Auto-immune hepatitis following COVID-19 Vaccination and SARS-COV2 infection : A narrative Review

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Abstract

Background and objectives : Since the onset of the COVID-19 pandemic, both SARS-CoV-2 infection and vaccination have been implicated as potential triggers for de novo autoimmune hepatitis (AIH). This review summarizes published cases, outlining clinical and biological features, treatment approaches, and outcomes.

Methods : A PubMed search identified reports of new-onset AIH following SARS-CoV-2 infection or COVID-19 vaccination up to February 1, 2025. Inclusion criteria encompassed case reports, series, and reviews. Data were extracted on demographics, vaccine type, onset timing, laboratory findings, histology, treatments, and outcomes.

Results : A total of 74 post-vaccination AIH cases and 22 post-infection cases were included. Post-vaccination AIH predominantly affected older women (median age 62) and occurred mainly after mRNA vaccines, with a median onset of 14 days. Most patients showed marked transaminase elevation, high IgG, and positive ANA (74.3%). Liver biopsies (performed in 92% of cases) showed features compatible with AIH. A total of 80% of the 50 cases of our study with available serology and liver histology were classified as probable / definite AIH, according to the simplified AIH score. Corticosteroid therapy was effective in most cases (survival 95.9%). Post-infection AIH cases showed similar features but affected younger individuals (median age 47), with uniformly favorable responses to immunosuppression.

Conclusions : New-onset AIH can occur following both SARS-CoV-2 infection or vaccination. Although these events remain rare, recognition of this association is essential for timely diagnosis and management. (Acta gastroenterol belg., **2026,** 89**, 341-354).**

Keywords: Coronavirus Disease 2019, Vaccine, Autoimmune Hepatitis, Vaccine-induced liver injury.

Introduction

Since its initial identification in Wuhan, China, in late 2019, the novel coronavirus SARS-CoV-2 has precipitated a global health crisis, causing extensive morbidity and mortality worldwide. Although respiratory manifestations remain predominant, hepatic involvement has been increasingly recognized, with liver function abnormalities reported in up to 50% of infected COVID-19 patients (1–4).

Among the autoimmune complications triggered (1–4) by COVID-19, autoimmune hepatitis (AIH), a chronic inflammatory liver disease characterized by immune-mediated hepatocyte damage, has increasingly been reported. AIH typically arises in predisposed individuals following exposure to specific environmental triggers, including viral infections such as Epstein–Barr virus (EBV) (5).

Emerging evidence suggests that SARS-CoV-2 infection may similarly precipitate autoimmune phenomena through mechanisms such as molecular mimicry, bystander activation, and dysregulated immune responses (6,7). Moreover, the rapid deployment of COVID-19 vaccines—although critical in mitigating the pandemic— has revealed rare immune-mediated adverse events, including cases of vaccine-associated AIH. Several reports describe the development of AIH following vaccination with mRNA (Pfizer-BioNTech and Moderna) and viral vector vaccines (AstraZeneca).

The pathogenesis of vaccine-associated AIH remains incompletely elucidated. Hypotheses include cross-reactivity between SARS-CoV-2 spike proteins and liver autoantigens, structural similarities between viral and human proteins, and adjuvant-induced immune activation. Although the absence of adjuvants in mRNA vaccines initially suggested a lower risk of autoimmunity, increasing reports now document AIH-consistent serological and histological findings post-vaccination (6). Importantly, distinguishing authentic AIH from vaccine-induced liver injury with autoimmune features (VILI) is complex, as these conditions display both overlapping phenotypes and distinct immunopathological signatures (8,9).

This review aims to synthesize current evidence on AIH occurrence following SARS-CoV-2 infection and vaccination, reviewing current case reports, diagnostic challenges and therapeutic considerations, while emphasizing the rarity of this complication and the continued importance of vaccination campaigns.

Methods

This review aims to provide a comprehensive analysis of the emergence of autoimmune hepatitis following SARS-coV-2 infection and COVID-19 vaccination. A PubMed search was conducted to identify relevant literature on both SARS cov2 infection and COVID-19 vaccination ; and new-onset autoimmune hepatitis published up to 1st February 2025. Inclusion criteria encompassed case reports, case series, original articles, letters to the editor, and reviews. Additionally, the references and related citations for the resulting articles

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were examined for potential inclusion. Search terms utilized included: “autoimmune hepatitis” , “COVID-19 “, “coronavirus” , “SARS-CoV-2”, “SARS CoV 2”, “vaccine”.

