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ENDOCRINOLOGY AND COVID-19

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Abstract: COVID-19 has been declared a global pandemic by the WHO and has affected millions of patients worldwide. COVID-19 disproportionately affects people with endocrine disorders, putting them at increased risk of serious illness. We discuss the mechanisms that put people with endocrine disorders at additional risk for severe COVID-19 and review the evidence. We also suggest precautions and management of endocrine conditions in the context of global curfews being imposed and offer practical tips for uninterrupted endocrine care.
Keywords: COVID-19, endocrinology, diabetes, hypertension, obesity, metabolic syndrome.

INTRODUCTION

The onslaught of SARS-CoV-2 infection, also known as COVID-19, has introduced rapidly evolving aspects of understanding and managing the full spectrum of medical information available to humanity. In fact, the landscape has changed so radically that many concepts of care and disability that were once accepted as immutable have now been inverted.

Among the medical subspecialties that were uniquely affected by COVID-19 is the discipline of endocrinology. It is well known that the treatment of diabetes constitutes the bread and butter of most clinical endocrinologists. The COVID-19 pandemic has affected multifaceted aspects of endocrine care. It is now well established that patients with diabetes are at a much higher risk of contracting more severe forms of the disease; in fact, the relationship appears to be bidirectional. Individuals with diabetes are at increased risk of life-threatening complications, primarily of a cardiopulmonary and renal nature. Obese people with pre-existing pre-diabetes or mild diabetes, when exposed to the SARS-CoV-2 virus, develop a very advanced form of hyperglycemia that often requires life-sustaining care and hospitalization. Furthermore, apparently new variations of the disease appear to have emerged that point to the possibility that the virus has a diabetogenic strain. Treatment regimens for patients with advanced COVID-19 infections, such as high-dose corticosteroids, are obviously implicated in worsening hyperglycemia.

Amidst the different aspects of diabetes care, the pandemic has enormously accelerated our propensity to employ all of our so-called big guns at our disposal. Situations that historically were conducive to a slow and methodical approach, perhaps influenced by inertia therapy, now require intensive treatment regimens and continuous blood glucose monitoring. In addition, combination therapies are gaining in popularity. The myriad of non-insulin agents for diabetes management that have appeared on the horizon in recent decades appear to have their own interaction with the COVID virus. For example, both major groups of incretin-based therapies have their own set of benefits in concomitant COVID-19 infection, acting both through and independently of glucagon-like peptide-1 receptors. Dipeptyl peptidase-4 inhibitor receptors are also a target for viral interaction, although the exact significance of this finding is not fully understood. Likewise, sodium-glucose transporter-2 inhibitors have an influence at the mechanistic level, which is still controversial.

Another big leap of logarithmic scale in the COVID era has been galactic advances in healthcare technology, covering two main aspects: glucose monitoring and telehealth delivery of medical care. The management of diabetes in the hospital setting has received a no-objection boost from the FDA to the use of continuous glucose monitoring techniques; This measure was initially taken to increase the protection of healthcare workers caring for

patients with a known or known COVID-19 virus.

However, an unintended and quite salubrious consequence of this action was to utilize CGM for full therapeutic use, including initiation into the inpatient setting and transition to discharge and outpatient use. Cloud-based and Bluetooth-based communication technologies have enabled informed and motivated patients to communicate their glycemic profiles with their physicians on a regular basis, aided by electronic communication outlined by portal as a component of electronic medical records. Complemented by the rapid adoption of the use of telemedicine, this has changed the face of diabetes healthcare delivery and brought high-quality care from the doctor's office to patients' doors and living rooms. The advantages in terms of convenience and safety are of such magnitude that it is fair to proclaim that telehealth is here to stay and grow.

