The Development or Exacerbation of an Autoimmune Disorder Associated with SARS-CoV-2 infection: a Systematic Review of Case Reports

Nuno Gonçalves (✉ nuno.mfg@hotmail.com)
University of Minho

Emídio Mata
University of Minho

Carlos Capela
University of Minho

Pedro Miguel Teixeira
University of Minho

Research Article

Keywords: Autoimmune diseases, Autoimmunity, Coronavirus Disease 2019, COVID 19, SARS CoV 2

DOI: https://doi.org/10.21203/rs.3.rs-344958/v1

License: ☕ ☀ This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Background: Infections have long been studied as environmental triggers of autoimmunity. Previous associations between coronavirus and autoimmune disorders make severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus identified in December 2019, a potential candidate for autoimmune disorder development. Indeed, an increasing number of these cases have been reported prompting a characterization and summarization of existing evidence.

Objectives: This review aims to characterize and summarize case reports documenting the development or exacerbation of an autoimmune disorders associated with SARS-CoV-2 infection.

Methods: A bibliographic search of Embase was performed from inception to July 2020. Studies included reported the development or exacerbation of an autoimmune disorder associated with SARS-CoV-2 infection. Quality was judge using Joanna Briggs Institute Critical Appraisal Checklist for Case Reports and piloted forms were used for data collection. Data were summarized using descriptive statistics and narrative synthesis.

Results: From 304 entries, 85 different cases were included, 41%-99% with good appraisal across quality domains. Sixty-two (72.9%) patients had no previous autoimmune disorder and 70 (82.4%) developed it De novo, the most frequent being Guillain–Barré syndrome and multisystem inflammatory syndrome in children. Eighteen (21.2%) cases of autoimmune disorders, mostly in remission, exacerbated. Organ-specific disease was found in 57 (67.1%) and systemic in 28. Disease affection was categorized into groups, the most frequent being neurological (36; 42.4%), vasculitis (19; 22.4%), blood (15; 17.6%), and connectivitis/systemic lupus erythematosus/antiphospholipid syndrome (6; 7.1%). The median coronavirus disease-2019 to De novo autoimmune disorder latency was 11 days (IQR = 5.75-16).

Conclusions: Although, as a systematic review of case reports, this study cannot verify causality, it provides support for further studies on the relationship between SARS-CoV-2 and autoimmune disorders. Furthermore, it delivers a characterization and summarization of existing reports making it a resource for clinicians to be aware of possible autoimmune disorder complications while taking care of their SARS-CoV-2 infected patients.

Background

Autoimmunity is an immune response directed against a self-antigen and its presence is a defining characteristic of an autoimmune disorder (AD). In the US, the estimated prevalence of ADs is 7.6–9.4% [1]. Infections are one of the most well-studied environmental triggers for autoimmunity [2-4], possibly through “molecular mimicry”, epitope spreading, “bystander activation”, and cryptic antigens processing and presentation [2]. Infections have also been associated with AD exacerbations, possibly via the same mechanisms [5].

In December 2019, a cluster of pneumonia cases was identified in Wuhan, China [6, 7], subsequently found to be caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [8, 9]. The infection is addresses as coronavirus disease 2019 (COVID-19) [10] and has already spread worldwide, leading to a global pandemic. Although most coronavirus infections are mild, two strains, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), have led to outbreaks and are associated with severe disease [11]. Infection by SARS-CoV-2 ranges from asymptomatic to critical condition and has already claimed millions of lives.

As SARS-CoV-2 infection has taken global proportions affecting a myriad of diverse patients, and has also been known to provoke hyperstimulation of the immune system through cytokine storm [12] and prolonged viral shedding [13], it is a potential candidate for AD association. Indeed, reports of ADs following COVID-19 have already been described (e.g. Kawasaki disease-like multisystem inflammatory syndrome in children (MIS-C)) [14, 15]. Additionally, SARS-CoV-2 forms a sister clave with SARS-CoV [9] (based on phylogeny, taxonomy, and established practice) which has cross-reaction with lung epithelial cells as a potential mechanism of pathogenesis [16, 17]. Moreover, MERS-CoV has also been associated with ADs such as Guillain-Barré syndrome (GBS) [18] and possibly immune thrombocytopenia [19]. Because of these findings and the increasing number of case reports, a characterization and summarization of existing evidence on the association of ADs and SARS-CoV-2 infection is necessary.

