Digestive Diseases and Sciences (2022) 67:4574–4580
https://doi.org/10.1007/s10620-022-07504-w

ORIGINAL ARTICLE

Autoimmune Hepatitis-Like Syndrome Following COVID-19 Vaccination: A Systematic Review of the Literature

Kenneth W. Chow[1] · Nguyen V. Pham[2] · Britney M. Ibrahim[2] · Kimberly Hong[2] · Sammy Saab[2,3]

Received: 23 November 2021 / Accepted: 15 January 2022 / Published online: 29 April 2022

Abstract

Objectives During the summer of 2021, case reports began to emerge documenting a small number of individuals who developed autoimmune hepatitis (AIH) following COVID-19 vaccination. These cases are rare and novel, and very little is known. In our systematic review, we analyzed every published case of AIH and reviewed their characteristic findings, treatment, and outcomes.

Methods We searched PubMed, Embase, and Web of Science from December 1, 2019, to November 1, 2021. Two researchers independently extracted information from the articles about vaccine type, patient history, laboratory values, histology results, treatment regimens, and disease course.

Results Thirty-two patients developed AIH-like syndromes after receiving a COVID-19 vaccine. Jaundice was the most frequently reported symptom (81%), and 19% of patients were initially asymptomatic and presented with elevated liver enzymes found during routine bloodwork. Mean alanine transaminase, aspartate transaminase, and total bilirubin were 1231 U/L, 921 U/L, and 14 mg/dL, respectively. Anti-nuclear antibody was positive in 56%, and anti-smooth muscle antibody in 28% of patients. Steroids were used in 75% of patients. Improvement or complete resolution was seen in 97% of patients. One patient died despite aggressive steroid treatment.

Conclusion COVID-19 vaccine-induced AIH is an uncommon association with just 32 documented cases in the literature. Clinicians should be vigilant for AIH in patients who present with liver injury following vaccination. These new findings should under not deter individuals from getting vaccinated, as the benefits of vaccination far outweigh the risks. Fortunately, COVID-19 vaccine-induced AIH appears amendable to corticosteroid therapy and appears to have a favorable outcome.

Introduction

The coronavirus 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to dramatic loss of life worldwide with devastating impacts to the economic and psychosocial livelihoods of the modern world. In response to the rapidly spreading infection rates and the rising death toll, vaccines against COVID-19 were developed at an unprecedented rate. On December 11, 2020, the Pfizer-BioNTech COVID-19 vaccine was issued emergency use authorization by the United States Food and Drug Administration (FDA), followed by the Moderna vaccine on December 18, 2020. The Oxford-AstraZeneca vaccine was approved by the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom on December 30, 2020. In the following months, billions of vaccine doses were administered worldwide, with an estimated 51% of the global population having received at least one dose of a COVID-19 vaccine at the time of this writing [1].

The Pfizer-BioNTech and Moderna vaccines are effective in preventing hospitalization due to COVID-19 infection in immunocompetent adults, with efficacy rates of 88% and 93% respectively [2]. The safety profiles of both vaccines have been extensively studied [3, 4]. Side-effects are typically mild and

An editorial commenting on this article is available at https://doi.org/10.1007/s10620-022-07509-5.

✉ Sammy Saab
SSaab@mednet.ucla.edu

[1] Department of Medicine, Harbor-UCLA Medical Center, Torrance, CA, USA

[2] Departments of Surgery, UCLA Medical Center, Pfleger Liver Institute, University of California at Los Angeles, 200 Medical Plaza, Suite 214, Los Angeles, CA 90095, USA