Lest it be assumed that the influence of COVID-19 has been limited to diabetes, other domains of endocrine health have not escaped the virus's onslaught. Endocrine hypertension, with fluctuations in adrenal and renal hormonal mechanisms, has gained new understanding. Pituitary function is extremely sensitive to inflammatory disturbances, and the pituitary-thyroid and pituitary-adrenal axes are prone to virus-induced derangements. The thyroid gland, a key player in metabolism and homeostasis, can be affected by the virus:

SARS-Co-2, manifesting functional changes and a picture similar to thyroiditis. Calcium and vitamin D metabolism and the parathyroid-gut-bone axis are also susceptible to virus-induced changes. Finally, although important, adipose tissue and the release of deleterious and pro-inflammatory cytokines may be key players in the vascular endothelial response. We must also consider the gender gap in the battle against COVID-19 and the consequent impact of genetics, comorbidities, inflammation and lifestyle on outcomes.

In addition to the direct effects on patients and patient care, the COVID-19 pandemic has affected endocrinology in other ways. Like other healthcare professionals, endocrinologists have had to learn and adapt to working in different and sometimes strange and difficult conditions with mandatory and necessary protective equipment. Even so, endocrinologists and their families have not been immune to COVID-19 infection, with sometimes serious consequences. Workdays were lost with obvious effects on patient care. However, some have been affected by COVID infection and have experienced the potentially devastating effects of the virus on themselves and their families firsthand. This also had effects on healthcare systems, which had to deal with less than 100% of the available workforce at any given time. In financial terms, health systems have been overburdened and stretched to, never seen before, with negative effects on medical and nursing education and research.

MATERIAL AND METOHDS

It was also hoped that this study could contribute to making development and implementation as successful as possible. Therefore, the objective of this study was to use the action research methodology to introduce, study and clarify the relationship between the repercussion in patients with chronic kidney diseases and the use of non-steroidal anti-inflammatory drugs in different contexts, in order to meet to the local needs of specific patients.

RESULTS

HYPERGLYCEMIA AND DIABETES

Etiology

The link between diabetes and SARS-CoV-2 is bidirectional. SARS-CoV-2 can

cause pancreatic damage through cytokine storm in the pancreas, resulting in pancreatic endocrine and exocrine damage. The latter was demonstrated in a study in 67 patients with severe COVID-19, with higher amylase levels seen in those with severe COVID-19 compared to mild cases.

In a 'catch-22' situation, hyperglycemia potentially exacerbates the cytokine storm seen in individuals with COVID-19. COVID-19 patients with diabetes had higher levels of IL6, C-reactive protein, and D-dimer than COVID-19 patients without diabetes.

POPULATION DATA (COVID-19)

Mortality related to COVID-19 varied depending on the type of diabetes and overall HbA1c. Adjusted for risk factors including cerebrovascular disease and age, the odds ratio of in-hospital death related to COVID-19 was 2.86 for type 1 diabetes and 1.80 for type 2 diabetes. Based on a population cohort study of people diagnosed with diabetes in England compared to people with HbA1c of 48 to 53 mmol/mol (6.5–7.0%), people with HbA1c of 86 mmol/mol (10.0%) or higher had higher COVID-19-related mortality (hazard ratio (HR) of 2.23 and 1.61 for type 1 and type 2 diabetes, respectively).

COVID-19 presents a unique set of challenges for clinicians as it can precipitate newly diagnosed diabetes and associated complications as a result of endocrine failure due to progressive destruction of the pancreas. In patients hospitalized for COVID-19, 2.8% were newly diagnosed with diabetes. On the other hand, a systematic review of 110 patients with COVID-19 showed that 10% had newly diagnosed diabetes mellitus. In this cohort, it also showed that the mortality rate of the mixed diabetic ketoacidosis group (CAD) and hyperosmolar hyperglycemic condition (HHE) was higher than the CAD-only group. Consequently, all patients admitted with COVID-19 must be screened for diabetes with random blood glucose on admission and HbA1c.

MANAGEMENT

Dexamethasone 6 mg for 10 days is recommended in patients with COVID-19 who require oxygen therapy and has been shown to reduce the mortality rate by up to a third. However, this therapy can exacerbate pre-existing insulin resistance that occurs in COVID-19 and can potentially precipitate hyperglycemia, CAD, and HHS. Even after stopping steroid therapy, it may take several days for insulin resistance to subside.

