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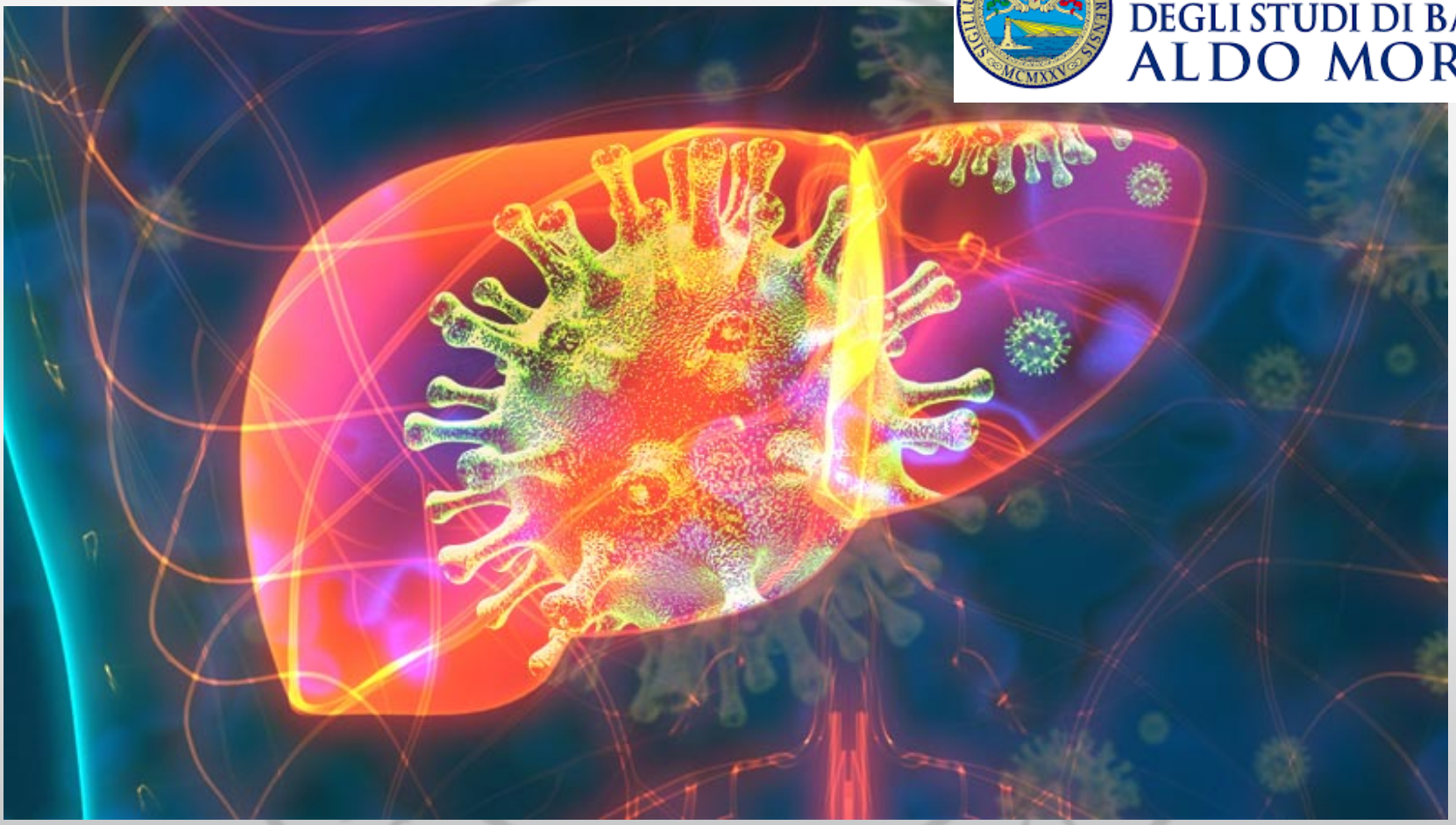

Liver and Covid-19

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- Prevalence of liver involvement
- Possible causes of Covid-19 liver injury
- Management of chronic liver disease

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… step back

Disease	Reference	Numbers of analyzed cases	Proportions of pre-existing liver diseases	Manifestations	Note
SARS	Chang et al[6]	346	2 (0.57%)	Mild to moderate elevation of ALT and AST	Non-survivors had a significantly higher level of AST than survivors
	Liu et al[7]	259	—	Abnormal ALT 146 (56.3%)	—
				Abnormal AST 96 (37.1%)	
	Lu et al[8]	250	NA	Abnormal ALT 87%	—
				Abnormal AST < 50%	
	Tie et al[9]	222	—	136 (61.7%)	The incidence of live injury in severe patients (74.4%) was markedly higher than that in mild patients (43.0%)
	Zhao et al[10]	169	—	Abnormal ALT 62.5%	Liver injury mainly appeared in the second and the third week after disease onset
	Yang et al[11]	168	12 (7.1%)	Abnormal ALT 52.5%	—
				Markedly decreased ALB	
	Duan et al[12]	154	4 (2.6%)	58 (37.7%)	The incidence of live injury in severe patients (48.4%) was markedly higher than that in mild patients (13.0%)
	Huang et al[13]	108	62 (57.4%)	38/38 (100%), in patients with HBV infection	
				33/46 (71.7%), in patients without pre-existing liver disease	
	Wang et al[14]	76	6	Abnormal ALT 59 (77.6%)	
				Abnormal AST 66 (86.9%)	—
	Jiang et al[15]	60	NA	Abnormal ALT 46 (76.6%)	Liver injury mainly appeared in the second week after disease onset
				Abnormal AST 24 (40.0%)	
				Abnormal TB 18 (30.0%)	
				Abnormal ALB 27 (45%)	
	Wu et al[16]	52	9 (17.3%)	Abnormal ALT and AST 53%	Liver injury mainly appeared in the second week after disease onset
	Duan et al[17]	43	3 (6.9%)	Abnormal ALT 33 (76.74%)	Liver injury mainly appeared in the second and the third week after disease onset
				Abnormal AST 21 (48.83%)	
MERS	Arabi[30]	330	21 (6.4%)	Abnormal ALT 142/252 (56.3%)	The incidence of live injury in non-survivors (91.3%) was significantly higher than that of survivors (77.9%) in ICU patients
				Abnormal AST 197/227 (86.8%)	
	Sad et al[27]	70	—	Liver dysfunction 22 (31.4%)	Low albumin was suggested as a predictor of disease severity
	Assiri[32]	47	NA	Abnormal ALT 5 (11%)	—
				Abnormal AST 7 (15%)	

