Considerations for Lupus patients during the COVID-19 pandemic

Ilana Abeles MD PhD

November 13th 2021

Outline

- Severity of COVID-19 infection and patients with SLE
- Safety data regarding COVID-19 vaccines in autoimmune rheumatologic population, with focus on the lupus population
- COVID-19 vaccine effectiveness in the lupus population

Lupus patients have high rates of hospitalization from COVID-19

Patient Source	Covid-19 +	Ethnicity/ Race	HCQ Use	Hospitalized	Reference
Columbia SLE (N=450) COVID Database (N = 835)	Confirmed = 10 Suspected = 8 (rate 16/450= 4%)	50% Hispanic 37 % Black	**72%**	7 (39%) Immunosuppression similar to non-hospitalized	*Gartshteyn Lancet Rheum, 2020*
Global Rheum Alliance Registry	Confirmed or suspected = 80 & 85		**64%**	45 (56%) (HCQ use similar to Non-hospitalized)	*Konig ARD, 2020* *Gianfrancesco M, ARD 2020*
France	Confirmed = 17		**100%**	14 (82%)	*Mathian, ARD, 2020*
NYU	Confirmed = 41	71.4% nonwhite	78%	24 (58.5%)	Fernandez-Luis 2020

Factors contributing to lupus patient hospitalization with COVID-19 are similar to those without lupus

- Factors contributing to hospitalization in lupus patients include:
  - Race/ethnicity
  - Co-morbidities including: older age, diabetes mellitus, cardiovascular disease, renal insufficiency, lung disease, increased body mass index

-Fernandez-Ruiz R, et al. Leveraging the United States Epicenter to Provide Insights on COVID-19 in Patients with Systemic Lupus Erythematosus. Arthritis Rheumatol. 2020.
-Gianfrancesco M, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Annals of the Rheumatic Diseases. 2020:annrheumdis-2020-217871.
-Tang W, Askanase AD, Khalili L, Merrill JT. SARS-CoV-2 vaccines in patients with SLE. Lupus Science & Medicine. 2021;8(1):e000479

COVID-19 Global Rheumatology Alliance

Characteristics Associated with Poor COVID-19 Outcomes in People with Systemic Lupus Erythematosus (SLE): Data from the COVID-19 Global Rheumatology Alliance (GRA)

Manuel Ugarte-Gil, Graciela Alarcón, Andrea Seet, Zara Izadi, Ali Duarte-Garcia, Cristina Reategui-Sokolova, Ann Clarke, Leanna Wise, Guillermo Pons-Estel, Maria José Santos, Sasha Bernatsky, Sandra Lúcia Ribeiro, Samar Al Emadi, Jeffrey Sparks, Tiffany Hsu, Kristin D'Silva, Naomi Patel, Emily Gilbert, Maria Valenzuela-Almada, Andreas Jonsen, Gianpiero Landolfi, Micaela Fredi, Tiphaine Goulenok, Mathilde Devaux, Xavier Mariette, Viviana Quayrel, Vasco C Romão, Graça Sequeira, Rebecca Hassell, Bimba Franziska Hoyer, Reinhard Voll, Christof Specker, Roberto Baez, Vanessa Castro Coello, Edgard Neto, Gilda Ferreira, Odirlei Andre Monticielo, Emily Sirotich, Jean Liew, Jonathan Hausmann, Paul Sufka, Rebecca Grainger, Suleman Bhana, Wendy Costello, Zachary Wallace, Lindsay Jacobsohn, Anja Strangfeld, Elsa Frazão Mateus, Kimma Hyrich, Laura Gossec, Loreto Carmona, Saskia Lawson-Tovey, Lianne Kearsley-Fleet, Martin Schaefer, Pedro Machado, Philip Robinson, Milena Gianfrancesco and Jinoos Yazdany

- Evaluated outcomes for 1734 patients with SLE with COVID-19
- More severe COVID-19 outcomes were associated with:
  - Older age, male gender, being outside of North/South America or Europe, patients on prednisone, no medications, chronic renal disease, cardiovascular disease/hypertension, number of co-morbidities, and moderate to high disease activity

ACR abstract 2021 -

ACR open rheumatology
American College of Rheumatology
Empowering Rheumatology Professionals

Original Article | Open Access

Poor Prognosis of COVID-19 Acute Respiratory Distress Syndrome in Lupus Erythematosus: Nationwide Cross-Sectional Population Study Of 252 119 Patients

Isabela Maria Bertoglio MD, Juliana Miranda de Lucena Valim MD, Danielle Daffre PhD, Nádia Emi Aikawa MD, PhD, Clovis Artur Silva MD, PhD, Eloisa Bonfá MD, PhD, Michelle Remião Ugolini-Lopes MD, PhD

- Study evaluated outcomes of 319 patients with SLE and 251,000 patients without SLE with COVID-19
- Those with lupus, had increased risk for mortality and combined poor outcomes as compared with those without lupus
- Lupus itself was associated with higher risk for poor outcomes including mortality

COVID-19 vaccination

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Efficacy and Safety of mRNA-1273 SARS-CoV-2 Vaccine

L.R. Baden, et al. DOI: 10.1056/NEJMoa2035389

CLINICAL PROBLEM

The Covid-19 pandemic continues and expands. Additional data regarding vaccines to prevent symptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are needed. The mRNA-1273 vaccine is a lipid-encapsulated mRNA vaccine encoding the prefusion stabilized spike protein of SARS-CoV-2.

CLINICAL TRIAL

A randomized, double-blind trial to evaluate the efficacy and safety of mRNA-1273.

30,420 participants ≥18 years old were assigned to receive either the vaccine or placebo in two intramuscular injections 28 days apart. Participants were followed for safety and the development of laboratory-confirmed, symptomatic Covid-19 over a median of 2 months after the second dose.

RESULTS

Safety:
Vaccine recipients had higher rates of local reactions (e.g., pain, erythema, swelling) and systemic reactions (e.g., headache, fatigue, myalgia) than placebo recipients. Most reactions were mild to moderate and resolved over 1–3 days.

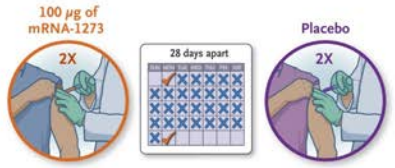
Efficacy:
The incidence of Covid-19 was lower among vaccine recipients than among placebo recipients as early as 14 days after the first dose. Protection in the vaccine group persisted for the period of follow-up.

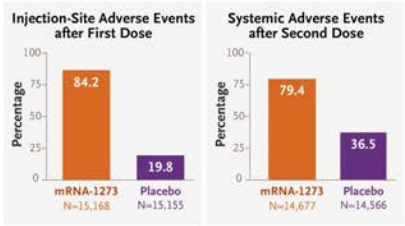
LIMITATIONS AND REMAINING QUESTIONS

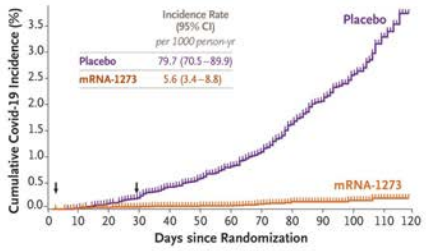
Further study is required to understand the following:

- Safety and efficacy over a longer period of time, in a larger population, and in pregnant women and children.
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to care for those who miss the second vaccine dose.

