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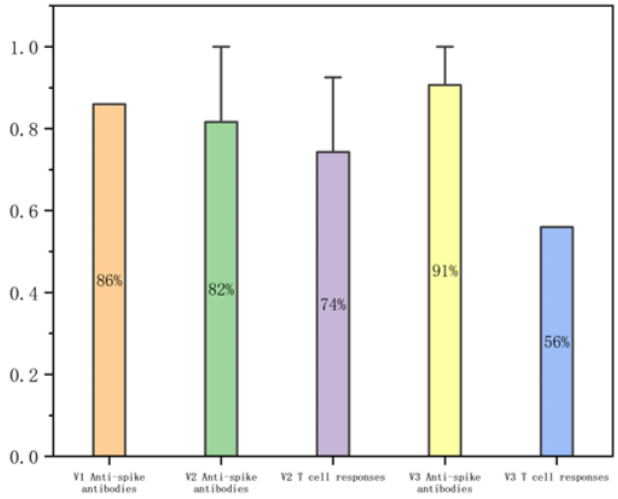
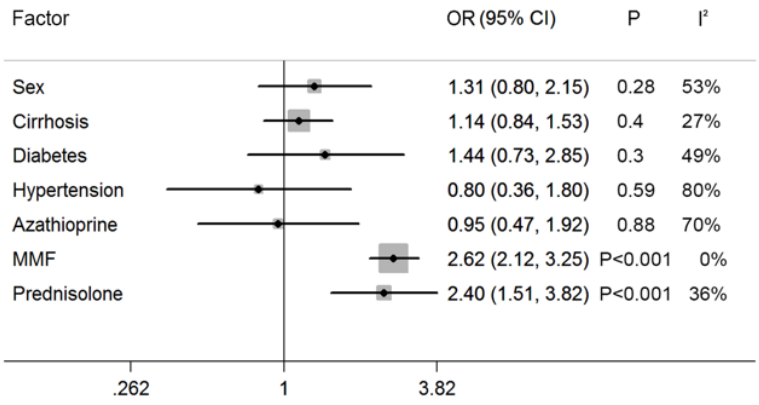


In patients with AIH, the immune response to SARS-CoV-2 vaccination is attenuated.



Treatment with mycophenolate mofetil and corticosteroids was associated with a notable decrease in seropositivity [pooled odds ratio (95% confidence interval): 2.62 (2.12–3.25) and 2.4 (1.51–3.82).

Author Tian, et al.

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Immunogenicity and risk factors for poor humoral immune response to SARS-CoV-2 vaccine in patients with autoimmune hepatitis: a systematic review and meta-analysis

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Author contributions: Tian ZX and Chen YH contributed equally to this work and share first authorship. Jin HB conceived and designed the study. Yao YX and Chen LH performed the literature search. Tian ZX, and Zhu XK performed the quality assessment of the literature. Chen YH, and Yang SW were responsible for data extraction. Shen ZC, and Chen YH conducted the statistical analysis. Tian ZX and Chen YH drafted the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data availability statement: the data supporting the findings of this study are included within the article and are available from the corresponding author upon reasonable request.

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Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

ABSTRACT

Background: research on the immunogenicity of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine in patients with autoimmune hepatitis (AIH) has produced varied results, and the determinants of the immunological response remain largely elusive.

Methods: a comprehensive search of three primary databases (PubMed, Embase, and Web of Science) yielded pertinent studies on the topic. The data extraction was a collaborative effort among three independent researchers, who subsequently reconvened to validate the key data that were collated. The primary outcomes were the magnitudes of humoral and cellular immune responses to the vaccines. The secondary outcomes were related to factors affecting the humoral immune response post-vaccination.

Results: this systematic review incorporated eight studies, and the meta-analysis involved three studies. The average antibody response rates after one, two, and three doses of the SARS-CoV-2 vaccine were 86 %, 82 %, and 91 %, respectively. Unexpectedly, the antibody concentrations of seropositive patients were markedly lower than those of their healthy counterparts. The cellular immune response rates after two and three vaccine doses were 74 % and 56 %, respectively. Treatment with mycophenolate mofetil and corticosteroids was associated with a notable decrease in seropositivity (pooled odds ratio [95 % confidence interval]: 2.62 [2.12-3.25] and 2.4 [1.51-3.82], respectively). In contrast, azathioprine had no discernable impact on the humoral response.