Xu L. et al. Liver Int. 2020

Prevalence of liver injury

- 2-11% of patients with COVID-19 had liver comorbidities
- 14-53% cases reported abnormal levels of alanine aminotransferase and aspartate aminotransferase (AST) during disease progression

	Patients with SARS-CoV-2 infection	Patients with pre-existing liver conditions	Patients with abnormal liver function	Notes
Guan et al[1]	1099	23 (2·3%)	AST abnormal (22·2%), ALT abnormal (21·3%)	Elevated levels of AST were observed in 112 (18·2%) of 615 patients with non-severe disease and 56 (39·4%) of 142 patients with severe disease. Elevated levels of ALT were observed in 120 (19·8%) of patients with non-severe disease and 38 (28·1%) of 135 patients with severe disease.
Huang et al[5]	41	1 (2·0%)	15 (31·0%)	Patients with severe disease had increased incidence of abnormal liver function. Elevation of AST level was observed in eight (62%) of 13 patients in the ICU compared with seven (25%) 25 patients who did not require care in the ICU.
Chen et al[6]	99	NA	43 (43·0%)	One patient with severe liver function damage.
Wang et al[7]	138	4 (2·9%)	NA	..
Shi et al[8]	81	7 (8·6%)	43 (53·1%)	Patients who had a diagnosis of COVID-19 confirmed by CT scan while in the subclinical phase had significantly lower incidence of AST abnormality than did patients diagnosed after the onset of symptoms.
Xu et al[9]	62	7 (11·0%)	10 (16·1%)	..
Yang et al[10]	52	NA	15 (29·0%)	No difference for the incidences of abnormal liver function between survivors (30%) and non-survivors (28%).
Our data (unpublished)	56	2 (3·6%)	16 (28·6%)	One fatal case, with evaluated liver injury.[13]

AST= aspartate aminotransferase. ALT= alanine aminotransferase. ICU=intensive care unit.

Table: **Comorbidity with liver disease and liver dysfunction in patients with SARS-CoV-2 infection**

Zang C. et al. Lancet G&H 2020

Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single center in Wuhan city, China

115 patients with Covid-19
114 patients with CAP

Levels of ALT, AST, TBIL, LDH and INR showed statistically significant elevation in severe COVID-19 cases compared with that in mild cases.

Majority of severe COVID-19 patients showed significantly decreasing in albumin level and continuously decreasing in the progress of illness.

Most of the liver function indexes in COVID-19 patients were correlated with CRP and NLR, the markers of inflammation. Logistic regression analysis further identified NLR as the independent risk factor for severe COVID-19, as well as age.

Variables		ALT	AST	TBIL	ALP	GGT	LDH	ALB	GLB	INR
CRP	r	0.302	0.219	0.03	0.443	0.375	0.648	-0.348	0.563	0.237
	P-value	0.001	0.001	0.058	0.001	0.001	0.001	0.001	0.001	0.001
NLR	r	0.360	0.607	0.562	0.121	0.326	0.439	-0.472	-0.008	0.361

Zang Y. et al. Liver Inter 2020

Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study

Key points

- Liver injury is prevalent in COVID-19 patients.
- Severe Lung lesions on CT might be related to higher incidence of liver injury.

- Nearly one-third patients had elevated ALT or AST.
- Even in non-critical COVID-19 patients, liver injury was common, while most patients had slight elevated aminotransferases and good prognosis.
- **The median values of ALT and AST were in the normal range.**

	Overall (n = 79)	Moderate (n = 51)	Severe (n = 28)	*P* value
Total bilirubin (μmol/L)	13.6 (8.8-17.6)	13.9 (8.9-18.7)	12.7 (8.1-15.4)	.38
ALT (IU/L, baseline)	34 (18-67)	30.0 (21.0-43.5)	36.5 (17.5-71.5)	.59
ALT (IU/L, post-treatment)	26 (20-31)	28 (19-34)	25 (20-32)	.63
AST (IU/L, baseline)	30 (23-50)	28 (22-48)	35 (25-55)	.23
AST (IU/L, post-treatment)	28 (20-33)	26 (22-30)	26 (23-32)	.35
γ-GT (IU/L)	31.5 (19.0-81.3)	25.5 (18.5-97.3)	35.5 (23.8-82.8)	.50
ALP (IU/L)	79.0 (59.0-100.0)	80 (60-114.3)	75.5 (59.0-93.0)	.56
Creatinine (μmol/L)	69.8 (59.0-79.6)	70.2 (57.7-79.3)	68.7 (60.8-80.3)	.63
C-reactive protein (mg/L)	13.9 (3.1-51.9)	11.0 (2.3-32.0)	35.2 (6.5-61.7)	.07