Links: Full article | NEJM Quick Take | Editorial







	mRNA-1273 Vaccine N=14,550	Placebo N=14,598
Symptomatic Covid-19	11	185
Severe Covid-19	0	30

Vaccine efficacy of 94.1% (95% CI, 89.3–96.8%; P<0.001)

CONCLUSIONS

Two doses of a SARS-CoV-2 mRNA-based vaccine were safe and provided 94% efficacy against symptomatic Covid-19 in persons 18 or older.

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

F.P. Polack, et al. DOI: 10.1056/NEJMoa2034577

CLINICAL PROBLEM

Safe and effective vaccines to prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 are urgently needed. No vaccines that protect against betacoronaviruses are currently available, and mRNA-based vaccines have not been widely tested.

CLINICAL TRIAL

A randomized, double-blind study of an mRNA vaccine encoding the SARS-CoV-2 spike protein.

43,548 participants ≥16 years old were assigned to receive the vaccine or placebo by intramuscular injection on day 0 and day 21. Participants were followed for safety and for the development of symptomatic Covid-19 for a median of 2 months.

RESULTS

Safety:
Vaccine recipients had local reactions (pain, erythema, swelling) and systemic reactions (e.g., fever, headache, myalgias) at higher rates than placebo recipients, with more reactions following the second dose. Most were mild to moderate and resolved rapidly.

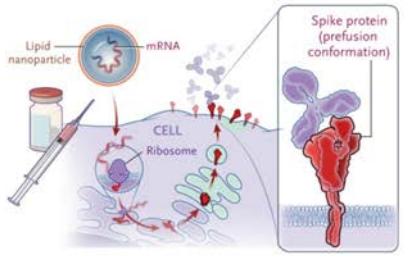
Efficacy:
The vaccine showed protection 7 days after the second dose; 95% efficacy was observed.

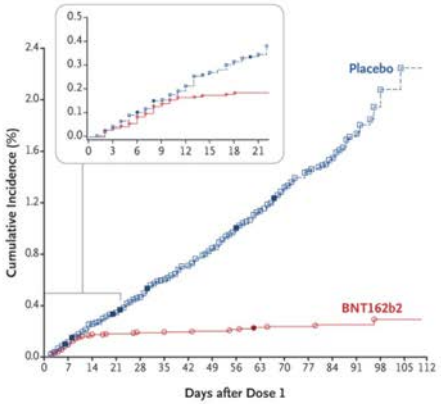
LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Safety and efficacy beyond 2 months and in groups not included in this trial (e.g., children, pregnant women, and immunocompromised persons).
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to deal with those who miss the second vaccine dose.

Links: Full article | Quick Take | Editorial





Vaccine efficacy of 95% (95% credible interval, 90.3 –97.6%)

CONCLUSIONS

Two doses of an mRNA-based vaccine were safe over a median of two months and provided 95% protection against symptomatic Covid-19 in persons 16 years of age or older.

Vaccine hesitancy

- A multi-faceted issue
- A study looking at vaccine hesitancy in patients with autoimmune disease found:
  - Like their counterparts without autoimmune disease, a common reason to refuse vaccination were concerns for adverse effects and no long term research
  - Patients specifically who were unsure of vaccination were more concerned that the vaccine might aggravate their autoimmune disease

Lancet Rheumatol. 2021 Apr;3(4):e241-e243. doi: 10.1016/S2665-9913(21)00037-0. Epub 2021 Feb 22

Established vaccines have not been linked to flare of lupus

- On multiple reviews of vaccination safety in patients with autoimmune inflammatory rheumatic diseases, including lupus, disease activity was not overall found to be significantly increased after vaccination
- Specifically, there is no evidence to support a link between HBV, HPV, flu or pneumococcal vaccines to flares of lupus disease activity
- We DO know that infection itself, like COVID-19 and influenza CAN exacerbate underlying disease activity.

Westra J, Rondaan C, van Assen S, Bijl M. Vaccination of patients with autoimmune inflammatory rheumatic diseases. Nat Rev Rheumatol. 2015 Mar;11(3):135-45.

EULAR COVID-19 vaccination registry and safety of COVID-19 vaccines

- Observational registry with data entered voluntarily by clinicians
- 1519 rheumatologic patients included
- Connective tissue diseases made up ~20% of the patient population.
  - SLE made up 7% of patient population
- Medications taken by all patients:
  - csDMARDs (leflunomide, mtx, sulfasalazine)
  - Glucocorticoids
  - bDMARDs (rituximab, TNFis)
  - Other: azathioprine, mycophenolate, cyclosporine, cyclophosphamide

http://dx.doi.org/10.1136/annrheumdis-2021-eular.5097

EULAR COVID-19 vaccination registry and safety of COVID-19 vaccines

- Vaccines administered: Pfizer, Astrazeneca, Moderna
- Disease flares were reported in 5% of patients (73/1375)
  - 1.2% flares determined to be severe
- Most common flare symptoms:
  - Arthritis, arthralgia, cutaneous flare (skin manifestations) and increased fatigue
- 31% of patients had typical side effects
  - Pain at injection site
  - Fatigue
  - headache

Tolerance of COVID-19 vaccination in patients with systemic lupus erythematosus: the international VACOLUP study

- N=696 participants answered 43 web based - questions -
- Primary outcome: occurrence of side effects - including flare -
- 100% participants received one dose and 343 (49%) patients received a second dose -

- Flares after vaccination in lupus patients occurred in 3%, or 21/696 patients
- Side effects predominantly were musculoskeletal symptoms and fatigue

	Patients (n=696)
Vaccination	
First dose	696 (100%)
First and second dose	343 (49%)
Vaccine received	
Pfizer-BioNTech	399 (57%)
Sinovac	156 (22%)
AstraZeneca	73 (10%)
Moderna	57 (8%)
Other*	11 (2%)
Side-effects after first vaccine dose	316 (45%)
Timing of onset of side-effects after first dose, days	0 (0–1)
Side-effects after second vaccine dose	181/343 (53%)
Timing of onset of side-effects after second dose, days	0 (0–1)
Consultations or admissions to hospital for side-effects (first and second doses together)	
Medical consultation	81/1039 (8%)
Emergency consultation	14/1039 (1%)
Admission to hospital	5/1039 (<1%)
SLE flare after vaccination	21 (3%)
SLE flare manifestations	
Fever (temperature >38°C or 100·4°F)	10/21 (48%)
Cutaneous (skin) flare (medically confirmed)	12/21 (57%)
Musculoskeletal symptoms (joint, arthritis, arthralgia, or myalgia; medically confirmed)	19/21 (90%)
Pleuritis or pleurisy (medically confirmed)	1/21 (5%)
Pericarditis (medically confirmed)	1/21 (5%)
Renal involvement (medically confirmed)	2/21 (10%)
Neuro-psychiatric manifestations (medically confirmed)	0
Cytopenia (anaemia, thrombocytopenia, or leukocytopenia; medically confirmed)	8/21 (38%)
Low complement (medically confirmed)	5/21 (24%)
Increase in anti-dsDNA antibody titre (medically confirmed)	7/21 (33%)
Fatigue	18/21 (86%)
Consequences of SLE flare	
Change in SLE treatment	15/21 (71%)
Medical consultation	21/21 (100%)
Admission to hospital	4/21 (19%)
COVID-19 after vaccination	0

Data are n (%), median (IQR), or n/N (%). *Other vaccines were Cansino (one patient), Curevac (one patient), Janssen (five patients), Sinopharm (two patients), Sputnik V (one patient), and unknown (one patient). SLE=systemic lupus erythematosus.