Results

Auto-immune hepatitis following coronavirus disease 2019 Vaccination

A total of 74 reported cases of autoimmune hepatitis (AIH) following COVID-19 vaccination were included in this review and were summarized in Table 1. The median age was 62 years (range: 20–85). The age distribution of the patients is shown in Figure 1. In addition, 60.8% of the patients were female. Most reported cases originated from Europe (59.5%) and Asia (32.4%). A pre-existing autoimmune disease was reported in 16.2% of patients, while 8.1% had a known history of liver disease. The majority of cases followed mRNA COVID-19 vaccination, with 44.6% receiving the Pfizer-BioNTech vaccine, 28.4% Moderna, and 18.9% AstraZeneca. The median delay between the last vaccine dose and symptom onset was 14 days (range: 2–56). The distribution of the delays between COVID-19 vaccination and AIH symptom onset is illustrated in Figure 2.

From a diagnostic standpoint, patients showed significantly elevated liver enzymes, with median ALT levels of 1026 U/L and AST levels of 720 U/L. The median total bilirubin level was 4.7 mg/dL, and immunoglobulin G levels were elevated in nearly 80% of cases (median: 1940 mg/dL). Autoantibodies were frequently detected : ANA in 74.3% of cases, ASMA in 23%, and AMA in 4.1%. Liver biopsies were performed in 91.9% of patients, all of which confirmed AIH. Treatment primarily involved systemic corticosteroids (91.9%), with azathioprine and therapeutic plasma exchange used in selected cases. Clinical outcomes were generally favorable with 95.9% of patients surviving, including one after liver transplantation, although 3 patients died.

The clinical and diagnostic features are reported in Tables 2 and 3.

Auto-immune hepatitis following SARS-Cov2 infection

The clinical and diagnostic features of reported cases of AIH following SARS-CoV-2 infection are analyzed in Table 4. The median age of affected individuals was 47 years, with a range spanning from 3 to 74 years, and a predominance of female patients (68.2%). Geographically, cases were distributed relatively evenly across America (36.4%), Asia (31.8%), and Europe (31.8%). Only a small proportion of patients had a history of autoimmune disease (9.1%), and none had pre-existing liver pathology. The median onset of AIH symptoms occurred 21 days after SARS-CoV-2 infection, with a wide variability from immediate onset to as late as 210 days post-infection.

Laboratory findings revealed markedly elevated liver enzymes, with a median alanine aminotransferase (ALT) of 848 U/L and aspartate aminotransferase (AST) reaching 1027 U/L. Total bilirubin levels were also significantly elevated (median 9.21 mg/dL). Immunoglobulin G levels were globally high (median 2260 mg/dL), and autoantibody testing showed ANA positivity in 50% and ASMA positivity in 36.4% of patients. Liver biopsies were conducted in 77.3% of cases and were compatible with AIH in all performed cases. Treatment mainly consisted of systemic corticosteroids (95.5%), with azathioprine used as a second-line agent in 50% of cases. Remarkably, all patients survived, underscoring the generally favorable prognosis of AIH post-COVID infection when appropriately managed.

All the 22 reported cases of AIH following SARS-CoV-2 infection are summarized in Table 5.

Discussion

The emergence of new-onset autoimmune hepatitis (AIH) following either SARS-CoV-2 infection or COVID-19 vaccination reflects a broader pattern of immune dysregulation triggered by viral antigens or vaccine-induced immune activation. This review summarizes 74 cases of vaccine-associated AIH and 22 cases following SARS-CoV-2 infection, highlighting clinical patterns, diagnostic features and treatment responses.

In the cases reviewed, many patients developed AIH after receiving mRNA vaccines, particularly Pfizer-BioNTech and Moderna, which together accounted for over 70% of vaccine-related AIH cases (6,7). The predominance of female patients and the median age of 62 years are consistent with typical epidemiological profiles of idiopathic AIH (5). The median 14-day interval between vaccination and symptom onset further supports a temporal association compatible with immune-mediated activation. In addition, the frequent presence of positive autoantibodies, marked elevations in liver enzymes and IgG, along with biopsy-confirmed interface hepatitis, reinforce the diagnosis of AIH and suggest a genuine autoimmune process rather than a nonspecifc liver injury.

However, despite these diagnostic arguments, distinguishing pure AIH from vaccine-induced liver injury (VILI) with autoimmune features remains particularly challenging. Primarily because the underlying pathophysiology is still poorly elucidated. Several mechanisms have been suggested - such as molecular mimicry between the SARS-CoV-2 spike protein and hepatic autoantigens, or vaccine-triggered immune stimulation in genetically predisposed individuals (7,73,5,74) - but none have been definitively demonstrated. The simplified AIH score classified 80% of assessable cases as probable or definite AIH, yet

Table 1. — **Reported cases of auto-immune hepatitis following coronavirus disease 2019 vaccination.**

