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COVID-19 in Pregnant Women With Rheumatic Disease: Data From the COVID-19 Global Rheumatology Alliance

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ABSTRACT. ***Objective.*** To describe coronavirus disease 2019 (COVID-19) and pregnancy outcomes in patients with rheumatic disease who were pregnant at the time of infection.

Methods. Since March 2020, the COVID-19 Global Rheumatology Alliance has collected cases of patients with rheumatic disease with COVID-19. We report details of pregnant women at the time of COVID-19 infection, including obstetric details separately ascertained from providers.

Results. We report on 39 patients, including 22 with obstetric detail available. The mean and median age was 33 years, range 24–45 years. Rheumatic disease diagnoses included rheumatoid arthritis (n = 9), systemic lupus erythematosus (n = 9), psoriatic arthritis/other inflammatory arthritides (n = 8), and antiphospholipid syndrome (n = 6). Most had a term birth (16/22), with 3 preterm births, 1 termination, and 1 miscarriage; 1 woman had yet to deliver at the time of report. One-quarter (n = 10/39) of pregnant women were hospitalized following COVID-19 diagnosis. Two of 39 (5%) required supplemental oxygen (both hospitalized); no patients died. The majority did not receive specific medication treatment for their COVID-19 (n = 32/39, 82%), and 7 patients received some combination of antimalarials, colchicine, anti–interleukin 1β, azithromycin, glucocorticoids, and lopinavir/ritonavir.

Conclusion. Women with rheumatic diseases who were pregnant at the time of COVID-19 had favorable outcomes. These data have limitations due to the small size and methodology; however, they provide cautious optimism for pregnancy outcomes for women with rheumatic disease particularly in comparison to the increased risk of poor outcomes that have been reported in other series of pregnant women with COVID-19.

Key Indexing Terms: anti-TNF, COVID-19, disease-modifying antirheumatic drug, rheumatoid arthritis, rheumatology

The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance, and do not necessarily represent the views of the American College of Rheumatology (ACR), the European Alliance of Associations for Rheumatology (EULAR), the (UK) National Health Service (NHS), the National Institute for Health Research (NIHR), or the (UK) Department of Health, or any other organization.

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Rheumatic diseases commonly occur in reproductive-aged women. The effect of pregnancy on the underlying rheumatic disease, the rheumatic disease's impact on pregnancy, and the limitations in the use of antirheumatic medications can make disease management challenging.[1,2] With the global outbreak of the novel coronavirus disease 2019 (COVID-19), an additional level of complexity has been added for women with rheumatic diseases who wish to become pregnant.

There are limited data to inform COVID-19 prognosis and pregnancy outcomes in women who are pregnant and infected with SARS-CoV-2. Data reported in November 2020 included 23,434 pregnant women with COVID-19, who were significantly more likely than nonpregnant women to be admitted to an intensive care unit, receive invasive ventilation and extracorporeal membrane oxygenation, and die.[3] However, none of these reports specifically included women with autoimmune or rheumatologic disorders, or those taking immunosuppressive therapy.

Among nonpregnant patients with rheumatic disease and COVID-19, initial reports from the COVID-19 Global Rheumatology Alliance (C19-GRA) physician registry of patients suggested that patients generally fared well.[4,5,6,7,8] Some medications were associated with poorer outcomes.[4,8] A large comparative study suggested that poorer outcomes in patients with rheumatic disease were likely mediated by comorbidities.[9] For the first time, to our knowledge, we report data from the C19-GRA registry on pregnant women with rheumatic disease who were diagnosed with COVID-19.

METHODS

Since March 24, 2020, healthcare providers globally have been able to enter data on people with rheumatic diseases diagnosed with COVID-19 into the C19-GRA provider REDCap survey.[10,11] Registry data elements include provider name, city, country, and clinic, as well as patient age, sex, race, and ethnicity. Rheumatic disease data include rheumatic disease medications (including glucocorticoids [GCs]), physician assessment of disease activity, and comorbidities. Data on COVID-19 include diagnosis date, symptoms, treatments, and outcomes, with available laboratory results also collected. Institutional review board exemption was granted for this registry. This study examines pregnant patients entered into the registry between March 24, 2020, and January 14, 2021.

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On July 1, 2020, and then again on January 15, 2021, a follow-up REDCap survey was sent to providers who had indicated that their patient was pregnant in the registry as of June 30, 2020, and January 14, 2021, respectively. Responses were received from providers who cared for 25 out of 44 women. Additional data requested included gravida, parity, number of fetuses in current pregnancy, gestational age at COVID-19 diagnosis, and obstetric outcomes. Five patients diagnosed on symptoms alone, including 3 with additional pregnancy data, were subsequently excluded. Data on whether drugs were stopped or continued through the COVID-19 illness were also reported if entered by the provider into the registry. As a comparison, we also included outcomes in nonpregnant women of childbearing age from the C19-GRA registry, aged 20–45 years, with data provided from registry inception until January 14, 2021. Data are reported using descriptive statistics.

