A Comprehensive Review of COVID-19–Associated Endocrine Manifestations

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Abstract: Coronavirus disease 2019 (COVID-19) has played a significant part in systematic damage, affecting lives and leading to significant mortality. The endocrine system is one of the systems affected by this pandemic outbreak. The relationship between them has been identified in previous and ongoing research. The mechanism through which severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) can achieve this is similar to that for organs that express angiotensin-converting enzyme 2 receptors, which is the primary binding site of the virus. Endocrine cells widely express angiotensin-converting enzyme 2 receptors and transmembrane serine protease 2, the primary mediators initiating the acute phase of the disease. This review aimed to identify and discuss the endocrine complications of COVID-19. This primary focus is on presenting thyroid disorders or newly diagnosed diabetes mellitus (DM). Thyroid dysfunction with subacute thyroiditis, Graves' disease, and hypothyroidism caused by primary autoimmune thyroiditis has been reported. Pancreatic damage leads to type 1 DM because of the autoimmune nature of the disease and type 2 DM because of postinflammatory insulin resistance. Because follow-up data on COVID-19 on the endocrine glands are limited, long-term investigations are needed to assess specific effects.

Key Words: COVID-19, diabetes mellitus endocrine, hyperthyroidism, hypothyroidism

The coronavirus disease 2019 (COVID-19) pandemic has had a massive impact, resulting in 500 million cases and nearly 7 million deaths (as of this writing).[1] The primary cause of this pandemic is a positive-sense, single-strand, enveloped RNA virus called severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2).[2] Moreover, it is transmitted mainly through the respiratory system via droplets and aerosol particles, potentially traveling up to 28 ft.[3] The disease process has both pulmonary and extrapulmonary signs and symptoms. General symptoms vary from mild acute symptoms such as fatigue, headache, loss of smell and taste, and muscle aches to severe long-term effects, from myocarditis (heart muscle inflammation) to irreversible pulmonary damage.[4] COVID-19 has been primarily known to target different organs such as the lungs, heart, and brain.[5] With continuous research and development, we are becoming more familiar with the extended and obscure multisystemic complications, including their widespread impact on the endocrine system. Endocrine organs affected by SARS-CoV-2 mainly include the hypothalamic–pituitary axis, thyroid gland, adrenal gland, and pancreas. It also can cause an imbalance in vitamin D and testosterone levels, resulting in malabsorption-related complications and infertility.[6,7] Pancreatic damage can lead to acute and chronic pancreatitis.[8] SARS-CoV-2 also plays a role in disrupting exocrine and endocrine functions. Exocrine insufficiency is one of the causes of COVID-induced acute diarrhea.[9] Some cases of new-onset type 1 diabetes mellitus (DM) in young children have been reported in a study conducted in London, UK, that have resulted from the endocrine involvement of the pancreas.[10]

Meanwhile, SARS-CoV-2 also has been significantly associated with subacute thyroiditis. Euthyroid sick syndrome (ESS) remains the most prevalent thyroid disorder, leading to a decremental decrease in triiodothyronine (T3) and thyroxine (T4)

Key Points

- Pulmonary, cardiovascular, renal, endocrine, and central neurological systems are affected by the coronavirus disease 2019 (COVID-19) infection. The thyroid, pancreas, and adrenal glands are some of the most typically afflicted endocrine organs.
- Both disorders of the thyroid spectrum, hyperthyroidism and hypothyroidism, are seen to be involved. The most prevalent manifestations are euthyroid sick syndrome and subacute thyroiditis.
- Diabetes mellitus has been found to be more common among COVID-19 patients in several investigations because of COVID-19–induced insulin resistance via the suppression of insulin-signaling pathways.

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levels from the cytokine storm.[7] As such, this article reviews the literature on the implications of COVID-19 for DM and thyroid disorders.