Flares after SARS-CoV-2 Vaccination in Patients with Systemic Lupus Erythematosus

Medha Barbhaiya*[1, 2,3], Jonah M. Levine[1], Caroline H. Siegel[1,2], Vivian P. Bykerk[1,2], Deanna Jannat-Khah[1,2], Lisa A. Mandl[1,2,3]

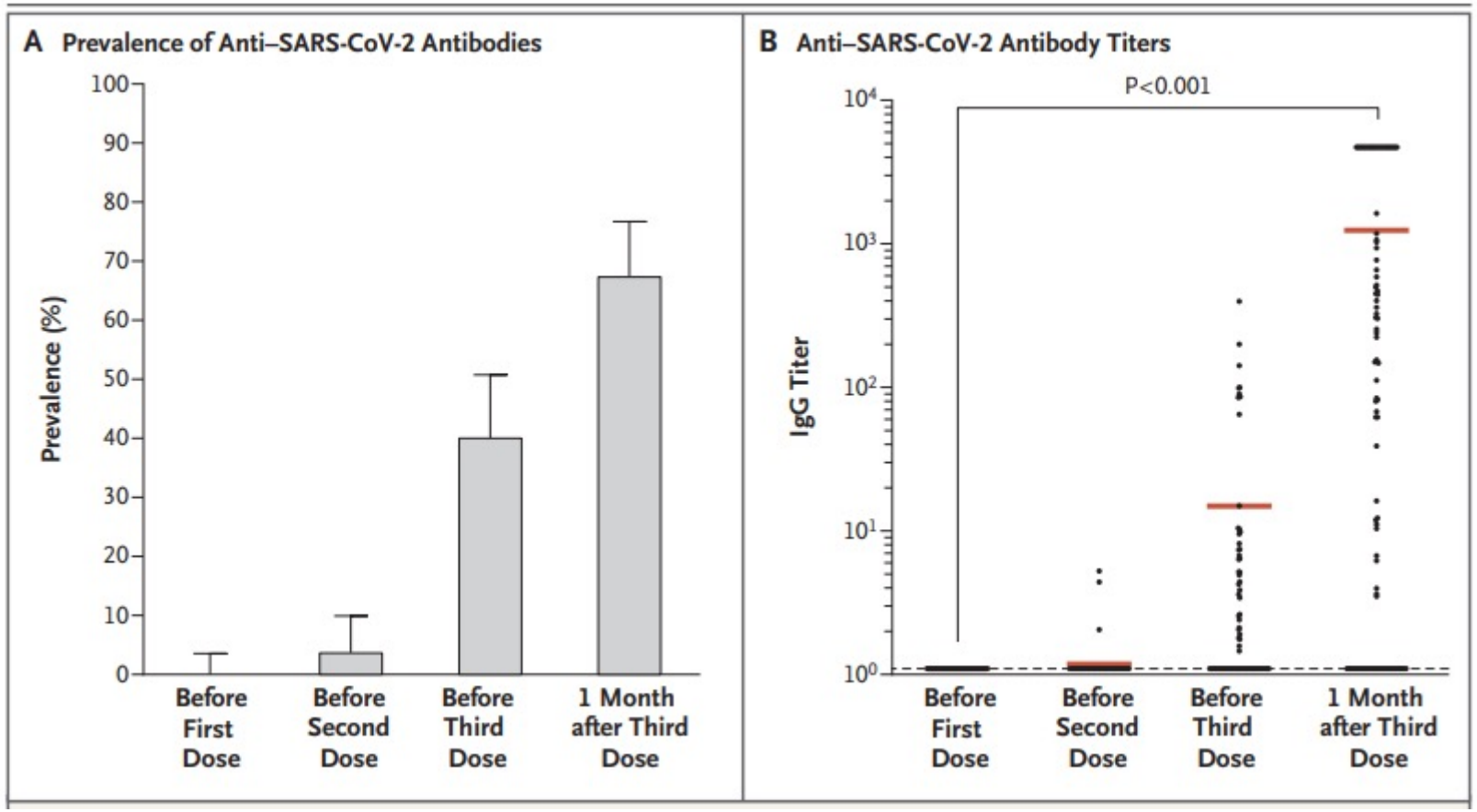
[1]Division of Rheumatology, Hospital for Special Surgery, New York, NY; [2]Department of Medicine, Weill Cornell Medicine, New York, NY; [3]Department of Population Health Sciences, Weill Cornell Medicine, New York, NY

- 183 patients with SLE responded to a survey regarding side effects from vaccination
- 11 patients reported a flare
- >91% of patients with lupus did not have a disease flare
- Most of the flares that were reported were mild or moderate
- Most flares resolved within 7 days of vaccine administration

The New York Times

C.D.C. Panel Recommends Third Dose of Covid Vaccine for Immunocompromised

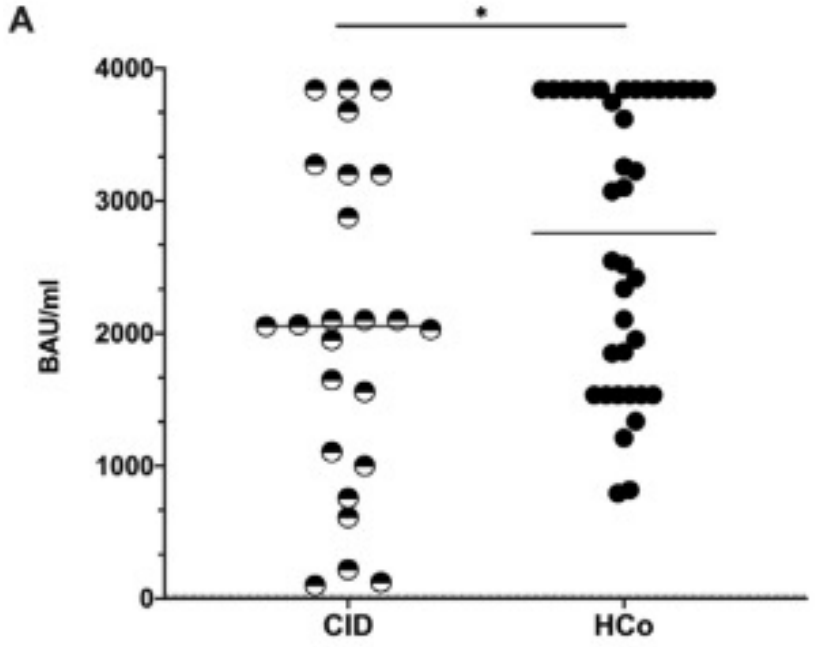
Third dose of mRNA vaccine increases seropositivity rate and antibody titers in solid organ transplant patients



Kamar et al. N Engl J Med 2021; 385:661-662 DOI: 10.1056/NEJMc2108861

Immunogenicity in autoimmune rheumatologic disease is there, it's just not optimal in some patients

- Overall, the majority of rheumatologic patients will seroconvert (>75-94% across the noted studies) but antibody levels may be decreased



Braun-Moscovici et al, Ann Rheum Dis, 2021
Deepak et al, MedRxiv, 2021
Haberman et al, Ann Rheum Dis, 2021
Mahil et al, Lancet Rheum, 2021
Ruddy et al, Ann Rheum Dis, 2021

Glucocorticoids and B Cell Depleting Agents Substantially Impair Immunogenicity of mRNA Vaccines to SARS-CoV-2

