Autoimmunity

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iaut20

The onset of *de novo* autoantibodies in healthcare workers after mRNA based anti-SARS-CoV-2 vaccines: a single centre prospective follow-up study

M.C Sacchi, C. Pelazza, M. Bertolotti, L. Agatea, P. De Gaspari, S. Tamiazzo, D. Ielo, P. Stobbione, M. Grappiolo, T. Bolgeo, P. Novel, M.M Ciriello & A. Maconi

To cite this article: M.C Sacchi, C. Pelazza, M. Bertolotti, L. Agatea, P. De Gaspari, S. Tamiazzo, D. Ielo, P. Stobbione, M. Grappiolo, T. Bolgeo, P. Novel, M.M Ciriello & A. Maconi (2023) The onset of *de novo* autoantibodies in healthcare workers after mRNA based anti-SARS-CoV-2 vaccines: a single centre prospective follow-up study, Autoimmunity, 56:1, 2229072, DOI: 10.1080/08916934.2023.2229072

To link to this article: https://doi.org/10.1080/08916934.2023.2229072

© 2023 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

Published online: 28 Jun 2023.

Submit your article to this journal

Article views: 2830

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=iaut20

AUTOIMMUNITY
2023, VOL. 56, NO. 1, 2229072
https://doi.org/10.1080/08916934.2023.2229072

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

The onset of *de novo* autoantibodies in healthcare workers after mRNA based anti-SARS-CoV-2 vaccines: a single centre prospective follow-up study

M.C Sacchi[a,b], C. Pelazza[c], M. Bertolotti[c], L. Agatea[d], P. De Gaspari[d], S. Tamiazzo[a], D. Ielo[e], P. Stobbione[f], M. Grappiolo[a], T. Bolgeo[c], P. Novel[d], M.M Ciriello[a] and A. Maconi[g]

[a]Autoimmunology and Analysis Laboratory Unit, "SS. Antonio e Biagio e Cesare Arrigo" Hospital, Alessandria, Italy; [b]Research Laboratory Facility, Research and Innovation Department (DAIRI), "SS. Antonio e Biagio e Cesare Arrigo" Hospital, Alessandria, Italy; [c]Research Training Innovation Infrastructure, Research and Innovation Department (DAIRI), "SS. Antonio e Biagio e Cesare Arrigo" Hospital, Alessandria, Italy; [d]Laboratory Department, Affiliated to Euroimmun, Padova, Italy; [e]Werfen, EEMEA, Milan, Italy; [f]Rheumatology Unit, "SS. Antonio e Biagio e Cesare Arrigo" Hospital, Alessandria, Italy; [g]Research and Innovation Department (DAIRI), "SS. Antonio e Biagio e Cesare Arrigo" Hospital, Alessandria, Italy

ABSTRACT

Nowadays, data concerning the risk of autoimmune disease after SARS-CoV-2 (COVID-19) vaccination is controversial. The aim of this single centre prospective follow-up study was to evaluate whether healthcare workers (HCWs) vaccinated with BNT162b2 mRNA and mRNA-1273 will show a development and/or a persistence of autoantibodies, focussing on the detection of antibodies against nuclear antigens (antinuclear antibodies, ANA). We enrolled 155 HCWs, however only 108 of them received the third dose and were considered for further analysis. Blood samples were collected before vaccine inoculation (T0), at 3 (T1) and 12 months (T2) after the first dose. All samples were analysed for the presence of a) ANA using indirect Immunofluorescence [IIF] (dilutions of 1:80, 1:160. 1:320 and 1:640), and anti-smooth muscle antibodies (ASMA); b) anti-myeloperoxidase (anti-MPO), anti-proteinase 3 (anti-PR3) and anti-citrullinated peptide antibodies (aCCP) [FEIA]; c) anti-phospholipid antibodies (anticardiolipin [aCL], anti-beta-2- glycoprotein I [anti-ß-2GPI] (Chemiluminescence). Line-blot technology was performed using the following kit: EUROLINE ANA profile 3 plus DFS70 (IgG). Our research suggests that mRNA based anti-SARSCoV-2 vaccines can induce the production of *de novo* ANA in 22/77(28,57%) of subjects and that the percentage of positivity seems to be directly correlated to the number of vaccine expositions: 6/77 (7,79%) after 2 doses; 16/77 (20,78%) after 3 doses. Since it is known that hyperstimulation of the immune system could lead to autoimmunity, these preliminary results seem to further sustain the idea that the hyperstimulation of the immune system might lead to an autoinflammatory mechanism and eventually to autoimmune disorders. However, the link between SARS-CoV-2 vaccination and the development of autoimmune diseases needs to be further investigated.