Pathophysiology

COVID-19 and Endocrinopathies

SARS-CoV-2 comprises four structural proteins: spike, envelope, membrane, and nucleocapsid.[11] Because of its complex structure and variability, its mechanism of action is diversified. Spike protein on its surface plays a vital part in binding to angiotensin-converting enzyme 2 (ACE2) receptors in host cells with the help of transmembrane serine protease 2. Spike protein is then separated into two subunits: S1 and S2. This results in structural changes to increase the stability of the binding process.[12] ACE2 expression has been reported in most tissues, including endocrine functions such as those of the hypothalamus, pituitary, thyroid, gonads, and pancreatic islets. It is greatly involved in regulating blood pressure and prevents inflammatory damage by breaking down angiotensin II (Ang II); however, when the virus occupies the ACE2 receptors, it eventually leads to inflammatory organ damage because of the increased availability of Ang II.[13] The virus-infected cells release inflammatory mediators, including interleukin-6, tumor necrosis factor-α, fibrinogen, and D-dimer, leading to an oxidative stress injury to various proteins and cellular structures, especially in the vascular compartment.

DM

SARS-CoV-2-induced inflammatory load affects the proper functionality of organs involved in insulin-mediated glucose uptakes, such as skeletal muscle and the liver.[14] In addition, viral infections can induce an integrated stress response, an intracellular signaling pathway, one of the host cell's protective mechanisms against cellular damage. To maintain cell homeostasis, kinases such as protein kinase RNA activated and protein kinase RNA-like endoplasmic reticulum kinase are activated, which can suppress the insulin-signaling pathway through the process of serine phosphorylation of insulin receptors.[15] These are some of the mechanisms through which this virus plays a part in worsening DM and causing insulin resistance.

Thyroid Disease

A mutation in the cellular structure of the spike protein on the surface of SARS-CoV-2 makes it possible for it to bind to and internalize via receptors other than the ACE2 receptors. One of the significant endothelial receptors it can use is the αVβ3 integrin receptor. These receptors interact with various proteins in the extracellular matrix and take an active part in the entry, replication, and proliferation of the SARS-CoV-2.[16] Thyroid hormones, especially T4, can regulate and promote the actions of these integrin receptors. This hormone–integrin interaction also can result in the transcription of cytokines and chemokines, eventually causing a cytokine storm.[17] T3 also has been found to suppress macrophage response to cytokines such as interleukin-6. In low T3 levels, such as in ESS, an exaggerated response by the macrophages can occur, eventually promoting the inflammatory mechanisms.[18]

Discussion

DM and COVID-19

Patients with DM already are at an increased risk of increased mortality and poor outcomes postviral infection, requiring advanced interventions. This increased risk is attributed to a higher level of ACE2 protein and immunodeficiency secondary to low complement levels in diabetic patients.[19] In one of the case series conducted in the initial stages of the pandemic, DM was the third most common comorbidity, with almost one-third of the patients having the disease.[20] The endocrine pancreas also can be damaged, resulting in metabolic dysfunction and increased hyperglycemia episodes in patients with type 2 DM. Moreover, the earlier use of glucocorticoids to treat COVID-19 may have affected the glucose levels of these patients.[19] One study showed that DM and hyperglycemia were seen in more than 50% of the cases. Meanwhile, almost one-third of the cases experienced diabetic ketoacidosis.[21] A recent analysis of a study indicated that COVID-19 patients were approximately 40% more likely to develop DM up to 1 year later when compared with the control group.[22] Similarly, a study involving the US Department of Veterans Affairs database showed an increased incidence of DM (burden per 1000 people at 12 months: 3.46, 95% confidence interval 12.11–14.84) and an increased risk of antihyperglycemic use (risk 1.85, 95% confidence interval 1.78–1.92).[23]

Because of the autoimmune nature of type 1 DM, diagnosis is confirmed by the positive results of several antibodies, including glutamic acid decarboxylase, insulin antibody, zinc transporter 8, and antityrosine phosphatase 2.[24] Worldwide criteria indicate that type 2 DM is diagnosed using fasting glucose, a 2-hour postoral glucose tolerance test, or hemoglobin A1c.[25]

Several drugs have been reported to be safe in diabetic patients with concurrent COVID-19 disease. These drugs include insulin, *dipeptidyl peptidase-4* inhibitors, metformin, glucagon-like peptide 1 analogs, α-glucosidase inhibitors, and thiazolidinedione.[14] In a study by Breton et al, insulin was combined with continuous glucose monitoring, which effectively reduced glucose levels reasonably and safely.[26] In a cohort study carried out by Massachusetts General Hospital, approximately 31% of patients were found to have a fluctuating course of hyperglycemia, initially mild and eventually self-resolving, sometimes going into remission, suggesting acute sequelae of postinflammatory stress response causing insulin resistance. Only one patient (11%) remained with persistent hyperglycemia.[27] A positive association can be determined between COVID-19 and new-onset DM incidence. It is unclear, however whether the damage to β cells is permanent, and further research is needed.