References	Age/ Sex	COVID Vaccin	Onset	Past History	ASAT/ ALAT (UI/L)	TB (mg/dl)	IgG (mg/dl)	Antibody	Histology	Simplified AIH score	Treatment	Outcome
Bril et al (10)	35/M	BNT162b2	7 days after 1st dose	Third month postpartum	754 / 2001	4.8	1081	ANA : 1:1280	AIH compatible	5	Prednisone (20 mg/d)	Improved
Rocco et al (11)	80/F	BNT162b2	7 days after 2nd dose	Hashimoto's disease	1401 / 186	10.5	3500	ANA : 1:160	AIH compatible	7	Prednisone	Improved
McShane et al (8)	71/F	mRNA-1273	4 days after 1st dose	Osteoarthritis	/ 1067	15.8	2177	ASMA : positive	AIH compatible	7	Prednisone 40 mg/d)	Improved
Rela et al (12)	38/F	AZD1222	20 days after vaccin	Hypothyroidism	1101 / 1025	2.86	1650	ANA : positive	AIH compatible	6	Prednisolone (30 mg/d)	Improved
Rela et al (12)	62/M	AZD1222	16 days after vaccin	None	1361 / 1094	19.2		ANA : negative	AIH compatible	-	Prednisolone (30 mg/d) + Plasma exchange	Death
Lodato et al (13)	43/F	BNT162b2	15 days after 1st dose	Dyslipidemia	132 / 171	29.15		ANA : negative	AIH compatible	-	Methyl-prednisolone 1 mg/kg/d)	Improved
Tan et al (14)	56/F	mRNA-1273	35 days after 1st dose	None	1124 / 1701	5.97	3260	ANA : positive ASMA : positive	AIH compatible	7	Budesonide	Improved
Londoño et al (6)	41/F	mRNA-1273	7 days after 2nd dose	Premature ovarian failure	993 / 1312	2.3	2080	ANA : 1:80 ASMA positive	AIH compatible	7	Prednisone (1 mg/kg)	Improved
Zhou et al (15)	36/F	mRNA-1273	10 days after 1st dose	Ulcerative colitis, Primary sclerosing cholangitis	581 / 588	1.9	2475	ANA : 1:2560	AIH compatible	7	Prednisone (50 mg/d)	Improved
Ghielmetti et al (16)	63/M	mRNA-1273	7 days after 1st dose	Type 2 diabetes, ischemic heart disease	1127 / 1038	11.98	1996	ANA : 1:640	AIH compatible	7	Prednisone (40 mg/d)	Improved
Vuille-Lessard et al (17)	76/F	mRNA-1273	3 days after 1st dose	Hashimoto's disease, urothelial carcinoma	811 / 579	3.8	3940	ANA : 1:1280 ASMA : positive	AIH compatible	7	Prednisolone (40 mg/d) + azathioprine	Improved
Garrido et al (18)	65/F	mRNA-1273	15 days after 1st dose	JAK2 V617F-positive polycythemia	1056 / 1092	1.14	1500	ANA : 1:100	AIH compatible	5	Prednisolone (60 mg/d)	Improved
Avci et al (19)	61/F	BNT162b2	30 days after 1st dose	Hashimoto's disease, hypertension	913 / 455	11.8	4260	ANA : 1:100 ASMA : positive	AIH compatible	7	Prednisolone (40 mg/d) + azathioprine	Improved

Table 1. — **Reported cases of auto-immune hepatitis following coronavirus disease 2019 vaccination - continued.**