[3] Departments of Medicine, UCLA Medical Center, Pfleger Liver Institute, University of California at Los Angeles, 200 Medical Plaza, Suite 214, Los Angeles, CA 90095, USA

resolve within 1–3 days after vaccine administration. These include injection site pain, fatigue, headache, muscle pain, and chills [5]. During the initial phase III pre-approval clinical trials, several potential adverse effects were identified, such as Bell's palsy [3] and lymphadenopathy [6]. Small imbalances between the vaccine and placebo groups were also observed in the incidence of myocarditis, appendicitis, hypersensitivity reactions, acute myocardial infarction, and cerebrovascular accidents [4]. Multiple follow-up studies suggest that these adverse effects are extremely rare and that the causality in the original trials cannot be conclusively determined due to small sample size and lack of power [4, 7]. However, safety remains a concern. Several case reports have linked the COVID-19 vaccine to the development of autoimmune diseases such as myocarditis and immune thrombocytopenic purpura (ITP) [8, 9]. Despite this uncertainty, the overwhelming scientific consensus remains that the benefits of the vaccine far outweigh the risks. As of November 4, 2021, the Centers for Disease Control and Prevention (CDC) recommends that all individuals above the age of 5 receive a COVID-19 vaccine. The CDC, FDA, and other federal agencies remain active in monitoring the safety and efficacy of the vaccines.

During the summer of 2021, case reports began to emerge documenting a small number of individuals who developed autoimmune hepatitis (AIH)-like syndromes shortly after receiving a COVID vaccine [10–25]. As of November 1, 2021, there are 16 case reports from throughout the globe that describe 32 such patients. Given the small number of cases, causality cannot be proven. However, the growing number of cases, along with recent reports describing cases of vaccine-associated myocarditis [8] and ITP [9], has raised concern for the possibility of vaccine-induced autoimmunity.

Autoimmune hepatitis is an immune-mediated disorder of unclear etiology, thought to be caused by loss of tolerance to hepatocyte-specific autoantigens [26] in genetically susceptible individuals. Triggers include infection, medications, and toxins [27]. AIH is classically associated with female gender, elevated transaminases, elevated levels of immunoglobulin G (IgG), and the presence of autoantibodies. Type 1 AIH is associated with the presence of anti-smooth muscle antibody (ASMA) with or without anti-nuclear antibody (ANA), while type 2 AIH is associated with anti-liver/anti-kidney microsome (anti-LKM) and anti-liver cytosol (anti-LC) antibodies. Estimates of AIH incidence range from 0.67 to 2 cases per 100,000 people per year [29]. In our systematic review, we analyzed all 32 documented cases of AIH following COVID-19 vaccination.

Methods

We conducted a systematic search of the literature using PubMed, Embase, and Web of Science from December 1, 2019, to November 1, 2021. A combination of keywords was used in the medical subjects heading (MeSH), including: "COVID-19," "COVID19," "COVID 19," "COVID," "coronavirus," "SARS-CoV-2," "SARS CoV 2," "2019 nCoV," "2019ncov," "2019-nCoV," "2019 novel coronavirus," "Novel coronavirus 2019," along with "vaccine," "vaccination," and "autoimmune hepatitis." We screened the bibliographies of all primary articles for additional cases. We limited our search to articles written in English. We limited our search to case reports, case series, and letters to the editor. Our search was in line with PRISMA guidelines, and our screening process is detailed on the flowchart in Fig. 1. A total of 79 records were identified by our literature search. Two reviewers (KC and BI) independently reviewed all records and identified 14 relevant articles. Two additional records were identified using a combination of Google Scholar and Google Search, resulting in a total of 16 eligible records. KC and BI independently extracted information from the 16 articles about vaccine type, patient history, symptom onset, characteristics, laboratory values, histology results, treatment regimens, and disease course.

Results

Demographics and Patient Information

We identified 32 cases of COVID-19 vaccine-induced AIH-like syndromes [10–25]. The mean age was 55.6 years with a standard deviation (SD) of 15.3 years, and 68.8% of patients were female. Six patients (18.8%) were Caucasian, and 26 patients (81.3%) had an unspecified race and ethnicity. Cases originated from throughout the globe with 17 patients from the USA, 11 from Europe, 3 from Asia, and 1 from Australia. Sixteen patients received the Pfizer-BioNTech vaccine, thirteen patients received the Moderna vaccine, and three patients received the Oxford-AstraZeneca vaccine.