Xie H. et al. Liver Int. 2020

Prevalence of chronic liver disease

Coronavirus disease 2019 (COVID-19) and prevalence of chronic liver disease: A meta-analysis

- Ten studies involved Chinese individuals, whereas one enrolled US patients.
- Patients with severe disease tended to have higher levels of liver enzymes, as well as a greater activation of coagulative and fibrinolytic pathways.
- The overall prevalence of chronic liver disease at baseline was relatively low, being 3%.

Mantovani A. et al. Liver Inter 2020

COVID-19 in long-term liver transplant patients

Three of our 111 long-term liver transplant survivors died

	Long-term liver transplant recipient (>10 years, n=111)	Short-term liver transplant recipient (<2 years, n=40)	p value
Age older than 65 years	55 (50%)	12 (30%)	0·04
Overweight or obesity (body mass index >25 kg/m²)	89 (80%)	24 (60%)	0·02
Diabetes	67 (60%)	9 (23%)	0·0001
Hyperlipidaemia	50 (45%)	7 (18%)	0·002
Arterial hypertension	111 (100%)	27 (68%)	0·0001
History of cardiovascular event	39 (35%)	2 (5%)	0·0015
Chronic kidney disease	44 (40%)	8 (20%)	0·03
Full immunosuppression*	11 (10%)	28 (70%)	0·0001
COVID-19-related deaths	3 (3%)	0	0·57

COVID-19=coronavirus disease 2019. *Ciclosporin concentration more than 150 ng/mL or tacrolimus concentration more than 5 ng/mL.

***Table*: Characteristics of liver transplant recipients in Istituto Nazionale Tumori, Milan**

Given that a reactive innate immune response might be responsible for severe clinical manifestations, immunosuppression might be protective, although this needs further clarification.

Bhoori S. et al. Lancet G&H 2020

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Chronic respiratory disease	
Asthma	479 (9)
Chronic obstructive pulmonary disease	287 (5.4)
Obstructive sleep apnea	154 (2.9)
Immunosuppression	
HIV	43 (0.8)
History of solid organ transplant	55 (1)
Kidney disease	
Chronic[c]	268 (5)
End-stage[d]	186 (3.5)
Liver disease	
Cirrhosis	19 (0.4)
Chronic	
Hepatitis B	8 (0.1)
Hepatitis C	3 (0.1)
Metabolic disease	
Obesity (BMI ≥30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥35)	791 (19.0)
No.	4170
Diabetes[e]	1808 (33.8)

0,5%

Findings In this case series that included 5700 patients hospitalized with COVID-19 in the New York City area, the most common comorbidities were hypertension, obesity, and diabetes. Among patients who were discharged or died (n = 2634), 14.2% were treated in the intensive care unit, 12.2% received invasive mechanical ventilation, 3.2% were treated with kidney replacement therapy, and 21% died.

Richardson S. et al. Jama 2020

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Table 5. Clinical Measures and Outcomes for Patients Discharged Alive, Dead, and In Hospital at Study End Point by Age

Clinical measure	Total discharged alive and dead patients (N = 2634)	Discharged alive			Died			In hospital		
		<18 y (n = 32)	18-65 y (n = 1373)	>65 y (n = 676)	<18 y (n = 0)	18-65 y (n = 134)	>65 y (n = 419)	<18 (n = 14)	18-65 (n = 1565)	>65 (n = 1487)
Invasive mechanical ventilation[a]	320 (12.2)	0	33 (2.4)	5 (0.7)	NA	107 (79.9)	175 (41.8)	4 (28.6)	449 (28.7)	378 (25.4)
ICU care	373 (14.2)	2 (6.3)	62 (4.5)	18 (2.7)	NA	109 (81.3)	182 (43.4)	5 (35.7)	490 (31.3)	413 (27.8)
Absolute lymphocyte count at nadir, median (IQR), $\times 10^9$/L (reference range, 1.0-3.3)	0.8 (0.5-1.14)	2.3 (1.2-5.0)	0.9 (0.7-1.2)	0.8 (0.5-1.1)	NA	0.5 (0.3-0.8)	0.5 (0.3-0.8)	2.0 (1.0-3.5)	0.7 (0.5-1.0)	0.6 (0.4-0.9)
No.	2626	32	1371	675		134	417	3	1564	1486
Acute kidney injury[b]	523 (22.2)	1 (11.1)	93 (7.5)	82 (13.1)	NA	98 (83.8)	249 (68.4)	2 (14.3)	388 (25.5)	457 (34.5)
No.	2351	8	1237	624		117	364	8	1400	1326
Kidney replacement therapy	81 (3.2)	0	2 (0.1)	1 (0.2)	NA	43 (35.0)	35 (8.8)	0	82 (5.4)	62 (4.4)
Acute hepatic injury[c]	56 (2.1)	0	3 (0.2)	0	NA	25 (18.7)	28 (6.7)	0	21 (1.3)	12 (0.8)
No.			1371	675		134	417	3	1564	1486

2,1%

9,5%

Acute hepatic injury was defined as an elevation in aminotransferase of more than 15 times the upper limit of normal.