The C19-GRA physician registry was determined "not human subjects research" under US Federal Guidelines assessed by the University of California, San Francisco, and patient consent was not required. Further details of the ethics procedures have been previously published.[8]

RESULTS

Patient and disease characteristics. Thirty-nine pregnant women were included in this study. Reported races/ethnicities were White (n = 13, 33%), Latin American/Hispanic (n = 9, 23%), Arab or Middle Eastern (n = 9, 23%), South or East Asian (n = 6, 15%), and Black (n = 2, 5%). The mean and median age was 33 years (SD 5.5, range 24–45 yrs). Patients were reported as nonsmokers (n = 28) and former smokers (n = 3); smoking status was unknown for 8 women. Comorbidities were reported in only 8 patients: prepregnancy hypertension (n = 3), morbid obesity (BMI > 40 kg/m^2, n = 2), obesity (BMI > 30 kg/m^2, n = 1), psoriasis (n = 1) and pregestational diabetes mellitus (n = 1). Rheumatic disease diagnoses (multiple diagnoses in the same patient are reported individually) were systemic lupus erythematosus (SLE; n = 9), rheumatoid arthritis (RA; n = 9), other inflammatory arthritis (n = 7), antiphospholipid syndrome (APS; n = 6), axial spondyloarthritis (n = 3), systemic sclerosis (n = 2), inflammatory myositis (n = 1), Sjögren syndrome (n = 1), mixed connective tissue disease (n = 1), gout (n = 1), Takayasu arteritis (n = 1), psoriatic arthritis (n = 1), antineutrophil cytoplasmic autoantibody–associated vasculitis (n = 1), and discoid lupus (n = 1). A common codiagnosis was SLE patients with coexisting APS (n = 2; Table 1). Rheumatic disease activity was reported as remission (n = 13), minimal or low (n = 18), moderate (n = 6), high (n = 1), and unknown (n = 1). Rheumatic disease treatment and COVID-19 treatment are shown in Table 1. About one-quarter of patients were using GCs (n = 9/39, 23%), most at low doses. Medication continuation data through the COVID-19 illness were reported for 6 medications: 2 anti–tumor necrosis factor drugs were stopped, sulfasalazine was stopped in 1 patient and continued in 1 other, and antimalarial drugs were stopped in 1 patient and continued in 1 other. No other continuation data were provided.

Most patients had COVID-19 diagnosed by PCR testing (n = 36), with the remainder by antibody serology, unknown, or other. Three patients reported no symptoms from their COVID-19. In those reporting symptoms of COVID-19 infection, those reported by ≥ 5 patients included cough (n = 24), fever (n = 21), headache (n = 12), anosmia (n = 11), myalgia (n = 11), shortness of breath (SOB; n = 11), vomiting or nausea (n = 8), arthralgia (n = 8), altered taste (n = 6), and sore throat (n = 6). Medication treatment for COVID-19 included nil (n = 32), hydroxychloroquine (n = 7), azithromycin (n = 3), lopinavir/ritonavir (n = 2), GCs (n = 2), interleukin 1β inhibitor (n = 1), and colchicine (n = 1; Table 1). Outcomes of

Table 1. Participant characteristics and COVID-19 treatments.

	Values
Rheumatic disease diagnosis[a]	
Systemic lupus erythematosus	9 (23)
Rheumatoid arthritis	9 (23)
Other inflammatory arthritis	7 (18)
Antiphospholipid syndrome	6 (15)
Axial spondyloarthritis	3 (8)
Systemic sclerosis	2 (5)
Inflammatory myositis	1 (3)
MCTD	1 (3)
Sjögren syndrome	1 (3)
Gout	1 (3)
AAV	1 (3)
Psoriatic arthritis	1 (3)
Takayasu arteritis	1 (3)
Discoid lupus	1 (3)
Rheumatic medication use at time of infection[a]	
No medications reported	17 (44)
HCQ	14 (36)
Anti-TNF	6 (15)
AZA	4 (10)
SSZ	4 (10)
Colchicine	1 (3)
IVIG	1 (3)
Medication combinations at time of infection	
HCQ + anti-TNF	2 (5)
HCQ + AZA	3 (8)
HCQ + SSZ	2 (5)
GC use at time of infection	
Any GC use	8 (21)
GC monotherapy	2 (5)
GC dose ≥ 10 mg/d	1 (3)
Daily GC dose, mg	
2.5	1
5	6
10	1
COVID-19 treatment[a]	
No treatment except supportive care	32 (82)
Antimalarials (i.e., HCQ)	7 (18)
Azithromycin	3 (8)
GCs	2 (5)
Lopinavir/ritonavir	2 (5)
IL-1β inhibitor	1 (3)
Colchicine	1 (3)

Values are expressed as n (%) unless otherwise indicated. [a] Not mutually exclusive. AAV: antineutrophil cytoplasmic antibody–associated vasculitis; AZA: azathioprine; COVID-19: coronavirus disease 2019; GC: glucocorticoid; HCQ: hydroxychloroquine; IL: interleukin; IVIG: intravenous Ig; MCTD: mixed connective tissue disease; SSZ: sulfasalazine; TNF: tumor necrosis factor.

