

## EDITORIAL

# Post-COVID-19 functional gastrointestinal disorders: Prepare for a GI aftershock

COVID-19 patients typically present with respiratory symptoms and fever, and we now know that gastrointestinal (GI) symptoms are not uncommon. Studies show that between 3% and 79% of COVID-19 patients additionally develop GI symptoms like diarrhea, abdominal pain, belching, vomiting, and GI bleeding.<sup>1</sup> COVID-19 patients with diarrhea were more likely to develop multi-organ damage and require intensive care unit (ICU) admission compared with COVID-19 patients with no or mild diarrhea.<sup>2</sup> It is increasingly recognized that a substantial number of COVID-19 patients develop long-term sequelae of the infection, in particular fatigue and breathlessness. Additionally, GI symptoms in post-COVID syndrome include abdominal pain, nausea, diarrhea, anorexia, and a reduced appetite.<sup>3</sup>



In this issue of JGH, Ghoshal *et al.* have reported that 9% of 288 adults with COVID-19 infection developed functional gastrointestinal disorders (FGIDs) (irritable bowel syndrome [IBS] 5.3%, uninvestigated dyspepsia 2.1%, and IBS/dyspepsia overlap 1.8%) at 6 months post infection, based on the Rome III criteria.<sup>4</sup> This was in contrast to a 0.38% FGID development rate at 6 months amongst 264 age and gender-matched historical control healthy adults. Predictive factors for the development of post-COVID-19 FGID included symptomatic patients at presentation, baseline GI symptoms, and more severe COVID-19 illness. The authors additionally explored psychological morbidity using a questionnaire and observed a higher rate of psychosocial disturbance amongst adults with FGID compared with those without. Although depression and anxiety increased significantly during the COVID-19 pandemic,<sup>5</sup> there is biological plausibility for the development of FGID post COVID-19. Direct viral invasion of the GI tract, presence of viral RNA in feces, increase in fecal calprotectin, gut microbiota dysbiosis, altered intestinal permeability, involvement of enteric nervous system, and mucosal damage on GI endoscopy are but some of the evidence for a “post-infectious” mechanism of FGID development.<sup>1</sup>

Post-infectious functional gastrointestinal disorders (PI-FGIDs) have been recognized following acute bacterial, protozoal, or viral gastroenteritis. The estimated risk of PI-FGID is about 1 in 10 adults following an acute GI infection.<sup>6</sup> Reported risk factors for PI-FGIDs include female gender, severe enteritis, the use of antibiotics during the infection, and psychological factors like anxiety and depression.<sup>7</sup> The frequency of post-COVID-19 FGIDs in this study appears to be lower than that of other PI-FGID, but this is not unexpected as COVID-19 is primarily a respiratory infection, with approximately 50% of patients developing acute GI symptoms.

So what is the concern if < 10% of adults with COVID-19 develop an FGID? FGIDs are disorders of brain–gut interaction and are notoriously difficult to manage.<sup>8</sup> Although FGIDs rarely lead to mortality, they have been shown to lead to increased healthcare utilization in both primary and secondary care, with similar rates of hospitalization to organic diseases such as inflammatory bowel disease and chronic liver disease.<sup>9</sup> To date, an

estimated 270 million of the global population have been infected with COVID-19.<sup>10</sup> If < 10% of these COVID-19 patients develop FGIDs globally, the potential for an increased healthcare, economic, and social burden from these post-COVID-19 FGIDs could be phenomenal.

The key to riding the potential tsunami of post-COVID-19 FGIDs includes education of patients about the nature of FGIDs, minimizing unnecessary investigations, managing expectations, and providing reassurance. The mechanisms, risk factors, and potential genetic predisposition for PI-FGID remain only partly elucidated. The COVID-19 pandemic has been a global disaster, but it may also provide an opportunity to study and investigate disease mechanisms in conditions such as PI-FGID. For the first time, there is a large homogenous group of FGID patients with a similar etiology (albeit different mechanisms) that will provide us with an opportunity to study disease mechanisms in conditions such as PI-FGID. Perhaps soon you will be asking your FGID patient: “Did you have your symptoms before or after COVID-19?”

Kewin Tien Ho Siah MBBS, MRCP, SAB \*<sup>†</sup> and Sanjiv Mahadeva MBBS, MRCP, CCST, MD <sup>‡</sup>

\*Division of Gastroenterology and Hepatology, University Medicine Cluster, National University Hospital, <sup>†</sup>Department of Internal Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; <sup>‡</sup>Division of Gastroenterology, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

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