Thyroid and COVID-19

The prevalence of thyroid dysfunction has been variable in several studies, ranging between 13% and 64% in COVID-19 patients.[28] In the thyrotoxicosis in patients with COVID-19 study, most of the patients had normal thyroid function (74.6%). In patients with an abnormal thyroid function test, hyperthyroidism (low thyroid-stimulating hormone [TSH]) was most commonly seen (20.2%) in comparison to hypothyroidism (5.2%).[29] The studies reported that the follicular epithelial cells and parafollicular cells of the thyroid gland are primarily affected.[30] Autopsies have shown damaged thyroid tissue in COVID-19–positive patients, and reports have suggested an increased mortality rate in patients with preexisting thyroid dysfunction.[19] SARS-CoV-2 has been known to affect both spectrums of thyroid disorders: thyrotoxicosis caused by Graves' disease or subacute thyroiditis and hypothyroidism caused by primary autoimmune thyroiditis or secondary hypothyroidism caused by pituitary dysfunction. Most of the cases reported were associated with subacute thyroiditis and ESS.[31] In one of the studies, pre-COVID thyroid function tests were compared with post-COVID tests in patients with and without COVID-19. Baseline TSH and free thyroxine (FT4) measurements were recorded. Patients who tested positive for COVID had a preadmission (in 2019) baseline median TSH of 1.59 mU/L (1.03–2.24 mU/L) versus 1.02 mU/L (0.6–1.65 mU/L) at admission ($P < 0.001$, until September 2020). Similarly, preadmission baseline mean FT4 measurements were recorded, and the mean (standard deviation) was 12.94 pmol/L (2.77 pmol/L) compared with 12.23 pmol/L (2.14 pmol/L) at admission ($P = 0.015$). TSH and FT4 levels for patients without COVID-19 showed no significant difference between baseline and admission (n = 62, $P = 0.72$ and n = 33, $P = 0.74$, respectively).[32] Case reports and case series show an association between COVID-19 and subacute thyroiditis.

Fever and neck pain were the most common symptoms in patients presenting with subacute thyroiditis. Approximately 65% of patients were diagnosed with thyroid function tests after COVID-19–inflicted symptoms were resolved. FT4 and free triiodothyronine (FT3) levels were twice the normal range. This was further supported by positive findings for subacute thyroiditis on imaging (eg, ultrasound, scintigraphy).[33] A study conducted in Milan, Italy enrolled 53 patients with thyroid test abnormalities post-COVID infection, with several of them presenting atypical features such as the absence of neck pain, mild thyroid