Camacho-Domínguez et al (20)	79/M	AZD1222	15 days after 1st dose	None	1194 / 2003	11.9	2058	ANA : 1: 80 ASMA : positive	AIH compatible	7	Prednisone (30 mg/d) + azathioprine	Improved
Goulas et al (21)	52/F	mRNA-1273	15 days after 1st dose	None	350 / 936	9.96	2396	ANA : 1:320 ASMA : positive	AIH compatible	7	Prednisolone (50 mg/d) + azathioprine	Improved
Tun et al (22)	47/M	mRNA-1273	3 days after 1st dose	None	/ 1048	11.12	2510	ANA : positive	AIH compatible	7	Prednisolone (40 mg/d)	Improved
Palla et al (23)	40/F	BNT162b2	30 days after 2nd dose	Sarcoidosis	160 / 180		2400	ANA : 1:640	AIH compatible	7	Prednisolone (40 mg/d)	Improved
Clayton-Chubb et al (24)	36/M	AZD1222	26 days after 1st dose	Hypertension	633 / 1774	0.99	1280	ANA : 1:160	AIH compatible	5	Prednisolone (60 mg/d)	Improved
Erard et al (25)	80/F	BNT162b2	10 days after vaccin	No AI history	538 / 541	4.56	2090	ANA : positive	AIH compatible	7	Steroids 1mg/Kg	Improved
Erard et al (25)	73/F	mRNA-1273	30 days after 1st dose	No AI history	1163 / 1027	19.54	1800	ANA : positive	AIH compatible	7	Steroids 1mg/Kg	Improved
Erard et al (25)	68/F	AZD1222	20 days after 1st dose	No AI history	2341 / 2029	43.99	1850	ANA : positive	AIH compatible	7	Liver Trans-plantation	Death
Suzuki et al (26)	80/F	BNT162b2	10 days after 2nd dose	Gastroesophageal reflux esophagitis	995 / 974	3.5	1936	ANA : 1:40	AIH compatible	6	Prednisone (0.8 mg/kg/d)	Improved
Suzuki et al (26)	75/F	BNT162b2	4 days after 2nd dose	Dyslipidemia				ANA : 1: 80	AIH compatible	≥ 6	Prednisone (1 mg/kg/d)	Improved
Suzuki et al (26)	78/F	BNT162b2	7 days after 1st dose	Primary biliary cholangitis				ANA : 1: 80	AIH compatible	≥ 6	Prednisone (0.6 mg/kg/d)	Improved
Kang et al (27)	27/F	BNT162b2	14 days after 2nd dose	None	1004 / 1478	8.6	1641	ANA : 1: 80	AIH compatible	6	Prednisolone (40 mg/d)	Improved
Fimiano et al (28)	63/F	BNT162b2	7 weeks atfer 2nd dose	Postmenopausal hypothyroidism	1625 / 1778	18.6	1760	ANA : negative ASMA : negative	AIH compatible	5	methylpred-nisolone 1 mg/kg/d) + azathioprine	Improved
Efe et al (29)	53/M	BNT162b2	30 days after 2nd dose		629 / 485	6.6	2830	ANA : negative ASMA : negative	AIH compatible	5	Prednisolone (40 mg/d) + Plasma exchange	Improved after Liver trans-plantation
Torrente et al (30)	49/F	AZD1222	21 days after 1st dose	Hypothyroidism, anemia	241 / 353		2016	ANA : 1:160	AIH compatible	7	Prednisone (30 mg/d) + azathioprine	Improved

Table 1. — **Reported cases of auto-immune hepatitis following coronavirus disease 2019 vaccination - continued.**

Mekritthikrai et al (31)	52/F	CoronaVac	7 days after 2nd dose	Hypertension Dyslipidemia	566 / 180	9.1	2712	ANA : 1:160 ASMA : positive	AIH compatible	7	Prednisolone (20 mg/d) + azathioprine	Improved
Barary et al (32)	35/M	AZD1222	8 days after 1st dose		1000 / 2000	4.7		ANA : negative ASMA : negative	Not performed	-	Dexa-methasone (40mg/d) + IVIG	Fulmi-nant hepatitis Death
Boettler et al(32)	52/M	BNT162b2	20 days after 2nd dose	Hypothyroidism	750 / 1939	2.9	1632	ANA : 1:200 AMA : positive ASMA : positive	Not performed	-	Budesonide + systemic steroid	Improved
Lasagna et al (34)	52/F	BNT162b2	10 days after 1st dose	Lung ADK under immunotherapy HBV	147 / 299	1.98	1400	ANA : negative	AIH compatible	4	Prednisone (1mg/kg)	Improved
Hasegawa et al (35)	82/F	BNT162b2	4 days after 1st dose	HCV	1682 / 1097	22.1	1809	ANA : positive	AIH compatible	7	Prednisolone (5 mg/d)	Improved
López et al (36)	76/H	BNT162b2	30 days after 3rd dose	history of hepatic cirrhosis secondary to PBC				ANA : positive	AIH compatible	-	Steroids + azathioprine	Improved
Pinazo-Bandera et al (37)	77/F	BNT162b2	2 days after 2nd dose	Hypertension	474 / 552	3.1		ANA : 1:160 ASMA : positive Anti-M2 : positive	AIH compatible	-	Prednisone (60 mg/d) + azathioprine	Improved
Pinazo-Bandera et al (37)	23/M	mRNA-1273	10 days after 2nd dose	None	702 / 587	2.3	1647	ANA : negative	AIH compatible	4	Prednisone (60 mg/d)	Improved
Shroff et al (38)	59/F	mRNA-1273	31 days after 1st dose	None	367 / 869	14.7	1750	ANA : 1:640	AIH compatible	6	Steroids	Improved
Zafar et al (39)	81/F	BNT162b2	28 days after 4th dose	None	/ 689	9.59	1380	ANA : positive	AIH compatible	5	Prednisolone 40 mg	Improved
Eslami et al (40)	21/F	BBIBP-CorV	4 days after vaccin	None	429 / 1700	7.8	2100	ANA : positive	AIH compatible	7	Prednisolone (10 mg/d) + azathioprine	Improved
Yoshida et al (41)	85/F	BNT162b2	14 days after 2nd dose	Sjögren's syndrome Hypertension Lacunar stroke	383 / 925	5.9	2126	ANA : 1:1280	AIH compatible	7	prednisolone (35 mg/d)	Improved
Shahrani et al (42)	63/F	AZD1222	14 days after 1st dose	Ulcerative colitis, primary sclerosing cholangitis	505 / 354	18.31	2030	ANA : positive	AIH compatible	7	Prednisolone (40 mg/d)	Improved

