The development of inflammatory arthritis following SARS-CoV-2 infection: a systematic review of the literature

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Abstract: Given the widespread impact of COVID-19, it is important to explore any atypical presentations and long-term sequelae associated with this viral infection, including the precipitation of inflammatory arthritis.

Objective: To identify and summarize clinical reports of acute inflammatory arthritis associated with COVID-19.

Methods: A systematic review of the PubMed (MEDLINE), Google Scholar, and Cochrane Central databases through January 31, 2022 was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. The inclusion criteria were: human subjects and English language. Data extraction and qualitative synthesis of the demographics, clinical presentations, treatments, and outcomes were performed. Quality assessment was performed using the Joanna-Briggs Institute critical appraisal tools.

Results: A total of 37 articles collectively describing the cases of 54 patients were included. The mean age was 48.2 years (6-78 years). 53.7% of patients were male and 46.3% were female. The onset of articular symptoms varied considerably, and the majority of cases were described as polyarticular (29). The classification of inflammatory arthritis in the included studies was as follows: reactive (19), post-viral (13), new-onset rheumatoid arthritis (RA) (8), crystal-proven arthropathy flare (4), acute viral (2), new-onset psoriatic arthritis (2), flare of preexisting RA (2), and other (4). Arthritis treatment regimens varied but consisted largely of NSAIDs and corticosteroids with most patients experiencing improvement or resolution of their joint symptoms.

Conclusion: There is limited low-level evidence suggesting that patients may develop acute arthritis during or after SARS-CoV-2 infection. This review highlights the need for further research to elucidate the relationship between COVID-19 and the development of inflammatory arthritis.

Introduction

As of early 2022, over 392 million individuals have been infected with SARS-CoV-2 globally.\textsuperscript{1} In light of the widespread impact of COVID-19, it is critically necessary to elucidate atypical presentations and long-term sequelae of this viral infection. Many viruses, including SARS-CoV-2, have been associated with rheumatological and autoimmune manifestations; these manifestations include acute inflammatory arthritis. There have been various associations between infectious processes and inflammatory arthritis described in the medical literature. Most notably, several pathogens, including Chlamydia trachomatis, Salmonella, Shigella, Yersinia, and Campylobacter, are known to trigger reactive arthritis, which typically presents within 2 to 4 weeks of the preceding infection as an acute asymmetric oligoarthritis involving the larger joints.\textsuperscript{2} Although more commonly associated with gastrointestinal and sexually-transmitted infections, there have been reports of reactive arthritis triggered by respiratory infections as well.\textsuperscript{3} It is also important to note that several viruses, such as parovirus B19, hepatitis B and C, chikungunya, and Epstein-Barr virus are associated with acute viral arthritis or post-infectious arthritis, which typically manifests as an acute onset polyarthritis.\textsuperscript{4} Moreover, there is also considerable literature, indicating that viruses are a major trigger of autoimmunity via various immune pathways.\textsuperscript{5,6} For example, Joo et al.\textsuperscript{6} reported that ambient respiratory viral infections, including other coronaviruses, are associated with an increased number of incident rheumatoid arthritis (RA) cases.

Therefore, it is imperative that clinicians have an awareness of the potential association between COVID-19 infection and acute inflammatory arthritis as such clinical presentations may become more prevalent over time given the increasing number of individuals who have contracted the SARS-CoV-2 virus to date and are, therefore, susceptible to developing rheumatological and autoimmune sequelae related to their prior COVID-19 infection at some point in the future. The purpose of this study was to identify and summarize all clinical reports of acute inflammatory arthritis associated with COVID-19.
COVID-19 and Inflammatory Arthritis

Key messages
- Several cases of acute arthritis during/after COVID-19 disease have been reported.
- Many of these cases were classified as reactive arthritis or post-viral arthritis.
- The included studies were low-level evidence (e.g. case reports, case series).
- Further research on the relationship between COVID-19 and acute arthritis is warranted.

Methods

Search strategy
The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was used in identification and selection of studies for this review.7 Two separate comprehensive literature searches of the PubMed (MEDLINE), Google Scholar, and Cochrane Central databases from inception through January 31, 2022 were performed in February 2021 and February 2022 to identify all clinical reports of inflammatory arthritis associated with SARS-CoV-2 infection. Various combinations of the following keywords were used in the search strategy: inflammatory arthritis, post-viral arthritis, reactive arthritis, acute arthritis, COVID-19, SARS-CoV-2, and novel coronavirus; no filters or limits were used in the search. Once the database search was complete, duplicates were removed, and the titles and abstracts of the remaining articles were screened by two independent reviewers. All clinical reports of human subjects in the English language were included in this review. Review articles, animal studies, cadaveric or otherwise in vitro studies, and non-English articles were excluded. Articles that met the inclusion criteria underwent full-text review by two independent reviewers. The references of all selected studies were reviewed to minimize exclusion of relevant studies. Any discrepancies in study selection were to be reviewed by a third more senior author to obtain consensus.

Data extraction and synthesis
Data extraction was performed by two independent reviewers using a standardized Microsoft Excel spreadsheet. Clinically relevant data were extracted from the selected articles and synthesized. When available, the following data were recorded: demographics (e.g. age, sex, and race), COVID-19 infection (e.g. testing, severity, and treatment), arthritis clinical manifestations (e.g. symptom onset in relation to acute COVID-19 infection, rheumatologic localization, associated findings, and arthritis classification), comorbidities, diagnostic evaluation (e.g. imaging findings and biomarkers), treatment rendered (e.g. topical/oral medications and injections), and clinical outcomes (e.g. symptom resolution and recovery). Due to heterogeneity of the clinical data points reported in the included clinical reports and the limited number of patients, meta-analysis was not performed. Therefore, the extracted data were synthesized qualitatively, and descriptive statistics were calculated to report demographics (e.g. age and sex) and clinical findings in aggregate using Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA). The data underlying this article are available within the article. A PRISMA checklist for this systematic review is available in the online supplementary material.

Quality assessment
Quality of the included studies was assessed using the Joanna-Briggs Institute (JBI) critical appraisal tools for case reports and case series.8 However, no predetermined cut-off scores were established for inclusion of studies as it was anticipated that a limited number of eligible clinical reports would be available for review in the peer-reviewed literature at the time of this review given that SARS-CoV-2 is a relatively novel virus.

Results

Study characteristics
Two systematic searches of the PubMed (MEDLINE), Google Scholar, and Cochrane Central databases yielded a total of 680 articles; 37 of these articles met our inclusion criteria and were, therefore, included for further review.5–45 A PRISMA flow diagram delineating our database search results and rationale for exclusion of articles is presented in Figure 1. Collectively, the 37 studies (30 case reports, 7 case series) described the cases of a total of 54 patients who developed inflammatory arthritis during acute COVID-19 infection or following COVID-19 infection. The mean JBI score for the included case reports was 6.8 (0.5) out of 8. The mean JBI score for the included case series studies was 5.4 (1.3) out of 10. Most articles originated from Italy (8) followed by Japan (4) Iran (3) and the USA (3). Details for each reported case are delineated in Table 1.

