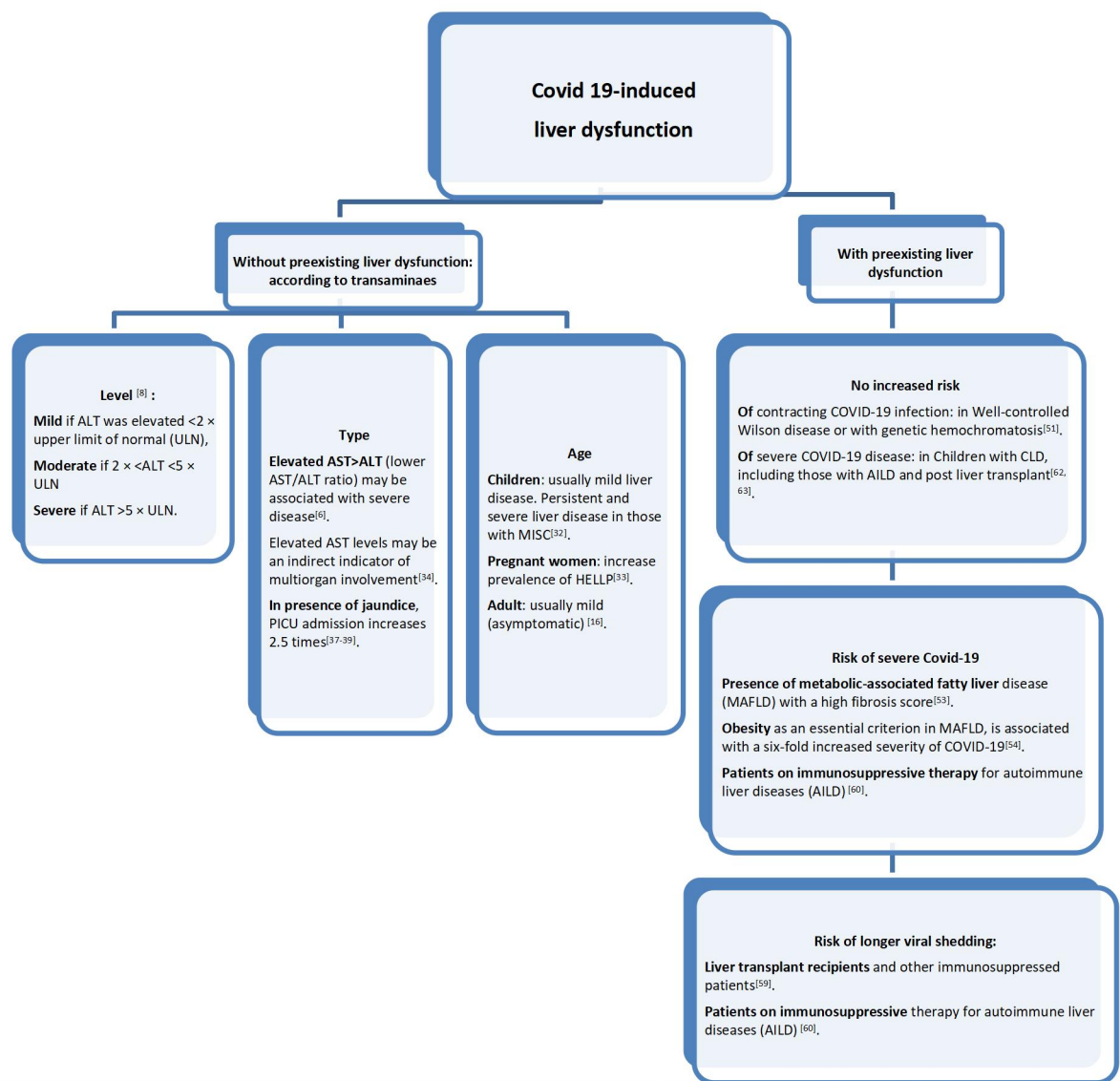


The manuscript is very well written except it is hard to keep the track of data numbers presented. It will be great for the reader if you can present various facts and the data in the form of some figures and (or) tables.



UNL: upper normal level; AST: aspartate transaminase; ALT: alanine transaminase; HELLP: hemolysis, elevated liver enzymes and low platelet; CLD: chronic liver disease; AILD: autoimmune liver diseases; MISC: multisystem inflammatory syndrome of children

Figure 1: Summary of Covid 19- induced liver dysfunction

The performed study is very innovative and good for society. The readability of the manuscript can be further extended by reducing grammatical mistakes and punctuation.

Another retrospective cohort study on 230 Covid-19 positive patients showed that the prevalence of abnormal liver tests among the sample population with severe COVID-19 infection were as follows: AST (77%), ALT (49%), ALP (12%) and γ GT (37%). A severe COVID-19 infection was more likely present in patients with abnormal levels of AST ($p = 0.015$), ALP ($p = 0.03$), and γ GT ($p = 0.022$) [31].