ARTICLE HISTORY
Received 21 December 2022
Revised 14 June 2023
Accepted 18 June 2023

KEYWORDS
Autoantibodies; SARS-CoV-2; mRNAvaccine; healthcare workers; autoimmune manifestations; follow-up

1. Introduction

Coronavirus disease 2019 (COVID-19) related to coronavirus 2 (SARS-CoV-2) infection, and characterised by severe acute respiratory syndrome, had a dramatic effect on the world's population leading to the most significant global health crisis[1]. Since March 11, 2020, when the pandemic status was declared by the World Health Organisation (WHO), the virus has caused severe critical health problems in several countries. This is also due to the series of multiple waves of COVID-19 outbreaks. SARS-CoV-2's rapid global spread and alarming clinical severity have accelerated the demand for vaccines that safely and effectively prevent the disease or reduce its severity[2]. The development of vaccines against SARS-CoV-2 infection proved to be the most effective and promising measure for a sustainable containment of this pandemic[3]. Therefore, the vaccination campaign started in Europe from the 27th of December 2020[4]. To date, 30 COVID-19 vaccines have received emergency use authorisation in at least one country and more than 5 billion people have been vaccinated. Evidence from clinical trials and observational studies overwhelmingly support the safety and efficacy/effectiveness of numerous COVID-19 vaccines[5], especially against disease severity and death in fully vaccinated individuals.

It is well known that vaccination can be followed by adverse events and can also cause transient or permanent autoimmune diseases[6,7]. The transitory appearance of autoantibodies has been observed in association with various environmental triggers, including vaccination[8]. The development of autoantibodies due to vaccination is related either to cross-reactivity between antigens or to the effect of

CONTACT Sacchi Maria Cristina csacchi@ospedale.al.it Autoimmunology and Analysis Laboratory Unit, "SS Antonio e Biagio e Cesare Arrigo" Hospital, Via Venezia 16 15121 Alessandria, Italy
© 2023 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

the adjuvant[9,10]. One of the most commonly inducible antibodies following infection and vaccination are the anti-phospholipid antibodies[11].

It has been already shown that viruses are a remarkable component of environmental factors that take part in the production of autoimmune antibodies, as well as autoimmune disease. Specific types of viruses can cause widespread non-specific lymphocytes B and T activation, promoting the production of autoantibodies and cytokines. For instance, the presence of the Epstein Barr Virus and the Parvovirus B19 correlates with Hashimoto's thyroiditis[12], the human T-lymphotropic virus-1, and the Human Foamy Virus with Graves' disease[13], and herpes simplex with postinfectious autoimmune encephalitis[14]. Similarly, SARS-CoV-2 shares features with autoimmune diseases in clinical manifestations, immune responses, and pathogenic mechanisms[15]. Robust immune reactions participate in the pathogenesis of both disease conditions. Autoantibodies as a hallmark of autoimmune diseases can also be detected in COVID-19 patients[16,17]. Thus, after a systematic review analysis, we found an association between COVID-19 and the tendency of patients to develop multiple types of autoantibodies [18–20] and autoimmune diseases[21,22], such as Guillain-Barré syndrome[23], systemic lupus erythematosus [24] and autoimmune hepatitis[25]. Indeed, an increase in new-onset autoimmune phenomena after COVID-19 vaccination have been reported recently (e.g. immune thrombotic thrombocytopenia, autoimmune liver diseases, IgA nephropathy, rheumatoid arthritis, and systemic lupus erythematosus)[26–37]. Molecular mimicry, the production of autoantibodies and the role of some adjuvants seem to be the principal contributors to these autoimmune phenomena[38].

