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COVID-19 after rituximab therapy in cSLE patients

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***Abstract*:** Childhood-onset systemic lupus erythematosus (cSLE) is an autoimmune disease associated with significant morbidity and mortality. Rituximab is a B-cell depleting therapy utilized in the treatment of SLE. In adults, rituximab has been associated with increased risk of adverse outcomes in patients who develop coronavirus disease 2019 (COVID-19). We aimed to assess the impact of prior rituximab treatment on clinical outcomes from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in children with SLE. To describe the impact of rituximab on outcomes from SARS-CoV-2 infection, we conducted a retrospective study of pediatric SLE patients in our center diagnosed with COVID-19 who had previously received rituximab between February 2019 and October 2022. Patients' clinical characteristics, disease activity, and outcomes were assessed. Of the eight subjects assessed, five required hospitalizations for COVID-19, four required ICU admission, and two were seen in the emergency department for their symptoms. One patient ultimately expired from her illness. The median time between rituximab administration and COVID-19 diagnosis was 3 months. We assessed the clinical outcomes, including the need of ICU admission and fatal outcome, of COVID-19 in our cSLE patient population after rituximab administration. Approximately 60% of our patients required hospitalization for their illness, and seven out of eight patients required healthcare utilization to include hospitalization and/or emergency department visits.

Keywords: COVID-19, cSLE, rituximab

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Introduction

Rituximab, an anti-CD20 therapy, is used widely across a variety of autoimmune conditions, including childhood-onset systemic lupus erythematosus (cSLE).[1] Rituximab administration is associated with prolonged B-cell depletion and decreased humoral response.[2,3] It remains unclear, however, whether treatment with rituximab therapy increases the risk of severe infection from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

Patients with persistent COVID-19 positivity by polymerase chain reaction (PCR) have been shown to have a more prolonged, often relapsing remitting course, and clinically have worse outcomes.[4–6] Patients who have recovered from COVID-19 infection develop T-cell and B-cell memory,[7] the latter of which is impaired with rituximab therapy and can affect rates of re-infection with COVID-19.[8] Additionally, a study by Furlan *et al.* demonstrated that depletion and/or functional impairment of T-cells through disease modifying antirheumatic drugs may account for the failure of convalescent plasma in B-cell-depleted individuals with autoimmunity; T-cell depletion or functional impairment may be one of the reasons why patients treated with disease modifying antirheumatic drugs who have also received B-cell depleting therapies should be considered high risk for poor outcomes and mortality associated with COVID-19.[9] The clinical course

of COVID-19 in patients with primary and secondary humoral immune deficiencies has been shown to be more severe, and although it has not been linked to higher prevalence of death,[4,6,10,11] the development of antibody response and viral clearance are affected by the time since exposure to rituximab.[12] A study by Levavi *et al.*[13] suggested that approximately 35% of adults receiving rituximab for non-malignant disease were admitted to the ICU for COVID-19 treatment. Given these findings, we sought to assess the impact of rituximab therapy on clinical outcomes from SARS-CoV-2 infection in our cSLE patient population.

Methods

We conducted a retrospective chart review of cSLE patients diagnosed with COVID-19 who had received rituximab from February 2019 to October 2022 and had followed up at the pediatric rheumatology clinic at Emory University and Children's Healthcare of Atlanta. All patients met at least 4 of the 17 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for systemic lupus erythematosus (SLE). For the SLICC criteria, this included at least one clinical and one immunologic criterion.[14] Nephritis was classified according to the International Society of Nephrology classification for lupus nephritis.[15] To provide for therapeutic effect, subjects were included if they had received rituximab between 1 and 8 months prior to positive COVID-19 testing. This time period was selected for the span of reported B-cell depletion after rituximab administration.[16] A confirmed case of COVID-19 was defined as a positive result on a reverse transcriptase polymerase chain reaction (RT-PCR) SARS-CoV-2 assay obtained by nasopharyngeal swab. Patients were included in the analysis regardless of the presence or absence of COVID-19-related symptoms at the time of RT-PCR testing. A retrospective chart review was conducted to evaluate clinical characteristics, epidemiological characteristics, disease and illness severity, and outcome. After consultation with the local institutional review board, no ethics board approval was required in accordance with the policy of our institution.

