Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Drug-induced diabetes and hepatoxicity in COVID-19 patients

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Dear Editor,

COVID-19, a newly found diabetes-related health risk, has been linked to diabetic ketoacidosis and drug-related liver disorders. SARS-CoV-2 may cause pleiotropic changes in glucose metabolism, which could exacerbate the pathophysiology of pre-existing diabetes or lead to new disease processes. In COVID-19 treatment, physicians often use glucocorticoid drugs such as methylprednisolone and dexamethasone to control the inflammatory changes during COVID-19 and prevent the severity. Corticosteroids stimulate endogenous glucose production, promote gluconeogenesis, and antagonize insulin's metabolic functions. They also increase the effects of other counterregulatory hormones, like glucagon and adrenaline, which stimulate endogenous glucose synthesis. It has also been demonstrated that the nuclear receptor peroxisome proliferator-activated receptor is required for the increase in endogenous glucose synthesis generated by corticosteroids. Corticosteroids inhibit peripheral glucose absorption in muscle and adipose tissue. Corticosteroids also reduce insulin synthesis and secretion from pancreatic β-cells, causing β-cell failure indirectly through lipotoxicity [1]. Normoglycemic individuals with

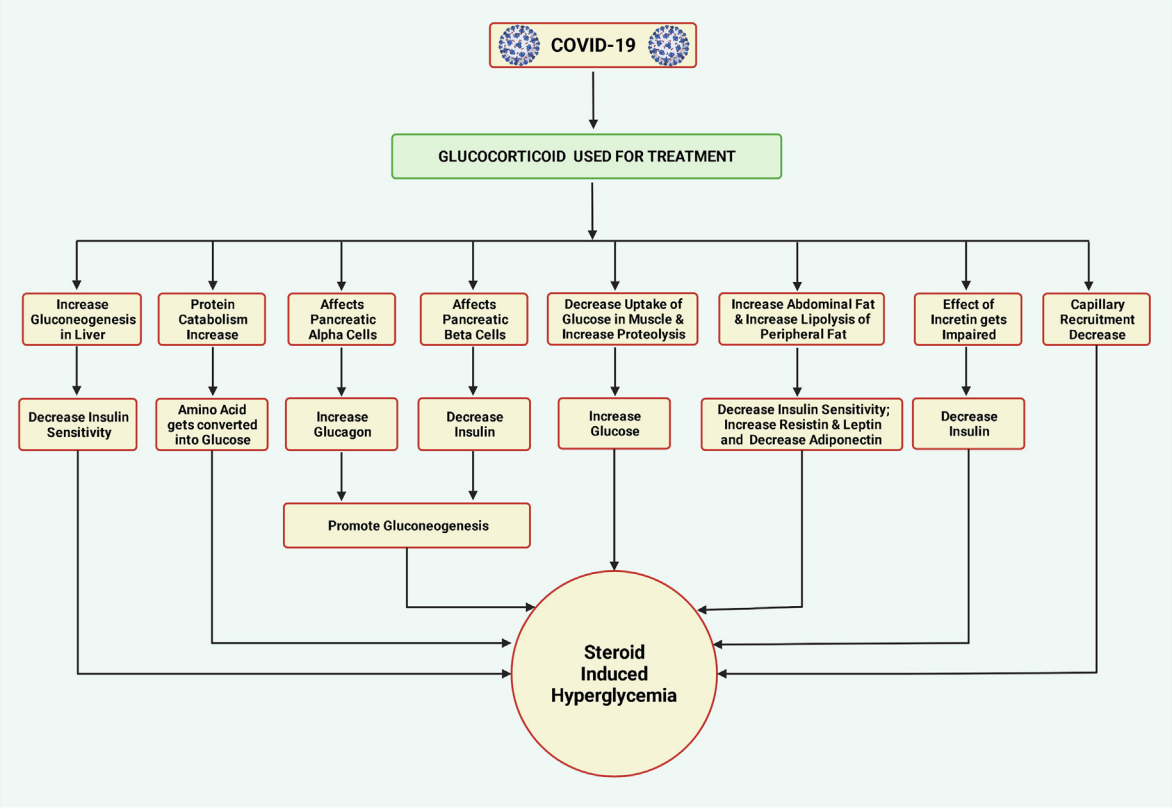

Fig. 1. Glucocorticoid-Induced Hyperglycemia [2]. **(Created with BioRender.com)**.

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decreased insulin sensitivity and insulin production at a low rate prior to steroid use who develop hyperglycemia as a result of the steroids they take (Fig. 1) [2]. Corticosteroids, which are produced from cholesterol metabolism, have the ability to disrupt numerous components of the body's glucose homeostasis. These compounds must be assessed since they alter liver metabolism and steatosis [3].

Various studies show drug-induced liver injury coupled with COVID-19 therapy. According to one study, more than half of the COVID-19 patients who had normal liver function indicators when they arrived had abnormal liver function markers one week later [4]. As per the randomized clinical trials lopivir-ritonavir treatment has been linked to increased AST, ALT, and bilirubin levels [5], whilst remdesivir has only been linked to elevated AST and ALT levels in both treated and control groups [6–8]. Additionally, the use of acetaminophen and hydroxychloroquine has been associated to abnormal liver markers [6,9]. Furthermore, the WHO safety report database clearly demonstrates that remdesivir use is associated with a statistically significant risk of liver damage [10]. The combination of angiotensin II receptor blockers and angiotensin-converting enzyme inhibitors causes increased liver enzymes [5]. Another study of 1040 COVID-19 patients recently revealed that 22.6% of the participants had elevated ALT/AST levels [11]. The tocilizumab medication group had a significantly higher ALT rise in the retrospective investigation of observational cohort analysis [12]. Favipiravir, an oral broad-spectrum, acting as an inhibitor of viral RNA-dependent RNA polymerase, causes cholestatic liver damage in those with ALD-related liver disease.

Declaration of competing interest

There are no financial and non-financial conflicts of interest.

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