*Letter to the editor*

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# Letter regarding "Elastase and COVID-19 relationship, and potential natural resource as elastase inhibitors: A comprehensive review"

Dear Editor,

I recently came across an article published in your journal titled "Elastase and COVID-19 Relationship, and potential natural resource as elastase inhibitors: A comprehensive review" by authors Ambarwati *et al*. [1]. The article gave an extensive outline of the path physiology of covid-19 caused by SARS CoV2 virus and emphasized the role of elastase in COVID-19 path physiology produced from neutrophils and the inflammatory response brought about in the form of cytokine storm and impact on the respiratory system.

However, it would like to point out an important oversight in the path physiological process which involves the development of severe COVID-19 infection. The SARS CoV2 virus enters the respiratory cells with the help of structural Spike protein S present on the surface. The Spike protein S has 2 domains S1 and S2. S1 binds with ACE (angiotensin-converting enzyme receptors) present in respiratory epithelium and S2 is cleaved by TMPRSS2 (transmembrane serine proteases) which activates S2 the domain of Spike protein and allows fusion of the S2 domain followed by entry inside respiratory cells. The SARS CoV2 virus upon entering the respiratory cells replicates and activates the innate immune system of the host through MAVS (mitochondrial antiviral signaling) cascade with the help of MDA-5 (melanoma differentiation-associated protein) and RIG-I (retinoic acid-inducible gene) pathways.

The innate system upon activation produces type 1 and type 3 interferon's. These interferons act in a paracrine and autocrine fashion via the plasma membrane receptors and lead to activation of JAK–STAT1/2 signaling cascade and results in the expression of interferon-stimulated genes (ISGs) that have direct and indirect antiviral functions [2].

The above path physiological process is an important mechanism explaining the severe covid19 infection leading to cytokine storm and death of patients. The inclusion of this path physiological process of severe COVID-19 infection will add to the existing Explanations described in the article and help us try to understand SARS-CoV2 COVID-19 infection better.

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## CONFLICTS OF INTEREST

Author declares that there are no conflicts of interest.

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