Conclusion: in patients with AIH, the immune response to COVID-19 vaccination is attenuated. Specific immunosuppressive agents, such as steroids and MMF, have been found to reduce antibody responses. Recognizing these determinants is crucial to formulating individualized vaccination strategies for patients with AIH. Further research with an emphasis on post-vaccination cellular immunity will be essential to

refine the vaccination approaches for this demographic.

Keywords: Autoimmune hepatitis. COVID-19 vaccination. Immunogenicity. Systematic review. Meta-analysis.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), has affected more than 770 million individuals worldwide, leading to approximately seven million deaths as of 29 September 2023 (1). Among those disproportionately impacted are individuals with chronic liver disease (CLD). Relative to the general population, individuals with CLD have higher rates of hospitalization and mortality following SARS-CoV-2 infection (2,3).

In light of this, both the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver recommend SARS-CoV-2 vaccination for all patients with CLD (4,5). Autoimmune hepatitis (AIH) is a specific subset of CLD that is closely associated with immune dysregulation (6). AIH is predominantly managed using corticosteroids, either as a monotherapy or in conjunction with azathioprine. Other therapeutic options include tacrolimus, mycophenolate mofetil (MMF) and rituximab. Patients with AIH typically require indefinite immunosuppressive therapy, which consequently elevates their susceptibility to bacterial and viral infections (7).

Due to the immune disturbances inherent to AIH and the administration of immunosuppressive agents in these patients, the repercussions of SARS-CoV-2 infection are accentuated in this cohort. The prevalence of SARS-CoV-2 among patients with AIH mirrors that of the broader community (8). Nevertheless, a large amount of evidence indicates significantly higher hospitalization and mortality rates in this group following exposure to the virus (9).

Numerous COVID-19 vaccines have shown potential to lower hospitalization and mortality rates among patients with AIH (10). However, emerging evidence suggests potentially attenuated immune responses to these vaccines in patients with AIH,

especially those receiving concurrent immunosuppressive treatments, although the data are somewhat discordant (11-14). Notably, isolated cases have suggested the possible onset of AIH following COVID-19 vaccination, fueling vaccine hesitancy (15). A comprehensive review assimilating these findings has not yet been performed. Therefore, this study aimed to collate the most recent insights on the immunogenicity of COVID-19 vaccines in patients with AIH and discern the factors that contribute to compromised immunogenicity within this demographic.

METHODS

Systematic review protocol

This systematic review was conducted in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (16).

Search strategy

Two authors independently conducted database searches of Web of Science, PubMed, and Embase, spanning from December 2020 to September 2023. As an example, in the PubMed search, relevant Medical Subject Headings (MeSH) terms related to COVID-19 vaccines were combined with all relevant free-text terms. Similarly, MeSH terms were used for AIH and their respective free-text terms in the search. No linguistic constraints were imposed; for non-English articles, Google Translate was used for the initial title and abstract screenings. To uphold the integrity of the data, articles from preprint databases that had not undergone peer review were excluded.

Study selection

A dual independent review was a cornerstone of the study assessment process. Clinical trials and a variety of observational studies were incorporated: prospective cohorts, retrospective cohorts and case-control studies. The inclusion criterion was studies delineating immunogenic responses after COVID-19 vaccination in patients with AIH. When clarification was needed, direct communication with the primary

authors was initiated, primarily concerning antibody assays. Disagreements among the reviewers were resolved through collective consensus.

Data extraction

To ensure meticulous data extraction, the Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modeling Studies (CHARMS) was used (17). Data extraction was a collaborative effort among two independent researchers, who subsequently reconvened to validate the key data that were collated. The data extracted included the study design, patient demographics, SARS-CoV-2 vaccine details, immunogenicity assessment methodologies, and study outcomes. The primary outcomes were the magnitudes of humoral and cellular immune responses to the vaccines. The seroconversion rate was calculated based on the responder count and total participants. "Responders" were classified as individuals exhibiting humoral or cellular responses surpassing the study-specified threshold. The secondary outcomes were related to factors affecting the humoral immune response post-vaccination. Essential metrics such as the number of responders, total participants and odds ratio (OR) with 95 % confidence interval (CI) were curated for factors influencing vaccine-induced immune responses.

