

## Gastrointestinal Symptoms and Liver Injury on Admission in a Hospitalised Population with COVID-19 Infection

### Sintomas Gastrointestinais e Lesão Hepática à Admissão numa População Hospitalizada com Infecção por COVID-19

**Keywords:** COVID-19; Gastrointestinal Diseases; Liver Diseases; SARS-CoV-2

**Palavras-chave:** COVID-19; Doenças do Fígado; Doenças Gastrointestinais; SARS-CoV-2

Dear Editor,

The novel coronavirus disease 2019 (COVID-19) may present with gastrointestinal symptoms and liver injury, but current evidence on their prevalence and association with disease-severity and severe outcomes is conflicting.<sup>1-3</sup>

We retrospectively analysed the prevalence of gastrointestinal manifestations and elevated liver enzymes in adult patients hospitalised in wards of a tertiary hospital in Portugal, with a COVID-19 diagnosis between March and August 2020. We studied their association with hospital mortality, intensive care unit (ICU) admission and hospital length of stay. The study was approved by the hospital's Ethics Committee.

A total of 561 patients were selected, mean aged 62 ± 20 years and 63% men. After excluding 25 patients due to previous gastrointestinal or liver disease, 536 patients were eligible for analysis. Gastrointestinal symptoms were present in 22% and included diarrhoea (14%), nausea/vomiting (10%) and abdominal pain/discomfort (5%). Elevated liver enzymes on admission were found in 30% of the patients. Seventeen percent (n = 93) presented with an isolated aspartate transaminase (AST) elevation [median 49 (43;62) UI/L] and 13% (n = 70) with both AST and alanine aminotransferase (ALT) elevated [median 66 (51;10) UI/L and 83 (65;109) UI/L, respectively], with a mean AST/ALT ratio of 0.94 ± 0.48.

We found an association between liver enzyme changes and mortality in multivariable analysis adjusted for age, gender and patients' comorbidities such as hypertension, obesity, diabetes mellitus and respiratory disease. Patients with isolated AST elevation and with both AST and ALT elevations were associated with greater hospital mortality [odds ratios (OR) of 2.28 (95% CI 1.19 - 4.35,  $p = 0.012$ ) and 2.68 (95% CI 1.12 - 6.45,  $p = 0.028$ ), respectively], compared to patients without liver changes. The presence

of gastrointestinal symptoms had no statistically significant association with hospital mortality ( $p = 0.078$ ) or ICU admission ( $p = 0.750$ ). Patients with isolated AST elevation had an OR of 2.33 (95% CI 1.37 - 3.98,  $p = 0.002$ ) of being admitted to an ICU than patients without liver changes, but these differences were not seen for patients with elevation of both enzymes (OR 1.65, 95% CI 0.88 - 3.09,  $p = 0.119$ ). Median hospital length of stay was 10 (5; 12) days, without differences between groups with gastrointestinal symptoms ( $p = 0.305$ ) or elevated liver enzymes ( $p = 0.259$ ).

In our Portuguese cohort, the prevalence of gastrointestinal symptoms and liver injury on presentation was similar to that of previous reports. Several mechanisms for these changes have been proposed, including the direct cytopathic effect of the virus mediated by ACE-2 receptors, which are highly expressed in intestinal epithelial cells, hepatocytes and cholangiocytes, and injury mediated by ischaemia and systemic inflammatory response in patients presenting with severe infection.<sup>4,5</sup>

While gastrointestinal manifestations were unrelated to worse outcomes, liver injury on admission, characterized by moderate AST and ALT elevations, was associated with greater hospital mortality. This should raise awareness to the possible prognostic value of elevated liver enzymes on admission in patients infected with SARS-CoV-2.

#### AUTHORS CONTRIBUTION

ROS, MIC: Data acquisition, statistics analysis, draft of the manuscript.

VA, JF, AD: Data acquisition.

ACR, DC, FM, AP, JC: Critical review of the paper.

#### DATA CONFIDENTIALITY

The authors declare having followed the confidentiality rules of their working centre regarding patients' data collection. Data was collected and stored in a pseudonymized database for statistical analysis. The authors further declare this work followed the regulations established by the Helsinki Declaration of the World Medical Association updated in 2013.

#### COMPETING INTERESTS

The authors declare no conflict of interest.

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