Regarding age, children appear to have a milder illness with significantly less need for inpatient admission or respiratory support and are less likely to have the multiple comorbidities present in older adults. Hepatitis is common in children with multisystem inflammatory syndrome and is associated with a more severe presentation and persistent elevation of LFTs in many patients [32]. Furthermore, older patients are not only more likely to develop more severe COVID-19 but also at greater risk of abnormal liver function. The latter is more common in patients with severe or critical presentations of COVID-19 [5]. Observational studies showed an increased prevalence of preeclampsia and hemolysis, elevated liver enzymes and low platelet (HELLP) syndrome in pregnant women with COVID-19. Despite a possible pathophysiology linkage between COVID-19 and HELLP syndrome, the evidence on temporality to prove a causal association between infection with severe acute respiratory syndrome coronavirus 2 and HELLP syndrome is lacking [33].

A cohort study reported that acute liver injury with a hepatocellular pattern was common in patients who tested positive for SARS-CoV-2 but was usually mild [16]. However, 6.4% of patients had a severe liver injury with a severe disease course, where elevated AST levels may be indirect indicators of multiorgan involvement [34]. There is also a recent case report of a young male with COVID-19 presenting with acute icteric hepatitis with a marked rise in bilirubin and liver transaminase levels without any respiratory symptoms [6]. Another case report found that COVID-19 infection could be a risk factor or comorbidity of acute liver failure, with only isolated hyperbilirubinemia indicating liver involvement [17]. Moreover, severe cases of COVID-19 followed by death were more often related to hypertransaminasemia and elevated bilirubin levels compared with cases of mild and moderate disease [14, 35]. Patients with severe liver injury were more likely to need ICU-level care, intubation, and renal replacement therapy and showed a greater risk of in-hospital mortality [6, 16, 36]. A high bilirubin level and liver stiffness (measured using shear wave elastography) have been reported as correlated with more severe outcomes [37, 38, 39]. Liver injury and failure are frequently observed in critically ill patients, and their occurrence is associated with increased morbidity and mortality [40-42]. Recently a potential link between Omicron variant infection and severe hepatitis of unknown etiology in children was observed, where it was postulated that previous infection or co-infection with SARS-CoV-2 increases the susceptibility to adenovirus infection [43]. Figure 1 summarizes the clinical and laboratory presentation of Covid 19-induced liver dysfunction.

COVID-19 in Patients with Preexisting Liver Disease

The impact of COVID-19 on chronic liver disease (CLD) is variable. Several studies have reported that patients with CLD, regardless of its etiology, may be at higher risk for severe illness from COVID-19 [44-47]. A systematic review of 40 studies with 908,032 participants (most of them from China and US) showed that COVID-19 patients with CLD had significantly higher odds of having a severe form of COVID-19 (pooled OR = 2.44; 95% CI, 1.89–3.16) and death (pooled OR = 2.35; 95% CI, 1.85–3.00) when compared with COVID-19 patients without CLD [48].

s. Shroff et al [66] noted that most cases of severe liver injury were described after SARS-CoV-2 mRNA vaccines. Most cases occurred after the first vaccination dose, and two developed ILI after the second dose. Interestingly, there was one case of ILI after both doses of vaccine. It is also notable that preexisting comorbidities (69.6%) were common, including liver disease in 26.1% and thyroid disorders in 13% of patients [67].

The authors described the liver involvement of COVID-19 and the effects of COVID-19 on liver function tests. The authors did not make any novel additions to the information in the literature but gave an excellent summary of the literature. Therefore, I think that this article will contribute to the literature.

31) Ibrahim N, Hosri J, Bteich Y, Dib A, Abou Rached A. COVID-19 and Liver Dysfunction. *Cureus*. 2022 16;14(1):e21302 PMID: 35186564; PMCID: PMC8849487

33) Nasa P, Juneja D, Jain R, Nasa R. COVID-19 and hemolysis, elevated liver enzymes and thrombocytopenia syndrome in pregnant women - association or causation? *World J Virol*. 2022 25;11(5):310-320. doi: 10.5501/wjv.v11.i5.310. PMID: 36188744; PMCID: PMC9523323.

39) Pierce T, Samir A , Ozturk A, Parameswaran M, Martin M, and Edenbaum H: COVID-19 patients show liver injury months after infection. Annual meeting of the Radiological Society of North America (RSNA), December 1, 2022, www.rsna.org/annual-meeting

43) Yi H, Lin Y, Lu B, Mao Y. The origin of severe hepatitis of unknown aetiology in children: SARS-CoV-2 or adenovirus? *J Hepatol*. 2023; 78(1):e16-e18.

doi: 10.1016/j.jhep.2022.08.032. Epub 2022 Sep 5. PMID: 36067884.

48) Nagarajan R, Krishnamoorthy Y, Rajaa S, Hariharan VS.: COVID 19 Severity and Mortality Among Chronic Liver Disease Patients: A Systematic Review and Meta-Analysis. *Prev Chronic Dis*. 2022 25;19:E53. doi: 10.5888/pcd19.210228. PMID: 36007255; PMCID: PMC9480842.

64) Wang Y., Hu M. and Yang H. Cirrhosis is an independent predictor for COVID-19 mortality: A meta-analysis of confounding cofactors-controlled data. *Letters to the Editor* 2023; 78(1): e28-e31 DOI: <https://doi.org/10.1016/j.jhep.2022.09.015>

66) Shroff H., Satapathy S.K., Crawford J.M., Todd N.J. and VanWagner L.B. Liver injury following SARS-CoV-2 vaccination: a multicenter case series. *J Hepatol*. 2022; 76: 211-214. doi: 10.1016/j.jhep.2021.07.024. Epub 2021 Jul 31. PMID: 34339763; PMCID: PMC8324396.