Title:

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Assessment of liver damage in patients with COVID-19 is sub-optimal: results of a survey of medical practitioners

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Dear Editor,

Liver damage, defined by an increase in liver biochemical parameters, is related to a more unfavorable severity and prognosis in patients with COVID-19 (1-3). These patients are also treated with immunomodulatory drugs capable of reactivating the hepatitis B virus (HBV), with indication for prophylaxis in specific situations (4-5). Due to its importance in this pathology, we wondered whether physicians should perform a systematic search for liver damage and HBV.

To this end, we distributed a self-developed survey that evaluated this search in different clinical scenarios and asked for respondents' opinions on the association between liver damage and severity and prognosis in patients with COVID-19. 173 responses were obtained from 13 hospitals. The respondents' medical specialties and

usual places of work with COVID-19 patients were varied. A total of 54.9% of respondents carried out a systematic search for liver damage, mainly because it is protocol at their place of work. Less than 45% of respondents carried out daily or sporadic searches for liver damage among hospitalized patients, including in patients with known liver disease, and less than 25% carried out a closer clinical / analytical follow-up when it presented. Only 41% performed outpatient lab monitoring in patients with liver damage upon discharge. A systematic search for HBV was performed by 36.4% of respondents, and 19.7% of them only ordered it if immunomodulating treatment was going to be initiated. Finally, 64.7% of respondents considered that there was no relevant association between liver disease and unfavorable severity/prognosis, while only 9.8% considered the association to be relevant (Fig. 1). This last percentage was just as low in the sub-analysis by medical specialty, except for Anesthesiology / Intensive Care, which was 26%.

In conclusion, respondents' search for liver damage and HBV is sub-optimal. We believe that strategies are required to raise awareness of its clinical and prognostic importance.

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1. What has been your engagement with COVID-19 patients in recent months?
Exclusive (28.9%); **Partial (56.6%)**; Sporadic (14.5%).

2. Where do you primarily care for these patients?
Hospitalization ward (61.3%); Emergency Room (11%); Intensive care unit (17.9%); Primary care (5.2%); Other (4.6%).

3. What is your medical specialty?
Internal Medicine/Infectious diseases (27.7%); Pneumology (8.6%); Anesthesiology/Intensive care (19.7%); Family Medicine (11.6%); Digestive diseases (21.4%); Other (11%).

4. What is your professional experience?
Residency (17.9%); **Specialised Doctor since less than 10 years (46.2%)**; Specialised Doctor since more than 10 years (35.8%).

5. Do you test for total bilirubin, AST, ALT, alkaline phosphate and GGT in the initial assessment of the COVID-19 patient?
Always (54.9%); Only if hospitalization is required (36.4%); Only if patient presents with known liver disease (0%); No (6.4%); DK/NR (2.3%).

6. What is the main reason for performing these tests?
It is protocol at my site (72.3%); I am performing an active search (23.1%); I think they are of prognostic importance (27.7%); There is no specific reason (4%); DK/NR (4.6%).

7. If these tests are normal for diagnosis of COVID-19 in hospitalized patients WITHOUT known liver disease, do you carry out additional tests during their hospital follow-up?
Daily (21.4%); **Sporadically (43.9%)**; Only if clinical outcome is unfavorable (13.3%); No (5.8%); DK/NR (15.6%).

8. If these tests are normal for diagnosis of COVID-19 in hospitalized patients WITH known liver disease, do you carry out additional tests during their hospital follow-up?
Daily (36.4%); **Sporadically (38.2%)**; Only if clinical outcome is unfavorable (5.8%); No (3.4%); DK/NR (16.2%).

9. If you are dealing with an asymptomatic or mild case and find it necessary to order a blood analysis, do you include these tests?
Always (50.9%); Only if patient presents with known liver disease (10.4%); Only on certain occasions (16.2%); Never (6.9%); DK/NR (15.6%).

10. Do you request viral hepatitis B serology in patients with COVID-19?
Always (36.4%); Only if they present with abnormal liver function parameters (12.1%); Only if I am going to prescribe immunomodulating treatment for COVID-19 (19.7%); No (25.4%); DK/NR (6.4%).

11. If patients are discharged with liver damage, do you perform subsequent liver biochemistry checks?
Always (31.2%); Only if patient presents with known liver disease (5.8%); Only if patient was severely ill or experienced a drastic change in condition (12.7%); No (9.2%); **DK/NR (41.1%)**.

12. If liver damage is confirmed, do you change patient handling or follow-up?
No (3.5%); I do not change treatment, but I follow up with more precise clinical/analytical work (22.5%); **I do not change treatment, but I request additional examinations and drug hepatotoxicity (46.8%)**; Yes, change or intensify treatment (13.3%); DK/NR (13.9%).

13. What do you think about the association between liver damage and the severity/prognosis of COVID-19 patients?
There is a relevant association with unfavorable severity/progression (9.8%); **There is a non-relevant association with unfavorable severity/progression (64.7%)**; There is an association with favorable severity/progression (1.2%); There is no association (9.8%;) DK / NA (14.5%).

Figure 1: List of questions and possible survey responses. Percentages are indicated in brackets after each answer, with the highest percentage in bold. Question 6 was the