Nucleic acid therapies have emerged as promising alternatives to conventional vaccine approaches. Therefore, genetically engineered nucleic acids are now used to generate immune responses safely. Comirnaty (BNT162b2) of Pfizer-BioNTech [39–41] and COVID-19 vaccine mRNA-1273 of Moderna/NIAID belongs to mRNA-based vaccines[42,43]. BNT162b2, a lipid nanoparticle-formulated nucleoside-modified mRNA vaccine, has been proved to significantly protect from SARS-CoV-2 [30]. It encodes the receptor-binding domain (RBD) of the spike protein1 of SARS-CoV-2. Dagan and collaborators have reported that mass vaccination with BNT162b2 is effective in COVID-19, and protects from most of the COVID-19 outcomes including severe conditions[44]. Notably, BNT162b2 is also very effective after 14 days of the second dose inoculation, against the COVID-19 and against its variants Alpha (B.1.1.7) and Beta (B.1.351), 89.5% and 75% respectively. In addition, it has a high protection level also in cases of severe and critical conditions[40]. The mRNA-1273 vaccine has successfully induced anti-SARS-CoV-2 immune response in all recipients[42]. This lipid nanoparticle–encapsulated mRNA vaccine is safe, and no safety concerns were observed, apart from a few transient local and systemic reactions. Furthermore, mRNA-1273 vaccines resulted to be safe also for people affected with chronic diseases[43].

The vaccines BNT162b2 and mRNA-1273 were the first ones to be approved and the first mRNA-based vaccines ever[39, 45]. Currently, their effects and possible ability to stimulate an autoimmune reaction are still poorly understood. Therefore, in this study we aimed to investigate their effects on the autoimmune profile of vaccinated healthcare workers (HCWs). Thus, we evaluated whether after three shots of mRNA COVID-19 vaccine these subjects demonstrated the production and/or a persistence of autoantibodies, particularly antibodies against nuclear antigens (antinuclear antibodies, ANA).

2. Methods

2.1. Ethics committee approval

The ethics committee of the "SS Antonio and Biagio and Cesare Arrigo" Hospital, Alessandria, Italy approved this study, and it was conducted under the ethical principles of the Declaration of Helsinki.

2.2. Study participants

All study participants worked at the "SS Antonio and Biagio and Cesare Arrigo" Hospital, Alessandria, Italy, and signed the informed consent for the study. From the 12th to 14th of January 2021 we enrolled 155 HCWs, but only 108 of them received the third dose and were considered for the further analysis. However, all 108 HCWs developed mild or no symptoms after receiving the vaccinations. Thus, blood samples of the 108 HCWs vaccinated with COVID-19 mRNA BNT162b2 (Pfizer- BioNTech) and mRNA 1273 (Moderna) were collected before the vaccine inoculation (T0), at 3 (T1) and 12 months (T2) after the first dose according with the vaccination programme. Only 77 resulted to be *naïve* from SARS-CoV-2 infection (60 females and 17 males, age range 26-67 years, median age 48). Blood samples were taken, collected and immediately centrifuged to obtain serum. The serum samples were stored at −20°C until further analysis.

2.3. Blood autoimmunity tests

All samples were analysed for the presence of a) antinuclear antibodies (ANA) using indirect Immunofluorescence [IIF] on the substrate Hep-2 EUROIMMUN; (dilutions of 1:80, 1:160. 1:320 and 1:640), and anti-smooth muscle antibodies (ASMA 1:80, 1;160) (IIF, Euroimmun); b) anti-myeloperoxidase (anti-MPO), anti-proteinase 3 (anti-PR3) and anti-citrullinated peptide antibodies (aCCP) ([FEIA], Thermo Fisher Scientific); c) anti-phospholipid antibodies (anticardiolipin [aCL], anti-beta-2- glycoprotein I [anti-ß-2GPI] (Chemiluminescence, Werfen). d) Line-blot technology was performed using the following kit: EUROLINE ANA profile 3 plus DFS70 (IgG). The test is specific for the following antigens: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, CENP B, PCNA, dsDNA, nucleosomes, histones, Protein P ribosomal, AMA-M2, DFS70. e) Anti-RF was measured using a fully automated spectrophotometric/immunoturbidimetric and ion selective electrode measurement system (Advia XPT analyser; Siemens).

2.4. Statistical analyses

Clinical data were collected using the REDCap software (REDCap version 10.2.3©2020 Vanderbilt University)[35,36]. Excel software was used to assess the presence of

autoantibodies in the vaccine cohort. The statistical analysis was performed using Graphpad prism 9 Software. In detail, the U Mann Whitney test was considered to compare the results within one time point (T1 or T2), whereas Friedman statistical tests was used to analyse T1 versus T2.

3. Results

This study, enrolled 155 subjects. Of these, 108 subjects were available for analysis at all time points. All subjects completed the full vaccination cycle and the booster dose (Figure 1). Thirty-one of the 108 subjects were excluded from the analysis because they were infected with SARS-CoV-2 before starting the vaccination cycle or after the booster dose (15 and 16 subjects respectively). A total, of 77 HCWs (60 females and 17 males, age range 26-67 years, median age 48) with no history of COVID-19 infection and no previous autoimmune disease were included in the analysis.