Visual Abstract for the COVaRiPAD Study (COVID-19 Vaccine Responses in Patients with Autoimmune Disease)

Methods/Cohort

Prospective Observational Study

2 Health Systems

133 Adults with Chronic Inflammatory Diseases (CID) and **53** Controls

Blood **before** and **1-2** weeks after SARS-CoV-2 vaccine

Humoral Response:
anti-SARS-CoV-2 spike (S) IgG+ binding and neutralizing titers, S-specific plasmablasts

Results

Adults with **CID** had **3x reduction** in antibody (anti-S IgG) titers (p=0.009) and neutralization response (p<0.0001)

Reduction in Antibody Titers by Medication:

36-fold B-cell depleting Rx
10-fold glucocorticoids *not dose dependent
4.5 fold JAK inhibitors
3.0 fold antimetabolites
2.5 fold TNF inhibitors

Most patients with CID mount a **reduced** response following COVID-19 vaccination, most severely affected by **B-cell depleting therapy** and **glucocorticoids**

PRE-PRINT

Created by @MithuRheum
Review by @alhkim (PI)

Several studies have shown decreased antibody responses to COVID-19 vaccines in rheumatologic population

Study	N	Antibody response in patients v controls	Medication considerations	Other factors
Boyarsky et al. Ann Rheum Dis. 2021; Ruddy JA Ann Rheum Dis. 2021	N = 404 SLE = 87	Decreased response after 1st and 2nd vaccine doses	Those on MMF, RTX, dual therapies led to decreased ab levels	
Deepak et al. medRxiv. 2021	N = 133 SLE = 15	Patients had a 3 fold reduction in antibody response	Patients were on b cell depleting therapies, steroids and antimetabolites (like MTX)	
Furer et al. Annals of Rheum Diseases 2021	N = 686 SLE = 101	Overall decreased antibody response in patients	Steroids, rituximab, MMF and abatacept associated with decreased antibodies	Older age

First study looking at response to COVID-19 vaccination specifically in Lupus patient cohort

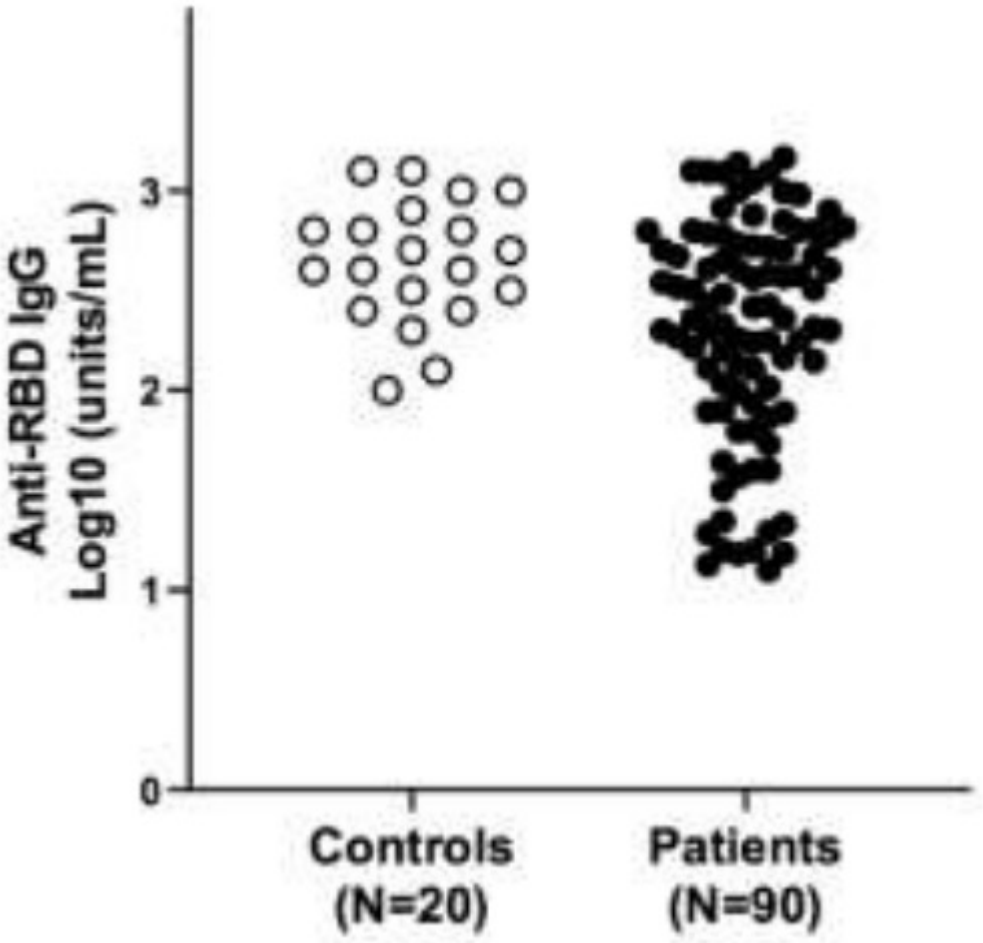
- Number of patients included
  - 90 patients and 20 controls

Medications	% patients taking
Hydroxychloroquine	79%
At least one immunosuppressing med	42%
Steroids (mean of 7 mg)	29%
Mycophenolate	21%
Belimumab	11%
More than 1 immunosuppressant	17%

Izmirly PM et al. Evaluation of Immune Response and Disease Status in SLE Patients Following SARS-CoV-2 Vaccination. Arthritis Rheumatol. 2021 Aug 4:10.1002/art.41937. doi: 10.1002/art.41937.

Antibody response to COVID-19 vaccination decreased in Lupus patients

- Overall the post vaccine antibody level in patients is lower than controls
- Predictors of low antibody response:
  - **Being on any immunosuppression (other than hydroxychloroquine**)