Risk-of-bias assessment

The Newcastle-Ottawa Scale was used to evaluate the risk of bias among all included studies (18). This instrument scrutinized studies on patient selection, comparability and outcome ascertainment, and the maximum score was 9. Studies with a score of ≥ 7 were considered as high-quality, those with a score of 4-6 were considered as moderate-quality, and those with a score of ≤ 3 were considered as potentially bias-prone.

Data analysis

Descriptive statistical methods were employed to examine the humoral and cellular immune responses post-vaccination. The humoral and cellular immune response rates were discerned via weighted means. For homogeneous indicators reported

across at least two clinical trials, Stata 18 (StataCorp, College Station, TX, USA) was used for the statistical analysis, targeting risk determinants linked to attenuated humoral immune responses. Binary or categorical variables are presented with their ORs and 95 % CIs. When presented with both adjusted and unadjusted ORs, the former was prioritized; in its absence, unadjusted ORs were derived from the primary data. Heterogeneity was evaluated using the Chi-squared test. When the heterogeneity was > 50 %, a random-effects model was used; otherwise, a fixed-effects model was used. If a sufficient number of studies were included, a sensitivity analysis was performed via a stepwise exclusion strategy and funnel plots were used to gauge potential publication bias (19).

RESULTS

Characteristics of selected studies and patients

From an initial pool of 844 articles, 709 remained after the removal of duplicates. After a preliminary screening of the titles and abstracts, 95 articles remained. Subsequently, 87 articles were excluded for various reasons: incomplete data sets, non-conforming study designs, misaligned study populations, or redundancy with another cohort (Fig. 1). Ultimately, eight pertinent studies were incorporated into this systematic review (11-14,20-23). An overview of these studies is presented in table 1. Collectively, the eight studies involved 303 patients with AIH (median age: 58.6 years) and originated from Australia, Germany, the United Kingdom, Italy and Japan. The patients predominantly received mRNA and adenovirus vaccines, with the humoral immune response evaluated through anti-SARS-CoV-2 spike protein receptor-binding domain levels. Post-vaccination evaluations were performed after two to 12 weeks. Three studies that examined factors modulating the vaccine immune response were entered into the meta-analysis (11-13). Quality assessment using the Newcastle-Ottawa Scale showed that five studies were high-quality (11-13,20,21,23), one was moderate-quality (14), and two were potentially bias-prone (13,22) (Table 2).

Humoral immune response

One study (14) showed an 86 % humoral immune response following the first vaccine dose. Six studies (11,13,14,20,21,23) reported the response following the second dose, which averaged 82 % (range 40-92 %), with the antibody assay typically performed approximately 5.4 weeks post-vaccination (range: 2-12 weeks). Three studies (12,13,22) reported the humoral immune response following the third vaccine dose, which averaged 91 % (range: 81-100 %), with an average testing interval of 4.3 weeks (range: 3-5 weeks) (Table 3 and Fig. 2).

Cellular immune response

The cellular immune response following the second vaccine dose was the focal point of two studies (11,20), and the response rate averaged 74 % (range: 56-92 %). Both studies used distinct methodologies for assessment: the interferon gamma ELISpot Assay (R&D Systems, Minneapolis, MN, USA) and activation-induced CD154 and CD137 markers. Another study (12) reported the cellular immune response following the third dose, which averaged 55 % (Table 3).

Risk factors for reduced humoral immune responses after two vaccine doses

Three studies (11-13) were evaluated to identify factors potentially influencing humoral immunity subsequent to a dual vaccine regimen in patients with AIH. Constraints induced by original data scarcity and variances in assay thresholds restricted our meta-analysis to specific parameters: sex, associated medical conditions (diabetes, hypertension, and cirrhosis) and medication regimens (azathioprine, MMF, and prednisolone) (Table 4). Sex was not associated with the antibody response (pooled OR: 1.13; 95 % CI: 0.8-2.15; $p = 0.28$; $I^2 = 0$ %). Similarly, prevalent conditions such as cirrhosis, diabetes and hypertension did not significantly affect the antibody response rate. With respect to medications, the influence of azathioprine on the antibody response was not statistically significant. In contrast, treatments with MMF and corticosteroids were inversely correlated with antibody response rates, as shown by their pooled ORs and 95 % CIs (Fig. 3).

