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Mild Pancreatic Enzyme Elevations in COVID-19 Pneumonia: Synonymous With Injury or Noise?



Dear Editors:

We read the article¹ by Dr Wang and colleagues with interest. They suggest that pancreatic enzyme elevations signify pancreatic injury due to cytotoxic effects of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Although preliminary data² suggest that the transmembrane protease serine 2 (TMPRSS2) and angiotensin-converting enzyme 2 (ACE2), which mediate cellular entry of SARS-CoV-2, are found on pancreatic ductal cells, the pathologic consequences of this are not clear at the current time. The use of serum pancreatic enzyme elevations to delineate the presence or degree of pancreatic injury is not validated or recommended, for example, in asymptomatic patients for monitoring of checkpoint inhibitor-induced pancreatic toxicity³ or for determining the degree of pancreatic injury in trauma patients.⁴

The clinical significance of serum amylase and lipase elevations primarily centers on their role in diagnosing acute pancreatitis. In the absence of imaging, none of the 9 patients in this series met the revised Atlanta classification criteria for acute pancreatitis, as there was no report of abdominal pain and the pancreatic enzymes were not above 3 times the upper limit of normal (ULN). Serum lipase is widely recommended over amylase for diagnosing acute pancreatitis because of its improved sensitivity. Therefore, any potential clinical merits of this study lie primarily in those 5 patients (cases 1, 4, 5, 8, and 9) with elevated lipase levels. However, lipase can be elevated without obvious major clinical sequelae for a variety of reasons not related to direct cytotoxic effects of SARS-CoV-2, including intensive care unit critical illness (case 4), diabetes (cases 1 and 5), and opioid use (not detailed).⁵⁻⁷ Of the 5 cases of mildly elevated lipase, only 2 (cases 8 and 9) do not have obvious alternative explanations as delineated previously, and the lipases in those cases are 85 and 77 U/L (ULN was 70 U/L), respectively. This could be within the margin of error for the laboratory assay. Our own laboratory, for example, has a serum lipase ULN of 63 U/L with a 10% margin of error (personal communication, 2020); therefore, the application of this margin of error to case 9 would bring their lipase into the normal range. We would also point out that 7 of the 9 patients received corticosteroids (cases 1, 3, 4, 5, 6, 7, 8), which has been associated with elevated lipase levels.⁸

In summary, most of the patients in the study by Wang et al.¹ have alternative explanations for their lipase elevations besides SARS-CoV-2 infection, and the mild enzyme elevations themselves are of equivocal clinical significance. Future studies are needed to evaluate if SARS-CoV-2 infection of pancreatic cells leads to injury on a mechanistic level before translation to clinical practice settings.

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Conflicts of interest

Vikesh K. Singh is a consultant for AbbVie and Theraly, medical advisory board participant for Cook Medical, and receives grant support from Orgenesis. These financial interests do not pertain directly to this work. The remaining authors disclose no conflicts.

Most current article

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Reply. We read with great interest the letter by Dr Enrique de-Madaria et al¹ and Dr Aditya Ashok.² de-Madaria et al¹ highlighted that the definition of pancreatic injury in our study lacked specificity, because many factors could lead to increased pancreatic enzyme (PE) levels, not just pancreatic injury. Ashok et al² indicated that it was not recommended to use the serum PE elevations to delineate the presence or degree of pancreatic injury.² They all mentioned that none of our cases met the revised Atlanta classification criteria for acute pancreatitis. Indeed, our study mainly proposed and emphasized the potential pancreatic injury caused by the novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]).³ Because it was reported for the first time, the underlying mechanism confused us until now.

Currently, several studies have focused on pancreatic injury in patients with Coronavirus Disease 2019 (COVID-19). Naren et al⁴ reported the occurrence of acute necrotizing pancreatitis in a patients with COVID-19 in the absence of any known risk factors. Severe acute