## Why Children are Less Likely to Contract COVID-19 Infection than Adults?

The novel coronavirus disease of 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>[1]</sup> The reported cases of COVID-19 among children have been less severe than those in adults.<sup>[2]</sup> Dong *et al.*,<sup>[3]</sup> in a recent clinical study of more than 2000 infants and preschool-aged children with suspected COVID-19, found that 4% of virologically confirmed cases were symptomatic and among children who were symptomatic, 5% experienced dyspnea and hypoxemia, and only 0.6% progressed to acute respiratory distress syndrome, a substantially lower percentage rate than has been reported in adults.

The findings of children that are less likely than adults to become severely ill from COVID-19 are challenging to discern [4]

Previous data from clinical trials suggest that children and adults who are healthy have a balanced renin-angiotensin system (RAS)—both the angiotensin-converting enzyme (ACE)/angiotensin II and angiotensin-converting enzyme 2 (ACE2)/angiotensin (1–7) pathways.<sup>[5,6]</sup> However, as we age and/or develop disease (hypertension, chronic kidney disease, diabetes, cardiovascular disease), we have relatively more ACE/angiotensin II compared to ACE2/angiotensin (1–7).<sup>[7,8]</sup> The ACE2 pathway increases to compensate, but only to a point, at which time the ACE pathway is essentially unopposed.<sup>[9,10]</sup>

Remember ACE2 degrades angiotensin II ("bad") into angiotensin (1–7) ("good").

We definitely have data that this shift in the RAS occurs more in children than in adults with hypertension, chronic kidney disease, and cardiovascular disease.<sup>[11]</sup>

In COVID-19, the hypothesis is that children have plenty of ACE2 but it easily counteracts the ACE pathway. Thus, children have the same (or higher) risk of infection with SARS-CoV-2, but are protected (in part) from the (likely) angiotensin II-mediated acute lung (and possibly heart/kidney/brain) injury that we see in COVID-19.

For sure, there are many other factors, which may play major role in the pathogenesis of COVID-19 disease. This is just one theory that could be involved.

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Received: 17 Apr 20 Accepted: 18 Apr 20

Published: 19 Jun 20

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Quick Response Code:	Website: www.ijpvmjournal.net/www.ijpm.ir  DOI: 10.4103/ijpvm.IJPVM_199_20

**How to cite this article:** Assadi F. Why children are less likely to contract COVID-19 infection than adults? Int J Prev Med 2020;11:74.