the HPA axis is inevitable in patients taking the equivalent of 15 mg/day or more of prednisolone for ≥ 3 weeks. Hence, the evaluation of the HPA axis may be performed after tapering and stopping glucocorticoids.
- e. Morning serum cortisol/ACTH levels may, however, be estimated in post-COVID patients with surrogate evidence of AI, that is, recent onset anorexia, involuntary weight loss, diarrhea, hyponatremia and/or hyperkalemia, and/or eosinophilia.
- f. Patients with COVID-19 with biochemically documented AI during the acute phase of the disease should undergo a morning serum cortisol/ACTH test estimated with/without Synacthen stimulation test at 12 weeks after discharge, withholding hydrocortisone 24 h prior to the test.
- g. Any documentation of central AI (in the absence of a prior history of glucocorticoid intake) should prompt the evaluation for other anterior pituitary hormone deficiencies.



Pituitary

- a. Patients with COVID-19 complaining of new-onset headache and visual disturbance post-recovery should be suspected of having pituitary apoplexy, and a noncontrast computed tomography of the head should be performed at the earliest. The possibility of pituitary apoplexy should be kept higher on the cards, especially in those already known to have an underlying pituitary adenoma, pregnant women, and those on antiplatelet medications.
- b. Patients with COVID-19 diagnosed with pituitary apoplexy in the acute phase of the disease and not found to have any anterior pituitary hormone deficiency should be reevaluated at 6 weeks for incident hormone deficiencies.
- c. Patients with COVID-19 diagnosed with pituitary apoplexy in the acute phase of the disease and found to have 1 or more anterior pituitary hormone deficiencies and supplemented with the respective hormones should be reevaluated at 6 weeks for other incident hormone deficiencies.



gonads

- a. Men with COVID-19 with biochemically documented hypogonadism (either primary or secondary) during the acute phase of the disease should undergo serum total testosterone, LH, and FSH tests performed at 3 months after discharge.
- b. Men with COVID-19 with normal gonadal function documented during the acute phase of the disease do not require a routine reevaluation of gonadal hormones on follow-up.
- c. Men with COVID-19 in whom the gonadal function was not estimated during the acute phase of the disease do not require a routine assessment of gonadal hormones on follow-up.
- d. Men who have recovered from COVID-19 and complaining of new-onset erectile dysfunction and/or low/loss of libido should undergo serum total testosterone, LH, and FSH tests performed irrespective of the gonadal status during the acute phase of the disease. A psychiatry opinion should be sought to exclude psychogenic erectile dysfunction in such men with normal gonadal function.
- e. On follow-up, men found to have hypogonadism (low serum total testosterone level) with low/normal LH/FSH levels after recovery should be evaluated for other anterior pituitary hormone deficiencies. In addition, the serum prolactin level should also be estimated.
- f. On follow-up, in men found to have hypogonadism (low serum total testosterone level) with elevated LH/FSH levels after recovery, a possibility of a primary testicular failure should be kept in mind.
- g. In either scenario, a semen analysis may be performed for men of reproductive age if they wish to father children.
- h. Routine semen analysis in men of the reproductive age group desirous of a future child is not recommended.
- i. Hitherto, there is no robust evidence to recommend a routine evaluation of gonadal function in women of childbearing age who have recovered from COVID-19.

Bone and mineral metabolism

- a. We do not recommend the routine estimation of serum calcium in post-COVID patients.
- b. Patients with COVID-19 with symptomatic hypocalcemia during the acute stage of the disease should undergo a repeat estimation of serum calcium at 2 weeks after discharge.
- c. The 25-hydroxyvitamin D levels may be estimated in post-COVID patients, and vitamin D be supplemented accordingly.

COVID-19 vaccination and endocrine systems

- a. Subjects complaining of involuntary weight loss, palpitations, tremors, and/or neck pain after vaccination with vector-based or mRNA-based SARS-CoV-2 vaccines should be suspected of having thyrotoxicosis, and a thyroid function test should be performed.