Results

We identified eight patients with cSLE treated with rituximab and subsequently diagnosed with COVID-19 at our center. Patient disease characteristics and epidemiologic data are summarized in Table 1. All patients were female. Of the eight subjects assessed, five required hospitalization for COVID-19 to the General Ward, four required ICU admission, and two were seen in the emergency department for their symptoms. One patient ultimately expired from her illness. The median time between most recent rituximab administration and COVID-19 diagnosis was 3 months. We have outlined patients' immunosuppressive regimens, clinical course, and COVID-19 treatments as well as time since last rituximab administration (Table 1).

Patient 1

A 16-year-old female originally presented at 14 years of age with symptoms of limited range of motion, swelling, and pain in her knees, along with intractable headache and fever. She was diagnosed with Systemic Lupus Erythematosus (SLE) with antinuclear antigen (ANA) and Smith antibody positive and was subsequently started on mycophenolate mofetil, hydroxychloroquine, and prednisone at her home facility. She also developed worsening creatinine and proteinuria conditions and subsequently started hemodialysis. Renal biopsy was not obtained prior to starting these therapies. She presented to our center in 2022 in order to establish care for her worsening disease, which included worsening creatinine and eye pain in the setting of newly diagnosed retinal detachment by recent ophthalmologic evaluation.

Additional work up on admission to our facility revealed microhemorrhage on brain imaging with concern for central nervous system (CNS) vasculitis, ground glass opacities on chest imaging consistent with pulmonary vasculitis, and left main coronary and left anterior artery dilation on echocardiogram. Patient had end-stage renal disease due to lupus nephritis, with renal biopsy revealing 100% glomerulosclerosis with tubular atrophy. She was admitted to our center for intravenous (IV) pulse dose methylprednisolone, cyclophosphamide and rituximab infusions (last administered September 2022). During the end of her hospitalization in October 2022, she developed tachypnea and crackles on lung auscultation. She was found to be hypogammaglobulinemic with an IgG of 271 mg/dL (Table 1). Due to respiratory distress, she was transferred to the

Table 1. Chronology of clinical features, laboratory results, and treatment modalities. Table 1 depicts the disease course and immunosuppression for patients who developed COVID-19 after rituximab use. All patients were found to be COVID-19 PCR positive.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Clinical features	Hypoxic respiratory failure requiring high flow nasal cannula	Cough, fever, fatigue, myalgia, nausea and sore throat	Fever, chills, sore throat, along with myalgia and arthralgia and cough ultimately progressing to altered mental status and seizures in setting of hypoxic respiratory failure requiring intubation	Diffuse myalgia without fever or further symptoms	Cough and nasal congestion with headache, chest pain and shortness of breath	Cough, hemoptysis and fever	Nasal congestion with fever for 1 week progressing to hypoxic respiratory failure requiring high flow nasal cannula	Fever, chest pain and shortness of breath
Age at COVID-19 onset	16 years of age	17 years of age	19 years of age	19 years of age	18 years of age	16 years of age	20 years of age	19 years of age
Level of care	ICU	Outpatient	ICU	Hospital admission	Emergency department	Emergency department	ICU	ICU
Outcome	Recovery	Recovery	Death	Recovery	Recovery	Recovery	Recovery	Recovery
Duration of COVID-19 related hospitalization	11 days	None	24 days	1 day	None	None	6 days	8 days
Disease severity classification (WHO)	Severe	Mild	Critical	Moderate	Mild	Moderate	Severe	Severe
Days requiring respiratory support	3 days	None	24 days	None	None	None	4 days	7 days
Time from treatment to clinical response	3 days	7 days	Not applicable	Not applicable	10 days	7 days	4 days	7 days
Immunoglobulin G level (mg/dL)	271	880	142	Not assessed	813	1149	434	837
Absolute B lymphocyte count (cells/μL)	<1	1	54	143	<1	92	None obtained	4
Absolute T lymphocyte count (cells/μL)	245	1519	544	1453	616	1548	None obtained	1104
Absolute NK cell count (cells/μL)	55	254	119	158	88	262	None obtained	28
Absolute neutrophil count (thousand cells/μL)	2.35	4.26	13.12	5.19	2.25	6.94	3.09	5.00
COVID-19 treatments	Remdesivir (200 mg × 1 day followed by 100 mg daily × 4 days) IVIG 500 mg/kg	Nirmatrelvir/ritonavir 300–100 mg twice daily × 5 days	Remdesivir (200 mg × 1 day followed by 100 mg daily × 4 days) IVIG 500 mg/kg Dexamethasone 8 mg daily × 5 days	None	Dexamethasone 16 mg × 1 dose	Secondary bacterial pneumonia treated with amoxicillin for 7 days	Convalescent plasma IVIG 500 mg/kg Prednisone 60 mg Secondary bacterial pneumonia treated with IV ceftriaxone	Remdesivir (200 mg × 1 day followed by 100 mg daily × 4 days) Dexamethasone 6 mg × 8 days Secondary bacterial pneumonia treated with azithromycin for 7 days