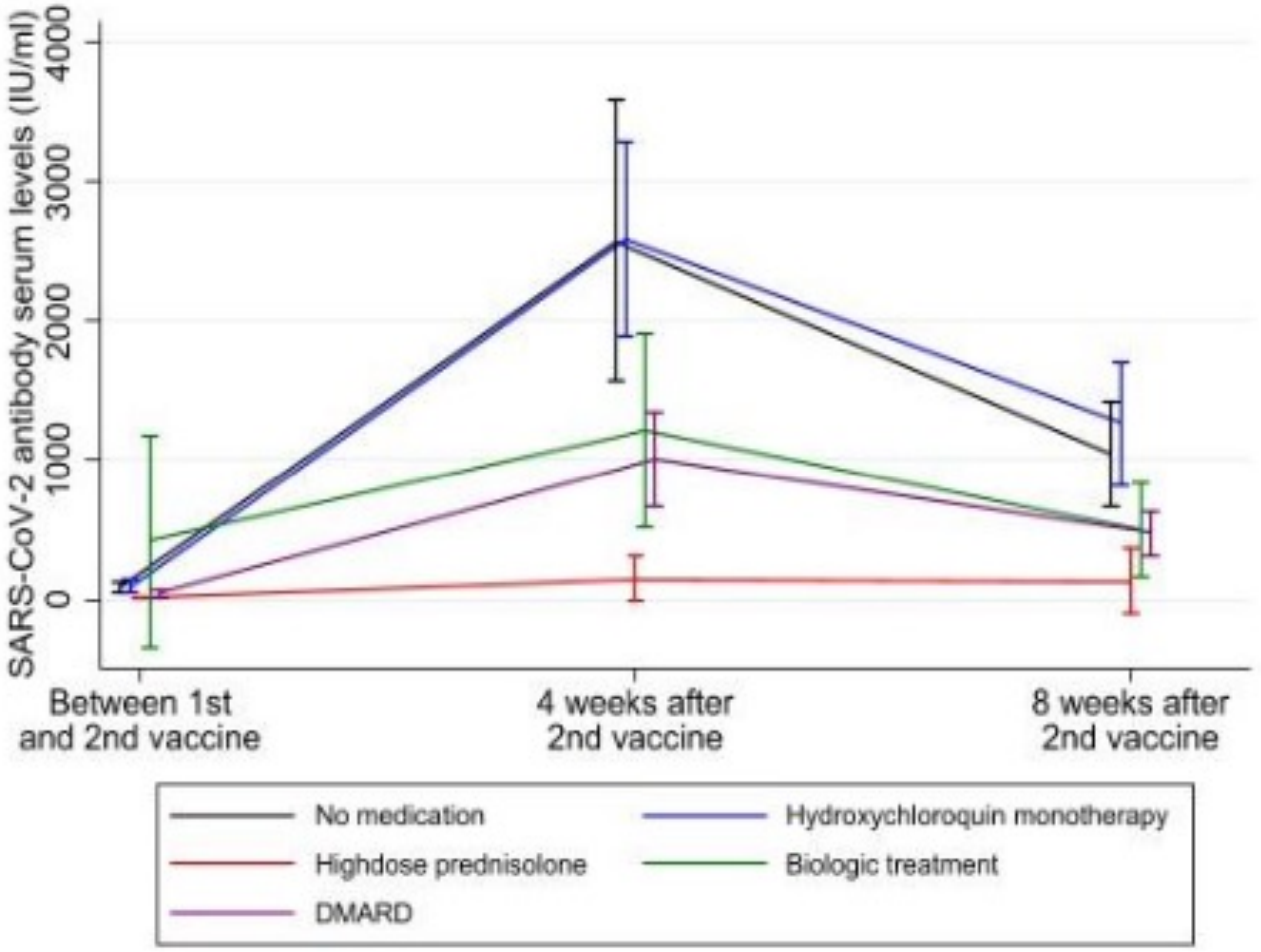
Disease activity remained stable in lupus patients post COVID-19 vaccination

- **No significant difference found in SLEDAI scores before vs after vaccination.**
- No changes in disease monitoring labs
- 9/79 patients had post-vaccination flare
- 8/9 flares were considered mild/moderate (arthritis and pericarditis treated with NSAIDs)
  - One severe flare of arthritis necessitating treatment with methotrexate (patient was not on any medication prior to vaccination)

Antibody response in patients with Systemic Lupus Erythematosus (SLE) after a two-dose regimen with SARS-CoV-2 vaccines

Emilie Stavnsbjerg Larsen, MD; **Anna Christine Nilsson**, MD, **Sören Möller**, Cand.scient., Ph.D; **Anne Boertman Voss**, DMSc; **Isik Somuncu Johansen**, DMSc.
Dept. of Rheumatology, dept. of Clinical Immunology and dept. of Infectious Diseases at Odense University Hospital, Denmark

- 83.7% of patients with SLE mounted an adequate antibody response
- At 4 weeks after 2nd vaccine dose, patients on prednisone >7.5mg, DMARDs and biologics had significantly decreased antibody titers as compared to those treated with HCQ only
- But at 8 weeks, only being on DMARDs and prednisone decreased antibody levels significantly versus HCQ



Future directions

- Rheumatologic patients, including those with SLE, are participating in studies looking at antibody responses to the third dose in the vaccine series

Summary

- Patients with lupus have high rates of hospitalization with COVID-19
- Factors contributing to poor outcomes in patients with SLE may include race/ethnicity, co-morbidities like cardiovascular disease and chronic kidney disease, older age, increased BMI, immunosuppression
- Vaccination with current COVID-19 vaccines carries low risk of disease flare, and is generally tolerated similarly to the population without lupus or rheumatologic disease
- Patients with lupus may mount a decreased antibody response to two dose vaccine series which is associated with medication regimens
- A third dose in the vaccine series for mRNA vaccines (and booster for J/J vaccine) is recommended given decreased antibody responses in patients with lupus on immunosuppressive medications

Thank you!

Clinical Outcomes of Patients with Systemic Rheumatic Diseases Hospitalized for COVID-19 at a Large Academic Center in New York City

Caroline H. Siegel[1,2], Jacky Choi[3], Debra D'Angelo[3], Paul Christos[3], Lindsay Lally[1,2], Parag Goyal[2], Lisa A. Mandl[1,2,3], Medha Barbhaiya[1,2,3]
1. Division of Rheumatology, Hospital for Special Surgery, NY; 2. Department of Medicine, Weill Cornell Medicine, NY; 3. Department of Population Health Sciences, Weill Cornell Medicine, NY

- Concluded that in a large observational inpatient cohort in a COVID-19 hot spot of NYC during the first wave, patients with systemic rheumatic disease were 1.27 times more likely to experience mechanical ventilation, ICU admission or in hospital death

Risk of Hospitalization, Admission to Intensive Care and Mortality Due to COVID-19 in Patients with Rheumatic Diseases: A Population-based Matched Cohort Study

Ana Michelle Avina-Galindo[1], Shelby Marozoff[1], Zahra Fazal[1,3], Jessie Kwan[1,3], Na Lu[1], Alison Hoens[2,3], Diane Lacaille[1,3], Jacek Kopec[1,3], Hui Xie[1,4], and J. Antonio Avina-Zubieta[1,3]
1 Arthritis Research Canada, 2 Arthritis Research Canada Arthritis Patient Advisory Board, 3 University of British Columbia, Vancouver, BC, Canada, 4 Simon Fraser University, Burnaby, BC, Canada

- Increased risk of hospitalization and ICU admission in patients with rheumatic disease than without.

ACR abstract 2021

Flares after SARS-CoV-2 Vaccination in Patients with Systemic Lupus Erythematosus

Medha Barbhaiya*[1, 2,3], Jonah M. Levine[1], Caroline H. Siegel[1,2], Vivian P. Bykerk[1,2], Deanna Jannat-Khah[1,2], Lisa A. Mandl[1,2,3]

[1]Division of Rheumatology, Hospital for Special Surgery, New York, NY; [2]Department of Medicine, Weill Cornell Medicine, New York, NY; [3]Department of Population Health Sciences, Weill Cornell Medicine, New York, NY

INTRODUCTION

- Vaccination against SARS-CoV-2 is particularly important for patients with systemic lupus erythematosus (SLE), who may be at increased risk of severe COVID-19.
- Their most common reason for vaccine refusal is fear of an SLE flare and SARS-CoV-2 mRNA vaccines could potentially induce interferon production, associated with increased SLE activity.

METHODS

- We emailed a secure web-based survey to 466 outpatients with SLE from a Rheumatology Division in New York City in March 2021.
- We used ICD-10 algorithms to identify patients with SLE.
- Patients reported adverse events (AE) within 7 days of vaccination.
- Separately, patients reported "typical" disease flares ("a sudden worsening of your rheumatology condition or arthritis") within two weeks of vaccination.