Patient demographics
The percentage of males and females were 53.7% (n = 29) and 46.3% (n = 25), respectively. The mean age for patients was 48.2 years (6–78 years); exact age was not reported for two cases.18,34 Only 9 of the included studies explicitly stated the patient’s race or ethnicity as noted in Table 1. The overwhelming majority of patients did not have a personal history of preexisting joint symptoms or autoimmune disease. Pertinent comorbidities included preexisting RA in one of the cases described by Alivernini et al.9 as well as one of the cases described by Derksen et al.,17 gout with recurrent acute arthritis in three of the cases described by Lopez-Gonzalez et al.,30 gout in each of the cases described by Ouedraogo et al.33 and Shimoyama et al.,40 unspecified recurrent acute arthritis in one of the cases described by Lopez-Gonzalez et al.,29 remote history of septic arthritis in one of the cases described by Sinaei et al.,42 chronic intermittent monoarticular joint pain in the case described by Kuschner et al.,37 sarcoidosis in one of the cases described by Derksen et al.,17 and autoimmune hypothyroidism in two cases described by Colatutto et al.14 A comprehensive list of the comorbidities reported for each
A positive family history of autoimmune disease was reported in two cases; Talarico et al.'s case had a family history of ankylosing spondylitis, and Novelli et al.'s case had a family history of psoriasis.

COVID-19 disease course
Patients in the included studies were confirmed to have active or prior SARS-CoV-2 infection either via real-time polymerase chain reaction (RT-PCR) or serology. In terms of disease severity, 35 cases were described as being mild or moderate, 16 cases were described as either moderate-to-severe or severe, and 3 cases did not have sufficient details to ascertain COVID-19 disease severity. Treatment for acute COVID-19 infection varied considerably with the most common pharmacological treatment being antibiotics \( n = 17 \) followed by hydroxychloroquine \( n = 13 \). The need for supplemental oxygen/mechanical ventilation was reported in 6 cases. The specific COVID-19 treatment regimens reported for each case are detailed in Table 1. Of note, specific details on COVID-19 treatment regimens were not reported for 24 of the included cases.

Clinical Manifestations of Acute Arthritis
The classification of acute inflammatory arthritis in the included studies was as follows: reactive (19), post-viral (13), new-onset RA (8) crystal-proven arthropathy flare (4), acute viral (2), new-onset psoriatic arthritis (2), flare of preexisting RA (2), and other (4). Figure 2 illustrates the classifications of arthritis for cases included in this review. Onset of articular symptoms ranged from 6 weeks prior to acute COVID-19 infection to 3.5 months following acute COVID-19 infection with the mean onset being approximately 4 weeks after acute COVID-19 symptom onset. The cases varied considerably in terms of rheumatologic localization with most cases being described as polyarticular \( n = 29 \) followed by monoarticular \( n = 12 \), oligoarticular \( n = 8 \), axial \( n = 3 \), and oligoarticular/axial \( n = 1 \). One case did not provide sufficient details on rheumatologic localization. There was considerable variability in terms of the joints involved as detailed in Table 2. Associated cutaneous findings were reported in six cases and included maculopapular rash, urticaria, lesions consistent with psoriasis, palpable purpura, pruritic clearly demarcated erythematous scaly patches, and leukoderma with an associated unspecified rash. The diagnostic work-up varied across cases with most authors reporting results of one or more inflammatory markers and auto-antibody panels. However, arthrocentesis with synovial fluid analysis was only reported for 19 cases. In addition, imaging findings were reported for 35 cases with the most frequently reported findings being consistent with non-specific inflammation, including joint effusion, synovial tissue thickening, and increased vascularity. Detailed biomarker and imaging findings are outlined in Table 2.

Treatment and outcomes of acute arthritis
The majority of cases were treated with non-steroidal anti-inflammatory agents (NSAIDs) and/or systemic corticosteroids. Disease-modifying antirheumatic drugs (DMARDs),
| Primary author | Design (JBI score) | Country | Age | Sex | Race/ethnicity | Comorbidities | COVID-19 diagnosis | COVID-19 treatment | COVID-19 severity |
|----------------|-------------------|---------|-----|-----|---------------|--------------|------------------|--------------------|------------------|
| Alivernini²  | Case series (5)   | Italy   | 61  | M   | NR            | NR           | Nasal RT-PCR     | Lopinavir-Ritonavir, HCQ | Mild             |
| (Patient 1)    |        |         |     |     |               |              |                  |                    |                  |
| Alivernini²  | Case series (5)   | Italy   | 50  | F   | NR            | RA: (+) ACPA/RF in 2017; in sustained remission on Methotrexate 15 mg/wk (held during admission) | Nasal RT-PCR | Lopinavir-Ritonavir, HCQ, Ceftriaxone, Azithromycin | Severe           |
| (Patient 2)    |        |         |     |     |               |              |                  |                    |                  |
| Baimukhamedov¹⁰ | Case report (7)   | Kazakhstan | 67  | M   | NR            | NR           | RT-PCR          | Ceftriaxone, Azithromycin, Ibuprofen | Moderate         |
| Ben-Chetrit¹¹ | Case report (6)   | Israel  | 55  | F   | NR            | NR           | RT-PCR          | NR                 | Mild infection followed by asymptomatic re-infection 5 months later |
| Chandrashekara¹² (Patient 1) | Case series (4) | India | 66  | M   | NR            | NR           | NR               | NR                 | NR               |
| Chandrashekara¹² (Patient 2) | Case series (4) | India | 78  | M   | NR            | Diabetes mellitus, asthma | Serology         | NR                 | NR               |
| Chandrashekara¹² (Patient 3) | Case series (4) | India | 31  | F   | NR            | Serology      | Unspecified antipyretics and antibiotics | Mild             |
| Chandrashekara¹² (Patient 4) | Case series (4) | India | 39  | F   | NR            | Serology      | NR               | Mild             |
| Coath¹³       | Case report (7)   | United Kingdom | 53  | M   | Lumbar disc herniation in mid-20s with resulting radiculopathy and foot drop s/p discectomy (successful management), hyperlipidemia | Serology       | NR               | Mild             |
| Colatutto¹⁴ (Patient 1) | Case series (5) | Italy | 58  | F   | NR            | Autoimmune hypothyroidism | Nasal RT-PCR     | HCQ, Azithromycin | Mild             |
| Colatutto¹⁴ (Patient 2) | Case series (5) | Italy | 53  | F   | NR            | Autoimmune hypothyroidism | Nasal RT-PCR     | HCQ, Azithromycin | Mild             |
| Crivelenti¹¹ | Case report (7)   | Brazil  | 11  | F   | Brazilian     | NR           | Serology         | Human immunoglobulin, aspirin | Severe (complicated by MIS-C) |
| Dansaer⁶⁶    | Case report (7)   | USA     | 37  | F   | NR            | Congestive heart failure, asthma, GERD, morbid obesity s/p bariatric surgery | Positive unspecified test | NR                 | Mild             |
| Derksen⁷ (Patient 1) | Case series (5) | Netherlands | 67  | M   | NR            | NR           | Positive unspecified test | NR                 | Moderate-to-severe |
| Derksen⁷ (Patient 2) | Case series (5) | Netherlands | 49  | M   | NR            | Preexisting RA previously in remission for 5 years | Positive unspecified test | NR                 | Moderate-to-severe |
| Derksen⁷ (Patient 3) | Case series (5) | Netherlands | 70  | F   | NR            | Sarcoidosis   | Positive unspecified test | NR                 | Moderate-to-severe |
| Derksen⁷ (Patient 4) | Case series (5) | Netherlands | 67  | F   | NR            | Positive unspecified test | NR                 | Moderate-to-severe |
| Derksen⁷ (Patient 5) | Case series (5) | Netherlands | 65  | M   | NR            | Positive unspecified test | NR                 | Moderate-to-severe |
| Primary author | Design (JBI score) | Country | Age | sex | Race/ethnicity | Comorbidities | COVID-19 diagnosis | COVID-19 treatment | COVID-19 severity |
|---------------|-------------------|---------|-----|-----|----------------|---------------|-------------------|-------------------|-----------------|
| De Stefano18   | Case report (6)    | Italy   | 30sM| NR  | NR             | NR            | Nasal RT-PCR     | Supportive care   | Mild            |
| Di Carlo19     | Case report (7)    | Italy   | 55M | NR  | NR             | None          | Nasal RT-PCR     | NR                | Mild            |
| Drosos20       | Case report (7)    | Greece  | 46  | F   | NR             | NR            | RT-PCR           | Supportive care (paracetamol) | Mild            |
| Fragata21      | Case report (7)    | Portugal| 41F | NR  | NR             | NR            | Nasal/Oropharyngeal RT-PCR | Supportive care | Mild            |
| Gasparotto22   | Case report (7)    | Italy   | 60  | M   | Caucasian      | None          | Nasal RT-PCR     | HCQ, Ceftriaxone, Azithromycin, anticoagulation prophylaxis, mechanical ventilation | Severe          |
| Hønge23        | Case report (7)    | Denmark | 53  | M   | NR             | None          | Oropharyngeal RT-PCR | Remdesivir, Dexamethasone, supplemental oxygen | Severe          |
| Houshmand24    | Case report (7)    | Iran    | 10M | NR  | NR             | NR            | Nasal/Oropharyngeal RT-PCR | Acetaminophen, Cefixime, Cetirizine, Desloratadine, Hydroxyzine | Mild            |
| Jal25          | Case report (7)    | Saudi Arabia | 39F | F   | Saudi Arabian | NR            | Nasal RT-PCR     | NR                | Mild            |
| Kocyigit26     | Case report (7)    | Turkey  | 53  | F   | Hypertension   | NR            | Nasal RT-PCR     | HCQ, Favipiravir, Azithromycin, anticoagulant, supplemental oxygen | Moderate         |
| Kuschner27     | Case report (6)    | USA     | 73  | M   | Hypertension; chronic, intermittent right wrist pain | Positive unspecified test | Nasal/Oropharyngeal RT-PCR | HCQ | Mild          |
| Liew28         | Case report (7)    | Singapore | 47M | Indian | NR         | Nasal/Oropharyngeal RT-PCR | HCQ | Mild          |
| Lopez-Gonzalez29 (Patient 1) | Case series (8)  | Spain   | 71M | NR  | Gout (on Allopurinol), recurrent acute arthritis | Nasal RT-PCR | HCQ | Severe         |
| Lopez-Gonzalez29 (Patient 2) | Case series (8)  | Spain   | 61M | NR  | Gout (on Allopurinol), recurrent acute arthritis | Nasal RT-PCR | HCQ, Azithromycin, Tocilizumab, Methylprednisolone | Severe          |
| Lopez-Gonzalez29 (Patient 3) | Case series (8)  | Spain   | 64M | NR  | Recurrent acute arthritis (no prior work-up or treatment) | Nasal RT-PCR | HCQ, Azithromycin, Lopinavir-Ritonavir, Tocilizumab | Severe          |
| Lopez-Gonzalez29 (Patient 4) | Case series (8)  | Spain   | 45M | NR  | Gout (on Allopurinol; held during admission), recurrent acute arthritis | Serology | HCQ, Tocilizumab, Methylprednisolone | Severe          |
| Mukarram30     | Case series (5)    | Pakistan | 65  | F   | Hypertension   | NR            | Self-reported     | NR | Mild            |
| Mukarram30     | Case series (5)    | Pakistan | 35  | M   | None          | NR            | Self-reported     | NR | Mild            |
### Table 1. Continued