(Continued)

Table 1. (Continued)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Immunosuppressive regimen prior to COVID-19	Cyclophosphamide (1 gram) Prednisone 60 mg daily 1000 mg IV Methylprednisolone weekly	Mycophenolate sodium 540 mg twice daily Hydroxychloroquine 400 mg daily	Cyclophosphamide (17 gram) Hydroxychloroquine 400 mg daily Mycophenolate mofetil 1000 mg twice daily Prednisone 50 mg daily	Methotrexate Mycophenolate mofetil 1000 mg twice daily Hydroxychloroquine 300 mg daily Prednisone 40 mg daily	Mycophenolate sodium 720 mg twice daily Hydroxychloroquine 300 mg daily Prednisone 2.5 mg every other day	Mycophenolate mofetil 500 mg every morning/1000 mg every evening Hydroxychloroquine 300 mg daily	Cyclophosphamide (8.825 gram) Mycophenolate sodium 360 mg twice daily Tacrolimus 7 mg twice daily Hydroxychloroquine 200 gm daily Prednisone 5 mg daily	Mycophenolate mofetil 1500 mg twice daily Hydroxychloroquine 400 mg daily Prednisone 5 mg daily
Total rituximab doses (cumulative to date)	2 g	6 g	9 g	2 g	8 g	6 g	8.5 g	10 g
Months between rituximab and COVID-19 development	1 month	4 months	1 month	4 months	3 months	1 month	7 months	5 months
COVID-19 re-infection	None	None	Not applicable	None	None	None	COVID-19 re-infection 4/202 with fever and shortness of breath that did not require admission or treatment	None
COVID-19 vaccination status	Unvaccinated	Unvaccinated	Unvaccinated	Unvaccinated	3 doses (Pfizer)*	Unvaccinated	2 doses (Pfizer)*	1 dose (Pfizer)*

*Patient received her second COVID-19 vaccination 4 months prior to acute infection; patient 7 received her COVID vaccine 11 months after acute infection; and patient 8 received her COVID-19 vaccine 9 months after acute infection.
ANA, antinuclear antibody; dsDNA, double-stranded deoxyribonucleic acid; PCR, polymerase chain reaction; RNP, ribonucleoprotein.

Pediatric Intensive Care Unit (PICU) where she tested positive for COVID-19. She received remdesivir as well as a replacement dose of intravenous immune globulin (IVIG) 500 mg/kg. She weaned from high flow nasal cannula and transferred to the floor 5 days later prior to discharge from the hospital 2 weeks later. Patient was COVID-19 unvaccinated.

Patient 2

A 17-year-old female originally presented at 14 years of age with autoimmune hemolytic anemia, hypocomplementemia, elevated inflammatory markers along with ANA and double-stranded DNA (dsDNA) and was diagnosed with cSLE. Patient was originally maintained on prednisone, azathioprine, and hydroxychloroquine. She developed persistent headaches with vomiting and underwent brain magnetic resonance imaging (MRI), which showed leptomeningeal enhancement with concern for CNS disease and prompted initiation of rituximab therapy (last administered April 2022) along with transition from azathioprine to mycophenolate mofetil and subsequently mycophenolate sodium due to nausea. She also underwent lumbar puncture with concern for idiopathic intracranial hypertension for which she started acetazolamide.

She developed cough, fever, fatigue, myalgia, nausea, and sore throat and had a positive at home test for COVID-19 PCR in August 2022. She was treated with nirmatrelvir/ritonavir because of prolonged headaches and fatigue when seen in clinic approximately 1 month after diagnosis. She did not require hospitalization. Patient was COVID-19 unvaccinated.