Although case reports cannot verify causality between the infection and ADs, it can identify unrecognized associations, generate hypotheses for subsequent studies and warn clinicians of possible complications. For these purposes, a systematic review of case
reports was performed documenting the development of an AD, related complications and autoimmune comorbidity exacerbation associated with the SARS-CoV-2 infection.

Methods

This systematic review followed the recommendations of the PRISMA statement [20].

Eligibility criteria

Studies were eligible when they reported a case of SARS-CoV-2 infection and the development of an AD, related complication, or exacerbation of a preexisting autoimmune comorbidity with a temporal relation with COVID-19. Studies with no explicitly stated SARS-CoV-2 infection diagnosis or with autoimmune comorbidities without exacerbations were excluded. The study designs considered eligible were any case report/series where the patient’s case information was provided separately. Studies where information about a case could not be distinguished from another were excluded.

Information sources and search

A bibliographic search was performed in Embase on 21/07/2020. The search strategy consisted of terms related to COVID-19 or SARS-CoV-2 AND AD (including autoimmunity-related terms and specific ADs) AND Case report or Case series. Each term was subsequently extended using synonyms and the subject headings functions of Embase (complete query in Additional file 1).

Study selection

Resulting entries were organized using EndNote X9.2. Duplicates were removed using the automated function. Title and abstract screening was carried out by two independent reviewers (NG and EM) and any entry which met eligibility criteria, where abstracts could not be obtained, or had insufficient information to access eligibility were considered for full-text review. Full text was then independently reviewed by the same two reviewers. A third researcher (CC) resolved disagreements. Publications not written in English or Portuguese were translated to English using Google Translate.

Data collection process and data items

A data extraction form was piloted with 15 random eligible entries. One reviewer (NG) extracted the data regarding studies’ characteristics (author, publication date, methodology, country, number of cases), participants’ characteristics (age, sex, comorbidities, AD comorbidities status and treatment), and cases characteristics (clinical features by area, COVID-19 confirmation test and treatment, laboratory, imaging, and other tests requested and findings, AD diagnosed and treatment, COVID-19 to AD latency, complications, hospitalization and intensive care unit (ICU) admission, patient outcome). Articles reporting on the same patient were counted as one case and combined to obtain more data.

Quality assessment

Quality was assessed independently by two reviewers (NG and EM) using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports [21]. Disagreements were resolved with a third researcher (CC). Each of the eight domains was given an answer of: yes (information present and clearly described), unclear (information present but not clearly described), no (information not present), and not applicable.

Data synthesis and analysis

A summary of the paper’s publication, authorship, study design, patient’s characteristics, and main findings was provided through detailed tables. The ADs retrieved for this review were diagnosis collected from the studies. When a diagnosis was not explicit, the
most probable cause was determined by reviewing the case's characteristics. A narrative synthesis was performed, and data were summarized using descriptive statistics: for categorical variables frequencies and percentages; for continuous variables means and standard deviations (SD), and medians and interquartile ranges (IQR) for skewed distributions (assessed with Shapiro–Wilk test).

**Results**

**Study selection**

The PRISMA flowchart details the selection process and the reasons for full-text exclusion (Figure 1). In summary, out of 304 entries 69 regarding 85 cases were considered eligible. Two articles reporting on the same patient were merged and therefore counted together.

**Study characteristics**

Main case characteristics are summarized in Table 1 and Additional file 2 and 3. Studies comprised 6 case series and 63 case reports published from January to June 2020, spanning 15 countries.

