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Letter to the editor

It is too soon to attribute ADE to COVID-19

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In the article “Is COVID-19 receiving ADE from other coronaviruses?” author has suggested the possibility of antibody dependent enhancement (ADE) of SARS-COV-2 disease (COVID-19) as a potential mechanism of the increase in severity of the disease [1]. Although it’s an interesting hypothesis, we should be careful in attributing ADE to enhanced severity of the current disease. As viruses from same group share cross reactivity, it is not uncommon to have cross reactive antibody responses [2]. Outside of the dengue virus serotypes family, which has demonstrated ADE in animal models, the ADE of the viruses using sub-neutralizing antibody levels has largely been restricted to *in-vitro* experiments. Cell culture experiments are considered pre-requisite to moving forward to animal experiments, however, not always result is translated to *in-vivo* setup. There is lack of collective innate/adaptive immune response *in-vitro*, which is presented *in-vivo* and the intricate interactions drive the disease pathology. Deliberate reduction in the neutralizing antibody levels in *in-vitro* assays and lack of innate immune response from other cells may result in an artificial ADE in cell-culture. As COVID-19 spread across the globe a common pattern of underlying morbid conditions such as diabetes and cardiovascular conditions is appearing. Such underlying conditions are known to present immune response dysfunction [3,4]. As reported by Channappanavar et al., immune dysregulation may contribute to lethal pneumonia induction by SARS-CoV [5]. To date, vaccines are the most effective way of protecting against infectious diseases.

Improper attribution of ADE in the absence of robust demonstration in animal models may hinder/scuttle the efforts to develop effective vaccines against SARS-CoV-2 and or other viruses of human health importance.

Opinions expressed herewith are those of the author and are not necessarily representative of those of the USUHS, DoD, or the United States Army, Navy or Air Force.

Conflict of interest

Author declares no conflict of interest.

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