Table 1. — **Reported cases of auto-immune hepatitis following coronavirus disease 2019 vaccination - continued.**

Shahrani et al (42)	59/F	AZD1222	12 days after 2nd dose	Dyslipidemia	962 / 1178	7.37	1740	ANA : negative	AIH compatible	4	Prednisolone (40 mg/d)	Improved
Shahrani et al (42)	72/F	BNT162b2	10 days after 2nd dose	None	1452 / 2280	1.7	1940	ANA : negative AMA positive	AIH compatible	7	Prednisolone (40 mg/d)	Improved
Ferronato et al (43)	30/F	mRNA-1273	30 days after 2nd dose	Hashimoto's thyroiditis	/ 2400	1.96	1642	ANA : positive	AIH compatible	6	N-acetyl-cysteine	Improved
Ferronato et al (43)	26/M	mRNA-1273	30 days after 2nd dose	Vitiligo	/ 76	0.9	1749	ANA : positive	AIH compatible	6	No treatment	Improved
Gips et al (44)	72/M	BNT162b2	15 days after 1st dose	Pulmonary sarcoidosis	1177 / 1221	7.2	3480	ANA : positive ASMA : positive	AIH compatible	7	Prednisone (60 mg /d)	Improved
Mathew et al (45)	20/M	AZD1222	10 days after 1st dose	Cluster headache Irritable bowel syndrome	1855 / 1790	4.91	2 700 000	ANA : positive AMA : positive	AIH compatible	7	Prednisolone (40 mg/d) + azathioprine	Improved
Izagirre et al (46)	72/M	BNT162b2	46 days after 2nd dose	30 g/d alcohol consumption	204 / 248	12.3	1670	ANA : 1:1280	AIH compatible	6	Prednisone 50 mg+ Azathioprine	Improved
Izagirre et al (46)	62/F	AZD1222	4 days after 2nd dose	Coeliac disease	498 / 655	2.5	1684	ANA : 1:160	AIH compatible	6	Prednisone 40 mg + Azathioprine	Improved
Izagirre et al (46)	72/F	BNT162b2	14 days after 2nd dose	No comorbidities	866 / 570	2.3	1916	ANA : 1:320	AIH compatible	7	Prednisone 50 mg	Improved
Izagirre et al (46)	59/M	Pfizer	9 days after 1st dose	Hypothyroidism	1799 /1292	1.3	1978	ANA : positive	Not performed	≥ 6	No treatment	Improved
Izagirre et al (46)	47/F	AZD1222	24 days after 1st dose	Hypothyroidism	241 / 253	0.4	2016	ANA : 1:320	AIH compatible	7	Prednisone 20 mg + Azathio-prine 50 mg	Improved
Díez et al (47)	51/F	mRNA-1273	14 days after 2nd dose	No AI history	/ 1771	6.25		ANA : 1:2560 ASMA : positive	Not performed	-	Cortico -steroids + azathioprine	Improved
Díez et al (47)	80/M	BNT162b2	12 days after 1st dose	No AI history	/ 1628	10		ANA : 1:160 ASMA : positive	AIH compatible	-	cortico -steroids	Improved
Díez et al (47)	56/M	mRNA-1273	2 days after 3rd dose	No AI history	/ 1515	5.69		ANA : negative ASMA : positive	AIH compatible	-	Cortico-steroids + azathioprine	Improved
Ueno et al (48)	54/F	mRNA-1273	7 days after 3rd dose	Mild hypertension	2001 / 2472	11.1	1358	ANA : negative ASMA : positive	AIH compatible	5	Cortico-steroids + azathioprine	Improved

Table 1. — **Reported cases of auto-immune hepatitis following coronavirus disease 2019 vaccination - continued.**