All the subjects were vaccinated with 2 doses of BioNtech/Pfizer BNT162b2 mRNA. Half received a third dose of the same vaccine, whereas the other half received Moderna (Spikevax). Blood samples were taken before vaccination (T0) and at 3 (T1) as well as 12 months (T2) after the first dose. Therefore, at T1 all the subjects received two doses of vaccine and at T2 three doses.

Considering the total number of subjects enrolled (77), at T0, 25/77 were positive for ANA (23 maintained this positivity also at T1 and T2) and 52/77 were negative (Figure 2).

At T1, 46/52 remained negative, whereas 6/52 became ANA positive (5 were positive also at T2). At T2, 30/46 were still negative, instead 16/46 became ANA positive. In addition, there was also a statistically significant increase in ANA presence. (p-value: 0,0076).

At T1 and T2, five ANA patterns were considered: homogeneous; speckled; cytoplasmatic; nucleolar; other (e.g. midbody, centrosomes, spindle poles). At T1, the homogeneous pattern was observed in 5/6 samples, the speckled in 4/6 and the cytoplasmatic in 1/6 (Figure 3 A, D). At T2, the type of pattern observed increased: homogeneous was observed in 12/21, speckled in 6/21, nucleolar in 2/21, cytoplasmic in 1/21 and other patterns in 7/21 (Figure 3 C, E). The most common pattern was the homogeneous pattern, although one patient had more than one pattern. The homogeneous pattern is usually associated with the presence of anti dsDNA, nucleosomes, and histones antibodies. All the T2 homogeneous positive samples were tested with a confirmatory assay and resulted negative for these autoantibodies.

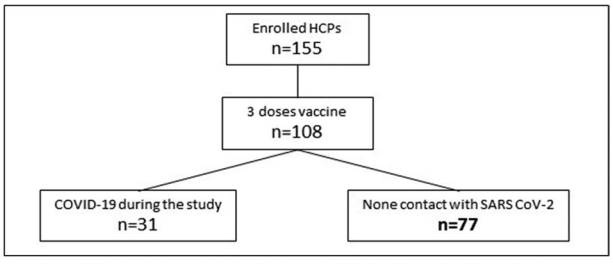


Figure 1. Flow chart of the population enrolled in the study.

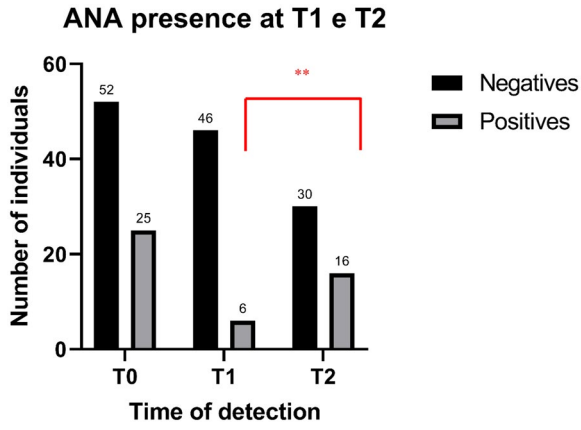


Figure 2. ANA presence at T0, T1, and T2.
The ANA presence was evaluated at T0 (before the vaccination), at T1 (after 2 doses of vaccine) and at T2 (after the booster dose). The graph shows a statistically significant increase of ANA presence from T1 to T2 (** $p < 0.05$).

We also evaluated the pattern distribution, which showed no statistical significance both within each time point (T1 and T2; p-value: 0,11642) and between them (T1 versus T2; p-value: 0,07364). In terms of antibody titres, none of the patterns analysed showed a statistical increase from T1 to T2.

We also evaluated other classic autoantibodies performed on solid phase technologies such as anti-rheumatoid factor (anti-RF), anti-myeloperoxidase (anti-MPO), anti-proteinase 3 (anti-PR3) anti-citrullinated peptide antibodies (aCCP), anti-phospholipid antibodies (anticardiolipin [aCL] and anti-beta-2- glycoprotein [anti-Beta2]) and ASMA (anti-alpha smooth muscle actin). Only aCL and ASMA antibodies showed a slight increase between T0 and T1, but this was not statistically significant (Figure 4).

The results highlighted that only ANA antibodies were increased after mRNA vaccination; however, their distribution and titre were not statistically significant.

