World Journal of Gastroenterology

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World J Gastroenterol 2021 December 14; 27(46): 7925-7942

DOI: 10.3748/wjg.v27.i46.7925

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

MINIREVIEWS

COVID-19 and gut immunomodulation

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Author contributions: Roy K and Agarwal S contributed equally; Roy K, Agarwal S, Banerjee R, Paul MK, and Purbey PK contributed to the draft preparation of the article; Paul MK and Purbey PK conceptualized and edited the article.

Conflict-of-interest statement: No Conflict-of-interest.

Country/Territory of origin: United States

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external

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Abstract

The disease coronavirus disease 2019 (COVID-19) is a severe respiratory illness that has emerged as a devastating health problem worldwide. The disease outcome is heterogeneous, and severity is likely dependent on the immunity of infected individuals and comorbidities. Although symptoms of the disease are primarily associated with respiratory problems, additional infection or failure of other vital organs are being reported. Emerging reports suggest a quite common co-existence of gastrointestinal (GI) tract symptoms in addition to respiratory symptoms in many COVID-19 patients, and some patients show just the GI symptoms. The possible cause of the GI symptoms could be due to direct infection of the epithelial cells of the gut, which is supported by the fact that (1) The intestinal epithelium expresses a high level of angiotensin-converting enzyme-2 and transmembrane protease serine 2 protein that are required for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry into the cells; (2) About half of the severe COVID-19 patients show viral RNA in their feces and various parts of the GI tract; and (3) SARS-CoV-2 can directly infect gut epithelial cells *in vitro* (gut epithelial cells and organoids) and *in vivo* (rhesus monkey). The GI tract seems to be a site of active innate and adaptive immune responses to SARS-CoV-2 as clinically, stool samples of COVID-19 patients possess proinflammatory cytokines (interleukin 8), calprotectin (neutrophils activity), and immunoglobulin A antibodies. In addition to direct immune activation by the virus,