| Primary author | Design (JBI score) | Country | Age sex | Race/ethnicity | Comorbidities | COVID-19 diagnosis | COVID-19 treatment | COVID-19 severity |
|----------------|--------------------|---------|---------|---------------|---------------|--------------------|-------------------|-----------------|
| Mukarram<sup>31</sup> (Patient 3) | Case series (5) | Pakistan | 25 F | NR | None | Self-reported | NR | Mild |
| Mukarram<sup>31</sup> (Patient 4) | Case series (5) | Pakistan | 32 F | NR | None | Self-reported | NR | Mild |
| Mukarram<sup>31</sup> (Patient 5) | Case series (5) | Pakistan | 40 M | NR | Diabetes mellitus | Self-reported | NR | Mild |
| Neves<sup>31</sup> | Case report (7) | Portugal | 28 M | NR | None | RT-PCR | Mechanical ventilation, Amoxicillin | Severe |
| Novelli<sup>32</sup> | Case report (6) | Italy | 27 F | NR | Irritable bowel disease (family history of psoriasis) | Serology | NR | Mild |
| Ohmura<sup>33</sup> | Case report (6) | Japan | 42 F | NR | Diabetes mellitus | RT-PCR | NR | Moderate |
| Ono<sup>34</sup> | Case report (7) | Japan | 50sM | NR | Steatohepatitis | Nasal RT-PCR | Favipiravir, Cefepime, Vancomycin; mechanical ventilation | Severe |
| Ouedraogo<sup>15</sup> | Case report (7) | USA | 45 M | Black | Chronic low back pain post spinal fusion; isolated episode of crystalline (<) podagra 12 years prior | Nasal RT-PCR | HCQ, Tocilizumab, Ceftriaxone, Azithromycin, mechanical ventilation, ECMO, hemodialysis | Severe |
| Parisi<sup>36</sup> | Case report (7) | Italy | 58F | White | NR | Nasal RT-PCR | Paracetamol | Mild |
| Perrot<sup>27</sup> | Case report (7) | France | 60F | NR | None | RT-PCR | HCQ, Azithromycin, Zinc Gluconate | Mild |
| Saricaoglu<sup>38</sup> | Case report (7) | Turkey | 73M | NR | Diabetes mellitus, hypertension, coronary artery disease | Nasal/Oropharyngeal RT-PCR | HCP, Ceftriaxone, Azithromycin, Enoxaparin | Moderate |
| Schenker<sup>39</sup> | Case report (7) | Germany | 65F | Caucasian | NR | Serology | NR | NR | Mild |
| Shimoyama<sup>40</sup> | Case report (7) | Japan | 37 M | NR | Gout, right ankle fracture | Nasal RT-PCR | Supportive care | Mild |
| Shokraee<sup>41</sup> | Case report (7) | Iran | 58 F | Iranian | Hypertension, coronary artery disease, diabetes mellitus | Nasal RT-PCR | Interferon beta-1, Dexamethasone, Ceftriaxone, Enoxaparin, Nortriptyline | Moderate |
| Sinaei<sup>42</sup> (Patient 1) | Case series (6) | Iran | 8 M | NR | None | Serology | NR | Mild |
| Sinaei<sup>42</sup> (Patient 2) | Case series (6) | Iran | 6 F | NR | Hydronephrosis, right hip septic arthritis 3 years prior | RT-PCR, serology | NR | Mild |
| Sureja<sup>43</sup> | Case report (7) | India | 27 F | NR | NR | Nasal RT-PCR | Methylprednisolone, Favipiravir | Moderate |
| Talarico<sup>44</sup> | Case report (8) | Italy | 45 M | NR | None (family history of ankylosing spondylitis) | Nasal/Oropharyngeal RT-PCR | None | Mild |
| Yokogawa<sup>45</sup> | Case report (6) | Japan | 57 M | Japanese | Hypertension, hyperlipidemia | Nasal RT-PCR | Supportive care | Mild vs. moderate |