**Quality appraisal**

Good appraisal ranged from 41% to 99% across quality domains (Figure 2). Although most cases clearly reported the patient's demographic characteristics, current clinical condition, diagnostic tests and methods, and summarized takeaway lessons, they lacked key elements of good reporting: intervention or treatment protocols, post-intervention clinical condition, adverse or unanticipated events, and patient's history.

**Demographical characteristics and clinical findings**

General population and case characteristics are summarized in Table 2. The patients’ age did not follow a normal distribution with a greater number of older patients (median: 53 (32-63 IQR) years) and ranged from 5 to 83 years old. Forty-five patients were male and 40 female (Table 2). Comorbidities were present in 45 (64.7%) cases, the most common: hypertension (24/45), diabetes mellitus (11/45), cerebrovascular disease (5/45), obesity (4/45), and psoriasis (4/45).

Clinical findings are detailed in Additional file 3. Most patients developed respiratory (72; 84.7%), mostly persistent cough, and non-specific symptoms (68; 80.0%), mainly fever. Additionally, nervous (48; 56.5%), gastrointestinal (27; 31.8%), and skin (21; 24.7%) clinical findings were also among the most common.

**COVID-19-related characteristics**

Nasopharyngeal and/or oropharyngeal swab real-time reverse transcription polymerase chain reaction (rRT-PCR) was used in 78 patients yielding 12 negative results (later confirmed through Immunoglobulin G (IgG) antibody serum testing). One patient was diagnosed only by IgG antibody serum testing and in six it was not clear which confirmation test was used. Additionally, one had positive rRT-PCR on cerebrospinal fluid (CSF) for SARS-CoV-2.

Seventy-nine (92.9%) cases requested general laboratory measurements, 66 (77.6%) inflammatory markers, 46 (54.1%) hemostasis system parameters and 43 (50.6%) immunological markers. Overall, the most requested laboratory tests were complete blood count (75.3%), c-reactive protein (63.5%), d-dimers (45.9%), ferritin (34.1%) and lactate dehydrogenase (LDH) (32.9%). The most common findings were high c-reactive protein, lymphocytopenia, high d-dimers, thrombocytopenia, leukocytosis, high ferritin, high LDH and anemia (Table 2).

Bilateral disease on chest computerized tomography (CT) and x-ray was found in 57 (67.1%) patients, while unilateral disease in six (7.1%), and nine (10.6%) had normal results. The most common findings were bilateral ground-glass opacities, bilateral pulmonary infiltrates, and diffused consolidations (Table 2).
Twenty-six patients (30.6%) received no COVID-19 treatment. Among the remaining, hydroxychloroquine was the most common. Forty patients (47.1%) required supportive therapies: intubation (24; 28.2%), mechanical ventilator support (19; 22.4%) and high flow oxygen therapy (14; 16.5%). Antibiotics, mainly azithromycin, and antivirals, mostly lopinavir/ritonavir, favipiravir, and/or oseltamivir were also common. Some patients received other therapies, primarily comprising of anticoagulant and immunosuppressive therapies (mostly corticosteroids) (Table 2).

While 52 (61.2%) patients had no complication (other than AD), the remaining presented mostly cardiovascular complications (22/33) and secondary infection (10/33). Almost all cases (83; 97.6%) required hospitalization with 35 (41.2%) admitted to the ICU. Mean hospital stay was 16.76 (10.18 SD) days (information not available in 39 cases). Favorable outcome (recovery or hospital discharge) was reported in 55 cases (23 male; mean age: 46.61 years) and death in nine (8 male; mean age: 66.3 years) (Table 2).

**AD-related characteristics**

Sixty-two patients (72.9%) had no previous AD. Eighteen (21.2%), mostly in remission (13/18), experienced an exacerbation (the most frequent: psoriasis, myasthenia gravis, antiphospholipid syndrome (APS)/systemic lupus erythematosus (SLE), Crohn's disease, immune thrombocytopenic purpura (ITP), multiple sclerosis), while 70 (82.4%) developed *De novo* AD (three had *De novo* AD plus exacerbation) (Table 2). The most common were GBS, MIS-C, ITP, acute disseminated encephalomyelitis (ADEM), autoimmune meningoencephalitis, APS and autoimmune hemolytic anemia (AIHA). A total of 22 different ADs developed, while 12 distinct AD exacerbations were found.

