

# Is there antibody-dependent enhancement in SARS Coronavirus 2?

Dear Editor,

As primary care physicians across the world cater to ongoing outbreak due to COVID-19 pandemic, it is perplexing to see the geographical discrepancy in the number of severe cases as well as deaths across countries. Although there are other significant factors, we raise a pertinent question, whether antibody-dependent enhancement (ADE) is a possible contributing factor.

When a virus enters the host, several types of antibodies are formed. Some of these antibodies are neutralising, which hinders the replication of the virus by inhibiting essential steps such as the interaction of the virus with the host cell receptor. In some viruses, such as flaviviruses, enhancing antibodies are being described, which may facilitate the entry of the virus into the host cells. This immune-mediated enhancement of entry and pathogenesis is termed as ADE.<sup>[1]</sup> ADE can be mediated by Fc receptors or complement receptors.<sup>[1]</sup> Besides, ADE has been associated with increased severity. Such an effect has been well-characterised with dengue, where antibody to one serotype enhances the severity of infection due to another serotype.

In coronaviruses, it has been suggested that the severity of severe acute respiratory syndrome (SARS) could have been partly due to ADE to other human coronaviruses such as 229E. *In-vitro* studies have shown that antibodies against SARS-CoV-1 at high dilutions resulted in ADE. However, ADE could not be demonstrated in vaccine models of rhesus macaques. Reports of ADE have also been described for the Middle East respiratory syndrome as well.<sup>[2-4]</sup>

In COVID-19, several reasons, such as higher median age has been put forward to explain a higher percentage of severity and mortality in certain regions. Whether ADE can serve as a possible explanation for the uneven geographic distribution of severity and mortality remains to be seen. Individuals in these areas may have been primed with pre-existing locally circulating human coronaviruses and ADE to these coronaviruses may have some role in the increased severity of COVID-19. The prevalence of four human coronaviruses (HCoV-OC43, 229E, NL63 and HKU1) before COVID-19 outbreak in regions with high reported mortality are as follows: 2.4% (Spain), 5.5% (Iran), 9.3% (France), Italy (10.5%) and China (23%).<sup>[5-9]</sup> There is a need

for serological surveys of human coronaviruses in serum samples of COVID-19 affected patients (mild and severe) to understand whether there is a correlation between pre-existing strain-specific antibodies to locally circulating human coronaviruses and severity of COVID-19. Convalescent plasma therapy from patients who have recovered from COVID-19 has been tried in several case series as a treatment with good results.<sup>[10]</sup> Vaccine trials across the world will start in the coming months.

Besides, understanding its possible role in severity, knowledge of ADE will be helpful for the primary care physicians to understand the safety and efficacy of convalescent plasma therapy and vaccines for COVID-19.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

**Rohit Kumar<sup>1</sup>, Nitin Gupta<sup>2</sup>,  
Parul Kodan<sup>3</sup>, Ankit Mittal<sup>1</sup>,  
Manish Soneja<sup>4</sup>, Naveet Wig<sup>5</sup>**

<sup>1</sup>Senior Resident, <sup>4</sup>Additional Professor, <sup>5</sup>Professor, Department of Medicine, AIIMS, New Delhi, <sup>2</sup>Assistant Professor, Department of Infectious Diseases, KMC Manipal, Karnataka, <sup>3</sup>Assistant Professor, Department of Medicine, Lady Hardinge Medical College and Dr. RML PGIMER, New Delhi, India

**Address for correspondence:** Dr. Manish Soneja, Department of Medicine, AIIMS, New Delhi - 110 029, India.  
E-mail: manishsoneja@gmail.com

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**Received:** 04-04-2020

**Revised:** 26-04-2020

**Accepted:** 08-05-2020

**Published:** 31-05-2020

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> <a href="http://www.jfmprc.com">www.jfmprc.com</a>
	<b>DOI:</b> 10.4103/jfmprc.jfmprc_540_20

**How to cite this article:** Kumar R, Gupta N, Kodan P, Mittal A, Soneja M, Wig N. Is there antibody-dependent enhancement in SARS Coronavirus 2? *J Family Med Prim Care* 2020;9:2589-90.

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