Patient 3

A 19-year-old female originally presented at 14 years of age with oral ulcers, palmar erythema, arthritis of her bilateral wrists and fingers, hypocomplementemia, elevated inflammatory markers along with positive ANA and anti-dsDNA and Smith antibodies. She was diagnosed with cSLE and was originally maintained on prednisone, mycophenolate mofetil, and hydroxychloroquine prior to transitioning to belimumab infusions in November 2017 due to poor compliance with oral medications. She developed worsening hypertension in 2017 and underwent renal biopsy which revealed Class V–II lupus nephritis prompting transition from belimumab and mycophenolate to cyclophosphamide infusions, as well as rituximab. Due to worsening renal function, she underwent repeat renal biopsy in April 2021 which revealed worsening lupus nephritis (Class V–IV) with 48% crescent formation. She subsequently underwent an additional course of cyclophosphamide infusions (1000 mg, six infusions), along with another course of rituximab. She required rituximab desensitization therapy due to hypersensitivity to the medication in December 2021. Further complicating her course, she developed a refractory headache in May 2021 due to cerebral venous sinus thrombosis. She began heparin and escalated her immunosuppression to weekly pulse dosing of methylprednisolone.

In December 2021 she developed a fever, chills, and sore throat with myalgia and cough prompting presentation to the emergency department and subsequent 3-day hospitalization at an outside facility. Patient was discharged and 3 days later had seizure activity and altered mental status. Her brain MRI was consistent with posterior reversible encephalopathy syndrome in the setting of hypertension, requiring admission to the PICU for nicardipine drip. She had a COVID-19 PCR positive on admission and started on remdesivir, IVIG 500 mg/kg given her hypogammaglobulinemia (IgG 142 mg/dL), as well as 5 days of dexamethasone. She clinically deteriorated and was empirically treated with vancomycin, cefepime, acyclovir, and micafungin in the setting of positive herpes simplex virus (HSV) serum testing. She was intubated due to altered mental status and hypoxic respiratory failure in the setting of acute COVID-19 infection. Later she required escalation to an oscillator with inhaled nitric oxide during her third week of hospitalization. Ultimately, the patient expired from pulmonary hemorrhage and disseminated intravascular coagulation despite these interventions in her fourth week of hospitalization. Patient was COVID-19 unvaccinated.

Patient 4

A 19-year-old female originally presented at 17 years of age with malar rash, vasculitic lesions, myalgias, and arthralgia of her bilateral wrists. She had hypocomplementemia, positive ANA, Coombs positive hemolytic anemia, lymphopenia, positive

anti-dsDNA antibody, and was diagnosed with SLE. She began methotrexate, prednisone, mycophenolate mofetil, and hydroxychloroquine for her disease but ultimately required escalation to rituximab in February 2020 given ongoing disease activity. In June 2020 she was admitted with diffuse body aches and initial concerns for a lupus flare, but ultimately found to be COVID-19 PCR positive (recent family COVID-19 exposure). She lacked fevers, shortness of breath, cough, nausea, and vomiting during her illness. She was discharged approximately 24 h after admission on an increased prednisone dose (40 mg daily). The patient was COVID-19 unvaccinated.

Patient 5

An 18-year-old female originally presented at 16 years of age with polyarthritis, malar rash, serositis, lymphopenia, positive anti-myeloperoxidase, ANA, and anti-dsDNA antibodies, Coombs positive hemolytic anemia. She was ultimately diagnosed with SLE. She also presented with coronary artery vasculitis involving her left anterior descending artery and Class IV lupus nephritis, prompting treatment with pulse dose methylprednisolone, cyclophosphamide (six doses), and rituximab (three courses, last administered September 2021). She was otherwise maintained on hydroxychloroquine, mycophenolate sodium, and prednisone for disease control. She developed a cough, nasal congestion, headache, chest pain, and shortness of breath, prompting presentation to the emergency department in December 2021. She did not require hospitalization. Prior to this illness, she received three doses of the COVID-19 vaccine (BNT162b2 [Pfizer/ BioNTech).

Patient 6

A 16-year-old female originally presented with headache, left facial numbness, and an MRI brain consistent with neuromyelitis optica. She had positive ANA, elevated erythrocyte sedimentation rate, positive anti-Ro/SSA antibody, and was diagnosed with SLE. She started pulse dose methylprednisolone, as well as rituximab upon diagnosis, and rituximab was continued for maintenance therapy, ultimately receiving a total of six doses, last administered in July 2022. She was also maintained on hydroxychloroquine and mycophenolate mofetil. She was seen in the emergency department in August 2022 with cough, hemoptysis, and fever and tested positive for COVID-19 by PCR. Chest X-ray was obtained and she was diagnosed with right lower lobe pneumonia with concern for secondary bacterial infection. She was treated outpatient with a 7-day course of amoxicillin and did not require hospitalization. Patient was COVID-19 unvaccinated.