DISCUSSION

To the best of our knowledge, this systematic review is the first investigation into the immunogenicity of COVID-19 vaccines in the context of AIH and the factors that may modulate the immune response. Our analysis revealed that patients with AIH exhibit a diminished humoral immune response to the COVID-19 vaccine compared with the healthy population. Notably, even among serologically positive individuals, a discernible decrease in antibody titers was evident. In the study by Jorgensen (13), for example, which included 46 patients with AIH and 1,114 healthy controls, the antibody levels in patients with AIH were significantly lower than those in the control group after the second dose (2,184 *vs* 3,355 AU/m). Similarly, Hartl (12) noted that although the antibody levels in patients with AIH increased after the third dose, they remained below those of the control group (10,908 *vs* 25,000 AU/ml, respectively). Such findings can be attributed to several factors. First, hepatic fibrosis can hinder the synthesis of innate immunity proteins and pattern recognition receptors. Second, the total counts and functions of B and T lymphocytes can be disrupted through various mechanisms, such as the downregulation of co-stimulation markers, the depletion of memory cells and T-cell exhaustion (24). Third, the widespread use of immunosuppressive treatments in patients with AIH may attenuate the immune response to the COVID-19 vaccine. Mechanisms of this attenuation might include the dampening of immune cell activity, a decrease in antibody production, and interference with T-cell responses (25). International medical organizations currently advocate for booster vaccines in immunocompromised patients. Consistent with this, our data underscore the potential of booster doses to bolster both the rate and magnitude of antibody responses in patients with AIH. However, questions regarding the optimal antibody concentration and its duration persist, especially considering that antibody levels are known to decline over time. Notably, Moriya (23) found that longer intervals between post-vaccination antibody tests in patients with AIH, such as 12-week intervals, revealed a significant decrease in serological response rates (down to 40 %). Given the protective role of elevated antibody concentrations against infection, timely administration of booster doses is crucial.

Notably, exclusively focusing on the humoral immune response may be too narrow in perspective. Hartl (12) demonstrated that following a booster dose, the cellular

immune response in patients with AIH showed no enhancement (56 % *vs* 55 %). Moreover, regardless of the group (patients with AIH or healthy controls), no direct relationship between the potency of cellular and humoral immunity was found (12). Cellular immune responses are pivotal to mitigating the severity of COVID-19, with numerous studies indicating that early SARS-CoV-2 T-cell responses correlate with milder disease manifestations (26-28). Current evidence suggests that effective vaccine protection may rely not only on high levels of neutralizing antibodies but also on other immune responses, such as non-neutralizing antibodies, T-cell reactions and innate immunity (29). Furthermore, circulating antibody levels do not always serve as reliable indicators of T-cell memory (30). Although there is evidence suggesting a decrease in the long-term protective effectiveness of SARS-CoV-2 vaccines, they consistently demonstrate the ability to safeguard against severe disease outcomes (31). Interestingly, one study of patients with AIH revealed that after the fourth dose, some patients demonstrated robust T-cell responses against both the wild-type and omicron (B.1.1.529) SARS-CoV-2 variants despite not exhibiting the expected antibody response (32). The immune responses induced by different types of vaccines appear to vary. For example, preliminary data indicate that although mRNA vaccines induce higher levels of antibodies than do adenovirus vector vaccines, the latter may more effectively induce strong T-cell responses. Overall, research on the cellular immune response to COVID-19 vaccines in patients with AIH remains limited, underscoring the importance of further studies.