Kim et al (49)	27/M	BNT162b2	15 days after 1st dose	None	640 / 1416	1.52	2069	ANA : positive	AIH compatible	7	Prednisolone (30 mg/d)	Improved
Zaiem et al (50)	37/M	mRNA-1273	56 days after 2nd dose	None	146 / 155		1920	ANA : 1:40	AIH compatible	6		Improved
Tamura et al (51)			10 days after vaccin							-	Prednisolone	Improved
Tamura et al (51)			10 days after vaccin							-	Prednisolone	Improved
Tamura et al (51)			10 days after vaccin							-	Prednisolone	Improved
Cao et al (52)	57/F	CoronaVac	15 days after 2nd dose	None	819 / 974	16.6	1744	ANA : 1:640	AIH compatible	6	Methylpre-dnisolone + azathioprine	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)	median age 62 yrs (range 32–80). 50% Fe-mals.	BNT162b2	median time from 1st & 2nd vaccine dose: 48 and 10 days, respectively	3 thyroiditis, 2 rheumatoid arthritis, 1 systemic lupus erythematosus	median 18 x ULN (range 5-85) / 23.8 x ULN (range 7-83),	median 3.8 x ULN (range 0.6-18.6)	median 1.2 x ULN (0.8-1.5)	8 patients had positive autoantibodies (6 ANA, 1 SMA, 1 LKM-1)	AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		BNT162b2							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		AZD1222							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		AZD1222							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		mRNA-1273							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		mRNA-1273							AIH compatible	-	Standard IS treatment	Improved
Rigamonti et al (53)		mRNA-1273							AIH compatible	-	Standard IS treatment	Improved

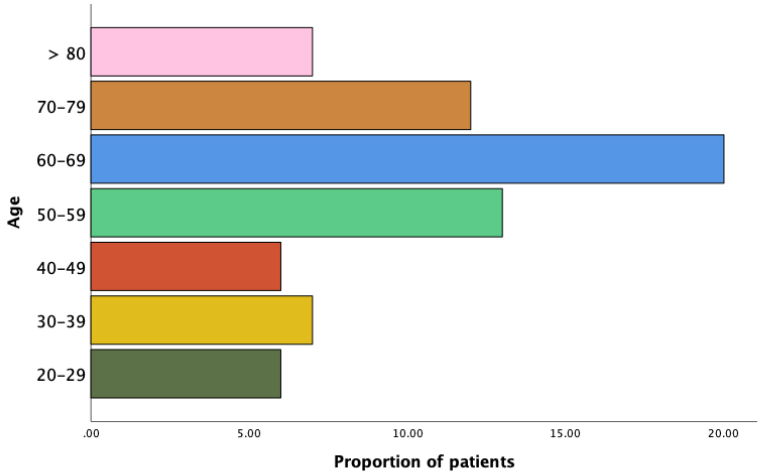

Figure 1. — Pre-vaccination age of patients with vaccine-associated AIH.

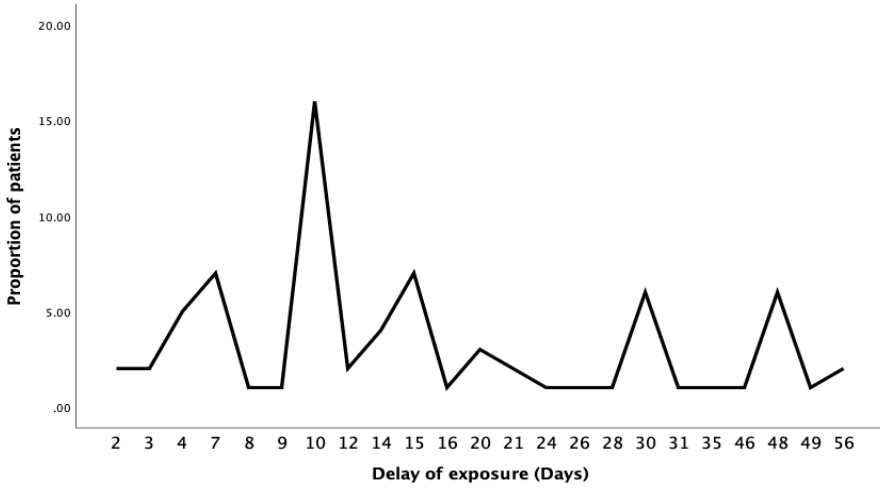

Figure 2. — Distribution of the delay between COVID 19 vaccination and AIH onset symptoms.

this scoring system does not fully resolve the overlap between AIH and VILI. Recent studies, including the work of Uzun et al. (9), highlight that VILI may represent a distinct immunopathological entity. While histomorphology appears similar between VILI and AIH, their molecular and cellular immune signatures diverge. VILI is characterized by enrichment of mitochondrial metabolism and oxidative stress pathways and is dominated by $CD8^+$ effector T cells, resembling drug-induced autoimmune-like hepatitis. In contrast, AIH typically shows $CD4^+$ T-cell predominance along with $CD79a^+$ B cells and plasma cells (9,33,75).

Treatment outcomes were generally favorable, with 95.9% of vaccine-related AIH patients surviving, and only a few progressing to liver failure requiring transplantation (29). First-line therapy involved systemic corticosteroids, while second-line immunosuppressive agents, such as azathioprine, were used in selected cases. These findings underscore the importance of early recognition and management, especially given the excellent response to conventional therapy.