NR: not reported; RT-PCR: reverse transcription polymerase chain reaction; HCQ: hydroxychloroquine; ACPA: anti-cyclic citrullinated peptide antibody; RF: rheumatoid factor; GERD: gastroesophageal reflux disease; JBI: Joanna-Briggs Institute critical appraisal tools; MIS-C: multisystem inflammatory syndrome in children and adolescents.
most commonly Methotrexate, Hydroxychloroquine, and Leflunomide, were initiated in 13 cases, most of which were described as flares of preexisting rheumatic disease (e.g. RA, psoriatic arthritis) or consistent with new-onset rheumatic disease. Three patients with gout flares thought to be triggered by SARS-CoV-2 infection were treated with colchicine. Approximately 11% (n = 6) of patients underwent intra-articular corticosteroid injections with or without local anaesthetics. More invasive treatments were reported in two cases. Neves et al. inserted a drainage catheter in a patient presenting with presumed septic arthritis with intra-articular steroid injection. It is important to note that most reports lacked details regarding treatment duration. Of note, one patient had no treatment rendered for their arthritis symptoms and still experienced resolution of symptoms within 4 weeks following symptom onset. The majority of authors reported symptomatic improvement or complete resolution of symptoms following treatment; however, clinical outcomes were not reported for 14 of the included cases. Resolution of articular symptoms ranged from 4 days to 5 months following onset for the cases where time to resolution was reported. The reported arthritis treatment regimens and clinical outcomes are summarized in Table 2.

**DISCUSSION**

The present systematic review provides a detailed summary of clinical reports of inflammatory arthritis observed both during and after SARS-CoV-2 infection. At the time of our database search, the available relevant literature was low-level evidence consisting of case reports and case series studies with a limited number of cases. Many of these cases were classified as reactive arthritis, although there were cases of new-onset psoriatic arthritis and RA as well as flares of preexisting crystal-induced arthropathy and RA reported in the literature as well. Given the arthritis presentation is suspected to be reactive arthritis, it is reasonable to assume that the COVID-19 reactive arthritis variation shares similar pathophysiology to that of other pathogens known to cause reactive arthritis. Although the relationship between SARS-CoV-2 infection and inflammatory arthritis has yet to be fully elucidated, the mechanism may involve systemic pro-inflammatory markers, such as IL-6 and TNF-α, which are known to be released in both alveolar and joint inflammation. Moreover, an ecological study by Joo et al. reported an association between ambient coronavirus, parainfluenza, and metapneumovirus infections and an increased rate of incident RA cases thereby, suggesting that viral respiratory infections may play a role in precipitating the onset of RA.

In the included studies, there was a slight predominance of males versus females. Moreover, patients had a mean age of 48.2 years; however, it is important to note that this demographic finding may be confounded by older patients being more likely to require medical care during and after COVID-19 infection. The overwhelming majority of patients had no documented preexisting autoimmune conditions. However, it is unclear if patients with preexisting autoimmune disease and/or preexisting chronic joint disease are more susceptible to developing acute arthritis after being infected with SARS-CoV-2. Patients in the included clinical reports had variable COVID-19 disease courses, although most of them experienced
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|---------------------------|--------------------------|---------------------------|---------------------|------------|-------------------------------|-------------|----------------------|---------|
| Alivernini9 (patient 1) | Simultaneous onset | Unspecified new-onset polyarthritis | Polyarticular | NR | (-) ACPA/RF, ↑ CRP and cytokines | No crystals, H&E stromal activation, oedema, inflammation, and peri-vascular diffuse infiltrates | U/S: Joint effusion, ST thickness, increased vascularity | Etoricoxib (200 mg/d) for 4 days with worsening symptoms followed by Baricitinib (4 mg/d) and Prednisone (10 mg/d) | Progressive symptom improvement with ↓ CRP after 8 days of treatment |
| Alivernini9 (patient 2) | Unclear (after respiratory symptom onset, during acute COVID-19 infection) | Flare of RA previously in sustained remission | Polyarticular | NR | ↑ CRP and cytokines | U/S-guided ST biopsy: severe inflammation (infiltrates forming aggregates and few follicles) with ST thickening and fibrin exudates | U/S: Joint effusion, ST thickness, increased vascularity | IV Sarilumab (400 mg) | Significant symptom improvement and ↓ CRP and cytokines with remission achieved |
| Baimukhamedov10 | 5 weeks after acute COVID-19 infection onset | New-onset RA | Polyarticular | Early morning stiffness | (+) ACPA/RF; ↑ CRP and ESR | NR | NR | Methotrexate (15 mg/week) and Methylprednisolone (8 mg/d) | ↓ ESR and CRP after 1 month of treatment with remission achieved after 3 months of treatment |
| Ben-Chetrit11 | 2 months after initial acute COVID-19 infection onset | Palindromic rheumatism followed by new-onset RA diagnosis after re-infection | Polyarticular | Early morning stiffness | (+) anti-CCP, (-) RF; borderline ANA; ↑ CRP and ESR | NR | NR | HCQ followed by Prednisone and weekly Methotrexate | No improvement with HCQ; significant improvement after initiating Prednisone and Methotrexate |
| Chandrashekara12 (Patient 1) | Unclear (after acute COVID-19 infection) | Post-COVID hyperinflammatory syndrome | Polyarticular | Bilateral panuveitis, CRAO with retinitis and macular vasculitis, leukoderma/rash | (-) APLA, ANA, ANCA ↑ ferritin and D-dimer | NR | NR | Deflazacort 36 mg/d | Patient being followed at time of report |
| Chandrashekara12 (patient 2) | Unclear (after acute COVID-19 infection) | Post-COVID hyperinflammatory syndrome | Unspecified joints in BLE | Significant bilateral pedal edema | ↑ CRP, ESR, LDH, D-dimer, and ferritin | NR | NR | Celecoxib 200 mg BID | NR |
| Chandrashekara12 (patient 3) | 3 weeks after acute COVID-19 infection onset | Post-COVID-19 arthritis | Polyarticular (large and small joints of upper and lower limbs) | Early morning stiffness | ↑ ESR (-) RF, anti-CCP, and ANA | NR | NR | Celecoxib | Patient responded well to NSAIDs |
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|--------------------------|-------------------------|----------------------------|---------------------|------------|-------------------------------|-------------|----------------------|---------|
| Chandrashekara12 (patient 4) | 1.5 months after acute COVID-19 infection onset | Post-COVID-19 arthritis | Polyarticular (large and small joints predominantly affecting the feet) | NR | ↑ ESR, CRP, RF, anti-CCP, and ANA; (-) Chikungunya IgG | NR | NR | HCQ 200 mg BID, NSAIDs | NR |
| Coath13 | Unclear (after acute COVID-19 infection) | Axial reactive arthritis | Axial (lumbar, thoracic, cervical anterior) | NR | ↑ CRP (+) HLA-B27 | NR | MRI: bone marrow edema in bilateral SI joints, left 1st costovertebral and costotransverse joints Hybrid PET-CT: focal increased FDG uptake at same sites as bone marrow edema on MRI | MR: Methylprednisolone 120 mg, Diclofenac 75 mg/d | Symptom resolution at 3 months with undetectable CRP and repeat MRI demonstrating near complete resolution of prior inflammatory changes |
| Colatutto14 (patient 1) | 1 month after acute COVID-19 infection onset | Post-COVID-19 sacroiliitis | Axial (sacroiliac) | Polymya-lgia | (-) RE, ANA, anti-SSA/SSB, and HLA-B27; ↑ CPK and cytokines | NR | NIR | NSAIDs for 10 days and then as needed | Symptomatic improvement with mild residual low back pain; normalization of inflammatory markers |
| Colatutto14 (patient 2) | 1 month after acute COVID-19 infection onset | Post-COVID-19 sacroiliitis | Axial (sacroiliac) | Polymya-lgia | (-) RE, ANA, and anti-SSA/SSB; ↑ CRP and cytokines | NR | MRI: Unilateral sacroiliitis with bone marrow edema | NSAIDs as needed | Symptomatic improvement with residual low back pain; normalization of inflammatory markers |
| Crivelenti15 | 3 days after acute COVID-19 infection onset | Chronic SARS-CoV-2-related arthritis | Polyarticular (ankles, knees, elbows, wrists, and IP joints) | Maculo-papular rash | (-) ANA and RF; ↑ ESR, CRP, and D-dimer | NR | U/S: Synovial hypertrophy | Aspirin and 2 weeks of corticosteroids | Resolution of symptoms 5 months after onset with the exception of residual morning stiffness |
| Danssaert16 | 12 days after acute COVID-19 infection onset | Reactive arthritis | Monoarticular (right hand) | NR | ANA speckled; CRP, ESR, uric acid, and lactic acid WNL; (-) Lyme serology and RF; mild leukopenia and anaemia noted | NR | MRI: Inflammation around extensor tendons of 2nd, 3rd, & 4th compartments with mild synovial enhancement of tendon sheaths Doppler U/S: negative for DVT U/S: Inflammation of extensor and flexor tendons of right hand | Voltaren gel, Neurontin, Dilaudid PRN; wrist support for associated tendinitis Pain initially improved down to 2/10 from 10/10 in severity; at time of manuscript, patient was undergoing OT and prescribed Ultram for continued pain | |
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|--------------------------|-------------------------|---------------------------|-------------------|-----------|-------------------------------|-------------|-------------------|---------|
| Derksen\(^a\)  (patient 1) | 6 weeks prior to acute COVID-19 diagnosis | New-onset RA | Polyarticular (small and large joints; upper and lower extremities) | NR | ↑ ESR; CRP WNL; (+) ACPA | NR | NR | NR | NR |
| Derksen\(^a\)  (patient 2) | 6 weeks after acute COVID-19 diagnosis | New-onset RA | Polyarticular (small and large joints; upper and lower extremities) | NR | ↑ ESR, CRP; (+) ACPA | NR | NR | NR | NR | Patient died unexpectedly during hospitalization (unclear cause of death) |
| Derksen\(^a\)  (patient 3) | 6 weeks after acute COVID-19 diagnosis | Flare of preexisting RA previously in remission for 3 years | Polyarticular (small and large joints; upper and lower extremities) | NR | ↑ ESR, CRP; (–) ACPA | NR | NR | NR | NR |
| Derksen\(^a\)  (patient 4) | 14 weeks after acute COVID-19 diagnosis | New-onset RA | Polyarticular (small joints; upper and lower extremities) | NR | ↑ ESR, CRP; (–) ACPA | NR | NR | NR | NR |
| Derksen\(^a\)  (patient 5) | 3 days after acute COVID-19 diagnosis | New-onset RA | Polyarticular (small and large joints; upper and lower extremities) | NR | ↑ ESR; CRP WNL; (+) ACPA | NR | NR | NR | NR |
| De Stefano\(^b\) | 40 days after acute COVID-19 infection onset | Reactive arthritis | Monoarticular (right elbow) | 3 pruritic clearly demarcated erythematous scaly patches on extensor surface of bilateral elbows and groin | (-) ANA, RF, anti-CCP, HLA-B27, and HLA-C*06 | No crystals; (–) SARS-CoV-2 RNA | U/S: Findings consistent with synovitis | Oral NSAIDs, topical steroids | Complete resolution of skin and joint symptoms in 6 weeks |
| Di Carlo\(^b\) | 1 month after acute COVID-19 infection onset | Reactive arthritis | Monoarticular (right ankle) | NR | ↑ ESR and CRP, lymphopenia; (-) HLA-B27; (-) Ureaplasma urealyticum, Mycoplasma hominis and Chlamydia trachomatis in GU system; (-) enterobacteriaceae in stool sample & serology | NR | U/S: Subtalar joint synovitis and tenosynovitis of the posterior tibial tendon sheath | Methylprednisolone 4 mg/d | Asymptomatic with normalization of ESR and CRP |