Different classes of immunosuppressive drugs can uniquely impact immune response to the COVID-19 vaccine. Our analysis indicated that azathioprine does not markedly alter the humoral immune response in patients with AIH, a finding mirrored in patients with rheumatoid arthritis after influenza vaccination (33). This could be attributed to the greater dependence of the vaccine-induced immune response on T-cell mechanisms (34), with azathioprine more potently inhibiting B-cell function (35). Thus, even with suppressed B-cell antibody production, T-cells can still mount an effective vaccine response. In contrast, both corticosteroids and MMF have been linked to significantly diminished immune responses, with the effect of MMF being especially pronounced. The vaccine's immunogenicity was compromised in various

patient groups undergoing treatment with MMF, including organ transplant recipients and patients with autoimmune inflammatory rheumatic diseases (36,37). Such effects can be ascribed to the mechanism of MMF and its potent immunosuppressive capabilities, which limit B- and T-cell proliferation, hinder antibody production, and obstruct memory cell development (38). Whereas the American Rheumatology Association recommends considering MMF dose modifications before COVID-19 vaccination in patients with autoimmune inflammatory rheumatic diseases (39), experts in hepatology have yet to offer a definitive guideline. The interplay between immunosuppressive drugs and COVID-19 vaccines in patients with AIH presents a complex scenario, as some drugs may reduce vaccine efficacy and increase the risk of infection, whereas their discontinuation may cause hepatitis flares. Our data suggest the need for a nuanced therapeutic strategy, possibly involving medication adjustments such as dose reduction, dose delay, or even an increase in the number of vaccine doses, to enhance immune responses in patients with AIH undergoing specific immunosuppressive regimens. Comprehensive clinical investigations are vital to balance the risk of infection with the potential for disease exacerbation.

To date, approximately 40 cases of AIH-like hepatitis associated with the COVID-19 vaccine have been documented, mirroring the clinical presentation of AIH and capturing significant attention from the medical community (15). Although the underlying pathophysiological mechanisms remain unclear, several theories have been proposed to explain this immune-mediated liver injury, such as molecular mimicry, vaccine adjuvants, bystander hepatitis or direct mRNA effects (40). Steroid treatments have been effective against post-vaccination AIH-like hepatitis, with most patients experiencing clinical improvement. Although COVID-19 vaccine-induced AIH-like hepatitis is rare and generally has a favorable prognosis, its cause is unknown. Nevertheless, the benefits of SARS-CoV-2 vaccination are evident, and when weighed against the potential risks, the case for vaccination remains compelling.

This systematic review had two main strengths. First, an exhaustive search strategy was used across multiple databases and key review processes underwent dual

review, minimizing errors. Second, our study adhered to the PRISMA guidelines, ensuring methodological rigor. However, there are limitations. The studies included in the review demonstrated considerable heterogeneity, possibly due to differences in vaccine types, use of a control group, age-matching, pre-vaccination infection status, and other factors. In particular, the data showed significant heterogeneity with respect to serological titer parameters. There is no universal consensus on defining immunogenicity and predicting protective efficacy, which remain challenging. Most studies in our review had small sample sizes, limiting their ability to make broad comparisons. Our review mainly focused on adult patients with AIH and was predominantly centered on European studies; only one Asian study was included. Thus, our findings might not fully represent the global AIH demographic. Finally, because of the limited number of studies in our meta-analysis, we could not perform a sensitivity analysis or assess publication bias.

CONCLUSION

In patients with AIH, the immune response to COVID-19 vaccination is attenuated. Although booster vaccines augment seroconversion and antibody levels, the antibody levels still do not reach those seen in individuals with typical immune responses. In addition, the enhancement of cellular immunity following vaccination is modest. Specific immunosuppressive agents, such as steroids and MMF, have been found to reduce antibody responses, whereas azathioprine appears to have a neutral effect. Recognition of these factors provides a foundation for tailoring vaccination regimens to individual patients with AIH. Further research, particularly focused on post-vaccination cellular immunity, is imperative to refine the vaccination strategies for this patient population.