Richardson S. et al. Jama 2020

TAKE HOME MESSAGE

- It appears unlikely that SARS-CoV-2 infection causes liver damage to an amount that substantially contributes to the overall disease burden.
- Liver injury is more prevalent in severe cases than in mild cases of COVID-19.
- Most patients had slight elevated aminotransferases.

Xie H. et al. Liver Int. 2020
Xu L. et al. Liver Int. 2020

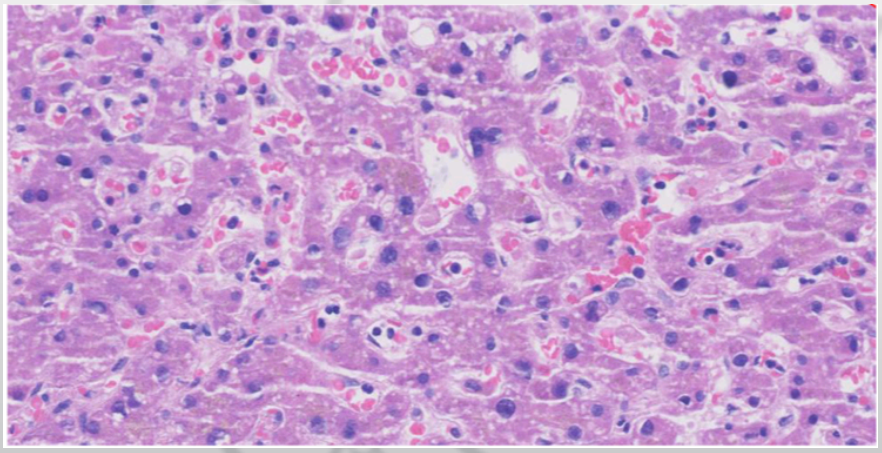
Possible causes

Data suggest that many patients admitted to hospital with COVID-19 have liver blood test abnormalities before admission.

- High levels of positive end expiratory pressure can contribute to hepatic congestion by increasing right atrial pressure and impeding venous return.

Bangash et al. Lancet G&H 2020

- Direct liver injury via a viral hepatitis: post-mortem liver biopsy from a patient with COVID-19 showed only microvesicular steatosis, a common finding in sepsis.



Increased serum levels of monocyte chemoattractant protein-1 (MCP-1), which is a chemokine known to exacerbate steatohepatitis

Bangash et al. Lancet G&H 2020
Boeckmans J. et al. Arc. Toxicol 2020
Zang Y. et al. Liv Int 2020

…myositis?

COVID-19 infection might induce a myositis similar to that observed in severe influenza infections.

	Group	Patients	Alanine aminotransferase (IU)	Aspartate aminotransferase (IU)	Prothrombin time (s)	Bilirubin (µmol/L)	Elevated lactate dehydrogenase, creatinine kinase, or myoglobin	Mortality (%)
Guan et al (2020)	ICU or death	67	Not known	Not known	Not known	Not known	Yes	22% (day 51)
Huang et al (2020)	ICU	13	49 (29–115)	44 (32–70)	12·2 (11·2–13·4)	14·0 (11·9–32·9)	Yes	38% (day 37)
Chen et al (2020)	Hospitalised	99	39 (22–53)	34 (26–48)	11·3 (1·9)	15·1 (7·3)	Yes	11% (day 24)
Wang et al (2020)	ICU	36	35 (19–57)	52 (30–70)	13·2 (12·3–14·5)	11·5 (9·6–18·6)	Yes	17% (day 34)
Shi et al (2020)	Hospitalised	81	46 (30)	41 (18)	10·7 (0·9)	11·9 (3·6)	Unclear	5% (day 50)
Xu et al (2020)	Hospitalised	62	22 (14–34)	26 (20–32)	Not known	Not known	Unclear	0% (day 34)
Yang et al (2020)	ICU	52	Not known	Not known	12·9 (2·9)*	19·5 (11·6)*	Not described	62% (day 28)
Extracted from all studies above	Chronic liver disease	42	Not known	Not known	Not known	Not known	Not known	0–2%†

Data is mean (SD) or median (IQR) depending on the original study. *Non-survivor intensive care unit (ICU) group. †One patient was either admitted to an intensive care unit or died. Details of references can be found in the appendix.

Table: **Liver test abnormalities from various COVID-19 studies, identifying the most severe disease categories where possible**

Bangash et al. Lancet G&H 2020

DILI?