\(^a\) Derksen, 2017
\(^b\) De Stefano, 2018
\(^b\) Di Carlo, 2019
### Table 2. Continued

| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|---------------------------|--------------------------|----------------------------|---------------------|------------|-------------------------------|-------------|---------------------|---------|
| Drosos         | 1 month after acute COVID-19 infection onset | New-onset seronegative erosive RA | Polyarticular (small joints of hands bilaterally) | Early morning stiffness; joint swelling | (-) RF, ACPA, and ANA; ↑ ESR and CRP | NR                  | X-ray: Erosions, joint space narrowing, soft tissue swelling | Methotrexate (15 mg/week), folic acid supplement, Prednisone 10 mg/d (tapered to 2.5 mg/d after 2 months) | Substantial clinical improvement with normal acute phase reactants 2 months after treatment initiation |
| Fragata        | 4 weeks after acute COVID-19 infection onset | Post-viral arthritis | Polyarticular (Right 3rd and 4th PIP joints; bilateral DIP and 1st MCP joints) | Early morning stiffness | (-) ANA, anti-dsDNA, RF, ACPA, ENAs, antibodies to echovirus, parvovirus b19, HIV 1 and 2, Hepatitis B and C; serum uric acid, ESR, and CRP | NR                  | X-ray: Erosions, joint space narrowing, soft tissue swelling | U/S: Erosive lesion | Oral NSAIDs (Ibuprofen 1200 mg/d), 5-day course of oral Prednisolone (5 mg/d) | Improvement in symptoms by day 5 of steroid course and complete resolution of symptoms 8 weeks after symptom onset |
| Gasparotto     | 4 weeks after acute COVID-19 infection onset | Post-COVID-19 arthritis | Oligoarticular (right ankle, knee, and hip) | Low-grade fever | (-) RF, ANA, and HLA-B27; ↑ CRP, ESR, D-dimer, fibrinogen, and Ferritin | No crystals; (-) SARS-CoV-2 RNA and culture; 20000/mm³ white blood cells | X-ray: No erosions or intraarticular calcifications | NSAIDs for ~4 weeks | ↓ CRP and complete resolution of symptoms at 6-month follow-up |
| Hønge          | 2 weeks after acute COVID-19 infection onset | Reactive arthritis | Oligoarticular (bilateral knees, right ankle, left foot) | Joint swelling | (-) RF, anti-CCP, ANA, HLA-B27, and HIV screening; ↑ CRP; mild leukocytosis | No crystals; (-) culture | X-ray: Fluid in joint space without evidence of arthritis | Piperacillin/tazobactam, oral NSAIDs, Prednisolone 2.5 mg/d for 6 days | ↓ CRP and resolution of symptoms 5 days after treatment initiation (sustained as of 4-month follow-up) |
| Houshmand      | 2 days after acute COVID-19 infection onset | Reactive arthritis | Oligoarticular (bilateral knees, right elbow) | Urticaria; early morning stiffness | (-) RF and ANA; ↑ ALP; D-dimer; C3, C4, CPK; and ferritin WNL; (-) urine and stool studies | Dry tap | X-ray right elbow: unremarkable | Acetaminophen, Cetirizine, Desloratadine, Hydroxyzine | Resolution of joint pain and urticaria 72 hours after initiating treatment (12 days following symptom onset) |
| Jali           | 3 weeks after acute COVID-19 infection onset | Reactive arthritis | Polyarticular (right 2nd/3rd PIP and 5th DIP joints; left 2nd PIP and 5th DIP joints) | NR | (-) RF, ANA, anti-CCP; hepatitis and HIV screenings; ESR and CRP WNL | NR | X-ray: Unremarkable | Celecoxib for 2 weeks | Complete resolution of symptoms after 2 weeks of treatment (sustained 2 months after discontinuation of NSAIDs) |
| Primary author       | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|---------------------|--------------------------|--------------------------|-----------------------------|---------------------|------------|-------------------------------|-------------|---------------------|---------|
| Kocyigit            | 6 weeks after acute COVID-19 infection | Reactive arthritis | Monoarticular (left knee) | Early morning stiffness, joint swelling, limited range of motion | ↑ ESR, CRP, and WBC; (−) RF, ANA, anti-CCP, HLA-B27; (−) urine and blood cultures | No crystals; mild inflammation; (−) culture | X-ray: unremarkable U/S; joint effusion | Diclofenac 150 mg/d (tapered after 6 weeks) | Completion resolution of symptoms and normalization of ESR/CRP following NSAID taper |
| Kuschner            | 2 weeks after acute COVID-19 infection onset | Reactive arthritis | Monoarticular (right wrist) | Joint swelling | ↑ ESR and CRP | No crystals; (−) gram stain and culture; (+) RT-PCR for SARS-CoV-2 | X-ray: diffuse degenerative changes | Ibuprofen without relief followed by 7-day course of Naproxen-sodium | Complete resolution of pain and swelling after 4 days of therapy |
| Liew                | 3 days after acute COVID-19 infection onset | Reactive arthritis | Monoarticular (right knee) | Painful glans penis with associated mild erythema and swelling | (−) HIV, syphilis, chlamydia, and gonorrhea | No crystals; (−) gram stain, gonococcal and chlamydia PCR, bacterial cultures, PCR and viral cultures for SARS-CoV-2 | X-ray: Right suprapatellar effusion with mild osteoarthritic changes and joint space narrowing | Etoricoxib, Intra-articular Triamcinolone (injected 1 week after NSAIDs due to effusion recurrence) | NR |
| Lopez-Gonzalez      | 8 days after acute COVID-19 infection onset | Acute arthritis due to crystal-proven flare (gout) | Monoarticular (1st MTP) | | | Monosodium urate crystals | | Intra-articular Triamcinolone with Mepivacaine, Colchicine | Flare successfully resolved |
| Lopez-Gonzalez      | 19 days after acute COVID-19 infection onset | Acute arthritis due to crystal-proven flare (gout) | Monoarticular (ankle) | | | Monosodium urate crystals; (−) RT-PCR for SARS-CoV-2 and culture | | Oral Prednisone, Colchicine | Flare successfully resolved |
| Lopez-Gonzalez      | 8 days after acute COVID-19 infection onset | Acute arthritis due to crystal-proven flare (caium pyrophosphate disease) | Oligoarticular (bilateral knees) | | | Calcium pyrophosphate crystals; (−) RT-PCR for SARS-CoV-2 and culture | | Intra-articular Triamcinolone with Mepivacaine | Flare successfully resolved |
| Lopez-Gonzalez      | 27 days after acute COVID-19 infection onset | Acute arthritis due to crystal-proven flare (gout) | Oligoarticular (knee and ankle) | | | Monosodium urate crystals; (−) RT-PCR for SARS-CoV-2 and culture | | Colchicine | Flare successfully resolved |
| Mukarram            | 8 weeks after acute COVID-19 infection | Post-COVID-19 inflammatory arthritis resembling RA | Polyarticular (symmetrical; wrists and PIP joints) | | | U/S: Synovitis involving wrists, MCP, and PIP joints; no bony erosions | | NSAIDs (temporary relief); Prednisone 10 mg/day taper, Etoricoxib, Leflunomide 20 mg/day, and HCQ 400 mg/day | NR |
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|--------------------------|--------------------------|---------------------------|--------------------|------------|-----------------------------|-------------|---------------------|---------|
