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

Pre-existing diabetes is worse for SARS-CoV-2 infection; an endothelial perspective

Sir,

We read with great interest the meta-analysis by Mantovani et colleagues [1] showing a greater risk of severe/critical illness and in-hospital mortality associated with COVID-19 (Coronavirus Disease-19) in patients with diabetes.

Covid-19 is caused by the beta-type coronavirus SARS-CoV-2, highly virulent for its ability to infect with high affinity human cells. It is possible that severe and fatal infections with COVID-19 occur more in subjects with impaired immune system, such as in diabetic patients, the elderly or in patients with cardiovascular diseases (CVD, in particular hypertension), involving multi-organ damage, particularly the cardiovascular system.

The pathogenic mechanism of COVID-19 is far from being understood, but recent evidence suggests that the severity of SARS-CoV-2 infection is attributable, rather than to the virus itself, to the pro-inflammatory cytokine storm and to exaggerated systemic inflammation [2], that triggers abnormal activation of the coagulation cascade and thrombotic states [3]. The incidence of thrombotic phenomena in patients admitted to intensive care units (ICU) is high: about 31% of 184 patients with COVID-19 pneumonia showed thrombotic complications [4,5]. Among in-patients with COVID-19, diabetes and/or hyperglycemia occurred frequently, and glycemic control is of prognostic value in diabetic in-patients [6].

The relationship between hyperglycemia and activation of the coagulation system has been associated in patients with diabetes mellitus [7,8]; more than half of the mortality in diabetes is related to CVD, and the increased risk is related to glycemic control; It is known that hyperglycemia causes endothelial damage, a hallmark of coagulation dysfunction. It is possible that the development of endothelial dysfunction, combined with platelet resistance to anti-aggregatory effects, leads to loss of control over platelet activation. Therefore, the virus infection seems to enhance the pre-existing endothelial damage and metabolic derangements typical of diabetes that, coupled to increased pro-thrombotic cytokines such as interferon-γ (IFNγ), interleukin (IL)-6, IL-17, IL-9, IL-1β, chemokine-ligand-2 (CCL2) and TGFβ [9], with a more deleterious effects, influencing the endothelial activation towards an up-regulation of coagulation factors, the anti-thrombin glycosylation and enhancing thrombosis.

Endothelial dysfunction is associated with several vascular conditions leading to multi-organ failure, and the severity of COVID-19 could be exacerbated in all manifestations of endothelial injury. The critical processes responsible for endothelial injury could be explained by the activation of signalling pathways, as 1) transcription factor nuclear factor kB (NF-kB) known mediator of inflammation, 2) molecules such as advanced glycated end products (AGEs), able to modify the components of the extracellular matrix (ECM), 3) changes in nitric oxide (NO) bioavailability and abnormalities of vascular permeability, that may favor inflammatory responses and the alteration in hemodynamics and shear stress.

We suggest that pre-existing diabetes could contribute to increased severity of COVID-19 by exaggerated pro-inflammatory response at the endothelial level; elevated glucose and oxidative lipids might also contribute to enhancing thrombotic phenomena and severity of infection.

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Declaration of Competing Interest

The authors have no conflict of interests with the contents of this letter.

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