ADs were categorized into organ-specific disease (57; 67.1%): neurological, blood, inflammatory bowel disease (IBD), skin, endocrinological, and ophthalmological; and systemic disease (28; 32.9%): vasculitis, connectivitis/SLE-APS, arthritis, endocrinological. Median COVID-19 to *De novo* AD latency was 12 (6-16 IQR) days (Table 2). Mean COVID-19 to AD exacerbation latency was 6.56 (8.14 SD) days.

**Organ-specific disease**

**Neurologic-related AD**

Median age was 54 (45.25-61.75 IQR), 16 were female and 30 had no previous AD. While four were exacerbations (two multiple sclerosis and two myasthenia gravis previously in remission), the majority were *De novo* ADs: GBS (14; 38.9%), ADEM (6; 16.7%), autoimmune meningoencephalitis (6; 16.7%), CNS vasculitis (2; 5.6%), anti-MOG associated encephalomyelitis (1; 2.8%), anti-NMDA receptor encephalitis (1; 2.8%), non-classified encephalitis (1; 2.8%), and oculomotor nerve palsy (1; 2.8%). Three subtypes of GBS were reported: four acute inflammatory demyelinating polyneuropathy, three acute motor and sensory axonal neuropathy, three acute motor and sensory axonal neuropathy, and three Miller-Fisher syndrome. Median COVID-19 to *De novo* AD latency was 12 (7-15 IQR) days (Table 2).

The most common laboratory finding was CSF high protein level: five cases with pleocytosis and five without. Five patients had high CSF IgG, one patient had positive anti-MOG antibody, another both anti-NMDA receptor and anti-cardiolipin antibodies, and another anti-ganglioside antibodies (Asialo GM1). Of 24 brain magnetic resonance imaging (MRI) requested, 12 were normal, with white matter lesions the most common feature found in the remainders. In 12, out of 14 cases with GBS, nerve conduction studies aided the diagnosis (Table 2).

Most patients received intravenous immunoglobulin (IVIG), corticosteroids, plasmapheresis, and plasma exchange, while 3 received no AD treatment. Four patients required supportive therapy (intubation and mechanical ventilator support) for GBS and myasthenia gravis exacerbation. Nevertheless, supportive therapy for COVID-19 was needed in 21. Mean hospitalization time was 19.2 (11.24 SD) days and death was reported in five (Table 2).

**Blood-related AD**

Median age was 53 (38-65 IQR), nine were female and 10 had no previous AD. Two had ITP exacerbations (previously in remission), and 13 experienced *De novo* ADs: ITP (8; 53.3%), AIHA (4; 26.7%) (one cold agglutinin disease and one warm agglutinin disease), and autoimmune thrombotic thrombocytopenic purpura (1; 6.7%). Median COVID-19 to *De novo* AD latency was 10 (6.25-15.75 IQR) days (Table 2).
The most common laboratory finding was thrombocytopenia and anemia. Other virus screens were negative (Epstein–Barr virus, hepatitis virus, Human Immunodeficiency Virus (HIV), Cytomegalovirus). Four patients had positive direct Coombs test, two with high cold agglutinin titers, one of these also with positive antinuclear antibodies (ANA). One case reported low ADAMTS-13 activity and positive ADAMTS-13 inhibitory antibodies, another antiplatelet antibodies, and another positive (albeit weak) anti-platelet factor 4/heparin antibodies. Two cases performed bone marrow aspirate, revealing normal cellularity with increased megakaryocyte count (Table 2). Chest and brain CT revealed two pulmonary embolism and two intracerebral hemorrhages.

All patients received AD treatment, the majority with corticosteroids, IVIG, platelet transfusions and red blood cell transfusions. For COVID-19, four required no treatment and only three required ICU admission. Mean hospitalization time was 19.85 (11.16 SD) days and one death was reported (Table 2).