| Mukarram (patient 2) | 6 weeks after acute COVID-19 infection | Post-COVID-19 inflammatory arthritis resembling RA | Polyarticular (symmetrical; wrists, MCP, and ankle joints) | Joint swelling | (-) RA and anti-CCP | U/S: Synovitis involving wrists, MCP, PIP, ankle, and MTP joints; no bony erosions | Prednisone 10 mg/day taper, Etoricoxib, Leflunomide 20 mg/day, and HCQ 400 mg/day | NR | NR |
| Mukarram (patient 3) | 8 weeks after acute COVID-19 infection | Post-COVID-19 inflammatory arthritis resembling RA | Polyarticular (symmetrical; wrists, MCP, ankles, and MTP joints) | Early morning stiffness | (-) RA and anti-CCP | U/S: Synovitis involving wrists, MCP, PIP, ankle, and MTP joints; bilateral Achilles tendonitis; no bony erosions | Prednisone 10 mg/day taper, Etoricoxib, Leflunomide 20 mg/day, and HCQ 400 mg/day | NR | NR |
| Mukarram (patient 4) | 10 weeks after acute COVID-19 infection | Post-COVID-19 inflammatory arthritis resembling RA | Polyarticular (symmetrical; wrists and MCP joints) | Early morning stiffness | (-) RA and anti-CCP | U/S: Synovitis involving wrists, MCP, and PIP joints; no bony erosions | Prednisone 10 mg/day taper, Etoricoxib, Leflunomide 20 mg/day, and HCQ 400 mg/day | NR | NR |
| Mukarram (patient 5) | 2 weeks after acute COVID-19 infection | Post-COVID-19 inflammatory arthritis resembling RA | Polyarticular (symmetrical; wrists and MCP joints) | Joint swelling | (-) RA and anti-CCP | U/S: Synovitis involving wrists and MCP joints; no bony erosions | Prednisone 10 mg/day taper, Etoricoxib, Leflunomide 20 mg/day, and HCQ 400 mg/day | NR | NR |
| Neves | 2 weeks after acute COVID-19 infection onset | Septic arthritis (presumed) | Oligoarticular (bilateral shoulders) | Soft tissue swelling; limited range of motion | ↑ CRP; (-) blood and urine cultures | CT: Scapulohumeral synovitis with multiple intra-muscular collections with glenohumeral joint continuity MRI: Infraspinatus and subscapular fossa collections with joint continuity | Gentamicin; drainage catheter insertion; physical therapy | Some improvement in range of motion following physical therapy |
| Novelli | Simultaneous onset | New-onset psoriatic arthritis triggered by SARS-CoV-2 infection | Axial/Oligoarticular (initially left ankle and left knee; followed by left knee, MTP joints, and bilateral SI joints 5 months later) | Single lesion in lumbar region resembling cutaneous psoriasis 3 months after acute infection | ↑ Inflammatory markers; (-) RF, anti-CCP, ANA, and HLA-B27 | (-) SARS-CoV-2 RNA; (+) anti-SARS-CoV-2 IgG | MRI Left Knee: arthritis, synovial effusion in subquadriacipital recess MRI Sacroiliac: Mild bilateral sacroiliitis | Intra-articular steroid injection | NR |
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|---------------|--------------------------|-------------------------|----------------------------|---------------------|------------|-------------------------------|-------------|----------------------|---------|
| Ohmura 33     | 5 weeks after acute COVID-19 infection onset | New-onset psoriatic arthritis triggered by SARS-CoV-2 infection | Polyarticular (bilateral hands, shoulders, knees, and feet) | Chronic skin lesions on hands (erythema with scale; biopsy consistent with psoriasis) | ↑ ESR and matrix metalloproteinase-3; (–) ANA, RF, ACPA, anti-SSA/SSB, anti-DNA, anti-Smith, anti-RNP, anti- aminoacyl-tRNA synthetase, HLA-B27; (–) Syphilis, Mycoplasma, Chlamydia pneumoniae, C. trachomatis, tuberculosis, parvovirus B19 | No crystals; (–) culture | X-ray: No erosive changes or entheseophytes | Celecoxib 400 mg/d for 4 weeks (failed); Prednisolone 30 mg/d (failed); Methotrexate (failed); combination of Certolizumab Pegol 400 mg every 2 weeks, Methotrexate, and Prednisolone (remission) | Remission achieved 12 weeks after initiation of combination treatment |
| Ono 34        | 21 days after acute COVID-19 infection onset | Reactive arthritis | Oligoarticular (bilateral ankles) | Mild enthesitis of right Achilles tendon | ↑ CRP and D-dimer (–) Syphilis, HIV, ASO, Mycoplasma, Chlamydia pneumoniae, Gonococcal & Chlamydia trachomatis (urine PCR), ANA, RF, anti-CCP, and HLA-B27 | No crystals; mild inflammation, (–) culture | X-ray ankle and feet: unremarkable | Intra-articular corticosteroid injection, NSAIDs | Moderate improvement |
| Ouedraogo 35  | 7 weeks after acute COVID-19 infection onset | Reactive arthritis | Polyarticular (bilateral shoulders, left elbow, left knee) | Joint, swelling, fever | ↑ ESR, CRP, WBC, and lactate; (–) blood and urine cultures; (–) RF, anti-CCP, EBV, Parvovirus B19 Enterovirus, CMV, Treponema pallidum, C. diff., HIV, Hepatitis B, Chlamydia, and Gonorrhea | No crystals; mild inflammation, (–) culture | X-ray Left Knee: Joint effusion and chondrocalcinosis | Oral Prednisolone; recurrence managed with second steroid taper and physical/occupational therapy | Significant improvement in pain and resolution of fever |
| Panisi 36     | 25 days after acute COVID-19 infection | Viral arthritis | Monoarticular (ankle) | NR | ↑ CRP, lymphopenia (–) ANA, anti-di DNA, RF, anti-CCP, and HLA-B27 | NR | U/S: Synovial hypertrophy in the tibiotarsal anterior and lateral recess, Achilles tendonitis | NSAIDs (Ibuprofen 600 mg BID) | Resolved |
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Arthritis treatment | Outcome |
|----------------|--------------------------|-------------------------|---------------------------|---------------------|------------|-------------------|---------|
| Perrot         | 37 days after acute COVID-19 infection | New-onset ACPA-positive RA, possibly triggered by SARS-CoV-2 infection | Polyarticular (right hand 5th MCP and IP joints; followed by spread to left hand 1st MCP and 2nd/3rd MCP joints 3–5 days later) | NR | X-ray Hands, Wrists, and Feet; US Duplex: Unremarkable | Methotrexate (10 mg/week) | Good clinical response |
| Sariclioglu     | 8 days after COVID-19 treatment | Reactive arthritis | Polyarticular | Joint swelling | CRP, ferritin, and D-dimer; (–) RF, ANA, and anti-CCP | NSAIDs | Complete resolution of symptoms and normalization of laboratory markers |
| Schmoerler      | 10 days after acute COVID-19 diagnosis | Reactive arthritis | Monarticular (right hip) | Joint swelling | CRP, ESR, HLA-B27, RF, ANA, anti-CCP, anti-CCP2, anti-CCP3, anti-SSB, anti-SSA, and anti-PAD2 and anti-PAD4 IgG | Prednisolone | Immediate regression of symptoms and CRP levels after steroid initiation |
| Shimoyama      | 6 days after acute COVID-19 diagnosis | Reactive arthritis | Monarticular (left hip) | Limited range of motion | CRP, ESR; (+) RF, ANA, and anti-CCP | NSAIDs (failed); intra-articular steroid injection (temporary relief followed by recurrence); arthroscopic synovectomy | Complete joint effusion, no recurrence post-operatively |
| Shokraee       | 2 weeks after acute COVID-19 diagnosis | Reactive arthritis | Monarticular (left hip) | Limited range of motion | CRP, ESR; (+) RF, ANA, and anti-CCP | NSAIDs (failed); intra-articular steroid injection (temporary relief followed by recurrence); arthroscopic synovectomy and BA | Dramatic improvement after treatment initiation with remission achieved after 14 days |