In our cohort, 10 patients (31.3%) had a history of liver disease, 9 patients (28.1%) had a history of autoimmune disease, and 5 patients (15.6%) had a history of both liver and autoimmune disease. This yielded 14 patients (43.8%) with a history of either liver or autoimmune disease, and 18 patients (56.3%) with a history of neither liver nor autoimmune disease. One patient was three months postpartum [10], and another was taking substitutive hormonal therapy

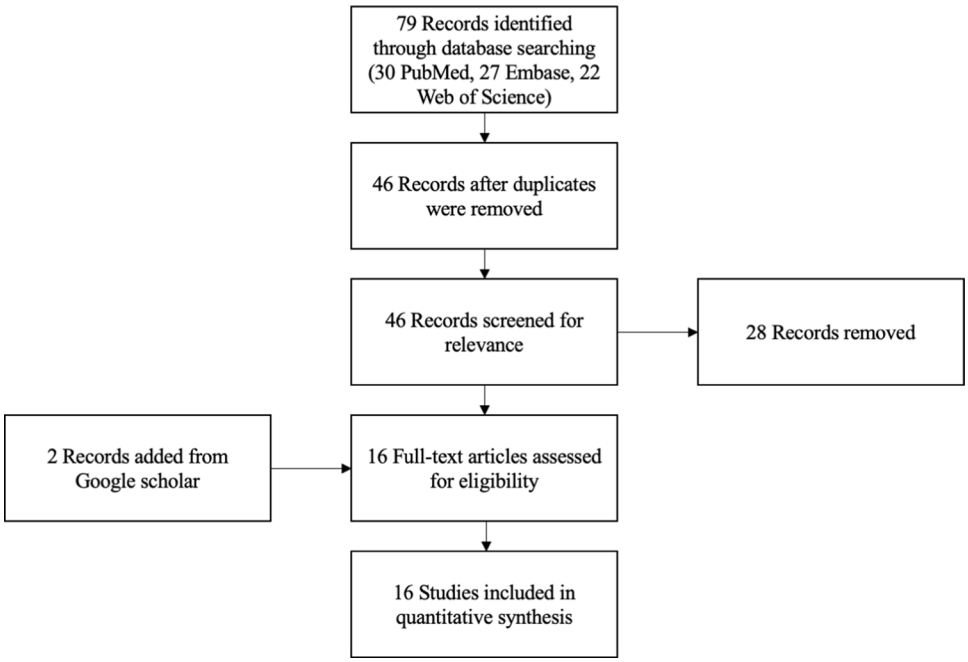

Fig. 1 PRISMA flowchart describing the study screening and selection process

due to premature ovarian failure [16]. One patient had a history of untreated sarcoidosis [18], three patients had a history of hypothyroidism [19, 20, 24], and one patient had a history of primary sclerosing cholangitis and ulcerative colitis [25]. Three patients had a prior history of AIH which had since resolved [21], and one patient had a history of COVID-19 infection that resolved. [24] (Table 1).

Medication Use

Four patients took acetaminophen shortly after receiving the first dose. Three patients were on chronic statin therapy. Twelve patients were taking potentially hepatotoxic medications including Pegylated interferon for polycythemia vera [12], levothyroxine [19, 20, 24], and nitrofurantoin [21]. However, each patient had been taking their medications for many years without recent changes to their medication regimens. The patient who reported nitrofurantoin use had completed a three-day course approximately 90 days prior vaccination, and thus nitrofurantoin-induced liver injury was deemed to be highly unlikely.

Presentation

The mean time to first symptom onset was 21.1 days after receiving the first COVID-19 vaccine dose. This latency time ranged from as little as two days to two months. Symptoms were recorded in 16 patients and were undocumented in 16. The most common symptoms were jaundice (81.3%), choluria (18.8%), fatigue (25.0%), anorexia (25.0%), pruritus (12.5%), abdominal pain (12.5%), and fever (6.3%). Three patients (18.8%) were initially asymptomatic and presented with elevated liver enzymes on routine bloodwork.

One patient [23] initially presented for malaise and jaundice that began 3 days after her first dose. Her symptoms resolved without treatment but returned shortly after she received her second dose 2 months later. Similarly, another patient [16] presented with abdominal pain, nausea, and vomiting one day after her first dose. Her symptoms persisted for 3 weeks but self-resolved. After an undisclosed time, she received her second dose and her symptoms reappeared at a higher intensity, this time with choluria and jaundice. Another patient [15] developed pruritus 15 days after her first dose. She received her second dose on day 21 and developed jaundice on day 23.