Table. Studies comparing changes in endocrine parameters in COVID-19 Patients

Author	Year	Parameters	Prevalence of changes in endocrine parameters in COVID-19 patients (n)	Conclusion
Chen et al[30]	2021	Thyroid function changes (TSH, FT4, FT3)	n = 50 Abnormal TFT: 32/50 (64%) TSH lower than the normal range was present in 56% (28/50) FT3/FT4: not reported	The more severe the COVID-19, the lower the TSH and T3 levels, with statistical significance ($P < 0.001$). The degree of the decreases in TSH and T3 levels was positively correlated with the severity of the disease.
Khoo et al[32]	2021	Thyroid function changes (TSH, FT4, T3)	n = 334 Abnormal TFT: 45/334 (13.5%) Low TSH: 18/343 (5.4%) Normal TSH: 297/3343 (88.9%) High TSH: 19/343 (5.7%) Low FT4: 10/289 (3.4%) FT3: not reported	TSH and FT4 levels were somewhat decreased, which is consistent with a state of nonthyroidal disease. Most COVID-19 patients were euthyroid (86.5%); none were overtly hyperthyroid (as defined by a low TSH and high FT4) and only a small number had overt hypothyroidism (0.6%).
Lania et al[29]	2020	Thyroid function changes (TSH, FT4, FT3)	n = 287 Abnormal TFT: 73/287 (25.4%) Low TSH: 58/287 (20.2%) Normal TSH: 214/287 (74.6%) High TSH: 15/287 (5.2%) High FT3-FT4: 31/73 (42%) Low FT3-FT4: 2/73 (2.8%)	58 patients (20.2%) were found with thyrotoxicosis, 15 (5.2%) with hypothyroidism, and 214 (74.6%) with normal thyroid function.
Cromer et al[27]	2022	Newly diagnosed DM criteria: no DM history and HbA1c ≥6.5% or RBG ≥11.1 mmol/L	n = 1902 Of 1902 individuals admitted with COVID-19, 594 (31.2%) had DM; 77 (13.0%) of these had NIDDM. Of 64 survivors with NIDDM, 36 (56.3%) continued to have DM, 26 (40.6%) regressed to normoglycemia or pre-DM, and 2 were unable to be classified at a median follow-up of 323 d.	
Li et al[43]	2020	No DM history and FPG ≥7.0 mmol/L	n = 453 Of 453 individuals admitted with COVID-19, 98 (21.6%) had DM; 94 (20.8%) of these had newly diagnosed DM.	
Lampasona et al[44]	2020	Newly diagnosed DM criteria: no DM history and mean FPG ≥7.0 mmol/L during hospitalization	n = 509 DM affected 139 (27.3%) of the individuals with confirmed COVID-19: comorbid DM was detected in 90 patients (17.7%), whereas admission-stage DM was discovered in 49 patients (9.6%) (newly diagnosed).	

COVID-19, coronavirus disease 2019; DM, diabetes mellitus; FPG, fasting plasma glucose; FT3, free triiodothyronine; FT4, free thyroxine; HbA1c, hemoglobin A1c; NIDDM, noninsulin-dependent diabetes mellitus; RBG, random blood glucose; TFT, thyroid function test; TSH, thyroid-stimulating hormone; T3, triiodothyronine.

dysfunction, and higher prevalence of thyrotoxicosis in men (64%) as compared with women (36%).[34] Nonsteroidal anti-inflammatory agents are recommended in an acute episode of subacute thyroiditis followed by low-dose prednisone, up to 20 to 25 mg/day, if needed.[35] As indicated by the SANASA polyclinic database, there has been an increase in the number of patients with hypothyroidism and subclinical hypothyroidism post-COVID infection since the pandemic started. This may have been caused by incidental findings following regular visits to the clinics postpandemic or because of the inflammatory damage.[36] Hypothyroidism is either overt or subclinical.

Measurement of serum TSH is the primary screening test for thyroid dysfunction. It usually shows an elevated serum TSH level and a low serum-free T4 level in hypothyroidism.[37] The American Association of Clinical Endocrinology has recommended continuing regular treatment with levothyroxine as required for patients with recently diagnosed hypothyroidism after COVID-19 infection.[38] As reported by multiple studies, ESS also is associated with SARS-CoV-2. The most common abnormality in ESS is the low level of serum T3. It is usually observed in 70% of the patients who are hospitalized. A low serum level of total T4 is associated with a bad prognosis. Both the low levels of serum T3 and T4 are seen in seriously ill patients.[39] One of the studies conducted to determine the changes in thyroid function tests during hospitalization in COVID-19 patients revealed a decrease in TSH, FT3 levels, and FT3:FT4 ratio, with the levels improving with disease progression.[40] A retrospective cohort study conducted in China showed that COVID-19 patients with ESS had a more severe clinical presentation with fever, hypertension, and shortness of breath than non-ESS patients. As such, it was concluded that ESS was associated significantly with disease severity in COVID-19 patients.[41] Management of ESS includes treating the underlying illness, in this case treating COVID-19. There is no need for thyroid hormone replacement in patients with ESS.[42] A summary of studies that have investigated the relation between COVID-19, new-onset DM, and thyroid dysfunction is described in the Table.