AIH following SARS-CoV-2 infection displayed similar features, although the median age was lower (47 years), and symptom onset was more variable, ranging from immediate presentation to as long as 7 weeks post-infection (71). Like vaccine-associated cases, these patients demonstrated elevated liver enzymes, IgG levels, and autoantibodies. Liver biopsies, when performed, were consistently compatible with AIH, and all patients responded well to corticosteroids, often supplemented with azathioprine or other immunosuppressive agents (54,59,60).

Conclusion

COVID-19 infection and vaccination may trigger autoimmune hepatitis in a small number of susceptible individuals, highlighting the need for careful clinical evaluation and timely management. However, distinguishing true AIH from vaccine-induced liver injury with autoimmune features (VILI) remains difficult due to limited understanding of their underlying mechanisms. Further longitudinal studies are required

Table 2. — **The clinical features of the reported cases of AIH following COVID 19 Vaccination.**

Patient information	
Number of patients	74 (100%)
Age, (median)	62 (20-85)
Gender	
Male	26 (35.1%)
Female	45 (60.8%)
Unknown	3 (4.1%)
Geographic location	
Africa	1 (1.4%)
Australia	1 (1.4%)
America	4 (5.4%)
Asia	24 (32.4%)
Europe	44 (59.5%)
Predisposing conditions	
History of liver disease	6 (8.1%)
History of autoimmune disease	12 (16.2 %)
None of the above	54 (73 %)
COVID Vaccin	
Pfizer-BioNTech (BNT162b2)	33 (44.6%)
Moderna (mRNA-1273)	21 (28.4%)
AstraZeneca (AZD1222)	14 (18.9%)
Sinopharm (BBIBP-CorV)	1 (1.4%)
CoronaVac	2 (2.7%)

Table 3. — **Diagnostic features of the reported cases of AIH following COVID 19 Vaccination.**

Diagnostic	
Delay of exposure (median)	14 (2 - 56)
Peak laboratory values (median)	
Alanine aminotransferase (U/L)	1026 (76 – 2472)
Aspartate aminotransferase (U/L)	720 (132- 2341)
Bilirubin (mg/dL)	4.7 (0.4 – 43.99)
Immunoglobulin G (mg/dL)	1940 (1081 – 2 700 000)
IgG > 1600 mg/dL	59 (79.7 %)
Antibodies	
Anti-nuclear antibody	55 (74.3 %)
Anti-smooth muscle antibody	17 (23 %)
Anti-mitochondrial antibody	3 (4.1 %)
Liver biopsy	
Performed	68 (91.9 %)
Compatible with AIH	68 (100 %)
Not performed	6 (8.1 %)
Treatment	
First agent	
Systemic steroids	68 (91.9 %)
Budesonide	1 (1.4 %)
N-acetylcysteine	1 (1.4 %)
Liver transplantation	1 (1.4 %)
No treatment	3 (4.1 %)
Second agent	
Azathioprine	18 (24.3 %)
Therapeutic plasma exchange	2 (2.7 %)
Intravenous immunoglobulins	1 (1.4 %)
Clinical outcomes	
Alive	71 (95.9 %)
Dead	3 (4.1 %)

Table 4. — **The clinical and diagnostic features of the reported cases of AIH following SARS-CoV-2 infection.**

Patient information	
Number of patients	22 (100%)
Age, (median)	47 (3 - 74)
Gender	
Male	7 (31.8 %)
Female	15 (68.2 %)
Geographic location	
America	8 (36.4 %)
Asia	7 (31.8 %)
Europe	7 (31.8 %)
Predisposing conditions	
History of liver disease	0
History of autoimmune disease	2 (9.1 %)
Onset (median in days)	21 (0 - 210)
Peak laboratory values (median)	
Alanine aminotransferase (U/L)	848 (106 – 1316)
Aspartate aminotransferase (U/L)	1027 (70 – 2305)
Bilirubin (mg/dL)	9.21 (1 – 28.5)
Immunoglobulin G (g/L)	2260 (1070 – 5295)
Antibodies	
Anti-nuclear antibody	11 (50 %)
Anti-smooth muscle antibody	8 (36.4 %)
Liver biopsy	
Performed	17 (77.3 %)
Compatible with AIH	17 (77.3 %)
Not performed	5 (22.7 %)
Treatment	
First agent	
Systemic steroids	21 (95.5 %)
Ursodeoxycholic acid	1 (4.5 %)
Second agent	
Azathioprine	11 (50 %)
Monoclonal antibody	1 (4.5 %)
Tacrolimus	1 (4.5 %)
Mycophelonate	1 (4.5 %)
Clinical outcomes	
Alive	22 (100%)