RESULTS

- 183 patients responded (39.3%)
  - 136/183 (74.3%) had at least one vaccine dose
  - 81 patients (59.6%) received Pfizer and 48 (39.3%) received Moderna

RESULTS

AEs: Reported by 100 patients (74%)
- 61% reported after 1st first dose
  71% reported after 2nd dose
- Pain at injection site (54%), fatigue (45%), headache (36%), sore shoulder (34%), and muscle aches (26%) were most common AEs.

Patients who Flared: (Table)
- 11 patients (8.1%) reported a flare
- Mean age 59.8 [SD 14.3] versus 54.2 [SD 13.9] years.
- White: 90.9% versus 65.6% in non-flare group.
- 12.5% who received Moderna (N=6), 6.2% who received Pfizer (N=5).
- 1/7 who received both vaccine doses flared both times.

Flares:
- 8/12 flares occurred after 1st dose
  4/12 occurred after the second.
  - 87.5% of flares after the first dose were 'mild'
  - 75% after the second were 'moderate'
- 6/12 flares started 1 day after vaccination and 4/12 started 4-7 days later.
- None started >7 days post-vaccine.
- Most flares resolved within 7 days
  - 3/12 lasted 8-21 days
  - 2/12 lasted >21 days

Rheumatology Research Foundation

Table. Characteristics of Patients with Systemic Lupus Erythematosus Reporting "Typical" Flares* After COVID-19 Vaccination

					Flare Symptoms**							Adverse Events (AE)	
Study ID	Vaccine Type	Flare Onset (days after vaccine dose)	Flare Severity (1Mild 2Moderate 3Severe)	Flare Duration (days)	Fever	Joint pain	Joint swelling	Skin rash	Fatigue	Muscle aches	Other	Any AE	Non-flare AE symptoms
Typical Flare After Vaccine Dose #1													
1	Moderna	1	Mild	1 days	0	1	0	0	1	1	Mouth sores	1	Pain at injection site
2	Moderna	1	Mild	4 days	0	1	1	0	0	0		1	Hand pain, pain at injection site, sore shoulder
3	Pfizer	1	Severe	20 days	0	1	0	0	1	0	Brain fog	1	Chills, flue-like feeling, hot, headache, pain at the injection site, sore shoulder
4	Moderna	1	Mild	21 days	0	1	0	1	1	1		1	Headache, itching, Rash at injection site, Redness or swelling at injection site
5	Moderna	1	Mild	22 days	1	0	0	0	1	0		1	Pain at the injection site, sore shoulder
6	Moderna	1	Mild	6 days	0	0	0	0	1	1		1	Pain at the injection site, sore shoulder
7	Pfizer	1	Mild	22 days	1	0	0	0	1	1		1	Pain at injection site, Redness or swelling at the injection site, sore shoulder
8	Pfizer	7	Mild	7	0	0	0	1	0	0		1	Tiredness/fatigue
Typical Flare After Vaccine Dose #2													
9	Moderna	1	Mild	4	1	0	0	0	1	0		1	Pain at the injection site, sore shoulder
9	Moderna	1	Moderate	3 days	0	1	1	0	1	1		1	Headache, pain at the injection site, redness or swelling at the injection site, sore shoulder
10	Pfizer	3	Moderate	8 days	0	1	1	0	1	1	Increased neuropathy neck pain, knee pain	1	Muscle weakness, neck pain, numbness and/or tingling in hand
11	Pfizer	7	Moderate	2 days	0	1	0	1	1	1		1	Chest pain, chills, headache, nausea/vomiting, numbness and/or tingling in hand

*11 patients reported 12 flares (1 patient flared at 2/2 vaccine doses)
**0=None, 1=Yes

CONCLUSIONS

- **>91% of patients with SLE did not flare** post-SARS-CoV-2 vaccination, and most flares were mild or moderate.
- 74% reported a vaccine related AE, similar to AE prevalence reported in the landmark Pfizer SARS-CoV-2 vaccine trial.
- We acknowledge possible misclassification of AEs as flares in the absence of confirmatory laboratory studies. However, we specifically asked patients to report symptoms concordant with their typical flares, separately from AEs.
- When flares occur the vast majority are mild or moderate; this information is reassuring and can help inform vaccine decision-making.

Characteristics Associated with Severe Outcomes in Patients with Systemic Rheumatic Diseases Hospitalized for COVID-19 in New York City

Caroline H. Siegel[1,2], Jacky Choi[3], Debra D'Angelo[3], Paul Christos[3], Lindsay Lally[1,2], Parag Goyal[2], Lisa A. Mandl[1,2,3], Medha Barbhaiya[1,2,3]

1. Division of Rheumatology, Hospital for Special Surgery, NY; 2. Department of Medicine, Weill Cornell Medicine, NY; 3. Department of Population Health Sciences, Weill Cornell Medicine, NY

INTRODUCTION

- Patients with systemic rheumatic diseases (SRDs) may have disproportionate risk of severe outcomes from COVID-19
- Older age, medical comorbidities, and steroid use have been identified as potential risk factors for COVID-19-related hospitalization in SRD patients

OBJECTIVE

To identify characteristics associated with severe COVID-19 in patients with underlying SRD hospitalized for COVID-19 in a U.S. "hotspot" during the initial wave of the pandemic in New York City.

METHODS

- Patients aged ≥18 years with SRD hospitalized for COVID-19 at any of 3 NewYork-Presbyterian hospitals (March – May 2020)
- Exposure: SRD
- Outcome: Severe COVID-19 (mechanical ventilation, ICU admission, or in-hospital death)
- Covariates: Baseline demographics, comorbidities, outpatient medications, presenting symptoms, laboratory values, COVID-19 treatment, and inpatient complications
- Wilcoxon rank sum, Chi-square, and Fischer's exact tests were used to compare covariates between patients with and without severe COVID-19

RESULTS

- 92/3,680 (2.5%) patients hospitalized with COVID-19 had SRD
- SRD Cohort: Mean age 66.3 [16.5] years; 82% female, 40% White, 26% Hispanic/Latinx; mean BMI 28.2 [6.7] kg/m²
- 35/92 (38%) SRD patients had severe COVID-19; compared to SRD patients without severe COVID-19:
  - More likely to be older, male, White or Asian, have a history of pulmonary disease or cerebral vascular accident [Table 1]
  - No difference in baseline immunosuppressive medications [Table 1]
  - Less likely to present with fever, cough, myalgia, diarrhea, or chest pain [Table 2]
  - Higher peak white blood cell count (WBC), serum creatinine (Cr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and inflammatory markers [Table 2]
  - No difference in inpatient treatments [Table 2]
  - More likely to develop thromboses, cardiac complications, renal dysfunction, or require vasopressor support [Table 2]

TABLES

Table 1. Baseline Demographics, Medical Comorbidities and Medication Use in Patients with Systemic Rheumatic Disease[1] Hospitalized with COVID-19, Stratified by Outcome[2]

