

## Long COVID and ophthalmology: New insights into underlying disease mechanisms

Dear Editor,

With interest, we read the article by Ling *et al.* about the ophthalmic implications of COVID-19 and we must congratulate the authors for bringing out this thought-provoking article.<sup>[1]</sup> These findings of this study have a number of important implications, but no mention is made of long-term vision complications in patients with COVID-19. It is therefore necessary to discuss this particular topic that will be useful for readers.

The term “long COVID” denotes the effects of COVID-19 that persists for weeks or months following the initial recovery. The clinical symptoms of long COVID are versatile, and different organ systems can be involved. Based on the existing literature, 30%–80% of COVID-19 survivors are likely to experience at least one long symptom. Some of them cannot return to normal life and are not able to perform their daily routine duties. Hence, continuous monitoring of COVID-19 symptoms is an inevitable stage of successful containment of the pandemic and minimizing the risk of an outbreak.

SARS-CoV-2 has an organotropism beyond the respiratory tract, including the ocular system. This feature could be related to the angiotensin-converting enzyme (ACE2) expression (an entry receptor for SARS-CoV-2) in different ocular tissues including aqueous humor, retina, corneal, and conjunctival epithelium. Ophthalmic manifestations may be the presenting feature of infected patients or may develop several weeks after recovery. These manifestations vary greatly and affect the visual system in the form of neurological morbidities, coagulopathy, and other ocular disabilities. For instance, corneal nerve loss and increased corneal dendritic cell density have been reported in patients who have recovered from COVID-19, particularly in long-COVID-19 cases with persistent symptoms. Moreover, a significant association was found between corneal nerve fiber loss and the severity of long COVID.<sup>[2]</sup>

These findings are consistent with those of Azab *et al.* They present a case of a 32-year-old male patient who had post-COVID optic neuritis.<sup>[3]</sup> A recent study in Egypt also shows that several ocular morbidities could be more likely to occur in long COVID patients including retinal vascular occlusion, uveitis, and central

serous chorioretinopathy.<sup>[4]</sup> Moreover, some recent reports indicate surface abnormalities (including dry eye disease and tear osmolarity alteration) following infection with COVID-19.<sup>[5]</sup> In addition, eye movement alterations have been reported in post-COVID-19 conditions. The exact mechanism underlying the vision deterioration in long COVID patients still remains unclear. Nonetheless, several hypotheses have been proposed to explain how ocular manifestations develop during or following SARS-CoV-2 infection. The long-term course of the disease can be caused by direct or indirect mechanisms. ACE2 expression in normal human ocular tissues provides a route for virus entry and tissue damage. The detection of SARS-CoV-2 viral RNA in tears and conjunctival specimens has provided evidence for this possibility. Recent research suggests that impairment of endothelial function, hypercoagulability/thrombosis,<sup>[4]</sup> and neurological dysfunctions<sup>[3]</sup> are other pathophysiological mechanisms of ocular manifestations in long-COVID. Immune dysregulation seems to play a role in long-term effects of SARS-CoV-2. It can lead to uncontrolled chronic inflammation and autoimmunity by various mechanisms including excessive production of inflammatory cytokines and production of autoantibodies.

Overall, emerging evidence has shown that the long-term effects of COVID-19 can lead to various vision problems. These symptoms raise questions about the causes of these abnormalities. Elucidating the mechanisms that primarily affect the eyes allows insight into the understanding of the pathophysiology and treatment of clinical symptoms of coronavirus. These findings also confirm the importance of ocular follow-up of COVID-19 patients after recovery.

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### Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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