Table 5. — **Reported cases of auto-immune hepatitis following SARS-Cov2 infection.**

Reference	Age / Sex	Onset (after SARS COV2 infection)	Past History	ASAT/ ALAT (UI/L)	TB (mg/ dl)	IgG (mg/dl)	Antibody	Histology	Simplified AIH score	Treatment	Outcome
Hong et al (54)	54/M	1 month	Rheumatoid arthritis, Scleritis.	1084 / 1238	25	3151	ANA : positive ASMA : positive	AIH compatible	7	Prednisone (40 mg/ day) + Monoclonal antibody	Improved
Kulkarni et al (55)	50/M	Few days		203 / 113	7.8	5052		Not performed	-	Prednisone + Azathiorpine	Improved
Mostafavi et al (56)	13/F	3 months		488 / 343	1	6365	ANA : positive ASMA : positive	AIH compatible	7	Prednisone 40 mg /d + azathioprine	Improved
Osborn et al (57)	3/F	3 weeks		1321 / 939	5.5	1070	LKM : positive	AIH compatible	5	Methylprednisolone (2mg/kg/d) + azathioprine	Improved
Montón et al (58)	60/F	COVID + at the diagnosis	Hypothyroidism	1830 / 1422	11.73	2775	ANA : negative ASMA : negative	AIH compatible	5	Corticosteroid + azathioprine	Improved
Kabaçam et al (59)	72/F	2 days			11.2	4250	ASMA : positive	Not performed	≥ 6	Prednisone 40 mg/d +Tacrolimus 4 mg/d	Improved
Kabaçam et al (59)	49/M	20 days			1.6	2260	ANA : positive	Not performed	≥ 6	Predn 30 mg/d +Azathioprine	Improved
Durazo et al (60)	49/F	7 weeks	None	614 / 851	8.93	2093	ANA : negative ASMA : negative	AIH compatible	5	Prednisone 40 mg + Mycophelonate	Improved
Andrés et al (61)	38/F	6 weeks	Asthma	1112 / 1255	1.7	1890	ASMA : positive	AIH compatible	7	Prednisone + azathioprine	Improved
Andrés et al (61)	74/F	15 days	None	1055 / 1011	5.3	2180	ANA : positive	AIH compatible	7	Prednisone + azathioprine	Improved
Cunha-Silva et al (62)	45/M	2 weeks	None	70 / 156	28.5	1509	ANA : positive ASMA : positive	AIH compatible	6	prednisone 40mg/ day+ UDCA	Improved
Singh et al (63)	57/M	1 month	Hypertension Prediabetes B-thalassemia mino	137 / 106	1	4049	ASMA : positive AMA : positive dsDNA : positive	Not performed	≥ 6	Ursodeoxycholic acid (AIH-PBC Overlap syndrom)	Follow-up
Martini et al (64)	42/M	2 weeks		1405 / 1047	15.8	3668	ANA : positive ASMA : positive	AIH compatible	7	Steroids and N-acetylcysteine + azathioprine	Improved
Lee et al (65)t	39/F	COVID + at the diagnosis	None	1270 / 1057	7.6	< 1800	ANA : negative ASMA : negative LKM : négative	AIH compatible	≤ 5	prednisone	Improved
Fanni et al (66)	52/F	20 days	Hashimoto thyroiditis	628 / 607	20.2	3317	ANA : positive ASMA : negative	AIH compatible	7	Methylprednisolone and Ursodeoxycholic acid + azathioprine	Improved

Table 5. — **Reported cases of auto-immune hepatitis following SARS-Cov2 infection - continued.**

Marabotto et al (67)	37/F	During hospitalisation for COVID-19 infection	Metabolic syndrom	1135 / 1417	normal	2270	ANA : positive ASLA : positive	AIH compatible	7	Steroids + azathioprine	Improved
Zhou et al (68)	39/F	3 weeks	None	2305 / 612	11.8	1757	ANA : positive	AIH compatible	6	Methylprednisolone (80mg/d)	Improved
Abe et al (69)	15/F	COVID + at the diagnosis	Immune thrombocytopenic purpura	650 / 845	9.5	1439	ANA : positive Anti-M2 : positive	AIH compatible	5	Prednisolone (40 mg/d)	Improved
Folman et al (70)	40/F	1 month		1000 / 1300	22	2190	ANA : positive	AIH compatible	7	Prednisone (1 mg/kg)	Improved
Lenci et al (71)	Middle-aged/F	7 months		x 10 normal values				AIH compatible	-	Steroids	Improved
Lenci et al (71)	Middle-aged/F	2 months		x 10 normal values				AIH compatible	-	Steroids	Improved

to clarify this relationship and improve diagnostic and management accuracy.

Declarations

Competing interests: All authors report no conflict of interest.

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