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Table 1. Study characteristics

Study	Age	Country	Proportion of male (%)	Study design	Number of patients	Vaccine	Vaccine (dose)
Jorgensen, 2022	Median age 56 years	Norway	0.3	Prospective	46	BNT 162b2	3
Zecca, 2022	NA	Italy	NA	Prospective	22	mRNA-1273/BNT162b2	2
Schneider, 2022	53.5	Austria	0.33	Prospective	12	BNT162b/mRNA-1273	3
Chauhan, 2022	NA	Austria	NA	Prospective	11	NA	3
Barnes, 2023	NA	UK	0.33	Prospective	68	BNT162b2/AZD1222	2
Duengelhoef, 2021	53	Germany	0.21	Prospective	94	AZD1222/BNT162b2/mRNA-1273	2
Moriya, 2023	61	Japan	0.2	Prospective	15	BNT162b2	2
Hartl, 2022	60	Germany	0.17	Prospective	81	AZD1222/ BNT162b2/mRNA-1273	3

NA: not available.

Table 2. Newcastle-Ottawa Quality Assessment Scale of included studies

Selection				Comparability	Outcome			
Representativeness	Selection of the non-exposed cohort	Ascertainment	Outcomes of interest do not present at start	Comparability	Assessment of outcome	Follow-up duration	Adequacy follow-up	Total score
1	0	1	1	1	1	1	1	7
1	0	1	1	1	1	1	1	7
1	0	1	0	1	1	1	1	6
1	1	1	1	1	1	1	1	8
1	0	1	1	2	1	1	1	8
1	0	1	0	0	1	1	1	5
1	1	1	1	2	1	1	1	9
1	0	1	0	0	1	1	1	5

Table 3. Humoral and cellular immune response after COVID-19 vaccines

Study	Antibody measurement	Seroconversion definition	Timing to Ab testing	Responders/total (seroconversion rate)	Antibody concentration (AU/ml)	Cellular immune response measurement	Timing to cellular immune response testing	Responders /total
Jorgensen, 2022	Anti-SARS-CoV-2 spike RBD	Values greater than 70 AU/ml	3-5 weeks	V2: 89 % V3: 91 %	V2: median 2,184 (IQR 245-8,763) *vs* HCs 3355 (IQR 896-7,849) V3: 264 (IQR 115-6,485] to 6,383 (IQR 1,480-9,412)	NA	NA	NA
Zecca, 2022	Anti-SARS-CoV-2 spike RBD	Values greater than 8 RU/ml	NA	V2: 81 %	NA	NA	NA	NA
Schneider, 2022	Anti-SARS-CoV-2 spike RBD	Values greater than 0.8	V1: 2-3 weeks	#V1: 86 % V2: 100 %	V2: 2,500 (IQR 459-2,500) *vs*	NA	NA	NA

		BAU/ml	V2:4-6 weeks V3: 6 weeks		controls 1,499 (IQR 577.250-2,002) V3: 707 (IQR 388.75-1,208.25) to 2,500 (IQR 2,500-2,500) and HCs 577 (IRQ 240-893.25) to 2,500 (IQR 2,500-2,500)	

		Values greater than 0.8 BAU/ml						
Chauhan, 2022	Anti-SARS-CoV-2 spike RBD	Values greater than 0.8 BAU/ml	4 weeks	V3: 81 %	NA	NA	NA	NA
Barnes, 2023	Anti-SARS-CoV-2 spike RBD	Values greater than 0.8 BAU/ml	4 weeks	V2: 92 %	NA	IFNγ ELISpot assay	4 weeks	V2: 92 %
Duengelhoef, 2021	Anti-SARS-CoV-2 spike RBD	Values greater than 100 BAU/ml	2 weeks	V2: 87 %	NA	Activation-induced markers CD154 and CD137	2 weeks	V2: 56 %
Moriya, 2023	Anti-SARS-CoV-2 spike RBD	Values greater than 100 BAU/ml	12 weeks	V2: 40 %	NA	NA	NA	NA
Hartl, 2022	Anti-SARS-CoV-2 spike RBD	Values greater than 0.8	5 weeks	V3: 100 %	V3: median 10,908 *vs* 25,000	Activation-induced markers	5 weeks	V3: 56 %

	BAU/ml		CD154 and CD137

		Values greater than 0.8 BAU/ml		

RBD: receptor binding domain; NA: not available; V1: following the first dose of vaccine; V2: following the second dose of vaccine; V3: following the third dose of vaccine.