Diagnosis

In our cohort, the most common pattern of liver injury was hepatocellular, with markedly elevated transaminases near the thousands. The mean alanine aminotransferase (ALT) was 1230.6 U/L, mean aspartate aminotransferase (AST) was 920.9 U/L, mean alkaline phosphatase was 296.6 U/L, and mean bilirubin was 13.8 mg/dL. Immunoglobulin G (IgG) was elevated (> 16 g/L) in 16 patients (50.0%). Levels of gamma glutamyl transferase (GGT) were documented in 16 patients and were elevated (> 30 IU/L) in 7 patients (43.8%). Twenty-two patients (68.7%) had at least one positive autoantibody. Ani-nuclear antibody (ANA) was positive in 18 (56.3%) patients, anti-smooth muscle antibody (ASMA) was positive in 9 (28.1%), and anti-double stranded DNA was positive in 2 (6.3%). The liver kidney microsome

Table 1 Demographics, patient information, and disease presentation

Patient information	
Number of patients	32
Age (mean ± SD)	55.6 (± 15.3)
Gender	
Male	10 (31.3%)
Female	22 (68.8%)
Race/ethnicity	
Caucasian	6 (18.8%)
Unspecified	26 (81.3%)
Geographic location	
Australia	1 (3.1%)
Asia	3 (9.4%)
Europe	11 (34.4%)
USA	17 (54.1%)
Predisposing conditions	
History of liver disease	10 (31.3%)
History of autoimmune disease	9 (28.1%)
None of the above	18 (56.3%)
Medications	
Acetaminophen	4 (12.5%)
Statin	3 (9.4%)
Other hepatotoxic medication	12 (37.5%)
Presentation	
Symptom onset, days after 1st dose (mean ± SD)	21.1 (± 15.0)
Symptoms	16 documented, 16 not documented
Abdominal pain	2 (12.5%)
Anorexia or weight loss	4 (25.0%)
Asymptomatic	3 (18.8%)
Choluria	6 (18.8%)
Fatigue or malaise	4 (25.0%)
Fever	1 (6.3%)
Jaundice	13 (81.3%)
Pruritus	2 (12.5%)

Table 2 Diagnostics, treatment, and clinical outcomes

Diagnostics	
Peak laboratory values (mean ± SD)	
Alanine aminotransferase (U/L)	1230.6 (± 978.2)
Aspartate aminotransferase (U/L)	920.9 (± 397.2)
Alkaline phosphatase (U/L)	296.6 (± 458.0)
Bilirubin (mg/dL)	13.8 (± 33.7)
Gamma glutamyl transferase (U/L)	366.3 (± 252.5)
Immunoglobulin G (g/L)	23.1 (± 8.4)
Antibodies	
Anti-nuclear antibody	18 (56.3%)
Anti-smooth muscle antibody	9 (28.1%)
Anti-double stranded DNA	2 (6.3%)
Other	3 (9.4%)
Liver biopsy	
Performed	26 (81.3%)
Not performed	6 (18.8%)
Eosinophils on histology	11
Treatment	
First agent	
Budesonide	1
N-acetylcysteine	2
Prednisone	11
Prednisolone	9
Unspecified intravenous steroids	2
No treatment	7
Second agent	
Azathioprine	3
Methylprednisolone	1
N-acetylcysteine	1
Therapeutic plasma exchange	1
Clinical outcomes	
Time to first improvement, days (mean ± SD)	5.5 (± 4.2)
Time to resolution, days (mean ± SD)	28.1 (± 14.5)
Alive	31 (96.9%)
Dead	1 (3.1%)

was negative in all 32 patients. A completely negative autoantibody panel was seen in 10 patients (31.3%).