	SRD Total (n=92)[3]	SRD, Severe Outcome[2] (n=35)[3]	SRD, No Severe Outcome[2] (n= 57)[3]	p-value[4]
Demographics				
Age	66.3 (16.5)	70.8 (12.8)	63.8 (17.1)	**<0.01**
Female	75 (82%)	24 (69%)	51 (89%)	**0.01**
Race				**0.03**
• White	37 (40%)	18 (51%)	19 (33%)	
• Asian	8 (9.0%)	5 (17%)	3 (5.3%)	
• Black	18 (20%)	4 (11%)	14 (25%)	
• Other	20 (22%)	4 (11%)	16 (28%)	
• Unknown	9 (9.4%)	2 (5.7%)	3 (5.3%)	
Ethnicity				0.13
• Hispanic/Latinx	24 (26%)	5 (14%)	19 (33%)	
• Not Hispanic/Latinx	53 (60%)	24 (69%)	31 (54%)	
• Other	3 (3.3%)	2 (5.7%)	1 (1.8%)	
• Unknown	10 (11%)	4 (11%)	6 (11%)	
BMI ≥ 30	31 (34%)	10 (30%)	21 (37%)	0.50
Ever smoker	29 (32%)	13 (37%)	17 (30%)	0.70
Comorbidities				
Coronary Artery Disease	20 (22%)	10 (29%)	10 (18%)	0.25
Hypertension	69 (75%)	26 (74%)	43 (75%)	>0.99
Diabetes	27 (29%)	10 (29%)	17 (30%)	0.99
Cerebral Vascular Accident	5 (5.4%)	3 (9%)	1 (1.8%)	**0.03**
Renal Disease	10 (11%)	3 (8.6%)	7 (12%)	0.73
Pulmonary Disease	28 (30%)	16 (46%)	12 (21%)	**0.04**
Transplant	4 (4.3%)	0 (0%)	4 (7.0%)	0.30
Outpatient Medications				
Hydroxychloroquine	21 (23%)	7 (20%)	14 (25%)	0.60
Systemic Corticosteroids	33 (36%)	12 (34%)	21 (37%)	0.99
Immunosuppressive Medication	13 (14%)	3 (8.6%)	7 (12%)	0.28
• Azathioprine	1 (1.1%)	1 (2.9%)	0 (0%)	0.40
• Methotrexate	10 (11%)	2 (5.7%)	8 (14%)	0.50
• Mycophenolate	3 (3.3%)	2 (5.7%)	1 (1.8%)	>0.99
• Tacrolimus	4 (4.3%)	0 (0%)	4 (7.0%)	0.30
• TNF-Alpha Inhibitor	2 (2.2%)	1 (2.9%)	2 (2.5%)	>0.99
• Other Monoclonal Antibody	4 (4.3%)	2 (5.7%)	2 (3.5%)	0.60

[1]RA (50%), SLE (10.9%), Vasculitis/PM/DSs/Myositis (10.9%), SLE-like/SSc/MCTD/APS (12%), PsA (3.2%), Spondylosis (2.2%)
[2]Composite Outcome of Intensive Care Unit Admission (N=15) or Mechanical Ventilation (N=20) or Death (N=24)
[3]Mean (SD); n (%)
[4]Wilcoxon rank sum test; Pearson's Chi-squared test, Fisher's exact test

Table 2. COVID-19 Presentation, Treatment, and Complications in Patients with Systemic Rheumatic Disease[1] Hospitalized with COVID-19, Stratified by Severe Outcome[2]

	SRD Total (n=92)[3]	SRD, Severe Outcome[2] (n=35)[3]	SRD, No Severe Outcome[2] (n= 57)[3]	p-value[4]
Clinical Presentation				
Presenting Symptom				
• Fever	61 (66%)	16 (46%)	45 (79%)	**<0.01**
• Cough	64 (70%)	20 (57%)	44 (77%)	**0.04**
• Dyspnea	62 (67%)	21 (60%)	41 (72%)	0.20
• Myalgia	16 (17%)	2 (5.7%)	14 (25%)	**0.02**
• Diarrhea	24 (26%)	5 (14%)	19 (33%)	**0.04**
• Chest Pain	15 (16%)	2 (5.7%)	13 (23%)	**0.03**
• Altered Mental Status	15 (16%)	9 (26%)	6 (11%)	0.05
• Anosmia	1 (1.1%)	0 (0%)	1 (1.8%)	>0.99
• Ageusia	1 (1.1%)	0 (0%)	1 (1.8%)	>0.99
Symptom Onset to Admission (Days)	6.1 (8.5)	7.0 (9.7)	5.7 (8.0)	0.70
Laboratory Values[5]				
• WBC	13.4 (9.4)	20.4 (10.7)	8.9 (4.5)	**<0.01**
• Creatinine	2.4 (3.2)	3.2 (3.4)	1.9 (3.0)	**<0.01**
• AST	161 (1,042.0)	376.4 (1,016.2)	62.1 (403.1)	**<0.01**
• ALT	102.0 (688.1)	174.8 (418.0)	55.4 (54.1)	**0.02**
• ESR	97.7 (33.6)	112.5 (28.5)	85.8 (33.2)	**<0.01**
• CRP	16.2 (11.3)	21.2 (11.9)	11.7 (9.7)	**<0.01**
• Ferritin	1,007.0 (5,713.4)	3,394.1 (8,578.2)	632.2 (741.5)	**<0.01**
• D-Dimer	3,769.7 (8,952.8)	7,207.1 (12,832.8)	1,256.2 (3,948.8)	**<0.01**
• LDH	609.0 (991.1)	892.7 (767.1)	418.4 (209.6)	**<0.01**
• Fibrinogen	706.3 (264.3)	831.6 (262.8)	587.9 (257.2)	**0.02**
Inpatient Treatment				
• Hydroxychloroquine	70 (76%)	26 (74%)	44 (77%)	0.80
• Remdesivir	6 (6.5%)	2 (5.7%)	4 (7.0%)	>0.99
• Steroids	47 (51%)	20 (57%)	27 (47%)	0.40
Steroid Duration (Days)	11.0 (18.1)	18.1 (25.5)	5.8 (4.8)	0.10
Complications				
• Thrombotic Events	6 (6.5%)	5 (14%)	1 (1.8%)	**0.03**
• Cardiac Complications[6]	15 (16%)	12 (34%)	3 (5.3%)	**<0.01**
• Renal Complications[7]	31 (34%)	20 (57%)	11 (19%)	**<0.01**
• Vasopressor Support	21 (23%)	19 (54%)	2 (3.5%)	**<0.01**

[1]RA (50%), SLE (10.9%), Vasculitis/PM/DSs/Myositis (10.9%), SLE-like/SSc/MCTD/APS (12%), PsA (3.2%), Spondylosis (3.3%)
[2]Composite Outcome of Mechanical Ventilation or ICU Admission or Death
[3]Mean (SD); n (%)
[4]Wilcoxon rank sum test; Pearson's Chi-squared test, Fisher's exact test
[5]Peak values during hospitalization
[6]Myocardial infarction, heart failure, new-onset arrhythmia
[7]Acute Kidney Injury or initiation of renal replacement therapy

CONCLUSIONS

Among SRD patients hospitalized for COVID-19 during the peak of the pandemic in NYC:

- **Demographic factors, medical comorbidities, and presenting symptoms were associated with severe outcomes**
- **Baseline immunosuppressive medication use was not associated with severe outcomes**
- **Patients with severe COVID-19 had higher peak inflammatory markers and increased frequency of clinical complications**

ACKNOWLEDGEMENTS

This study was supported by Hospital for Special Surgery COVID-19 Special Pilot grant. Dr. Siegel is supported by the National Center for Advancing Translational Sciences (NCATS) Grant # UL1TR02384 of the Clinical and Translational Science Center at Weill Cornell Medical College. Dr. Barbhaiya is supported by the Rheumatology Research Foundation and the Barbara Volcker Center for Women and Rheumatic Diseases.