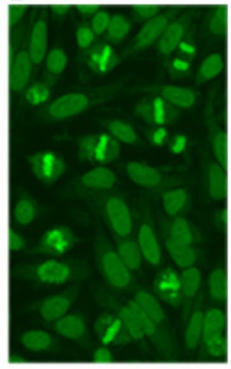
4. Discussion

Conventional vaccine approaches have largely failed to produce effective vaccines against viruses that cause repeated and chronic infections, such as HIV-1. Therefore, the development of more potent and versatile vaccine platforms has become crucial. Nucleic acid therapeutics have emerged as promising alternatives to conventional vaccine strategy. In this regard, mRNA vaccines have emerged as a promising alternative to conventional approaches due to their high efficacy, ability to be rapidly developed, potential for low-cost production and safe administration. BNT162b2 and mRNA-1273 vaccines were produced in a short period of time that can be considered a record[46]. The safety of these vaccines is still a matter of debate and there are several reports of autoimmune diseases that develop after SARS-CoV-2 vaccinations. Although the exact mechanism of post-vaccination autoimmune diseases is unknown, some possible mechanisms have been presented. These include an abnormal immune response induced by molecular mimicry, particularly in susceptible individuals[47]; and bystander activation, whereby microbial agents release sequestered self-antigens from host tissues that activate antigen-presenting

A

T1	homogeneous	speckled	cytoplasmatic
Total	5	4	1
% relative to total pattern found (10)	50,00	40,00	10,00
n subject			
patient 1	positive		positive
patient 2	positive	positive	
patient 3		positive	
patient 4	positive	positive	
patient 5	positive	positive	
patient 6	positive		

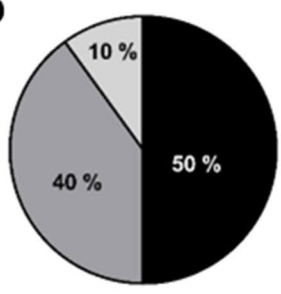
B



C

T2	homogeneous	speckled	nucleolar	cytoplasmatic	others
Total	12	6	2	1	7
% relative to total ANA positive pattern found (28)	42,86	21,43	7,14	3,57	25,00
n subject					
patient 1	positive			positive	
patient 2	positive		positive		
patient 3	positive	positive			
patient 4					
patient 5			positive		
patient 6	positive				
patient 7					positive
patient 8	positive				
patient 9	positive	positive			
patient 10	positive				
patient 11		positive			
patient 12	positive				
patient 13	positive				
patient 14	positive				
patient 15	positive	positive			
patient 16					positive
patient 17					positive
patient 18					positive
patient 19					positive
patient 20	positive				
patient 21		positive			positive
patient 22		positive			positive

D



E

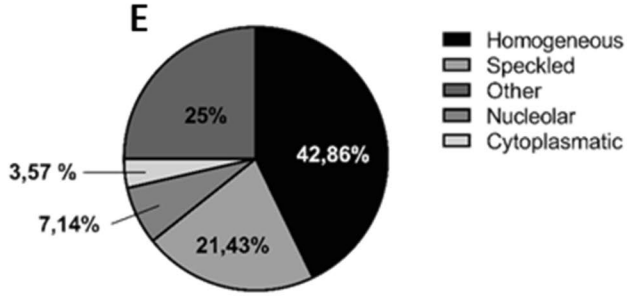


Figure 3. Pattern distribution of ANA positive samples at T1 and T2 (**A, C, D, E**). representative picture of a homogeneous positive sample at T2 (**B**).
The tables and the graphs summarised the relative percentage of the total patterns identified at T1 (**A, D**) and T2 (**C, E**). Patient4 resulted positive at T1 but negative at T2. The homogeneous pattern was observed in 50% of the positive samples at T1 and 42,86% at T2. The speckled one was detected in 40% at T1 and 21,43% at T2 and the cytoplasmatic in 10% and 3,57% respectively. In addition, at T2, the 7,14% of the samples had a nucleolar pattern, whereas the 25% showed other types of ANA positivity.

