Liver injury, hypoalbuminaemia and severe SARS-CoV-2 infection

We have read with interest the recent study published in *Gut* by Weber *et al*[1] outlining liver abnormalities in 217 patients admitted with COVID-19 infection in Germany. Along with respiratory failure, deranged liver blood tests have been demonstrated in many cohort studies of patients admitted with SARS-CoV-2 infection, the clinical relevance of which has been unclear to date.[2 3]

The authors of this study demonstrated that deranged liver blood tests on admission were associated with more severe morbidity and mortality. Notably, hypoalbuminaemia on admission in this cohort was associated with a severe COVID-19 disease course.

A review of 310 patients admitted with COVID-19 to our institution in Dublin revealed abnormal liver blood tests were present in almost 50% of patients, in particular raised gamma-glutamyl transferase (gGT) levels (table 1), similar to that noted by Weber and colleagues.[1] In our patient cohort, hypoalbuminaemia on admission to hospital was also an independent predictor of mortality, validating the findings of their prospective study. Multivariate analysis of our cohort showed a significant association between COVID-19-related mortality and serum albumin on admission (OR 0.90, 0.85–0.96; p=0.002); in a model incorporating older age, male sex, high MULBSTA score (a predictive score of viral pneumonia mortality[4]) and body mass index, hypoalbuminaemia predicted death, with area under the curve receiver operating characteristic at 0.8 (figure 1). A notable elevation in liver blood tests, especially gGT, was evident in this cohort, and no association between this elevation in liver blood tests and mortality was identified. The findings outlined here are taken from a local study entitled 'COVID-19 and liver blood test derangement'.

The exact relationship between SARS-CoV-2 infection, liver injury and hypoalbuminaemia has not yet been determined and warrants further investigation.[5]

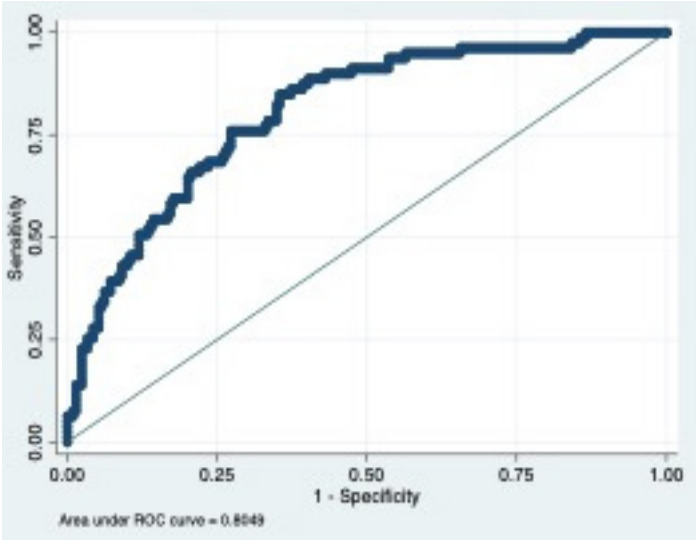

Figure 1 Hypoalbuminemia ROC when incorporated into model.

Naturally, albumin is a negative acute phase reactant, and decreased albumin levels may simply reflect severe systemic inflammation[6 7]; in our cohort albumin levels correlated significantly with other inflammatory markers such as C reactive protein (CRP) and white cell count (Spearman's r=−0.36 and r=−0.31 for albumin vs CRP and albumin vs white cell count, respectively; both p<0.0001).

The findings of both Weber *et al*[1] and our study highlight the potential clinical utility of albumin levels to identify admitted patients with COVID-19 at a higher risk of mortality. Further studies to elucidate the underlying pathophysiological mechanisms are warranted.

Table 1 Baseline characteristics and liver blood tests on admission for 310 COVID-19 patients

Baseline characteristics*	Patients with COVID-19 (N=310)
Age, median (years)	69 (range 21–95)
Male gender, % (n)	61 (188/310)
Ethnicity, % (n)	
Caucasian	96.5 (299/310)
Black	1.6 (5/310)
Romany	1.9 (6/310)
BMI (kg/m^2)	26 (15–55)
CRP (mg/L)	155 (1.6–510)
MULBSTA score, median	9 (range 2–19)
Death, % (n)	26.8 (83/310)
Liver blood tests on admission, % (n)	
Bilirubin >20 µmol/L (range 0–21 µmol/L)	5 (18/310)
ALT >40 IU/L (range 0–41 IU/L)	20 (62/310)
AST >40 IU/L (range 0–40 IU/L)	28 (87/310)
Alkaline phosphatase >130 IU/L (range 40–130 IU/L)	17 (54/310)
GGT >40 IU/L (range 0–59 IU/L)	48 (150/310)
Albumin <35 g/L (range 35–52 g/L)	23 (71/310)

*Mean (±SD) unless stated.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C reactive protein; GGT, gamma-glutamyl transferase.

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Contributors CEF collected and analysed the data. CM and KB carried out the statistics on the data. MB, NR, PR and AW collected the data. GC, EdB and JR supervised the project.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study where the findings outlined here were taken was approved by the Beaumont Hospital Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Foley CE, Mulvey C, Boylan M, *et al*. *Gut* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/gutjnl-2021-324570

Received 3 March 2021
Accepted 19 May 2021

Gut 2021;**0**:1–2. doi:10.1136/gutjnl-2021-324570

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