

COVID-19 in women with rheumatic disease who are pregnant: Data from the COVID-19 Global Rheumatology Alliance

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Downloaded on September 8, 2021 from www.jrheum.org

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Key Words:

COVID-19, rheumatology, rheumatoid arthritis, anti-TNF, disease modifying anti-rheumatic
drug

Disclosures:

Bonnie L. Bermas, Helen L. Tanner, Milena Gianfrancesco, Andrea Seet, Mathia C. Aguiar, Nasra K. Al Adhoubi, Samar Al Emadi, Bernardo Cunha, Rachel Flood, Daria A. Kusevich, Eoghan M McCarthy, Naomi J. Patel, Savino Sciascia, Faizah Siddique, Mario O. Valenzuela-Almadi, Angus Worthing, JoAnn Zell, Wendy Costello, Saskia Lawson-Tovey, Emily Sirotich, Paul Sufka declare no competing interests. Eric M. Ruderman declares consulting for AbbVie, Amgen, BMS, Horizon, Janssen, Lilly, Novartis, Pfizer, unrelated to this work. Research grants from Corrona, Pfizer unrelated to this work. Sebastian E. Sattui declares funding from Vasculitis Clinical Research Consortium and Vasculitis Foundation outside of the submitted work. Leanna Wise declares consulting for Aurinia outside the submitted work. Suleman Bhana declares non branded consulting for AbbVie, Horizon, Pfizer, and Novartis. Ali Duarte-Garcia declares grants from the Centers for Disease Control and Prevention, the Rheumatology Research Foundation Scientist Development Award, the Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, the Women's Health Career Enhancement Award, and the Eaton Family Career Development Award. Rebecca Grainger declares Abbvie, Cornerstones, Janssen, Pfizer all outside the submitted work. Laure Gossec declares research grants: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi; Consulting fees: AbbVie, Amgen, BMS, Biogen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, all outside of the submitted work. Jonathan S. Hausmann declares grants from the Rheumatology Research Foundation and salary support from the Childhood Arthritis and Rheumatology Research Alliance (CARRA). Consulting for Novartis, Biogen, Pfizer (<\$10,000) all unrelated to this work. Kimme Hyrich declares honoraria from Abbvie, Grants from BMS, Pfizer and UCB. Jean Liew declares research funding from Pfizer unrelated to this work. Jeffrey A. Sparks declares research support from Amgen and Bristol-Myers Squibb and performed consultancy for Bristol-Myers Squibb, Gilead, Inova, Janssen, and Optum unrelated to this work. Zach S. Wallace declares grant support from Bristol Myers Squibb and Principia and has received consulting fees from MedPace and Viela Bio for unrelated work. Pedro M. Machado declares consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, and is supported by the National Institute for Health Research (NIHR), University College London Hospitals (UCLH), Biomedical Research Centre (BRC). Anja Strangfeld declares lecture honoraria from Abbvie, BMS, Celltrion, MSD, Pfizer, Roche, UCB outside the submitted work. Megan Clowse declares consulting for GSK, Astra-Zeneca,

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UCB; Grants from from GSK, Pfizer; outside the submitted work Jinoos Yazdany declares personal fees from AstraZeneca, personal fees from Eli Lilly, grants from Pfizer and Gilead, outside the submitted work. Philip C. Robinson declares Abbvie, Atom Bioscience, Gilead, Eli Lilly, Novartis, Roche, UCB, BMS, Janssen, Pfizer all outside the submitted work.

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Abstract

Objectives

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 (GRA) 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/other inflammatory arthritides (n=8) and anti-phospholipid antibody syndrome (n=6). Most had a term birth (16/22), with 3 pre-term births, one termination, one miscarriage and one woman yet to deliver at time of report. A quarter (n=10/39) of pregnant women were hospitalised following COVID-19 diagnosis. Two of 39 (5%) required supplemental oxygen (both hospitalised); no patient died. The majority did not receive specific medication treatment for their COVID-19 (n=32/39, 82%), seven patients received some combination of anti-malarials, colchicine, anti-IL-1beta, azithromycin, glucocorticoids, and lopinavir/ritonavir.