In ten cases, scoring systems such as the Simplified AIH score [28] and the Revised Original Score [29] guided the diagnosis of AIH. In 22 cases, the diagnoses were author-defined and guided by clinical suspicion, laboratory data, and liver biopsy results. Liver biopsy was performed in 26 patients (81.3%) [10–25], of which 7 had findings "typical" of AIH [10, 12, 14, 16, 19, 23, 24] and 19 had findings "compatible with" AIH. "Typical" histology findings are defined as the presence of all three of: (1) interface hepatitis with lymphocytic or lymphoplasmacytic portal inflammatory infiltrates extending into the lobule, (2) hepatocyte rosette formation, and (3) emperipolesis. "Compatible" histology findings are defined as chronic hepatitis with lymphocytic infiltration that do not meet requirements to be considered "typical." [30] Eosinophils, which can also be seen in drug-induced liver injury (DILI), were observed in 11 of the 26 liver biopsies (42.3%). [10, 12–15, 17, 19, 22, 23, 25] (Table 2).

Treatment and Outcomes

Steroids were used as a first-line agent in 23 patients (71.9%). *N*-acetyl cysteine was used as first-line treatment in two patients, one of whom failed to improve and required methylprednisolone to be added as a second agent [15], while the other fully recovered without additional therapy

[21]. Of those who received steroids as first-line treatment, 11 received prednisone, 9 received prednisolone, 2 received unspecified intravenous steroids, and 1 received budesonide. Seven patients received no treatment, all of whom recovered. The mean time to first improvement was 5.5 days, and the mean time to disease resolution was 28.1 days. Improvement or complete resolution was seen in 31 out of 32 patients (96.9%).

One death was observed in our review [19]. The patient was a 62-year-old male from India who developed AIH 13 days after receiving the first dose of the Oxford-AstraZeneca vaccine. He was initially treated with 30 mg of prednisolone per day with transient improvement in his liver enzymes before deteriorating due to unclear reasons. A liver transplant was offered, but the patient's family declined. The patient received five cycles of therapeutic plasma exchange which failed to improve his condition. He died 3 weeks after admission.

Discussion

As of November 4, 2021, an estimated 4 billion individuals worldwide have received at least one dose of the COVID-19 vaccine [1]. In the USA, approximately 250 million Pfizer-BioNTech and 162 million Moderna have been administered, with an estimated 234 million individuals who have received at least one dose [1]. COVID-19 vaccine-induced AIH is extremely rare with just 32 documented cases in the literature (17 cases in the United States). Although causality cannot be proved, this phenomenon should not be treated as coincidence. Clinicians should be vigilant for vaccine-induced AIH in patients who present with jaundice and abnormal liver enzymes following vaccination. We estimate the risk of AIH due to COVID-19 vaccination to be at least 1 in 14 million, although we acknowledge not all cases of vaccine-induced AIH have been documented in the literature. In comparison, the estimated incidence of idiopathic AIH ranges from 0.67 to 2 cases per 100,000 people per year. [31].

Vaccine-induced AIH is not unique to the COVID-19 vaccine. Case reports have documented AIH following vaccinations such as influenza [32, 33], hepatitis A [34, 35], measles, mumps, and rubella (MMR), typhoid, polio, and diphtheria/tetanus [34, 36]. Presentation of AIH was heterogenous in most cases, but all were acutely symptomatic with non-specific findings such as jaundice and abdominal pain. Interestingly, evidence of chronic liver disease was observed on the initial histologic examination of many patients. Nevertheless, all patients documented received steroid therapy with positive responses.

Molecular mimicry is thought to play a significant role in the development of autoimmune disease associated with other vaccines, such as vaccines for influenza and hepatitis B (HBV). In the influenza vaccine, cross-reactivity between a peptide sequence of surface-exposed influenza nucleoprotein A and the extracellular domain of Hypocretin receptor reportedly led to an increase in narcolepsy incidence in patients receiving the Pandemrix or Arepanrix vaccine [37, 38]. In the HBV vaccine, small HBV surface antigens in the vaccine exhibited similarity to multiple sclerosis autoantigen myelin basic protein (MBP) and myelin oligodendrocyte glycoprotein (MOG). Increased reactivity between vaccine HBV surface antigen and MOG was subsequently observed in over 60% of vaccinated subjects, predisposing them to multiple sclerosis [37, 39]. Although the pathophysiological mechanism behind COVID-19 vaccine-induced AIH is unclear, molecular mimicry likely plays a role. Antibodies against spike protein S1 have been shown to have a high affinity toward other human tissue proteins [40]. Vojdana et al. demonstrated that 21 out of 50 tissue antigens had moderate to strong reactions with the SARS-CoV-2 antibodies, suggesting that cross-reaction between SARS-CoV-2 proteins and other human tissue may exist. The Pfizer-BioNTech and Moderna vaccines are mRNA vaccines that lead to the production of spike protein, and thus antibodies against the spike protein. Molecular mimicry may lead to autoimmune tissue damage in susceptible individuals, contributing to the development of AIH.