Conclusions

The COVID-19 infection affects multiple organ systems such as the pulmonary, cardiovascular, renal, endocrine, and central nervous systems. Endocrine organs, including the thyroid gland, pancreas, and adrenal gland are commonly affected. The interaction among the viral surface component, spike protein, and ACE2 receptor found abundantly in endocrine organs is one of the proposed mechanisms that causes endocrine dysfunction. Moreover, the release of inflammatory mediators caused by the COVID-19 virus is another way by which it causes damage to the organs. Both hyperthyroidism and hypothyroidism are seen in COVID-19 patients, with the ESS and subacute thyroiditis being the most common presentations. Damage to the endocrine pancreas and activation of different cellular protein kinases have been shown to suppress insulin signaling pathways and may lead to insulin resistance. Several studies have reported an increased incidence of DM in COVID-19 patients. The management for all of these conditions remains the same as in COVID-19–negative patients. More extensive research is needed to determine the exact cause and extent of endocrine dysfunction in COVID-19 patients and correctly differentiate the new-onset endocrine pathologies secondary to COVID-19 from the already existing but undiagnosed endocrine pathologies.

References

1. World Health Organization. WHO coronavirus (COVID-19) dashboard. https://covid19.who.int. Accessed January 17, 2023.
2. V'kovski P, Kratzel A, Steiner S, et al. Coronavirus biology and replication: implications for SARS-CoV-2. *Nat Rev Microbiol* 2020;19:155–170.
3. Ranga U. SARS-CoV-2 aerosol and droplets: an overview. *VirusDisease* 2021;32:190–197.
4. Viner RM, Ward JL, Hudson LD, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. *Arch Dis Child* 2021;106:802–807.
5. Carfì A, Bernabei R, Landi F, et al. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020;324:603–605.
6. Abdel-Moneim A, Hosni A. Insights into the possible impact of COVID-19 on the endocrine system. *Arch Physiol Biochem* 2021 March 3:1–9 [online ahead of print].
7. Soldevila B, Puig-Domingo M, Marazuela M, et al. Basic mechanisms of SARS-CoV-2 infection. What endocrine systems could be implicated? *Rev Endocr Metab Disord* 2021;23:137–150.
8. Huang BZ, Sidell MA, Wu BU, et al. Pre-existing pancreatitis and elevated risks of COVID-19 severity and mortality. *Gastroenterology* 2022;162:1758-1760.e3.
9. Patel HK, Makker J, Alemam A, et al. Diarrhea due to SARS-CoV-2-related exocrine pancreatic insufficiency. *Case Rep Gastrointest Med* 2021;2021:1–5.
10. Unsworth R, Wallace S, Oliver NS, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. *Diabetes Care* 2020;43:e170–e171.
11. Wang MY, Zhao R, Gao LJ, et al. SARS-CoV-2: structure, biology, and structure-based therapeutics development. *Front Cell Infect Microbiol* 2020;10:587269.
12. Yang J, Petitjean SJL, Koehler M, et al. Molecular interaction and inhibition of SARS-CoV-2 binding to the ACE2 receptor. *Nat Commun* 2021;12:2996.
13. Sriram K, Insel PA. A hypothesis for pathobiology and treatment of COVID-19: the centrality of ACE1/ACE2 imbalance. *Br J Pharmacol* 2020;177:4825–4844.
14. Lim S, Bae JH, Kwon HS, et al. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol* 2020;17:11–30.
15. Santos A, Magro DO, Evangelista-Poderoso R, et al. Diabetes, obesity, and insulin resistance in COVID-19: molecular interrelationship and therapeutic implications. *Diabetol Metab Syndr* 2021;13:23.
16. Nader D, Fletcher N, Curley GF, et al. SARS-CoV-2 uses major endothelial integrin αvβ3 to cause vascular dysregulation in-vitro during COVID-19. *PLOS One* 2021;16:e0253347.
17. Davis PJ, Lin HY, Hercbergs A, et al. Coronaviruses and integrin αvβ3: does thyroid hormone modify the relationship? *Endocr Res* 2020;45:210–215.
18. Lisco G, de Tullio A, Jirillo E, et al. Thyroid and COVID-19: a review on pathophysiological, clinical and organizational aspects. *J Endocrinol Invest* 2021;44:1801–1814.
19. Shekhar S, Wurth R, Kamilaris CDC, et al. Endocrine conditions and COVID-19. *Horm Metab Res* 2020;52:471–484.
20. Landstra CP, de Koning EJP. COVID-19 and diabetes: understanding the interrelationship and risks for a severe course. *Front Endocrinol* 2021;12:599.
21. Müller JA, Groß R, Conzelmann C, et al. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. *Nat Metab* 2021;3:149–165.