Conclusion

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

Rheumatic diseases commonly occur in reproductive-aged women. The impact of pregnancy on the underlying rheumatic disease, the rheumatic disease impact on pregnancy, and the limitations in the use of anti-rheumatic 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 and found they were significantly more likely than non-pregnant women to be admitted to an intensive care unit (ICU), receive invasive ventilation, receive 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 non-pregnant 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(4-8). 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 co-morbidities(9). For the first time 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 health care 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 the provider name, city, country, and clinic; patient age, sex, race and ethnicity. Rheumatic disease data includes rheumatic disease medications (including glucocorticoids), physician-assessment of disease activity and comorbidities. Data on COVID-19 includes 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 24th 2020 and January 14th 2021.

On July 1, 2020 and then again on the 15th of January 2021 a follow-up REDCap survey was sent to providers who had indicated their patient was pregnant in the registry as of June 30th 2020 and 14th January 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 three with additional pregnancy data, were subsequently excluded. Data on whether drugs were stopped or continued through the COVID-19 illness was also reported if entered by the provider into the registry. As a comparison we also included outcomes in non-pregnant women of child bearing age from the C19-GRA registry, aged 20-45 years old, with data provided from registry inception until the 14th of January 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 to be sought. Further details of the ethics procedures have been previously published (8).

RESULTS

Patient & Disease Characteristics

Thirty nine pregnant women were included in this study. Reported race/ethnicity were White (n=13, 33%), Latin American/Hispanic (n=9, 23%), Arab or Middle East (n=9, 23%), South or East Asian (n=6, 15%) and Black (n=2, 5%). The mean and median age was 33 years (standard deviation (SD) ± 5.5), range 24-45 years. Patients were reported as non-smokers (n=28) and former smokers (n=3); smoking status was unknown for eight women. Co-morbidities were reported in only eight patients, pre-pregnancy hypertension (n=3), morbid obesity (BMI >40 kg/m², n=2), obesity (BMI >30 kg/m², n=1), psoriasis (n=1) and pre-gestational diabetes mellitus (n=1). Rheumatic disease diagnoses were (multiple diagnoses in the same patient are reported individually) systemic lupus erythematosus (SLE) (n=9), rheumatoid arthritis (n=9), other inflammatory arthritis (n=7), anti-phospholipid syndrome (n=6), axial spondyloarthritis (n=3), systemic sclerosis (n=2), inflammatory myositis (n=1), Sjogren's syndrome (n=1), mixed connective tissue disease (n=1), gout (n=1), Takayasu vasculitis (n=1), psoriatic arthritis (n=1), ANCA-vasculitis (n=1) and discoid lupus (n=1). A common co-diagnoses was SLE patients with co-existing antiphospholipid syndrome (n=2). 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 a quarter of patients were using glucocorticoids (n=10/44, 23%), most at low dose (see Table 1). Medication continuation data through the COVID-19 illness was reported for six medications; two anti-TNF drugs were stopped,

sulfasalazine was stopped in one patient and continued in one other, anti-malarial drugs were stopped in one patient and continued in one other. No other continuation data was provided.

Most patients had COVID-19 diagnosed by polymerase chain reaction 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 five or more patients included cough (n=24), fever (n=21), headache (n=12), anosmia (n=11), myalgia (n=11), shortness of breath (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), glucocorticoids (n=2), IL-1 β inhibitor (n=1) and colchicine (n=1). Outcomes of COVID-19 infection were: not hospitalised (n=29), hospitalised and no oxygen given (n=8) and hospitalised requiring supplemental oxygenation (n=2). None of the patients died. Outcomes compared to non-pregnant women of child bearing age from the COVID-19 Global Rheumatology Alliance are shown in Table 2.

Patients Requiring Supplemental Oxygen

Two patients required supplemental oxygen. The first was a 31-year-old woman with rheumatoid arthritis. She was on no specific anti-rheumatic treatment or glucocorticoids. COVID-19 was diagnosed by PCR. Her symptoms were of fever, cough, shortness of breath (SOB), myalgia and malaise. She was hospitalised and was lymphopaenic. She was treated with anti-malarials and glucocorticoid for COVID-19. She was symptomatic for ten 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 anti-rheumatic treatment or

glucocorticoids. She was reported to have been diagnosed with COVID-19 by an unknown laboratory test. Her presenting symptoms were of cough and SOB. She was hospitalised and her lymphopaenia status was not reported. She received no specific COVID-19 treatment. She was symptomatic for seven days from onset of COVID-19 symptoms.

Pregnancy Information

Pregnancy information was available on 22 of 39 patients. Most were singleton pregnancies with one set of twins. The mean previous pregnancies per women were 3.6 (SD 2.5), and mean previous live births were 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 10 caesarean deliveries, 8 vaginal deliveries, 2 not delivered at the time of the report, one miscarriage and one termination (9 weeks, reasons not specified).