Patient 7

A 20-year-old female originally presented at 9 years of age with lymphadenopathy and arthritis of her shoulders and elbows. Subsequent lab workup revealed positive ANA, hypocomplementemia, and positive anti-dsDNA antibody with ultimate diagnosis of SLE. She began hydroxychloroquine and prednisone. Her course was complicated with development of Class IV–Class V lupus nephritis, and she underwent renal transplant in 2017. She was induced with cyclophosphamide and rituximab, with her last infusion prior to COVID-19 infection being in February 2020. She was maintained on tacrolimus, mycophenolate mofetil, prednisone, and hydroxychloroquine. In September 2020 she developed nasal congestion along with 1 week of fevers. Patient was admitted and tested positive for COVID-19 via PCR.

She was treated with IV ceftriaxone with concern for secondary bacterial pneumonia per chest X-ray on admission. Additionally, she was administered IVIG 500 mg/kg and was diagnosed with hypogammaglobulinemia (IgG 434 mg/dL). She required transfer to the PICU for increased respiratory support via high flow nasal cannula. She required a six-day total hospitalization, four of which were spent in the PICU. She received convalescent plasma due to worsening hypoxia and the presence of hypogammaglobulinemia in the setting of severe B-cell depletion after optimization of her prednisone dosing (60 mg daily) and lack of clearance of the virus. Patient had significant clinical improvement approximately 72 h after administration of convalescent plasma. Repeat COVID-19 PCR testing was not performed prior to discharge. Patient had received two doses of the COVID-19 vaccine (Pfizer).

Patient 8

A 19-year-old female originally presented at 16 years of age with fatigue, malar rash, and

weight loss. She had positive ANA, positive anti-dsDNA antibody, and hypocomplementemia and was diagnosed with SLE. She received prednisone and hydroxychloroquine, along with rituximab, for disease control, with last infusion in September 2019. In January 2021, she developed fever, chest pain, and shortness of breath after exposure to multiple ill family members and had COVID-19 PCR positive. She was originally seen at an outside emergency department where a chest computed tomography scan showed concern for pneumonia. She was prescribed a 7-day course of azithromycin and discharged home. Approximately 1 week later, she re-presented to the emergency department due to persistent fevers and development of tachypnea. She was admitted to the floor but ultimately transferred to the PICU for increased respiratory support of high flow nasal cannula, which was discontinued after 5 days. She required an additional 2 days of nasal cannula on the General Ward prior to discontinuation of respiratory support. Patient received remdesivir for a total of 5 days as well as dexamethasone for 8 days prior to discharge home. She had received one dose of the COVID-19 vaccine (Pfizer).

Discussion

Since the start of the COVID-19 pandemic, there has been an attempt to identify which patients are at highest risk of poor outcomes from infection. Data from studies in adults has demonstrated that rituximab in particular may place patients at risk of severe infection. Our case series evaluated the severity of COVID-19 infection after rituximab therapy in children with cSLE. Patients treated with B-cell-depleting therapies often develop a failure to seroconvert after primary infection, independent of viral load and time to viral clearance as well as impairment of vaccine response.[4,17,18] Studies have shown that rituximab therapy depletes memory B cells, which in turn may cause persistent hypogammaglobulinemia with the possibility for infection-related complications.[3]

A study by Ihlow *et al.*[19] found that in COVID-19 deceased adult patients there was B-cell depletion in either bone marrow or spleen with complete plasma cell depletion and severe lymphocytopenia in the peripheral blood. The authors also found there was a tendency toward higher pulmonary SARS-CoV-2 ribonucleic acid load in COVID-19 patients with B-cell depletion in the setting of active disease.[19] In contrast, a study by Shuwa *et al.*[20] found alterations in B- and T-cell function in hospitalized adult patients with active COVID-19. Specifically, the authors found a propensity for pro-inflammatory (IL-6+) B-cell expansion in acute COVID-19, as well as increased expression of CD8+ T-cells, as well as perforin, granzyme, and CD107a during the acute disease process. Of note, for our patient cohort the patients with the lowest absolute total T-cell counts as well as IgG levels less than 300 were overall associated with severe to critical disease (Table 1). Previous studies have shown T-cell responses are impaired in severe SARS-CoV-2 infection, and T-cell immunity plays a vital role in the control of SARS-CoV-2.[21] Additionally, a study by Govender *et al.*[22] elucidated long-term alterations in T-cell populations associated with COVID-19 pathogenesis. This suggests T-cell depletion and/or functional impairment in the setting of B-cell depletion and hypogammaglobulinemia with rituximab use may play a role in worse outcomes in the cSLE patient population, although this association needs to be evaluated with further studies.