Idiopathic AIH is heterogenous in its natural course but often has a chronic subclinical phase with fluctuating symptoms accompanied by acute exacerbation or even fulminant hepatic failure [41, 42]. Treatment consists of prednisone or prednisolone with or without azathioprine, or alternatively budesonide and azathioprine. It is associated with high remission rates and favorable outcomes [31, 42]. Vaccine-induced AIH is a new phenomenon with limited understanding of its natural history. Patients were diagnosed incidentally on laboratory surveillance or were acutely symptomatic. Patients with asymptomatic AIH typically exhibited lower liver enzyme elevations compared to those with symptoms [43]. However, acute versus chronic presentation of AIH was not shown to influence prognosis or response to treatment [44]. Despite various associations between different vaccines and rare instances of vaccine-induced AIH, patients with vaccine-induced AIH responded to treatment similarly to patients with idiopathic AIH. However, there are insufficient data to draw definite conclusions about the overall relapse rate and long-term outcomes of vaccine-induced AIH. In our cohort, 3 patients (9.4%) had a prior history of idiopathic AIH, while 29 patients (90.6%) had de novo AIH.

Despite its effectiveness, vaccine hesitancy has rapidly grown in certain subgroups [45]. Spurred by social media, misinformation has spread and ideologies from anti-vaccination groups are threatening to erode public confidence in the

vaccine. Clear and concise data are needed to ensure that public opinion regarding the vaccine is grounded in facts and science. Our results should not deter the public from vaccination. Rather, our study highlights the rarity of this phenomenon. Nevertheless, clinicians need to be aware of this rare but real complication.

There are several limitations to our study. The data extracted from the published articles were limited to retrospective case reports, case series, and letters to the editor. In certain articles, information about patient symptoms and laboratory values was incomplete. We did not have full access to each patient's medical history and detailed treatment courses. In the case series by Shroff, et al. [21], six patients did not undergo liver biopsy. Of those six patients, all had elevated transaminases, two had positive autoantibodies, and two were treated with steroids. Levels of IgG were not documented. Assessment of the diagnosis of immune-mediated hepatitis was limited by the patient information documented in the original article. It is possible that the incidence of vaccine-induced AIH is underestimated, as some patients may be asymptomatic and cases can go unreported. Publication bias may be present in the published case reports. Since this is a retrospective systematic review, we cannot confirm causality of the vaccine leading to AIH.

COVID-19 vaccine-induced AIH is extremely rare and has an excellent prognosis. Clinicians should consider AIH in patients who present with jaundice or elevated liver enzymes following COVID-19 vaccination, and promptly refer to hepatology for further work-up and treatment with steroids. Laboratory values typically show a hepatocellular pattern of injury and findings suggestive of type 1 AIH rather than type 2. Presence of autoantibodies is common, but its absence cannot rule out AIH. These new findings should under no circumstances deter individuals from getting vaccinated, as the overwhelming scientific consensus remains that the benefits of vaccination far outweigh the risks.

Author's contribution SS was involved in study concept and design; KC and BI acquired the data; KC, NP, BI, and SS analyzed and interpreted the data; KC drafted the manuscript; KC, NP, BI, KH, and SS critically revised the manuscript for important intellectual content; KC and NP were involved in statistical analysis; SS was involved in administrative, technical, or material support; SS was involved in study supervision. All authors approved the final draft submitted.

Declarations

Conflict of interest All authors report no conflict of interest.