22. Sun B, Huang S, Zhou J, et al. Perspectives of antidiabetic drugs in diabetes with coronavirus infections. *Front Pharmacol* 2021;11:592439.
23. Xie Y, Al-Aly Z. Risks and burdens of incident diabetes in long COVID: a cohort study. *Lancet Diabetes Endocrinol* 2022;10:311–321.
24. d'Annunzio G, Bassi M, de Rose EL, et al. Increased frequency of diabetic ketoacidosis: the link with COVID-19 pandemic. *Front Clin Diabetes Healthc* 2022;3:846827.
25. Sherwani SI, Khan HA, Ekhzaimy A, et al. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomark Insights* 2016;11: 95–104.
26. Breton MD, Patek SD, Lv D, et al. Continuous glucose monitoring and insulin informed advisory system with automated titration and dosing of insulin reduces glucose variability in type 1 diabetes mellitus. *Diabetes Technol Ther* 2018;20:531–540.
27. Cromer SJ, Colling C, Schatoff D, et al. Newly diagnosed diabetes vs. pre-existing diabetes upon admission for COVID-19: associated factors, short-term outcomes, and long-term glycemic phenotypes. *J Diabetes Complications* 2022;36:108145.
28. Giovanella L, Ruggeri RM, Ovčariček PP, et al. Prevalence of thyroid dysfunction in patients with COVID-19: a systematic review. *Clin Transl Imaging* 2021;9:233–240.
29. Lania A, Sandri MT, Cellini M, et al. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. *Eur J Endocrinol* 2020;183: 381–387.
30. Chen M, Zhou W, Xu W, et al. Thyroid function analysis in 50 patients with COVID-19: a retrospective study. *Thyroid* 2021;31:8–11.
31. Naguib R. Potential relationships between COVID-19 and the thyroid gland: an update *J Int Med Res* 2022;50:3000605221082898.
32. Khoo B, Tan T, Clarke SA, et al. Thyroid function before, during, and after COVID-19. *J Clin Endocrinol Metab* 2021;106:E803–E811.
33. Scappaticcio L, Pitoia F, Esposito K, et al. Impact of COVID-19 on the thyroid gland: an update. *Rev Endocr Metab Disord* 2021;22:803–815.
34. Muller I, Cannavaro D, Dazzi D, et al. SARS-CoV-2-related atypical thyroiditis. *Lancet Diabetes Endocrinol* 2020;8:739–741.
35. Martins JRM, Villagelin DGP, Carvalho GA, et al. Management of thyroid disorders during the COVID-19 outbreak: a position statement from the Thyroid Department of the Brazilian Society of Endocrinology and Metabolism (SBEM). *Arch Endocrinol Metab* 2021;65:368–375.
36. Burekovic A, Halilovic D, Sahbaz A, et al. Hypothyroidism and subclinical hypothyroidism as a consequence of COVID-19 infection. *Med Arch* 2022; 76:12–16.
37. Gaitonde DY, Rowley KD, Sweeney LB, et al. Hypothyroidism: an update. *Am Family Physician* 2012;86:244–251.
38. Pramono LA. COVID-19 and thyroid diseases: how the pandemic situation affects thyroid disease patients. *J ASEAN Fed Endocr Soc* 2020;35:155–157.
39. Chopra IJ. Euthyroid sick syndrome: is it a misnomer? *J Clin Endocrinol Metab* 1997;82:329–334.
40. Campi I, Bulgarelli I, Dubini A, et al. The spectrum of thyroid function tests during hospitalization for SARS COV-2 infection. *Eur J Endocrinol* 2021; 184(5):699–709.
41. Zou R, Wu C, Zhang S, et al. Euthyroid sick syndrome in patients with COVID-19. *Front Endocrinol* 2020;11:566439.
42. Inaba H, Aizawa T. Coronavirus disease 2019 and the thyroid—progress and perspectives. *Front Endocrinol* 2021;12:708333.
43. Li H, Tian S, Chen T, et al. Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. *Diabetes Obes Metab* 2020;22:1897–1906.
44. Lampasona V, Secchi M, Scavini M, et al. Antibody response to multiple antigens of SARS-CoV-2 in patients with diabetes: an observational cohort study. *Diabetologia* 2020;63:2548–2558.