Drug	Mechanism of action, rationale for COVID-19	Considerations for patients with liver diseases or after liver transplantation
Remdesivir	• NUC/viral RNA polymerase inhibitor (completed phase III for Ebola treatment) • Inhibits SARS-CoV-2 *in vitro*[24] • Case reports with COVID-19[26]	• No relevant drug-interactions expected[34] • No experience in liver cirrhosis but a NUC might be safer than other drug classes based on experience with NUCs in chronic hepatitis B and C • Liver toxicity (↑ALT) possible
Chloroquine/ Hydroxychloroquine[35] ± azithromycin	• Interference with the cellular receptor ACE2[24] • Endosomal acidification fusion inhibitor • Generally used for treatment of malaria and amoebiasis • *In vitro* and *in vivo* data[32,36]	• Exclude G6PD deficiency before application • Drug-interactions with immunosuppressive drugs: close monitoring of drug level is required for cyclosporine, tacrolimus, sirolimus, everolimus[34] • Hydroxychloroquine therapy has not been associated with ALT abnormalities and is an extremely rare cause of clinically apparent acute liver injury (LiverTox).
Lopinavir/ritonavir	• Lopinavir/ritonavir are approved PIs for HIV • *In vitro* data, experience in patients with SARS, case reports with COVID-19[37] • No proven efficacy *in vivo* in severe COVID-19[28] • Many centres have discontinued its use	• Known and well-studied drug-interactions with immunosuppressive drugs. mTOR inhibitors (sirolimus, everolimus) should not be co-administered, close monitoring of drug level are required for calcineurin-inhibitors (cyclosporin, tacrolimus)[34] • Data for patients with liver cirrhosis exist[38] • The risk of lopinavir-associated hepatotoxicity in patients with very advanced liver disease is low • Based on experience with PIs in HCV, patients with decompensated cirrhosis should not be treated
Tocilizumab	• Humanised mAb targeting interleukin-6 receptor • Treat cytokine release syndrome observed in COVID-19[7]	• ALT elevations are frequent but clinically apparent liver injury with jaundice seem to be rare[39] • Patients with decompensated cirrhosis should not be treated • Consider risk of HBV reactivation[40]
Methylprednisolone (steroids)	• Corticosteroids bind nuclear receptors to dampen proinflammatory cytokines • Mostly used in patients with septic shock • Currently NOT recommended by WHO[41]	• The risk of other infections (*e.g.* SBP) and viral shedding may increase in patents with decompensated liver cirrhosis • Consider antimicrobial prophylaxis • Consider risk of HBV reactivation

EASL-ESCMID position paper 2020

Convalescent plasma	• Case reports with COVID-19[42]	• No experience in patients with chronic liver disease
Umifenovir (Arbidol)*	• May inhibit viral entry into target cells and stimulate the immune response, used to treat influenza in some countries[31]	• Possible drug interactions between arbidol and CYP3A4 inhibitors and inducers[43] • Potentially metabolised in liver and intestines in humans. Caution in patients with liver cirrhosis
Favipiravir/favilavir*	• Guanine analogue, RNA-dependent RNA polymerase (RdRp)- inhibitor, approved for influenza in Japan • Preliminary results from a study with 80 COVID-19 patients[31]	• Metabolised by aldehyde oxidase and xanthine oxidase. CYP450 isoenzymes are not involved in the metabolism • Elevation of ALT and AST possible. • No data in cirrhosis available
Sofosbuvir* maybe combination with ribavirin	• Nucleotide analogue, RdRp-inhibitor • Approved for treatment of chronic hepatitis C • *In vitro* data show binding to SARS-CoV-2 RdRp[44]	• Good experience in patients with chronic hepatitis C including patients with decompensated cirrhosis • For drug-interaction details see[45] • Ribavirin may cause severe haemolytic anaemia
Baricitinib*	• Janus kinase inhibitor, might interrupt endocytosis of the virus and intracellular assembly of virus particles[46] • Could affect both inflammation and cellular viral entry	• Associated with transient and usually mild elevations of ALT[47] • Patients with decompensated cirrhosis should not be treated
Camostat*	• Blocks serine protease TMPRSS2 *in vitro* which is required for S protein priming[48] • Licensed in Japan for treatment of chronic pancreatitis	• Patients with chronic viral hepatitis and cirrhosis are excluded from clinical trial for chronic pancreatitis.[49] • Drug-interactions unknown
Emapalumab*	• mAb targeting interferon-gamma • Treat cytokine release syndrome observed in COVID-19[7] • Approved for haemophagocytic lymphohistiocytosis • Clinical trial for COVID-19 planned[50]	• Associated with mild and transient ALT elevations typically arising a few weeks after start of treatment • Risk of reactivation of tuberculosis, pneumocystis jirovecii, herpes zoster • Risk of HBV reactivation may be lower
Anakinra*	• Interleukin 1 receptor antagonist • Clinical trial for COVID-19 planned[50]	• Minimal hepatic metabolism