Table 2. Outcomes in pregnant patients compared to nonpregnant patients.

	Pregnant, n = 39	Nonpregnant, n = 1878
Not hospitalized	29 (74)	1584 (84)
Hospitalized	10 (26)	126 (7)
Hospitalized with supplemental oxygen	2 (5)	127 (7)
Died	0 (0)	41 (2)

Values are expressed as n (%).

COVID-19 infection were as follows: not hospitalized (n = 29), hospitalized and no oxygen given (n = 8), and hospitalized requiring supplemental oxygenation (n = 2; Table 2). None of the patients died. Outcomes compared to nonpregnant women of childbearing age from the C19-GRA are shown in Table 2.

Patients requiring supplemental oxygen. Two patients required supplemental oxygen. The first was a 31-year-old woman with RA. She was on no specific antirheumatic treatment or GCs. COVID-19 was diagnosed by PCR. Her symptoms included fever, cough, SOB, myalgia, and malaise. She was hospitalized and had lymphopenia. She was treated with antimalarials and GCs for COVID-19. She was symptomatic for 10 days from the onset of COVID-19 symptoms to their resolution. The second patient who received supplemental oxygen was a 29-year-old woman with the reported diagnosis of "other inflammatory arthritis." She was also on no specific antirheumatic treatment or GCs. She was reported to have been diagnosed with COVID-19 by an unknown laboratory test. Her presenting symptoms included cough and SOB. She was hospitalized and her lymphopenia status was not reported. She received no specific COVID-19 treatment. She was symptomatic for 7 days from onset of COVID-19 symptoms.

Pregnancy information. Pregnancy information was available for 22 of 39 patients. Most were singleton pregnancies; there was 1 set of twins. The mean number of previous pregnancies per woman was 3.6 (SD 2.5), and mean previous live births was 2.0 (SD 1.3). Three women were diagnosed with COVID-19 in the first trimester (0–12 weeks), 13 in the second trimester (13–28 weeks), and 6 in the third trimester (≥ 29 weeks). The mean gestation at COVID-19 infection was 23.3 (SD 9.0) weeks. Pregnancy outcome at the time of data collection is shown in Table 3. No women delivered due to their COVID-19 infection. There were 9 cesarean deliveries, 8 vaginal deliveries, 1 miscarriage, and 1 termination (9 weeks, reasons not specified); 1 was not delivered at the time of the report.

Table 3. Pregnancy outcomes (n = 22).

Pregnancy Status	No.	Gestation, weeks
Termination	1	9
Miscarriage	1	< 20
Ongoing	1	19
Preterm birth (< 37/40 weeks)	3	32, 35, and 36
Term birth (≥ 37/40 weeks)	16	39 (median)

DISCUSSION

Using data from a global registry, we report on outcomes of 39 pregnant women with rheumatic diseases who developed COVID-19. Ten patients were hospitalized but only 2 required supplemental oxygen. There were no deaths.

The C19-GRA have previously reported that in persons with rheumatic conditions, poorer outcomes were associated with older age, comorbidities, higher doses of prednisone, high disease activity, and some specific medications.[4,8] However, information on outcomes of pregnant women with rheumatic conditions remains limited. Recent data from the Centers for Disease Control suggest that pregnant women with COVID-19 infection are more likely to be hospitalized and require mechanical ventilation, and may have a higher likelihood of death compared to nonpregnant women.[3]. Similarly in a report from the UK of 427 pregnant women admitted to hospital, 10% required mechanical ventilation and 1% died.[12] Importantly, half of these hospitalized patients were from racial and ethnic minorities. Similarly, in the nonpregnant patients from the GRA registry, odds of poor outcome were increased in ethnic minorities in the US.[13] The presence of rheumatic disease and rheumatic disease medication also has the potential to influence outcomes in pregnant women.

In our small patient series, the coexistence of a systemic rheumatic disease and pregnancy did not portend worse outcomes from COVID-19 infection than what has been observed in the general population of pregnant women.

Our study is limited in that the patient number is small and we have incomplete data on obstetric outcomes. As the C19-GRA registry data are voluntarily submitted, there may be selection bias in reported cases, with more complex rheumatic diseases and active disease being reported, as well as the bias that more severe COVID-19 cases are more likely to be included in the registry. Thus, the data in the registry cannot address the individual risk of infection, morbidity, or pregnancy outcome. In addition, our patients were young, had few comorbidities, and were on low GC doses, all of which may have contributed to a more benign course. Finally, these findings are purely descriptive. Further data that are collected on pregnant patients within the C19-GRA registry will be analyzed to inform disease and pregnancy outcomes for women with rheumatic diseases who are pregnant and have COVID-19. A priority is collecting data on obstetric and fetal outcomes in this group of patients.

In conclusion, pregnancy and COVID-19 outcomes in pregnant patients with systemic rheumatic disease were relatively benign in this patient series. However, data on all pregnancy outcomes and whether there were any cases of vertical transmission to infants are not available. Additional cases with greater granularity of data regarding pregnancy and fetal outcomes in the rheumatic disease population will greatly enhance our knowledge in this area.

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