Consequently, optimal glucose control has been advocated in inpatients in several international diabetes guidelines, with a blood glucose goal of less than 10 to 12 mmol/L and considering variable rate insulin and/or intermediate-acting insulin if target glucose levels are not reached. Not infrequently, large doses of insulin may be required (1-2 units/kg) during acute admission, even in those who had not previously received insulin. International guidelines also emphasized the need to highlight sick days rules in a person with diabetes through educating them about the symptoms of high glucose and encouraging them to check their blood glucose and ketones more often when they are not feeling well. They must never stop their insulin and must have an ample supply of their regular medications and glucose/ketone monitoring equipment.

Treatment for diabetes and hypertension has been widely discussed in this pandemic, as pioglitazone, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs) increase the expression of ACE2 levels and are believed to possibly increase the risk of SARS-CoV-2 viremia. However, to date, there have been no

reports of increased mortality or morbidity in those treated with these drugs and current guidance suggests continuing with these drugs. 19,20 However, metformin, sodium-glucose cotransporter 2 (SGLT2) and glucagon-like peptide-1 (GLP-1) receptor agonists may need to be discontinued during illness, as they may potentiate dehydration and increase the risk of acidosis and CAD.

In vitro studies have demonstrated immunosuppressive effects of dipeptidyl peptidase-IV (DPP-IV) inhibitors and have been suggested as a potential target in reducing of the cytokine storm in COVID-19. A UK observational cohort study looking at type 2 diabetes and COVID-19-related mortality found a non-significant increase in COVID-19-related mortality in those prescribed with DPP-IV inhibitors (HR 1.07); however, this was confounded by the fact that this drug tends to be prescribed in an older and frail population.

ADRENAL INSUFFICIENCY

Adrenal insufficiency can be one of the manifestations of COVID-19. The mechanism is thought to be due to the hypercoagulable state of the infection that causes acute adrenal infarction.

Adrenal insufficiency and COVID-19 have a bidirectional effect on each other, as patients with adrenal insufficiency are also at increased risk of infection. This can be explained by reduced cortisol secretion in adrenal insufficiency. Cortisol mediates the immune system through the upregulation of cytokines secreted by T helper 2 (TH2) cells, cells that produce antibodies against pathogens. Although unrelated to COVID-19, based on a retrospective cohort study of 1,580 patients in the UK, patients with adrenal insufficiency were at least twice as likely to develop lower respiratory tract infection.

DISCUSSION

Overall, nephrotic syndrome is more common in men. The glomerular capillaries are lined by a fenestrated endothelium that lies on the glomerular basement membrane, which in turn is covered by glomerular epithelium, or podocytes, which surround the capillaries with cell extensions called foot processes (pedicelles), these processes interdigitate with junctions cells called the filtration slit diaphragm that together form the glomerular filter. Normally, larger proteins (greater than 69 kD) are excluded from filtration. Destruction of podocytes above a critical mass also leads to irreversible glomerular damage.

FINAL CONSIDERATIONS

In conclusion, endocrinologists routinely care for a high proportion of patients vulnerable to COVID-19 who are at increased risk of life-threatening complications. Physicians must advise patients on emergency preparedness, contingency plans, maintaining adequate but not excessive supplies, social distancing, and access to reliable information resources. In addition, care must be based only on available evidence and caution must be exercised in basing decisions on incomplete or inconclusive evidence. These measures can mitigate some of the risks faced by our vulnerable patient population in this unprecedented crisis.

It is extremely important that a timely and up-to-date compendium is brought together with the vast amount of endocrinology-related knowledge and data that has been acquired since the beginning of the COVID-19 pandemic. With this lofty goal in mind, the editors of the special issue invite research articles and reviews pertaining to the unique and ever-evolving interface of COVID-19 and endocrinology. Following the lead of the great North American

clinician and professor Dr. William Osler, who declared that "medicine is a science of uncertainty and an art of probability", we hope, with this effort, to bring some guidance and clarity to this ever-changing landscape.

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