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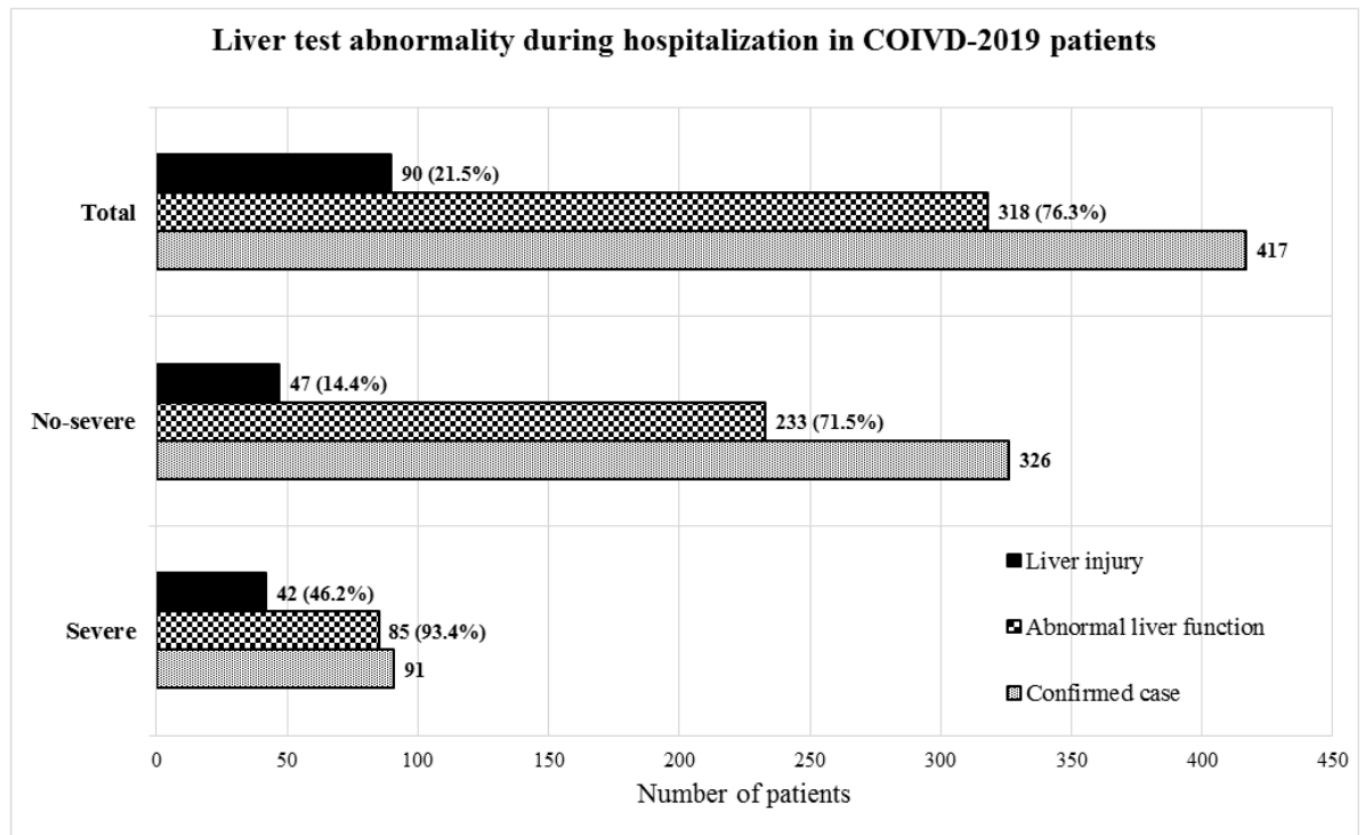
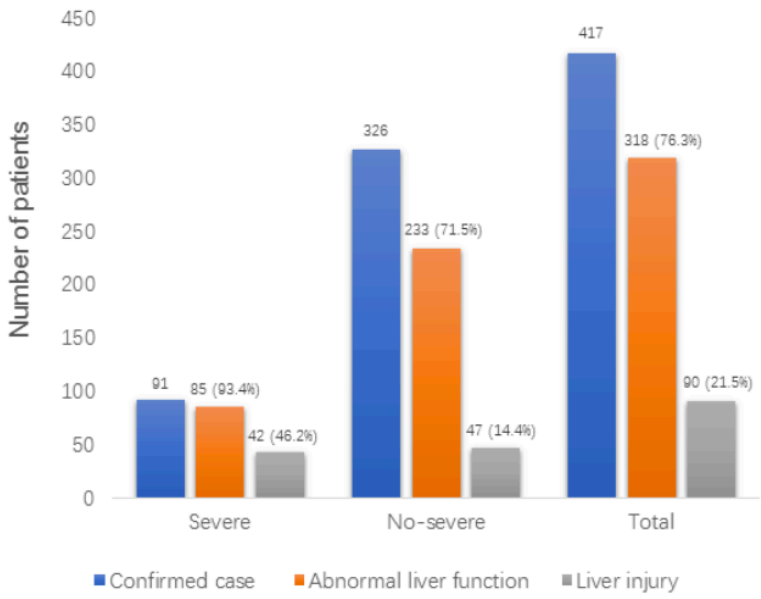
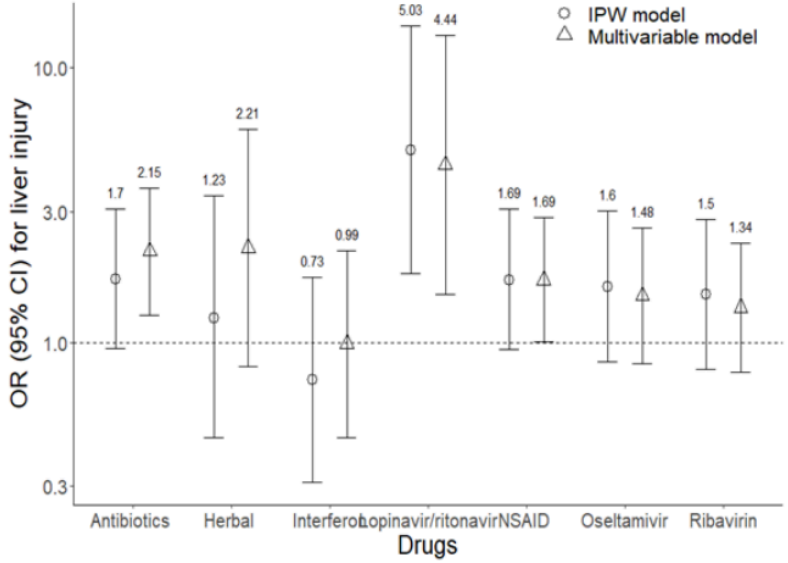
Patients with abnormal liver tests, especially in hepatocyte type or mixed type, had significantly higher odds of developing severe pneumonia.