Table 4. The effect estimates of factors influencing the humoral immune response

Study	Factor	Measure of association between factor and immune response (OR)	
		Univariable (95 % CI)	**Multivariable (95 % CI)**
Duengelhoef, 2021	Sex	0.48 (95.0 % CI: 0.25-0.92)	0.87 (95.0 % CI: 0.41-1.84)
	Cirrhosis	0.82 (95.0 % CI: 0.43-1.56)	NA
	Diabetes	3.42 (95.0 % CI: 1.37-8.57)	2.48 (95.0 % CI: 0.89-6.91)
	Hypertension	1.97 (95.0 % CI: 1.08-3.59)	1.32 (95.0 % CI: 0.64-2.72)
	Azathioprine	1.60 (95.0 % CI: 0.88-2.89)	NA
	MMF	2.35 (95.0 % CI: 0.51-10.78)	NA
	Prednisolone	2.51 (95.0 % CI: 1.26-4.97)	2.71 (95.0 % CI: 1.22-6.02)
Jorgensen, 2022	Azathioprine	0.241 (95.0 % CI: 0.012-4.716)	NA
	Prednisolone	0.347 (95.0 % CI: 0.037-3.253)	NA
	Prednisolone + azathioprine	1.450 (95.0 % CI: 0.298-7.051)	NA
Hartl, 2022	Sex (female)	1.53 (95.0 % CI: 1.36-1.57)	NA
	Cirrhosis	1.22 (95.0 % CI: 1.04-1.42)	NA

	Diabetes	1.15 (95.0 % CI: 0.83-1.58)	NA
	Hypertension	0.57 (95.0 % CI: 0.5-0.65)	NA
	Azathioprine	0.73 (95.0 % CI: 0.6-0.88)	NA
	MMF	2.63 (95.0 % CI: 2.12-3.33)	NA
	Prednisolone	2.65 (95.0 % CI: 2.12-3.1)	NA

NA: not available; OR: odds ratio; CI: 95 % confidence interval; MMF: mycophenolate mofetil.

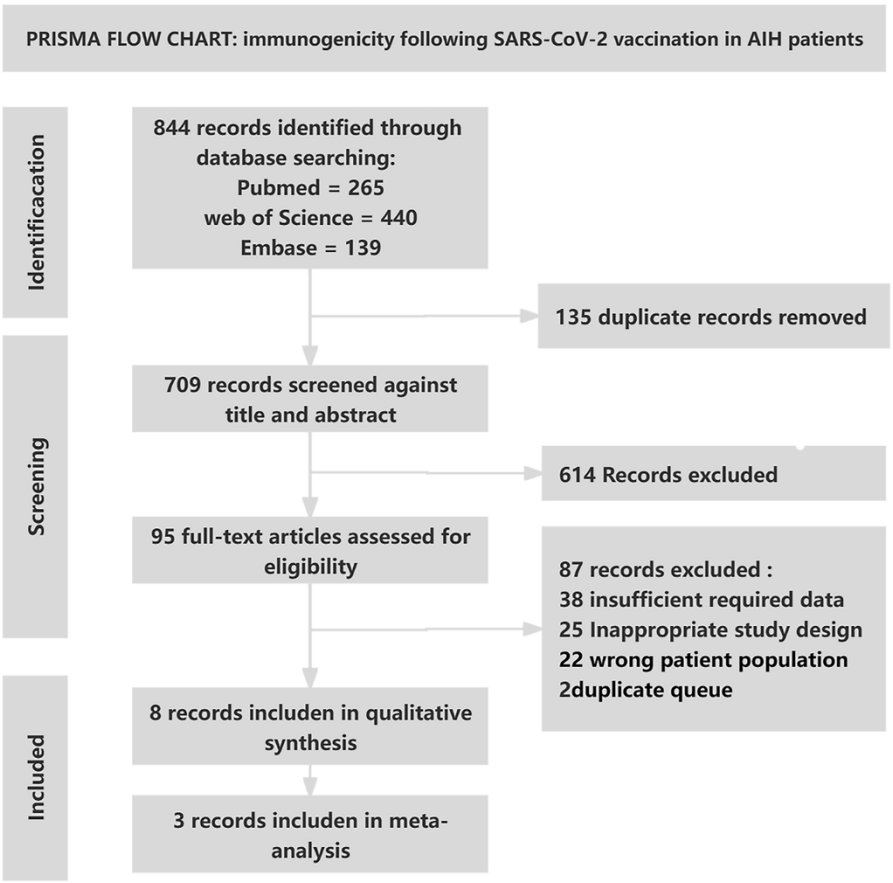

Fig. 1. PRISMA FLOW CHART immunogenicity following SARS-CoV-2 vaccination in patients with autoimmune hepatitis (AIH). PRISMA: Preferred Reporting Items 91 for Systematic Reviews and Meta-Analyses.

