


# Raised serum amylase in patients with COVID-19 may not be associated with pancreatitis

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Dear Editor

COVID-19 is a global health emergency that principally causes respiratory illness. However, a myriad of extrapulmonary organ systems may be affected, and it has been proposed that pancreatic injury occurs as a result of SARS-CoV-2 infection. A recent study<sup>1</sup> reported pancreatic injury in 17 per cent of 52 patients admitted with severe COVID-19, although this was defined by an increase in serum amylase level alone. In a further study<sup>2</sup> of 64 patients with severe COVID-19, 18 per cent had an increased serum amylase concentration, which was also attributed to pancreatic injury. Further observations, case reports, and a case series of patients with COVID-19 suffering from pancreatitis have been published, strengthening the notion of COVID-19-related pancreatic injury<sup>3–5</sup>. However, it should be acknowledged that the majority of these articles reported isolated observations and, as reported in *BJS*, there is a deficiency in ‘serum amylase measurements exist[ing] in the international literature, requiring urgent rectification’<sup>6</sup>. Altogether, ‘actual evidence of clinical pancreatitis secondary to SARS-CoV-2 is dubious’<sup>5</sup>.

The authors therefore undertook a retrospective analysis of all patients with COVID-19 admitted to the ICUs at three London teaching hospitals between 14 March and 22 May 2020 in order to investigate the prevalence of either biochemical and/or radiological evidence of pancreatic injury. Peak and mean serum amylase concentrations were studied in relation to ICU mortality. An abnormally raised peak amylase concentration refers to a peak concentration greater than the upper limit of normal (ULN) (over 100 units/l).

Among 234 patients included in the study, the ICU mortality rate was 37.2 per cent (87 of 234) (*Table 1*). In total, 158 of 234 patients (67.5 per cent) had an abnormally raised peak amylase level during ICU admission, and in 52 (22.2 per cent) the peak value was more than three times greater than the ULN. Furthermore, 97 patients in this cohort (41.5 per cent) had a mean amylase concentration greater than the ULN. Sixty-one patients (26.1 per cent) met local clinical criteria for cross-sectional imaging of the abdomen, after which four (1.7 per cent) met the revised Atlanta criteria (rAC) for acute pancreatitis. Of these four patients, two survived ICU admission and two did not.

**Table 1 Patient demographics, duration of organ support, and mean and peak amylase concentrations in survivors and non-survivors**