Cai Q. et al. J Hepatol 2020





- The use of lopinavir/ritonavir increased the odds of liver injury by 4-fold.

- **After admission, the use of drugs, especially lopinavir and ritonavir, was the most important risk factor for liver damage.**

Cai Q. et al. J Hepatol 2020

DILI?

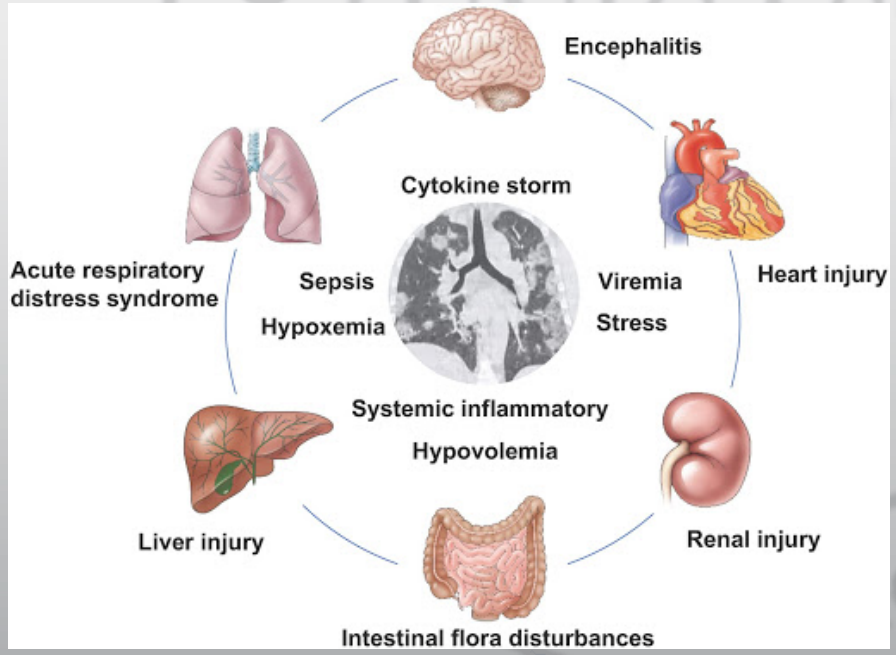
- Drug-induced liver injury is a possible contributing factor to the observed abnormal liver blood test abnormalities after therapeutics begin and should be considered by clinicians, but mild liver test derangement is present at baseline.
- The presence of abnormal liver biochemistries does not seem to represent a contraindication to using investigational or off-label therapeutics for COVID-19, although strict monitoring is advisable.

Sun J. et al. Liver Int. 2020

Bangash et al. Lancet G&H 2020

…bystander hepatitis?

Greater activation of coagulative and fibrinolytic pathways, relatively depressed platelet counts, climbing neutrophil counts and neutrophil to lymphocyte ratios, and high ferritin levels that may reflect general innate immune activation caused by circulating cytokines.



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Hepatitis A virus (HAV) infection

Hepatocyte

Non-HAV-specific memory CD8+ T cells

IL-15

TCR-independent bystander activation

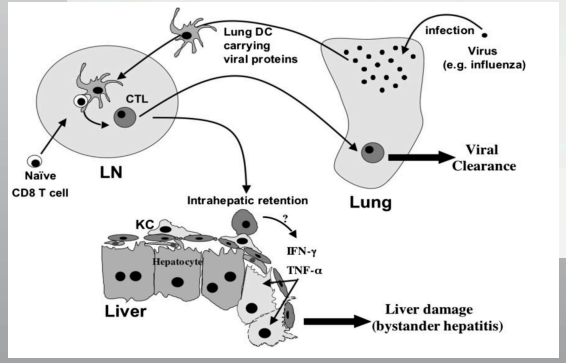
NKG2D
NKp30

Innate-like cytotoxicity

NKG2D
NKp30

Perforin
Granzyme

Liver injury



Kim J. et al. Immunity 2018

Management of chronic hepatitis

All patients with chronic liver disease should adhere to common rules of physical distancing

Patients with chronic liver disease
(including compensated cirrhosis)

- Visits to specialized centres can be postponed
- Routine laboratory testing can be performed locally/off-site
- Use telemedicine/visits by phone wherever possible

Specific considerations for

Patients with viral hepatitis:
- No increased risk of a severe course of COVID-19
- Send follow-up prescriptions for patients on antiviral therapy by mail

Patients with NAFLD or NASH:
- May suffer from diabetes, hypertension and obesity, putting them at increased risk of a severe course of COVID-19

Patients with autoimmune liver disease:
- We currently advise against reducing immunosuppressive therapy. Reduction should only be considered under special circumstances after consultation with a specialist
- Emphasis on the importance of vaccination for *Streptococcus pneumoniae* and influenza

Patients with compensated cirrhosis:
- Consider delaying hepatocelullar carcinoma) surveillance and screening for varices. Individualized and non-invasive risk assessment should be applied for stratification (see also section on "*Liver-related diagnostic procedures*")

Patients with decompensated liver disease
(including hepatocelullar carcinoma)

- Care should be maintained according to guidelines
- Minimal exposure to medical staff, by using telemedicine/visits by phone wherever possible/required to avoid admission
- Listing for transplantation should be restricted to patients with poor short-term prognosis, as transplantation activities/organ donations will likely be reduced in many countries and areas
- Reducing the in-hospital liver transplant evaluation program to the strictly necessary is recommended to shorten hospital stays
- Emphasis on the importance of vaccination for *Streptococcus pneumoniae* and influenza
- Guidelines on prophylaxis of spontaneous bacterial peritonitis and hepatic encephalopathy should be closely followed to avoid admission
- Include testing for SARS-CoV-2 in patients with acute decompensation or acute-on-chronic liver failure

Specific considerations for

Patients actively listed for transplantation:
- SARS-CoV-2 routine testing should be performed before transplantation in both donors and recipients, acknowledging that negative testing cannot completely rule out infection.
- Consent for diagnostic and therapeutic procedures related to transplantation should include the potential risk for nosocomial COVID-19
- Living-donor transplantations should be considered on a case-by-case basis.