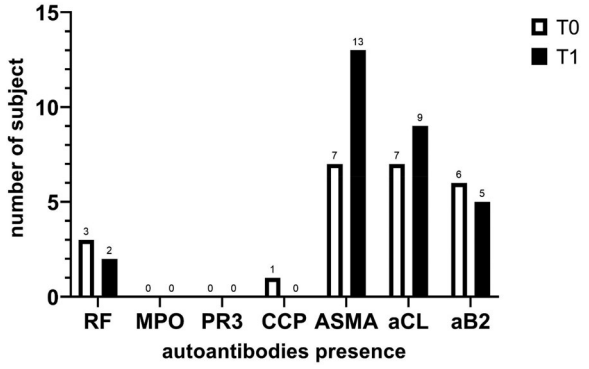


Figure 4. Distribution of positive blood autoimmunity tests at T0 and T1.
The presence of the blood autoimmunity markers was evaluated at T0 (before the vaccination), at T1 (after 2 doses of vaccine). RF: rheumatoid factor; MPO: myeloperoxidase; PR3: proteinase 3; CCP: anti-citrullinated peptide antibodies; ASMA:-alpha smooth muscle actin; aCL: cardiolipin; aB2: betaglycoprotein.

cells and dormant autoreactive T-helper cells[48,49]. For instance, multiple sclerosis has been reported following both COVID-19 infection and vaccination, as well as monoclonal antibodies targeting both diseases may be the future golden standard[6, 50]. Appropriate testing of vaccinated individuals is crucial, as today's societies are already susceptible to disease as more people become symptomatic[51].

In this single centre prospective follow-up study, we have focussed our attention on the effects of the mRNA based anti-SARS-CoV-2 vaccines on the development of potential autoimmune events in HCWs. We found that the common autoantibodies (i.e. MPO, PR3, aCCP, anticardiolipin [aCL], anti-beta-2- glycoprotein I, ASMA), showed no significant difference already at T0, T1. However, when we checked the presence of ANA, it emerged that a significant number of HCWs, developed *de novo* autoantibody production after receiving three doses of mRNA vaccines. Interestingly, the positivity developed at T1 was maintained over time. Most ANA positive samples showed a homogeneous pattern; however, the pattern was not associated with to any of the known related antigens. Interestingly, we found that already at T0, 35% of HCPs were ANA positive before vaccination. This data is in contrast when compared to literature (REF below) in which reported positivity rate of healthy individual when performing Hep-2 ANA is around 15%[52]. One possible explanation may be that some of those positive HCPs might have also encountered the COVID-19 infection before T0, thus explaining the elevated positivity rate of healthy individuals before vaccination. We can speculate that there may be another antigenic target responsible of this pattern and in the future, it will be interesting to elucidated and characterise which one it is.

Since autoantibody positivity does not imply the development of clinical manifestation, we planned to perform a perspective study to monitor these positive individuals and determine where they will develop any clinical sign of connective tissue disorders or autoinflammatory related conditions. Finally, we should consider the fact that every study has its limitations, and in this study no other autoimmune antibodies were analysed, but also, the possibility for false-positive and false negative serological test results is evident, as indicated in current literature.[53,54].

5. Conclusions

In conclusion, this study suggests that mRNA based anti-SARS-CoV-2 vaccines can induce the production of *de novo* ANA in 22/77(28,57%) of subjects and that the percentage of positivity seems to be directly correlated to the number of vaccine exposures: 6/77 (7,79%) after 2 doses; 16/77 (20,78%) after 3 doses. As it is known that immune stimulation can act as a double-edged sword, meaning infectious and endogenous defense versus autoimmune related hyper-stimulation[55,56], our preliminary results and the presence of *de novo* ANA antibodies in HCWs seem to be more prone to sustain this second consequence: hyperstimulation. However, the link between SARS-CoV-2 vaccination and the development of autoimmune diseases needs to be further investigated .

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Data availability statement

The data that support the findings of this study are available from the corresponding author, [MCS], upon reasonable request.