**Other organ-specific ADs**

Three cases had an exacerbation of IBD: one ulcerative colitis (UC) and one Crohn's disease previously in remission, and one active Crohn's disease. The Crohn's disease patients also presented *De novo* IgA vasculitis and Kawasaki disease. Age ranged from 14 to 26 years old. The UC case was a pregnant woman with proctitis, Disease Activity Index score of 3, and active chronic inflammation on biopsies, treated with methylprednisolone and cyclosporine, and ultimately undergoing spontaneous abortion. Abdominal CT and MRI enterography found ileitis in both Crohn's disease cases. One (previously in remission) also had perianal abscess and fistula requiring drainage, antibiotics, and infliximab, while the other received the regular adalimumab treatment (Table 1).

Concerning skin-related ADs, two exacerbations of psoriasis (one in remission) and one *De novo* livedo reticularis were reported. The psoriasis cases occurred in a 73-year-old male 14 days after COVID-19 onset, and in a 71-year-old female 4 days after, neither receiving AD treatment. The *livedo reticularis* case occurred in a 57-year-old male with high d-dimers and positive ANAs, 8 days after COVID-19 onset, and treated with low-molecular-weight heparin (Table 1).

For endocrinological-related ADs, one diabetes mellitus type 1 exacerbation in the form of diabetic ketoacidosis, and one autoimmune hypothyroidism exacerbation was reported. The diabetic ketoacidosis case occurred in a 60-year-old male 5 days after COVID-19 onset, complicating with secondary bacterial infection and pulmonary embolism. He was treated with insulin and required ICU admission. The autoimmune hypothyroidism exacerbation received no treatment and occurred concurrent with *De novo* ITP in a 65-year-old female with elevated thyroid peroxidase antibodies, 11 days after COVID-19 onset (Table 1).

An ophthalmological-related AD befell an 11-year-old male with left retinal vasculitis on ocular *fundus* examination, negative autoimmune panel, and chilblains (Table 1).

**Systemic disease**

**Vasculitis-related AD**

Median age was 13 (9-36 IQR), eight were female, and 15 had no previous AD. One had an exacerbation of anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis in the form of glomerulonephritis and 18 experienced *De novo* ADs: MIS-C (11; 57.9%), cutaneous small-vessel vasculitis (2; 10.5%), multisystem inflammatory syndrome in adults (MIS-A) (1; 53%), Kawasaki disease (1; 53%), immunoglobulin A (IgA) vasculitis (1; 53%), non-classified vasculitis (1; 53%), and gallbladder vasculitis (1; 53%). Median COVID-19 to *De novo* AD latency was 5 (0-13 IQR) days (Table 2). When MIS-C and Kawasaki disease are not counted, median age was 59 (25-83 IQR), two out of seven were female, and median COVID-19 to *De novo* AD latency was 13 (7.5-37 IQR) days. As previously mentioned, two cases had, concurrent with *De novo* AD, an exacerbation of Crohn's disease. Gastrointestinal (15; 78.9%) (mostly abdominal pain) and skin (13; 68.4%) findings were common clinical findings. Nine (47.4%) patients had no complications while the remaining experienced mainly cardiogenic shock (8; 42.1%), and acute kidney injury (6; 31.6%).

Fourteen (73.7%) cases had hemostasis system-related findings: high d-dimers, fibrinogen, INR, and prothrombin time; 16 (84.2%) inflammatory markers: high c-reactive protein, procalcitonin, ferritin, lactate dehydrogenase, and erythrocyte sedimentation rate; 6 (31.6%) increased serum interleukin 6, interleukin 8, and/or tumor necrosis factor-α; and 11 (57.9%) liver markers: high alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transferase, direct hyperbilirubinemia, and hypoalbuminemia. Seven (36.8%) cases reported high troponins and one (5.3%) elevated myoglobin. The IgA vasculitis case had high complement C4
and serum IgA, and one cutaneous small-vessel vasculitis case had anti-cardiolipin antibodies. The ANCA-associated vasculitis exacerbation case was cytoplasmic-ANCA positive, and the MIS-A case presented positive ANAs, anti-Ro/SSA and low complement C3 and C4. From 14 heart ultrasounds requested, seven reported depressed left ventricular systolic function, five coronary artery dilatation, and three pericardial effusion. Abdominal CT exams showed bowel inflammation (ileitis and/or colitis) in four cases. Three patients underwent skin lesion biopsy, all yielding leukocytoclastic vasculitis as the major finding (Table 2).