Patients with hepatocellular carcinoma

- Care should be maintained according to guidelines, including continuing systemic treatments and evaluation for liver transplantation
- Minimal exposure to medical staff, by using telemedicine/visits by phone wherever possible/required to avoid admission
- In case of COVID-19, early admission is recommended. See also section on "*Inpatient care*"

Patients after liver transplantation

- Maintain care according to guidelines
- Minimal exposure to medical staff, by using telemedicine/visits by phone wherever possible/required to avoid admission
- Emphasis on the importance of vaccination for *Streptococcus pneumoniae* and influenza
- In stable patients, perform local lab testing (including drug levels)
- We currently advise against reducing immunosuppressive therapy. Reduction should only be considered under special circumstances after consultation with a specialist

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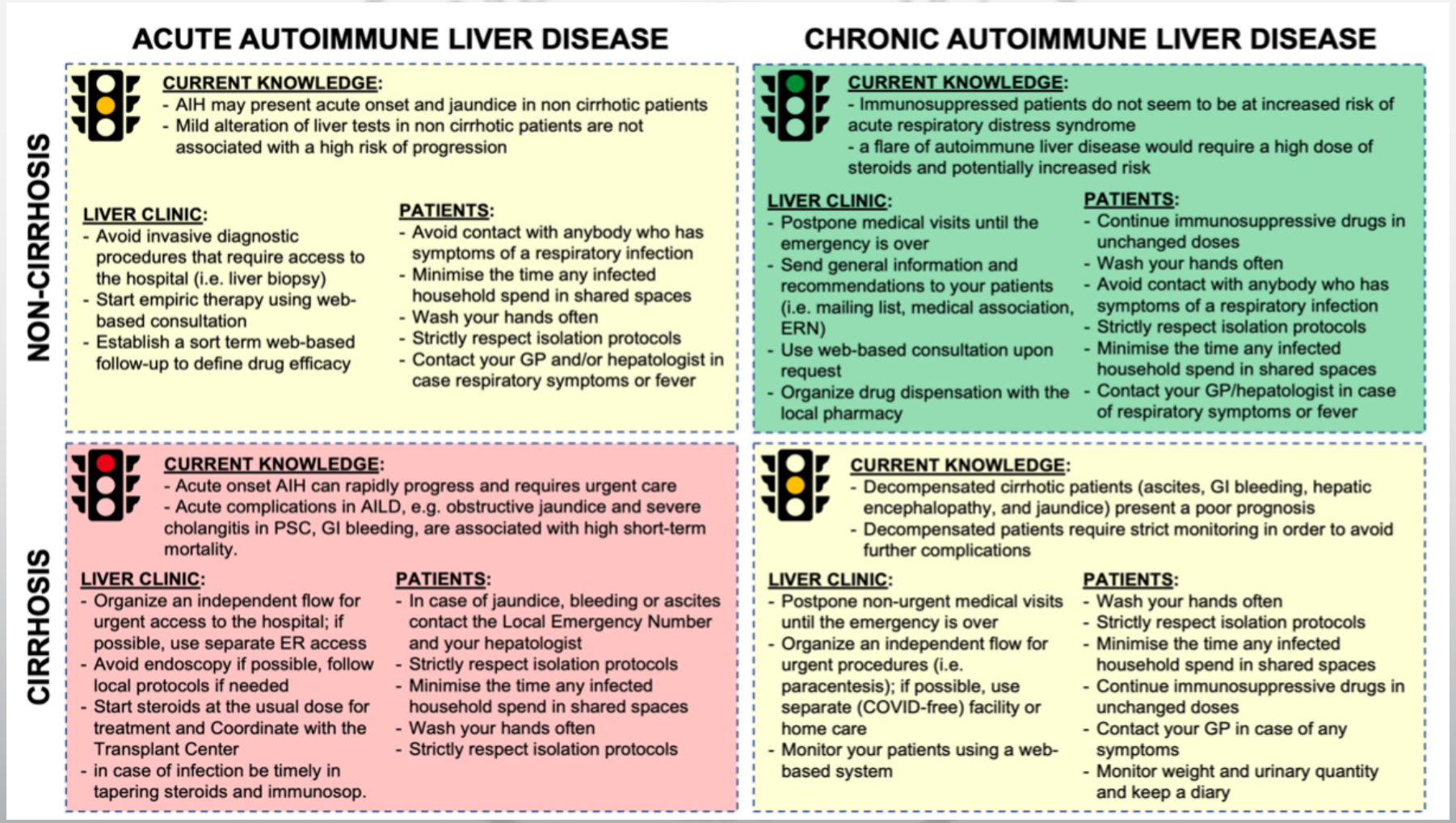
Management of chronic autoimmune hepatitis



Lleo A. et al. J Hepatol 2020