**Table 2.** Continued
| Primary author | Timing of arthritis onset | Arthritis classification | Rheumatologic localization | Associated findings | Biomarkers | Synovial fluid/tissue analysis | MSK imaging | Arthritis treatment | Outcome |
|----------------|--------------------------|--------------------------|----------------------------|---------------------|-----------|-----------------------------|------------|----------------------|---------|
| Sinaei[^2] (patient 2) | 1 week after acute COVID-19 infection onset | Reactive arthritis | Polyarticular (bilateral knees, wrists, and left hip) | Limited range of motion | ↑ CRP, ESR; (–) RF, ANA | NR | X-ray: Unremarkable | Ibuprofen 40 mg/kg/day | Recovery achieved with normalization of US findings 4 days after treatment initiation without recurrence at 45-day follow-up |
| Sureja[^3] | 2 weeks after acute COVID-19 symptom onset | Reactive arthritis | Polyarticular (knees, ankles, feet, right hand) | Joint swelling | (+) RF with low titers; (–) ACPA, ANA, and HLA-B27 | NR | NR | NSAI ds, Methylprednisolone (3-week taper), opioid analgesia | Significant improvement 4 weeks after treatment initiation |
| Talarico[^4] | 1 week prior to COVID-19 symptom exacerbation of arthritic symptoms 2 months after acute infection onset | Reactive arthritis versus chronic inflammatory process triggered by SARS-CoV-2 infection | Polyarticular (bilateral hands MCP and PIP joints) | NR | ↑ CPK and ESR; ↑; CRP WNL; (–) RF (+) anti-CCP | NR | U/S: Slight effusion of the right wrist, bilateral effusion of 5th PIP without synovial hyperplasia | Methylprednisolone (starting from 16 mg with progressive taper) | Complete resolution of articular symptoms during steroid course; slight exacerbation of arthralgia after discontinuing steroid taper at time of manuscript |
| Yokogawa[^5] | 17 days after acute COVID-19 infection onset | Viral arthritis | Oligoarticular (left wrist, right shoulder, bilateral knees) | NR | ↑ CRP; (–) ANA, RF, anti-CCP, hepatitis B surface antigen, anti-hepatitis C virus Ab, and HIV Ab | NR | None | Spontaneous resolution of articular symptoms on day 27 |