References

1. Ritchie H, Mathieu E, Rodés-Guirao L et al. Coronavirus pandemic (COVID-19). Our world in data. Published online March 5, 2020. https://ourworldindata.org/covid-vaccinations. Accessed November 4, 2021.
2. Self WH, Tenforde MW, Rhoads JP et al. Comparative effectiveness of moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) vaccines in preventing COVID-19 hospitalizations among adults without immunocompromising conditions—United States, March–August 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70:1337–1343.
3. Baden LR, El Sahly HM, Essink B et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021;384:403–416.
4. Barda N, Dagan N, Ben-Shlomo Y et al. Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *N Engl J Med.* 2021;385:1078–1090.
5. Riad A, Pokorná A, Attia S et al. Prevalence of COVID-19 vaccine side effects among healthcare workers in the Czech Republic. *J Clin Med.* 2021;10:1428.
6. Polack FP, Thomas SJ, Kitchin N et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* 2020;383:2603–2615.
7. Klein NP, Lewis N, Goddard K et al. Surveillance for adverse events after COVID-19 mRNA vaccination. *JAMA.* 2021;326:1390–1399.
8. Hines A, Shen JG, Olazagasti C et al. Immune thrombocytopenic purpura and acute liver injury after COVID-19 vaccine. *BMJ Case Rep.* 2021;14:e242678.
9. Jawed M, Khalid A, Rubin M et al. Acute immune thrombocytopenia (ITP) following COVID-19 vaccination in a patient with previously stable ITP. *Open Forum Infect Dis.* 2021;8:ofab343.
10. Bril F, Al Diffalha S, Dean M et al. Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: Causality or casualty? *J Hepatol.* 2021;75:222–224.
11. Clayton-Chubb D, Schneider D, Freeman E et al. Autoimmune hepatitis developing after the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine. *J Hepatol.* 2021;75:1249–1250.
12. Garrido I, Lopes S, Simões MS et al. Autoimmune hepatitis after COVID-19 vaccine - more than a coincidence. *J Autoimmun.* 2021;125:102741.
13. Ghielmetti M, Schaufelberger HD, Mieli-Vergani G et al. Acute autoimmune-like hepatitis with atypical anti-mitochondrial antibody after mRNA COVID-19 vaccination: A novel clinical entity? *J Autoimmun.* 2021;123:102706.
14. Goulas A, Kafiri G, Kranidioti H et al. A typical autoimmune hepatitis (AIH) case following Covid-19 mRNA vaccination. More than a coincidence? *Liver Int.* 2021. https://doi.org/10.1111/liv.15092.
15. Lodato F, Larocca A, D'Errico A et al. An unusual case of acute cholestatic hepatitis after m-RNABNT162b2 (Comirnaty) SARS-CoV-2 vaccine: coincidence, autoimmunity or drug-related liver injury. *J Hepatol.* 2021;75:1254–1256.
16. Londoño MC, Gratacós-Ginès J, Sáez-Peñataro J. Another case of autoimmune hepatitis after SARS-CoV-2 vaccination - still casualty? *J Hepatol.* 2021;75:1248–1249.
17. McShane C, Kiat C, Rigby J et al. The mRNA COVID-19 vaccine - A rare trigger of autoimmune hepatitis? *J Hepatol.* 2021;75:1252–1254.
18. Palla P, Vergadis C, Sakellariou S et al. Letter to the editor: Autoimmune hepatitis after COVID-19 vaccination. A rare adverse effect? *Hepatology.* 2021. https://doi.org/10.1002/hep.32156.
19. Rela M, Jothimani D, Vij M et al. Auto-immune hepatitis following COVID vaccination. *J Autoimmun.* 2021;123:102688.
20. Rocco A, Sgamato C, Compare D et al. Autoimmune hepatitis following SARS-CoV-2 vaccine: May not be a casuality. *J Hepatol.* 2021;75:728–729.