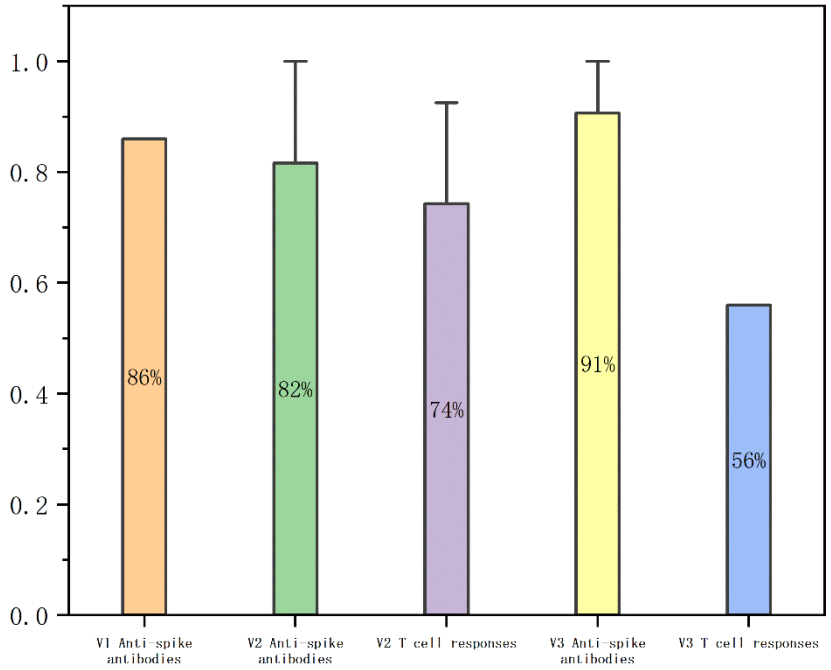

Fig. 2. Humoral immune response rates of SARS-CoV-2 vaccines. V1: following the first dose of vaccine; V2: following the second dose of vaccine; V3: following the third dose of vaccine.

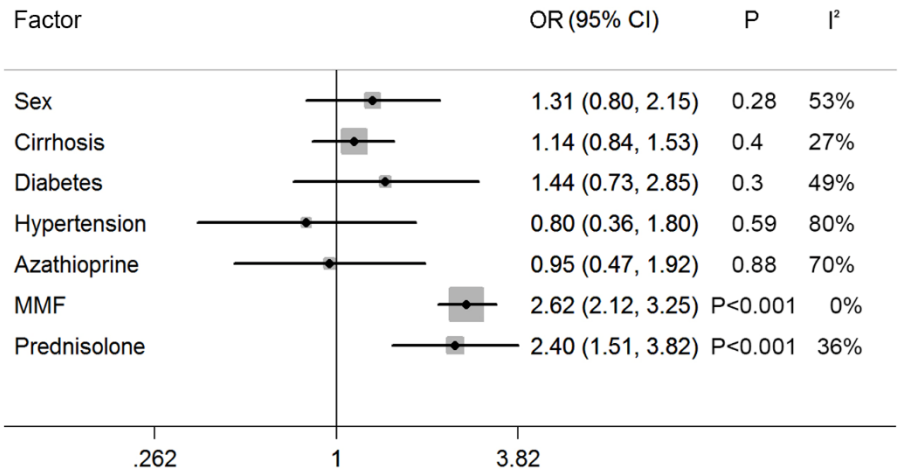

Fig. 3. Risk factors for poor humoral immune response to SARS-CoV-2 vaccine in patients with AIH. MMF: mycophenolate mofetil; OR: odds ratio; p: p-value; I2: inconsistency index.