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Cases of severe acute liver injury following inactivated SARS-CoV-2 vaccination

To the Editor:

Several cases of severe acute liver injury (ALI) with features of autoimmune hepatitis after SARS-CoV-2 infection or SARS-CoV-2 vaccination have been described.[1–7] Most cases developed ALI following mRNA or viral vector-based vaccines, while only a few reports described the development of ALI after inactivated SARS-CoV-2 vaccines.[1] Recently, Wong *et al.*[8] evaluated the risk of ALI in a large cohort of vaccine recipients. They reported that the risk of ALI did not increase due to any formulation of SARS-CoV-2 vaccination. We reviewed our cohort of patients who developed ALI after inactivated SARS-CoV-2 vaccination.

We included 13 cases (female/male:7/6) with a median age of 42 (22-67) years at the time of ALI presentation (Table 1). ALI was diagnosed a median 18 (range: 2–39) days after vaccination with either the Sinopharm (n = 4), Sinovac (n = 4), Covaxin (n=4) or CanSino (n = 1) vaccines. One patient had a diagnosis of primary biliary cholangitis (PBC). None of the individuals were taking any medication prior to the onset of liver injury. Aminotransferase levels had been checked in eight (61%) individuals a median of 80 (25-210) days prior to the onset of liver injury and were normal in all. Nine (70%) cases developed ALI after the first vaccine dose, while four (30%) were diagnosed after the second dose. A hepatocellular pattern of injury was noted in 12 and a cholestatic pattern in one case.

Anti-nuclear antibody was positive in eight cases, and three cases showed seropositivity for anti-smooth muscle antibody. The serum IgG levels were measured in 12 cases and were high in six of these. Liver biopsy was performed in three cases. Six (46%) cases reached probable or definitive autoimmune hepatitis according to simplified criteria. Most cases (11/13) had features of grade 1-2 (mild-moderate) liver injury, one had grade 3 (severe) and another case had grade 4 (fatal) liver injury.

Corticosteroid therapy was given to five patients and could be successfully withdrawn in four of them. The median time from ALI to complete biochemical resolution was 39 days (20-120) in treated and untreated patients, and no relapse was observed after a median 265 (20-450) days follow-up.

Wong *et al.*[8] did not report severe or fatal cases of ALI following SARS-CoV-2 vaccination in their study population. In our data, 15% (2/13) of cases had grade 3-4 liver injury. One of them responded to corticosteroid therapy, while another patient (not treated with corticosteroid) who had a PBC diagnosis progressed to decompensated liver failure (developed ascites and encephalopathy) 20 days after the second dose of Sinopharm. The patient underwent liver transplantation and is alive after 60 days of follow-up. To the best of our knowledge, this is the second patient who underwent liver transplantation following vaccine-induced liver injury.[9] Importantly, our case series contains observational data and does not suggest increased risk of ALI following SARS-CoV-2 vaccination. The association of SARS-CoV-2 vaccination and risk of ALI can be better postulated with case control studies as was done by Wong *et al.*[8]

The authors do not discourage SARS-CoV-2 vaccination. In our data, most patients (12/13) showed resolution of liver injury with or without therapy and no patient relapsed during follow-up. This outcome suggests that SARS-CoV-2 vaccine-induced ALI is usually transient. Similar results were also reported in other studies.[1,5] Vaccination has significantly reduced the risk of severe COVID-19 and mortality during the pandemic.[3,10] Compared to the billions of people vaccinated across the World, only a fraction of individuals may develop vaccine-induced ALI. Through this series, we only aim to increase the awareness of post-vaccination ALI and suggest close follow-up of individuals who present with ALI following SARS-CoV-2 vaccination.

Table 1. Characteristics of the study population.

Characteristics	
Patient number	N = 13
Age (years)	42 (22-67)
Sex, female, n (%)	7 (54)
Pre-existing liver disease, n (%)	1 (8)
Symptoms at liver injury onset, n (%)	11(85)
Peak ALT xULN	17.2 (2.2-56.6)
Peak AST xULN	10.8 (1.4-26)
Peak ALP xULN	1 (0.6-2.4)
Peak total bilirubin xULN	1.2 (0.4-27.6)
INR	1.1 (0.8-4.7)
Hepatocellular liver injury, n (%)	12(92)
IgG xUNL	1.04 (0.60-1.51)
ANA positivity, n (%)	56 (67.5)
SMA positivity, n (%)	15 (18.1)
Grade of liver injury (1-2)/(3-4), n (%)	11(85)/2(15)
Corticosteroid response, n (%)	5 (100)
Liver transplantation, n (%)	1 (8)

Values reported as median (range).
ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANA, anti-nuclear antibody; AST, aspartate aminotransferase; INR, international normalized ratio; SMA, smooth muscle antibody.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.
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Authors' contributions

CE, and AVK conceptualized the study. CE, LN, AVK, MA SW and ER contributed data and approved final manuscript.

Data availability statement

All relevant data that support the findings are presented in the manuscript.

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Supplementary data

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Author names in bold designate shared first authorship.

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Life's Essential 8 and MAFLD in the United States

To the Editor:

The American Heart Association (AHA) recently proposed Life's Essential 8 (LE8) as an update of Life's Simple 7 (LS7) to quantify cardiovascular health (CVH), which included five health behaviors (nicotine exposure, physical activity, diet, body mass index, and sleep health) and three health factors (blood lipids, blood pressure, and blood glucose).[1] By adding a new sleep metric and being redefined on a more continuous scale, LE8 better reflects recent clinical guidelines, interindividual difference and intraindividual change than LS7.[1] Previous studies have reported associations between LS7 and cardiometabolic disease (*e.g.*, cardiovascular disease [CVD] and diabetes).[2,3] Metabolic dysfunction-associated fatty liver disease (MAFLD) is a newly proposed nomenclature that has been reported to be associated with increased all-cause and cardiovascular mortality, and those with advanced fibrosis have higher risk of all-cause mortality compared to those without.[4] Since MAFLD shared similar lifestyle and metabolic risk factors with CVD, we aimed to investigate the associations of LE8 with MAFLD and clinically significant fibrosis (CSF) in participants with MAFLD.

We analyzed adults from the National Health and Nutrition Examination Survey (NHANES) 2017-2018. Individuals who were pregnant, under 20 years old, had ineligible elastography examination status, or had missing data on MAFLD or components of LE8 were excluded, leaving 1,812 individuals for the final analysis. Based on expert consensus and published NHANES research, MAFLD was determined by controlled attenuation parameter ≥285 dB/m with ≥1 of the following: i) overweight or obese (body mass index ≥25 kg/m^2), ii) diabetes mellitus, and iii) at least 2 metabolic risk abnormalities. Metabolic risk abnormalities consisted of i) waist circumference