References

[1] Mouliou DS, Pantazopoulos I, Gourgoulianis KI. COVID-19 smart diagnosis in the emergency department: all-in in practice. Expert Rev Respir Med. 2022;16(3):1–6.
[2] Mouliou DS, Pantazopoulos I, Gourgoulianis KI. Social response to vaccine against COIVD-19: the underrated power of influence. JPM. 2021;12(1):15.
[3] Viana J, Van Dorp CH, Nunes A, et al. Controlling the pandemic during the SARS-CoV-2 vaccination rollout. Nat Commun. 2021;12(1):3674.
[4] COVID-19 Vaccination and prioritization strategies in the EU/EEA. Available online: https://www.ecdc.europa.eu/en/pubblications-data/COVID-19-vaccination and priorization strategies-eueea. (accessed on 8 July 2021).
[5] Harder T, Koch J, Vygen-Bonnet S. Efficacy and effectiveness of COVID-19 vaccines against SARS-CoV2 infection: interim results of a living systematic review. Euro Surveillance. 2021;26(28):2100563.
[6] Mouliou DS, Dardiotis E. Current evidence in SARS-CoV-2 mRNA vaccines and post-vaccination adverse reports: knowns and unknowns. Diagnostics. 2022;12(7):1555.
[7] Vial T, Desctes J. Autoimmune diseases and vaccinations. Eur J Dermatol. 2004;14(2):86–90.
[8] Orbach H, Agmon-Levin N, Zandman-Goddard G. Vaccines and autoimmune diseases of the adult. Discov Med. 2010;9(45):90–97.
[9] Shoenfeld Y, Aron-Maor A. Vaccination and autoimmunity-"vaccinosis": a dangerous liaison? J Autoimmun. 2000;14(1):1–10.
[10] Guimaraes LE, Baker B, Perricone C, et al. Vaccines, adjuvants and autoimmunity. Pharmacol Res. 2015;100:190–209.
[11] Martirosyan A, Aminov R, Manukyan G. Environmental triggers od autoreactive responses: induction of antiphosholipid antibody formation. Front Immunol. 2019;10:1609.