NR—not reported; ANA—antineutrophil cytoplasmic antibodies; ACPA/anti-CCP—anti-cyclic citrullinated peptide antibody; APLA—antiphospholipid antibody; ANCA—atypical neutrophil cytoplasmic antibodies; HLA—human leukocyte antigen; CRAO—central retinal artery occlusion; RF—rheumatoid factor; CRP—C-reactive protein; ESR—erythrocyte sedimentation rate; US—ultrasound; MRI—magnetic resonance imaging; WNL—within normal limits; NSAIDs—nonsteroidal anti-inflammatory drugs; ST—synovial tissue; OT—occupational therapy
mild-to-moderate COVID-19 infection. Treatment regimens ranged from supportive care alone to antivirals with or without adjunct antibiotics or hydroxychloroquine. The onset of arthritis symptoms in the reviewed cases varied considerably with the mean onset being approximately 4 weeks after COVID-19 symptoms began with the exception of cases that had preceding joint symptoms prior to other COVID-19 symptoms and those with an unspecified symptom onset. The rheumatologic localization for the majority of cases was polyarticular. There was considerable variability in terms of the joints involved. The variation in clinical presentations lead to the authors classifying COVID-19 associated arthritis in a number of different ways. Some authors termed the presentation ‘post-COVID hyperinflammatory syndrome’, whereas others diagnosed their patients with ‘post-COVID-19 arthritis.’ When the presentation of the arthritis symptoms manifested concurrently with COVID-19 symptoms, the authors often classified it as an unspecified new-onset polyarthritis. When the arthritis symptoms clearly started after the onset of COVID-19 symptoms and in most cases following resolution of COVID-19 symptoms, the authors diagnosed it as reactive arthritis or post-viral arthritis. Most of the cases included in this review were classified as either reactive arthritis or post-viral arthritis, although there were also several cases of new-onset RA thought to be triggered by COVID-19.

In terms of associated extra-articular findings, six patients had cutaneous findings, including maculopapular rash, urticaria, lesions consistent with psoriasis, palpable purpura, pruritic clearly demarcated erythematous scaly patches, and leukoderma with an associated unspecified rash. Interestingly, there were no cases of keratoderma blennorrhagicum, classically presenting as painless vesiculopustular waxy lesions localized to the palms/soles; this cutaneous finding is estimated to occur in approximately 5–30% of reactive arthritis cases.47 In a single case described by Liew et al.,28 a patient presented with pain localized to the glans penis with mild erythema and swelling. However, there were no cases of patients presenting with the classic triad of reactive arthritis formerly termed ‘Reiter’s syndrome’ (conjunctivitis, arthritis, and non-infectious urethritis), although it has been estimated that only up to one-third of patients with reactive arthritis present with all three classic findings.48 Of note, Santacruz et al.49 described an unusual case of reactive arthritis 2 months after acute COVID-19 infection presenting exclusively with extra-articular findings, including conjunctivitis, oral aphthous ulcers, palatal erosions, keratoderma blennorrhagicum, and vulvitis without evident arthritis.

Although the diagnostic work-up in these cases was quite variable, many authors used both normalization of ESR and CRP and symptomatic improvement to determine treatment efficacy. Among cases where synovial fluid analyses were performed, the predominant finding was lack of crystals with H&E showing stromal activation, oedema, inflammation, and perivascular diffuse infiltrates. Moreover, there were mixed findings for synovial fluid testing positive or negative for SARS-CoV-2 RNA or antibodies. Authors who elected to obtain imaging of the affected joints often reported findings suggestive of non-specific inflammation, including joint effusion, synovial tissue thickening, and increased vascularity.

The treatment rendered for arthritis symptoms, regardless of geographic or demographic characteristics, consisted largely of NSAIDs. Corticosteroids were a close second with a majority of patients receiving both NSAIDs and corticosteroids. Corticosteroids were administered topically, orally, intra-articularly, or intramuscularly. Given the limitations of the review, it is difficult to definitively say which route of administration was the most clinically effective. Regardless of the administration route, corticosteroids played a crucial role in many of the cases with some patients failing to experience any symptomatic improvement until steroids were initiated. DMARDs were initiated in 13 cases, most of which were described as either flares or new-onset of rheumatic disease (e.g. RA, psoriatic arthritis), with good clinical response noted in the majority of cases. Intraarticular corticosteroid injections were performed in approximately 11% of cases. More invasive treatment measures, including surgical intervention, were reported only in a minority of cases. Resolution of articular symptoms ranged from 4 days to 5 months following onset. However, not all authors reported time to symptom resolution and some patients were still being followed at the time of publication, thereby making it impossible to ascertain how many patients had refractory symptoms or long-term sequelae. It is worth noting that in the existing literature on reactive arthritis, it has been reported that most patients have a self-limited disease course, whereas 15–30% may go on to have chronic or refractory symptoms.30 Moreover, there have been reports of symptomatic improvement following initiation of DMARDs among patients with chronic symptoms, although it is important to note that use of DMARDs or biologics in cases of reactive arthritis refractory to steroids and NSAIDs may not lead to a good clinical response in all cases.51

Limitations
This systematic review is not without its limitations. First, given that SARS-CoV-2 is still a relatively novel virus, there were only a limited number of clinical reports examining the potential association between COVID-19 infection and the development of acute inflammatory arthritis published when this systematic review was performed. Second, the studies published in the available literature are considered low-level evidence given that most are clinical case reports. Third, given the nature and brevity of case reports, some of the included articles lacked clinically relevant information, which limited our qualitative data synthesis. Fourth, there appear to be discrepancies in the nomenclature and classification of arthritis cases used by the authors. It is also important to note that different SARS-CoV-2 variants may be associated with different clinical presentations of inflammatory arthritis. Finally, although substantial effort was made to ensure that all relevant studies published at the time of the database search were included in this review, it is still possible albeit unlikely that relevant eligible studies were excluded.

Conclusion
Given the widespread impact of the COVID-19 pandemic, it is imperative for clinicians to not only have an understanding of how this disease affects patients acutely but to be cognizant of its longer-term sequelae, including its potential role in the precipitation of autoimmune and rheumatologic conditions. While the available literature does not allow for determination of causal associations, there is limited low-level evidence suggesting that patients may develop inflammatory arthritis during and after SARS-CoV-2 infection. Therefore, in the era of COVID-19, clinicians should consider including...
this in their differential diagnosis for patients presenting with new-onset inflammatory arthritis during or after acute SARS-CoV-2 infection. Needless to say, the present systematic review highlights the paucity of research in this area and a need for the emergence of high-level evidence to fully elucidate the relationship between SARS-CoV-2 infection and the development of inflammatory arthritis.

Acknowledgments
N/A

Supplementary material
Supplementary material is available at Family Practice online.

Author contribution
All authors contributed to the design of this protocol. ZSC and NN initiated the project. The protocol was drafted by ZSC and was reviewed and refined by AS and CR. ZSC and NN performed the literature search, data collection, and qualitative synthesis. All authors contributed to interpretation of data. ZSC and NN were responsible for drafting the manuscript. All authors contributed intellectual content, revised the manuscript, and approved the final draft for submission. ZSC serves as the guarantor and corresponding author for this manuscript.

Funding
There are no funders to report for this submission.

Conflict of interest
None declared.

Data Availability
The data underlying this article are available in the article and/or in its online supplementary material.

Registration
N/A

Protocol
Not prepared.

Ethics approval
N/A—this study did not require IRB approval as it is a systematic review.

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