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 two required supplemental oxygen. There were no deaths.

The C19-GRA have previously reported that in persons with rheumatic conditions, older age, comorbidities and higher doses of prednisone, high disease activity and some specific medications were associated with poorer outcomes (4, 8). However, information on outcomes of pregnant women with rheumatic conditions remain limited. Recent data from the Centers

for Disease Control (CDC) suggests 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 non-pregnant women(3). Similarly in a report from the United Kingdom of 427 pregnant women admitted to the hospital, 10% required mechanical ventilation and 1% died(12). Importantly, half of these hospitalized patients were from racial and ethnic minorities. Similarly, in the non-pregnant 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 outcome in pregnant women.

In our small patient series, the co-existence of a systemic rheumatologic 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 infection, morbidity or pregnancy outcome. In addition, our patients were young, had few co-morbidities and were on low glucocorticoid 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 analysed 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 is 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.

Disclaimer: 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 organisation.

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Table 1: Participant Characteristics and COVID-19 Treatments

| Rheumatic Disease Diagnosis* | Number (%) |
|---|------------|
| Systemic Lupus Erythematosus | 9 (23%) |
| Rheumatoid Arthritis | 9 (23%) |
| Other Inflammatory Arthritis | 7 (18%) |
| Antiphospholipid antibody syndrome | 6 (15%) |
| Axial spondyloarthritis | 3 (8%) |
| Systemic sclerosis | 2 (5%) |
| Inflammatory myositis | 1 (3%) |
| Mixed connective tissue disease | 1 (3%) |
| Sjogren's syndrome | 1 (3%) |
| Gout | 1 (3%) |
| ANCA vasculitis | 1 (3%) |
| Psoriatic arthritis | 1 (3%) |
| Takayasu arteritis | 1 (3%) |
| Discoid lupus | 1 (3%) |
| | |
| Rheumatic Medication Use at time of infection* | |
| No medications reported | 17 (44%) |
| Hydroxychloroquine | 14 (36%) |
| Anti-TNF | 6 (15%) |
| Azathioprine | 4 (10%) |
| Sulfasalazine | 4 (10%) |
| Colchicine | 1 (3%) |
| Intravenous immunoglobulin | 1 (3%)† |
| | |
| Medication Combinations at time of infection | |
| Hydroxychloroquine & anti-TNF | 2 (5%) |
| Hydroxychloroquine & azathioprine | 3 (8%) |
| Hydroxychloroquine & sulfasalazine | 2 (5%) |
| | |
| Glucocorticoid Use at time of infection | |
| Any glucocorticoid use | 8 (21%) |
| Glucocorticoid monotherapy | 2 (5%) |
| Glucocorticoid dose \geq 10 mg/day | 1 (3%) |
| | |
| Daily glucocorticoid doses | |
| 2.5mg | 1 |
| 5mg | 6 |
| 10mg | 1 |
| | |
| COVID-19 Treatment* | |

| | |
|--|----------|
| No treatment except supportive care | 32 (82%) |
| Anti-malarials (e.g. hydroxychloroquine) | 7 (18%) |
| Azithromycin | 3 (8%) |
| Glucocorticoids | 2 (5%) |
| Lopinavir/ritonavir | 2 (5%) |
| IL-1 β inhibitor | 1 (3%) |
| Colchicine | 1 (3%) |

*Not mutually exclusive; ANCA Anti-neutrophil cytoplasmic antibody; TNF tumour necrosis factor

Table 2: Outcomes in pregnant patients compared to non-pregnant patients

| | Pregnant N = 39 | Non-Pregnant N = 1878 |
|--|-----------------|-----------------------|
| Not Hospitalized | 29 (74%) | 1584 (84%) |
| Hospitalized | 10 (26%) | 126 (7%) |
| Hospitalized with supplement oxygen | 2 (5%) | 127 (7%) |
| Death | 0 (0%) | 41 (2%) |

Table 3: Pregnancy Outcomes (n=22)

| Pregnancy Status | Number | Gestation |
|-----------------------------|--------|---------------------|
| Termination | 1 | 9 weeks |
| Miscarriage | 1 | <20 weeks |
| Ongoing | 1 | 19 weeks |
| Pre-term birth (<37/40) | 3 | 32, 35 and 36 weeks |
| Term Birth ($\geq 37/40$) | 16 | Median = 39 weeks |