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

ACE2, COVID19 and serum ACE as a possible biomarker to predict severity of disease

Preliminary epidemiological data indicates that *symptomatic* Coronavirus disease 2019 (COVID-19) in children is uncommon. In a cohort of 44 672 confirmed cases in China, only 1% were younger than 10 years of age [1]. This could suggest that children are less susceptible to infection, or that infection in children leads to asymptomatic or mild disease that remains largely undetected.

Cellular entry of SARS-CoV-2, the causative agent for COVID-19, is facilitated by binding of viral spike proteins to Angiotensin Converting Enzyme 2 (ACE2) receptors on host membranes [2]. This raises the possibility that susceptibility to infection is related to expression of the target ACE2 receptor in virally exposed epithelium [2]. However, a complex too much/too soon relationship is at play here, as the related SARS-CoV virus has been shown to *downregulate* ACE2 after cell entry, a factor contributing to the severe lung pathologies associated with infection with this virus [3].

Evidence suggest that there is a counter-regulatory relationship between ACE2 and its homologue, Angiotensin Converting Enzyme (ACE), as they take part in opposite axes in the Renin-Angiotensin-System (RAS). For example, drugs that inhibit ACE activity induces ACE2 expression [4]. Therefore, high levels of ACE could indicate low levels of ACE2, and vice versa [4].

Children have higher ACE volumes in serum than adults [5]. Considering the inverse relationship between ACE and ACE2, could this difference similarly reflect a lower degree of ACE2 expression in children compared with adults? The same study found that adolescents had higher levels of circulating ACE than adults [5], and is interesting to note that COVID-19 in the age group 10–19 years also amounted to only 1% in the Chinese cohort [1].

It remains to be verified if the low frequency of symptomatic COVID-19 in children and adolescents can be attributed to lower levels of membrane bound ACE2 in this population. It is equally uncertain that serum ACE is inversely related to ACE2 expression in airway epithelium and other tissue. The hypothesis that serum ACE could serve as a biomarker for the severity of COVID-19 therefore hinges on the data being able to draw a line between the propositions outlined above.

Should such a relationship be established, it could provide us with a powerful tool for early intervention in and triage of COVID-19 patients. Low levels of circulating ACE in symptomatic patients could predict mild disease, whereas high levels could be indicative of a more severe progression, cf. the biphasic role of ACE2 found in airway infection with the related SARS-CoV virus [3].

Original publication

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Compliance with ethical standards

As this letter presents a theoretical hypothesis and contains no patient data, approval from the regional committees for medical and health research ethics in Norway was not required.

Declaration of Competing Interest

The author declares no conflict of interest.

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Espen Skarstein Kolberg[a,b,*]

[a] *Department of Clinical Pharmacy, Trondheim Hospital Pharmacy, Trondheim, Norway*

[b] *Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway*

E-mail address: espen.skarstein.kolberg@sykehusapoteket.no.

[*] Corresponding author at: Department of Clinical Pharmacy, Trondheim Hospital Pharmacy, Olav Kyrres gate 10, PB 8905, 7491, Trondheim, Norway.

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