[12] Tomer Y, Davies TF. Infection, thyroid disease, and autoimmunity. Endocr Rev. 1993;14(1):107–120.
[13] Wick G, Trieb K, Aguzzi A, et al. Possible role of human foamy virus in graves' disease. Intevirology. 1993;35(1-4):101–107.
[14] Jeffrey MG. Autoimmune encephalitis after herpes simplex encephalitis: insights into pathogenesis. Lancet Neurol. 2018;17(9):733–735.
[15] Liu Y, Sawalha AH, Lu Q. COVID-19 and autoimmune diseases. Curr Opin Rheumatol. 2021;33(2):155–162.
[16] Yazdanpana N, Rezaei N. Autoimmune complication of COVID-19. J Med Virol. 2022;94(1):54–62.
[17] Vlachoyiannopoulos PG, Magira E, Alexopoulos H, et al. Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19. Ann Rheum Dis. 2020;79(12):1661–1663. [17].
[18] Pascolini S, Vannini A, Deleonardi G, et al. COVID-19 and immunological dysregulation: can autoantibodies be useful? Clin Transl Sci. 2021;14(2):502–508.
[19] Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and antiphospholipid antibodies in patients with covid-19. N Engl J Med. 2020;382(17):e38.
[20] Sacchi MC, Tamiazzo S, Stobbione P, et al. SARS-CoV-2 infection as a trigger of autoimmune response. Clin Transl Sci. 2021;14(3):898–907.
[21] Li J, Liu HH, Yin XD, et al. COVID-19 illness and autoimmune diseases: recent insights. Inflamm Res. 2021;70(4):407–428.
[22] Caso F, Costa L, Ruscitti P, et al. Could SarS-coronavirus-2 trigger autoimmune and/or autoinflammatory mechanisms in genetically predisposed subjects? Autoimmun Rev. 2020;19(5):102524.
[23] Aladawi M, Elfil M, Abu-Esheh B, et al. Guillain barre syndrome as a complication of COVID-19: a systematic review. Can J Neurol Sci. 2022;49(1):38–48.
[24] Bonometti R, Sacchi MC, Stobbione P, et al. The first case of systemic lupus erythematous (SLE) trigger by COVID19 infection. Eur Rev Med Pharmacol Sci. 2020;24(18):9695–9697.
[25] Vuille-Lessard E, Montani M, Bosch J, et al. Autoimmune hepatitis triggered by SARS-CoV-2 vaccination. J Autoimmun. 2021;123:102710.
[26] Gracia-Ramos AE, Martin-Nares E, Hernández-Molina G. New onset of autoimmune diseases following COVID-19 diagnosis. Cells. 2021;10(12):3592.
[27] Liu Y, Shao Z, Wang H. SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia. Thromb Res. 2022;209:75–79.
[28] Cines DB, Bussel JB. SARS-CoV-2 Vaccine-Induced immune thrombotic thrombocytopenia. N Engl J Med. 2021;384(23):2254–2256.
[29] 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(1):222–224.
[30] Capecchi PL, Lazzerini PE, Brillanti S. Comment on "autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: causality or casualty? J Hepatol. 2021;75(4):994–995.
[31] Clayton-Chubb D, Schneider D, Freeman E, et al. Autoimmune hepatitis developing after the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine. J Hepatol. 2021;75(5):1249–1250.
[32] 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.
[33] Uchiyama Y, Fukasawa H, Ishino Y, et al. Sibling cases of gross hematuria and newly diagnosed IgA nephropathy following SARS-CoV-2 vaccination. BMC Nephrol. 2022;23(1):216.
[34] Abramson M, Mon-Wei Yu S, Campbell KN, et al. IgA nephropathy after SARS-CoV-2 vaccination. Kidney Med. 2021;3(5):860–863.
[35] Baimukhamedov C, Makhmudov S, Botabekova A. Seropositive rheumatoid arthritis after vaccination against SARS-CoV-2 infection. Int J Rheum Dis. 2021;24(11):1440–1441.
[36] Sakai M, Takao K, Mizuno M, et al. Two cases of systemic lupus erythematosus (SLE) after administration of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. Mod Rheumatol Case Rep. 2023;7(2):378–382.
[37] Hinterseher J, Hertl M, Didona D. Autoimmune skin disorders and SARS-CoV-2 vaccination - a meta-analysis. J Dtsch Dermatol Ges. 2023; Epub ahead of print.
[38] Chen Y, Xu Z, Wang P, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. Immunology. 2022;165(4):386–401.
[39] Polack FP, Thomas SJ, Kitchin N, WC, C4591001 Clinical Trial Group., et al. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. N Engl J Med. 2020;383(27):2603–2615.
[40] Abu-Raddad LJ, Chemaitelly H, Butt AA, National Study Group for COVID-19 Vaccination. Effectiveness of the BNT162b2 covid-19 vaccine against the B.1.1.7 and B.1.351 variants. N Engl J Med. 2021;385(2):187–189.
[41] Sahin U, Muik A, Derhovanessian E, et al. COVID. 19 vaccine BNT162b1 elicits human antibody and T(H)1 T cell responses. Nature. 2020;586(7830):594–599.
[42] Jackson LA, Anderson EJ, Rouphael NG, mRNA-1273 Study Group., et al. An mRNA vaccine against SARS-CoV-2—preliminary report. N Engl J Med. 2020;383(20):1920–1931.
[43] Baden LR, El Sahly HM, Essink B, COVE Study Group., et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384(5):403–416.
[44] Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA. Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med. 2021;384(15):1412–1423.
[45] Chilamakuri B, S Agarwal S. Diverse vaccine platforms safeguarding against SARS-CoV-2 and its variant. Expert Rev Vaccines. 2022;21(1):47–67.
[46] Oliver SE, Gargano JW, Marin M, et al. The advisory committeeon immunization pracrices'interim recommendation for use of moderna COVID-19 vaccine-United States. MMWR Morb Mortal Wkly Rep. 2021;69(5152):1653–1656.
[47] Perumalswami P, Peng L, Odin JA. Vaccination as a triggering event for autoimmune hepatitis. Semin Liver Dis. 2009;29(3):331–334.
[48] Vadala M, Poddighe D, Laurino C, et al. Vaccination and autoimmune diseases: prevention of adverse health effects on the horizon? Epma J. 2017;8(3):295–311.
[49] 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.
[50] Mouliou DS, Dardiotis E. Temelimab for MS and SARS-CoV-2: could it be a double-edged blessing? Mult Scler Relat Disord. 2022;64:103938.
[51] Mouliou DS, Kotsiou OS, Gourgoulianis KI. Estimates of COVID-19 risk factors among social strata and predictors for a vulnerability to the infection. IJERPH. 2021;18(16):8701.
[52] Tan EM, Feltkamp TE, Smolen JS, et al. Range of antinuclear antibodies in "healthy" individuals. Arthritis Rheum. 1997;40(9):1601–1611.
[53] Mouliou DS, Gourgoulianis KI. False-positive and false-negative COVID-19 cases: respiratory prevention and management strategies, vaccination, and further perspectives. Expert Rev Respir Med. 2021;15(8):993–1002.
[54] Mouliou DS. Managing viral emerging infectious diseases via current molecular diagnostics in the emergency department: the tricky cases. Expert Rev anti Infect Ther. 2022;20(9):1163–1169.
[55] Ryabkova VA, Churilov LP, Shoenfeld Y. Hyperstimulation of the immune system as a cause of autoimmune diseases. Annals RAMS. 2020;75(3):204–213.
[56] Hedrich CM. Shaping the spectrum-From autoinflammation to autoimmunity. Clin Immunol. 2016;165:21–28.