21. Shroff H, Satapathy SK, Crawford JM et al. Liver injury following SARS-CoV-2 vaccination: a multicenter case series. *J Hepatol.* 2021;76:211–214.
22. Tan CK, Wong YJ, Wang LM et al. Autoimmune hepatitis following COVID-19 vaccination: True causality or mere association? *J Hepatol.* 2021;75:1250–1252.
23. Tun GS, Gleeson D, Dube A et al. Immune-mediated hepatitis with the Moderna vaccine, no longer a coincidence but confirmed. *J Hepatol.* 2021;76:747–749.
24. Vuille-Lessard É, Montani M, Bosch J et al. Autoimmune hepatitis triggered by SARS-CoV-2 vaccination. *J Autoimmun.* 2021;123:102710.
25. Zhou T, Fronhoffs F, Dold L, Strassburg CP, Weismüller TJ. New-onset autoimmune hepatitis following mRNA Covid-19 vaccination in a 36-year-old woman with primary sclerosing cholangitis - should we be more vigilant? *J Hepatol.* 2022;76:218–220.
26. Sahebjam F, Vierling JM. Autoimmune hepatitis. *Front Med.* 2015;9:187–219.
27. Linzay CD, Sharma B, Pandit S. Autoimmune hepatitis. [Updated 2021 Aug 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459186/
28. Hennes EM, Zeniya M, Czaja AJ et al. Simplified criteria for the diagnosis of autoimmune hepatitis. *Hepatology.* 2008;48:169–176.
29. Alvarez F, Berg PA, Bianchi FB et al. international autoimmune hepatitis group report: review of criteria for diagnosis of autoimmune hepatitis. *J Hepatol.* 1999;31:929–938.
30. Tiniakos DG, Brain JG, Bury YA. Role of histopathology in autoimmune hepatitis. *Dig Dis.* 2015;33:53–64.
31. Mack CL, Adams D, Assis DN et al. Diagnosis and management of autoimmune hepatitis in adults and children: 2019 practice guidance and guidelines from the American association for the study of liver diseases. *Hepatology.* 2020;72:671–722.
32. Muratori P, Serio I, Lalanne C et al. Development of autoimmune hepatitis after influenza vaccination; trigger or killer? *Clin Res Hepatol Gastroenterol.* 2019;43:e95–e96.
33. Sasaki T, Suzuki Y, Ishida K et al. Autoimmune hepatitis following influenza virus vaccination: two case reports. *Medicine.* 2018;97:e11621.
34. van Gemeren MA, van Wijngaarden P, Doukas M et al. Vaccine-related autoimmune hepatitis: the same disease as idiopathic autoimmune hepatitis? Two clinical reports and review. *Scand J Gastroenterol.* 2017;52:18–22.
35. Berry PA, Smith-Laing G. Hepatitis a vaccine associated with autoimmune hepatitis. *World J Gastroenterol.* 2007;13:2238–2239.
36. Perumalswami P, Peng L, Odin JA. Vaccination as a triggering event for autoimmune hepatitis. *Semin Liver Dis.* 2009;29:331–334.
37. Segal Y, Shoenfeld Y. Vaccine-induced autoimmunity: the role of molecular mimicry and immune crossreaction. *Cell Mol Immunol* 2018;15:586–594.
38. Ahmed SS, Volkmuth W, Duca J et al. Antibodies to influenza nucleoprotein cross-react with human hypocretin receptor 2. *Sci Transl Med.* 2015;7:294ra105.
39. Bogdanos DP, Smith H, Ma Y et al. A study of molecular mimicry and immunological cross-reactivity between hepatitis B surface antigen and myelin mimics. *Clin Dev Immunol.* 2005;12:217–224.
40. Vojdani A, Kharrazian D. Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. *Clin Immunol.* 2020;217:108480.
41. European Association for the Study of the Liver. EASL clinical practice guidelines: autoimmune hepatitis. *J Hepatol.* 2015;63:971–1004.
42. Terziroli Beretta-Piccoli B, Mieli-Vergani G, Vergani D. Autoimmune hepatitis: standard treatment and systematic review of alternative treatments. *World J Gastroenterol.* 2017;23:6030–6048.
43. Jacob K, Rifat S, Yaffa A et al. Prognosis of symptomatic versus asymptomatic autoimmune hepatitis. *J Clin Gastroenterol.* 2002;35:75–81.
44. Nikias GA, Batts KP, Czaja AJ. The nature and prognostic implications of autoimmune hepatitis with an acute presentation. *J Hepatol.* 1994;21:866–871.
45. Puri N, Coomes EA, Haghbayan H et al. Social media and vaccine hesitancy: new updates for the era of COVID-19 and globalized infectious diseases. *Hum Vaccin Immunother.* 2020;16:2586–2593.