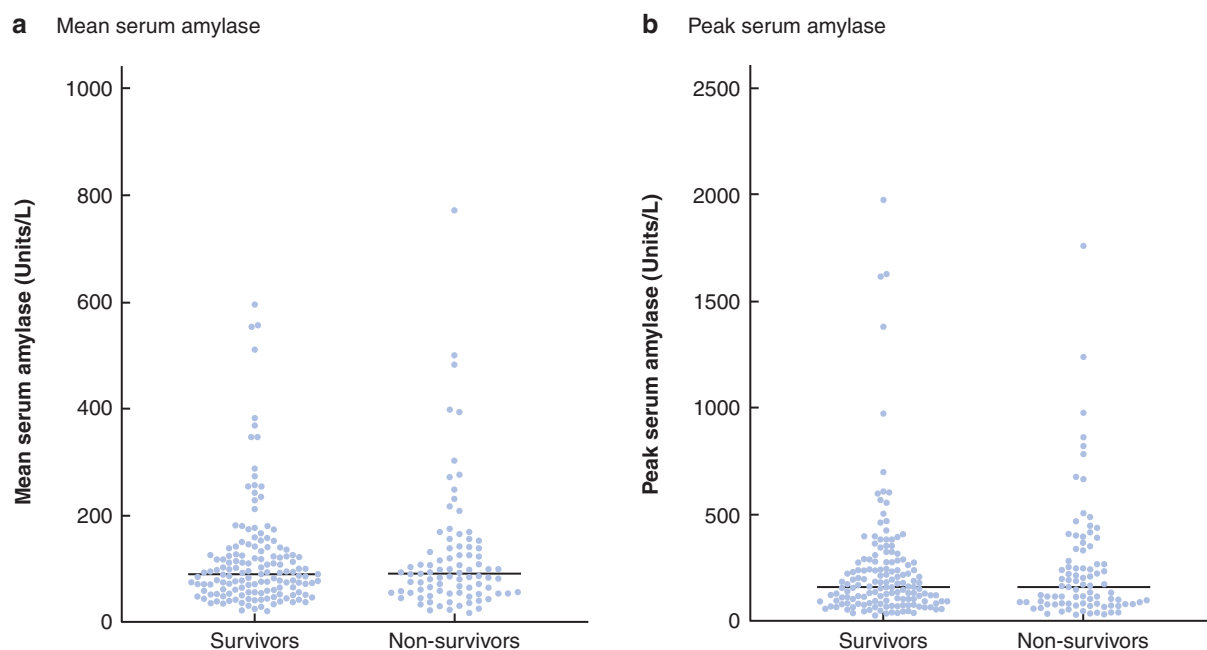
	All patients (n = 234)	Survivors (n = 147)	Non-survivors (n = 87)
Age (years)*	59 (51.0–64.3)	56.0 (47.0–63.0)	61.0 (57.0–66.0)
Men	167 (71.4)	101 (60.5)	66 (39.5)
BMI (kg/m <sup>2</sup> )*	27.7 (24.5–31.4)	27.6 (24.8–32.7)	27.6 (23.9–30.3)
Duration of ICU stay (days)*	14.7 (6.0–31.1)	16.0 (5.6–35.6)	12.1 (6.0–20.0)
Duration of advanced respiratory support days (days)†	13.0 (4.0–25.3)	13.0 (3.0–29.0)	13.0 (6.0–2–,0)
Mean amylase (units/l)*	90.3 (56.2–136.5)	90.0 (56.3–132.9)	90.5 (55.1–139.1)
Mean amylase > ULN (100 units/l)	97 (41.5)	63 (65)	34 (35)
Peak amylase (units/l)	158 (82.8–274.5)	157 (90.0–273.0)	160 (79.0–330.0)
Peak amylase > 3 × ULN (300 units/l)	52 (22.2)	30 (58)	22 (42)
Peak amylase > 2 × ULN (200 units/l)	94 (40.2)	58 (62)	36 (38)
Peak amylase > ULN (100 units/l)	158 (67.5)	103 (65.2)	55 (34.8)
Peak amylase ≤ ULN (100 units/l)	76 (32.5)	44 (57.9)	32 (42.1)

Values in parentheses are percentages unless indicated otherwise; \* values are median (i.q.r.). † Mechanical ventilatory support via endotracheal tube. ULN, upper limit of normal.

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**Fig. 1** Mean and peak serum amylase concentrations among survivors and non-survivors

**a** Mean and **b** peak serum amylase. Horizontal line indicates median value. Upper limit of normal 100 units/l.

There was no statistically significant difference in mean and peak amylase concentrations between ICU survivors and non-survivors ( $P = 0.890$  and  $P = 0.925$  respectively) (Fig. 1).

These results demonstrate that, although a significant proportion of critically unwell patients with COVID-19 disease had a raised serum amylase concentration, only a minority (1.7 per cent) had a confirmed diagnosis of acute pancreatitis as defined by the rAC. Furthermore, there was no statistical difference in amylase concentrations between patients who survived and those who died. Previous studies<sup>1-4</sup> have suggested that patients with COVID-19 are at increased risk of pancreatic injury, defined as an increase in serum amylase concentration beyond the normal laboratory range. Yet, the reported increases in pancreatic biomarkers were only mild to moderately abnormal, and the data do not corroborate this theory of pancreatic injury. A raised serum amylase level may be multifactorial given that multiple organs can produce and/or secrete amylase, for example in generalized gut inflammation or impaired renal excretion. Therefore, in practice, acute pancreatitis is usually diagnosed by multi-modal criteria and the rAC recommends correlating biochemical data (amylase level) with radiological imaging and clinical findings (such as typical abdominal pain).

The present results suggest that CT of the abdomen is not necessarily indicated in the context of a raised serum amylase level alone. It is proposed that a raised serum amylase value in patients with severe COVID-19 is most frequently not immediately attributable to acute pancreatitis or a clinically important pancreatic injury, but is more likely to be a non-specific manifestation of shock/critical illness. The authors hope this gives clinical teams reassurance when managing critically ill patients with COVID-19 who have an abnormally raised amylase level, and suggest that cross-sectional imaging should not be instigated

upon this finding, independent of other clinical suspicions of pancreatic injury.

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