Clinical Outcomes of Patients with Systemic Rheumatic Diseases Hospitalized for COVID-19 at a Large Academic Center in New York City

Caroline H. Siegel[1,2], Jacky Choi[3], Debra D'Angelo[3], Paul Christos[3], Lindsay Lally[1,2], Parag Goyal[2], Lisa A. Mandl[1,2,3], Medha Barbhaiya[1,2,3]

1. Division of Rheumatology, Hospital for Special Surgery, NY; 2. Department of Medicine, Weill Cornell Medicine, NY; 3. Department of Population Health Sciences, Weill Cornell Medicine, NY

INTRODUCTION

- There are conflicting data regarding risk of severe outcomes from COVID-19 among patients with systemic rheumatic diseases (SRDs)
- Prior studies have been limited by sample size, lack of comparator groups, and/or statistical analysis

OBJECTIVE

To determine whether patients with SRD hospitalized with COVID-19 in New York City during the first wave of the pandemic were at increased risk of severe outcomes compared to those hospitalized with COVID-19 without SRD.

METHODS

- Patients aged ≥18 years hospitalized with COVID-19 at any of 3 NewYork-Presbyterian hospitals between March 3 and May 15, 2020
- We obtained data on demographics, comorbidities, outpatient medications, COVID-19 symptoms, inpatient treatments, and outcomes
- We used Chi-Square, Fisher's Exact and T-tests to compare patients with and without SRD
- **We applied inverse probability of treatment weighting (IPTW) based on propensity scores to a logistic regression model to assess the multivariable association between SRD status and the primary composite outcome: mechanical ventilation, ICU admission, or in-hospital death**
- **We adjusted for covariates with an absolute standardized mean/proportion difference (SMD) ≥0.10 in the logistic regression outcome model**

RESULTS

- 92/3680 (2.5%) patients hospitalized with COVID-19 had SRD
- All COVID-19 patients: Mean age 63.7 [16.9] years; 41% female, 29% White; 34% Hispanic/Latinx
- Comparing patients with SRD to those without:
  - More likely female (82% vs. 40%), ever smokers (32% vs. 20%), White (40% vs. 29%) or Black (20% vs 12%); less likely Hispanic/Latinx (26% vs. 34%)
  - More with history of coronary artery disease, hypertension, pulmonary disease
  - More on outpatient HCQ, steroids, immunosuppressive medication
  - Higher proportion treated with steroids during hospitalization

RESULTS (Continued)

Table: Baseline Comorbidities, Outpatient Medications, Inpatient Treatment, and Clinical Outcomes in Hospitalized Patients with COVID-19 with and without Systemic Rheumatic Disease[1]

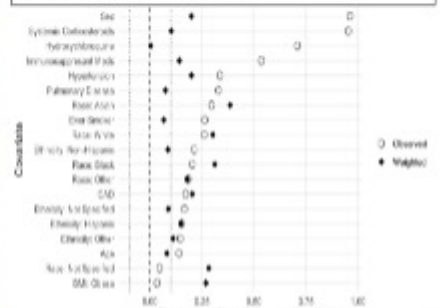
	Overall (n=3,680*)	SRD (n=92*)	No SRD (n=3,588*)	p-value[2]
Comorbidities				
Coronary Artery Disease	534 (15%)	20 (22%)	514 (14%)	0.05
Hypertension	2,619 (55%)	66 (72%)	1,953 (54%)	<0.01
Diabetes Mellitus	1,171 (32%)	27 (29%)	1,144 (32%)	0.60
Cerebral Vascular Accident	251 (6.8%)	6 (6.5%)	245 (6.8%)	>0.99
Chronic Kidney Disease	385 (9.8%)	10 (11%)	345 (9.8%)	0.70
Pulmonary Disease	580 (16%)	20 (30%)	572 (16%)	<0.01
Outpatient Medications				
Hydroxychloroquine	67 (1.8%)	21 (23%)	46 (1.3%)	<0.01
Systemic Corticosteroids	166 (4.5%)	35 (38%)	129 (3.4%)	<0.01
Immunosuppressives	73 (2.0%)	10 (11%)	65 (1.8%)	<0.01
- Azathioprine	5 (0.1%)	1 (1.1%)	4 (0.1%)	0.12
- Cyclosporine	3 (<0.1%)	0 (0%)	3 (<0.1%)	>0.99
- MTOR Inhibitor	2 (<0.1%)	0 (0%)	2 (<0.1%)	>0.99
- Methotrexate	19 (0.5%)	10 (11%)	4 (0.1%)	<0.01
- Mycophenolate	68 (1.8%)	6 (6.5%)	49 (1.4%)	0.02
- Tacrolimus	68 (1.8%)	4 (4.3%)	49 (1.4%)	0.04
- TNF-Alpha Inhibitor	4 (0.1%)	3 (3.3%)	1 (<0.1%)	<0.01
- Other Monoclonal Antibody	11 (0.3%)	4 (4.3%)	7 (0.2%)	<0.01
Inpatient Treatment				
Hydroxychloroquine	2,837 (80%)	70 (76%)	2,467 (80%)	0.13
Remdesivir	581 (16%)	6 (6.5%)	575 (16%)	0.50
Systemic Corticosteroids	663 (18%)	17 (81%)	606 (17%)	<0.01
Tocilizumab	166 (4.5%)	0 (0%)	166 (4.6%)	0.04
Sarilumab	24 (0.7%)	1 (1.1%)	23 (0.6%)	0.50
Anakinra	11 (0.3%)	0 (0%)	11 (0.3%)	>0.99
Convalescent Plasma	38 (1.0%)	0 (0%)	38 (1.1%)	>0.99
Clinical Outcomes				
ICU Admission/Mechanical Ventilation/Death	1,286 (35%)	35 (38%)	1,251 (35%)	0.60
ICU Admission	775 (21%)	19 (21%)	756 (21%)	>0.99
Mechanical Ventilation	746 (21%)	20 (22%)	726 (20%)	0.70
Death	883 (24%)	24 (26%)	859 (24%)	0.60

[1] RA (50%), SLE (16.3%), Vasculitis/PMR/GCA/Myositis (16.3%), SLE like/SS/MCTD/APS (12%), PsA (2.2%), Sarcoidosis (2.2%)
[2] Mean (SD); n (%)
[3] Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

ACKNOWLEDGEMENTS

This study was supported by Hospital for Special Surgery COVID-19 Special Pilot grant. Dr. Siegel is supported by the National Center for Advancing Translational Sciences (NCATS) Grant # UL1TR02384 of the Clinical and Translational Science Center at Weill Cornell Medical College. Dr. Barbhaiya is supported by the Rheumatology Research Foundation and the Barbara Volcker Center for Women and Rheumatic Diseases.

Figure 1. Standardized Mean Differences for Observed and Weighted Sample for Covariates Included in Propensity Score Model



Standardized mean differences for each covariate included in the propensity score model, pre and post differences before (i.e., observed) and after (i.e., weighted) weighting. No other covariates with SMD ≥ 0.1 were additionally adjusted for in the multivariable logistic regression model.

- **Weighted multivariable analysis: SRD patients had OR of 1.27 [95% CI 1.12-1.44, p<0.001] for composite outcome of mechanical ventilation, ICU admission, or in-hospital death after adjustment for covariates with absolute SMD ≥0.10**

CONCLUSIONS

In a large observational inpatient cohort in a COVID-19 "hotspot" during the initial peak of the pandemic, we found that patients with SRD were 1.27 times more likely to experience mechanical ventilation, ICU admission, or in-hospital death than patients without SRD, using IPTW to balance covariates. Our study illustrates the importance of appropriate modeling to account for confounding.