According to the Centers for Disease Control, during March to February 2022, weekly COVID-related hospitalization rates for children across the United States were 14.5 per 100,000.[23] Additionally, monthly ICU admission rates were approximately 3.5 times as high during the Omicron predominance peak (10.6) compared to the Delta predominance peak (3.0).[23] In-hospital death was associated with 0.6% of total hospitalizations.[23] In comparison, approximately 60% of our patient cohort required hospitalization for their symptoms as a result of immunocompromised status (Table 1). Of those admitted, 80% required ICU level care and ultimately one expired (12.5% of our cohort) (Table 1). Overall, our cohort required both higher rates of healthcare utilization and higher level care compared to national averages, although ultimately four patients recovered without need for hospitalization.

All patients in this series were taking additional immunosuppressive therapies, including mycophenolate mofetil, prednisone, and hydroxychloroquine. Three out of eight patients had

been exposed to cyclophosphamide previously. While these medications do not have the prolonged bioavailability of rituximab, many of these medications were repeatedly administered over the course of their treatment. The impact of these ancillary therapies on immune response to COVID-19 remains unclear and should be investigated in future studies in children.

Within our cohort, three patients were diagnosed with superimposed bacterial or viral pneumonia in the setting of acute COVID-19 infection, with one ultimately expiring in the setting of disseminated intravascular coagulation. Adult literature reports that, while co-infection at COVID-19 diagnosis is uncommon, patients with community-acquired co-infections and hospital-acquired superinfections had worse outcomes.[24,25] Patients undergoing immunosuppressive therapy for underlying diseases including malignancy and autoimmune diseases were reported to have several opportunistic infections at the time of COVID-19 diagnosis, to include HSV, *Mycobacterium tuberculosis*, and *Toxoplasma gondii*.[26] Specifically in rheumatologic patients receiving rituximab, many required hospitalizations with respiratory support due to clinical decompensation.[27] A report by Yarahmadi *et al.* indicated that, of a cohort of 13 adult patients who had received rituximab including three with SLE, three with systemic vasculitis, five with rheumatoid arthritis, and two with Sjögren syndrome, eight patients were hospitalized, and three ultimately died from acute respiratory distress syndrome.[27] As previously mentioned, there is limited data assessing COVID-19 outcomes in the childhood-onset SLE population prior to this report.

Limitations of our case series include the single center nature of our review, as well as small sample size. Additionally, the relationship between the timing of therapeutic intervention, onset and duration of PCR positivity, and disease-related outcomes was not assessed in our review given limited follow-up PCR data, and should be investigated in future studies. Further studies are required to elucidate the relationship between concomitant or past medication exposure and specific disease-related processes on the clinical course of COVID-19 infection and outcome after rituximab administration. Future studies should assess the relationship between lupus disease activity, such as through the SLE Disease Activity Index scoring as well as clinically distinct disease phenotypes, and COVID-19 severity both for patients who have received rituximab and those who have not received B-cell depleting therapies. Additionally, our study did not elucidate an association with COVID-19-related outcomes and vaccination status. Given previous reports of suboptimal immune responses in the setting of immunosuppression, additional studies should focus on serologic responses to COVID-19 vaccination in this particularly vulnerable patient population.[28]

Conclusion

We assessed the clinical outcomes, including the need of ICU admission and fatal outcome, of COVID-19 in our cSLE patient population after rituximab administration. Our review suggests T-cell depletion and/or functional impairment in the setting of B-cell depletion and hypogammaglobulinemia with rituximab use may play a role in worse outcomes in the cSLE patient population, although this association needs to be evaluated with further studies. Further investigation of this vulnerable patient population in larger sample sizes is required to further understand these relationships between COVID-19 immunity and immunomodulatory therapies.

Declarations

Ethics approval and consent to participate

This study was not considered Human Research by the Children's Healthcare of Atlanta Institutional Review Board.

Consent for publication

Telephone consent was obtained from the patients in our publication for ease of family and minimal risk of the study.

Author contributions

Meghan Corrigan Nelson: Conceptualization; Data curation; Writing – original draft; Writing – review & editing.

Cynthia K. Manos: Conceptualization; Validation; Writing – review & editing.

Elaine Flanagan: Conceptualization; Validation; Writing – review & editing.

Sampath Prahalad: Conceptualization; Project administration; Validation; Writing – review & editing.

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Competing interests
The authors declare that there is no conflict of interest.

Availability of data and materials
Data were ethically extracted from the patient's file. Data used in this study is available from the corresponding author upon request.

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