Most patients received antibiotic prophylaxis, IVIG, corticosteroids, immunosuppressive therapy (tocilizumab, anakinra, or cyclophosphamide), and acetylsalicylic acid, while two received no AD treatment. Most patients required ICU admission with one Kawasaki disease, and seven MIS-C patients requiring rescue and supportive therapy for cardiogenic shock. Nevertheless, most required no COVID-19 treatment. Death was reported in two and mean hospitalization time was 14.92 (10.48 SD) days (Table 2).

**Connectivitis/SLE-APS-related AD**

Median age was 67 (50-69.25 IQR) and three were female. Four cases had no previous AD and developed *De novo* APS, and two had APS/SLE (previously in remission) and APS exacerbations. Median COVID-19 to *De novo* AD latency was 25.5 (12-45 IQR) days (Table 2).

The *De novo* APS cases had positive anti-beta-2-glycoprotein I and anti-cardiolipin antibodies, and high d-dimers, while three had high fibrinogen, prothrombin and partial thromboplastin time, and one high fibrin degradation products (Table 2). Patients had multiple cerebral (5; 83.3%) and bilateral cerebellar (3; 50.0%) infarctions on brain CT. On doppler ultrasound one patient had bilateral jugular venous thrombi. One *De novo* APS case complicated with index finger dry gangrene and another with two digits and lower limbs bilateral ischemia.

Three cases received AD treatment, one with acetylsalicylic acid, low-molecular-weight heparin and plasma exchange, and two with IVIG, one of which with eltrombopag, platelet transfusions and prednisone. Five required COVID-19 treatment, three with supportive therapy. Mean hospitalization time was 21.17 (18.76 SD) days with four ICU admissions and one reported death (APS exacerbation) (Table 2).

**Other systemic AD**

For Arthritis-related ADs, one ankylosing spondylitis exacerbation (previously in remission) and one *De novo* non-classified arthritis were reported. The ankylosing spondylitis case occurred in a 53-year-old female 22 days after COVID-19 onset with normal brain MRI and nerve conduction studies, and was treated with etanercept. The non-classified arthritis case occurred in a 57-year-old male 20 days after COVID-19 onset with negative ANAs, rheumatoid factor and anti-cyclic citrullinated peptide antibodies, and the synovial fluid was crystal-free on polarized microscopic examination (Table 1).

One endocrinological-related AD case, a 32-year-old female with autoimmune polyglandular syndrome type 1, presented with hypoparathyroidism exacerbation with low serum calcium, and was treated with calcitriol and calcium supplementation. She required ICU admission for COVID-19 (Table 1).

**Discussion**

This review describes 22 different *De novo* ADs and 12 distinct AD exacerbations associated with SARS-CoV-2 infection.

As AD cases in children (<18 years) have been reported following SARS-CoV-2 infection, most notably MIS-C [14, 15], one could argue the existence of more associations. In this regard, entry age was not restricted, and besides MIS-C and Kawasaki disease, AIHA and retinal vasculitis were also found. The reported higher prevalence of older patients, cardiovascular risk factor comorbidity, and cardiovascular disease could be explained by their added risk of severe COVID-19 and hospital admission [91, 92], in line with this review’s inpatient cohort. Contrary to the literature on AD gender differences [93], there were more males than females found (9:8).

COVID-19 was predominantly diagnosed through rRT-PCR, the present recommendation. Laboratory and radiologic findings were similar to those found in the literature [7, 91, 94]. Treatment was heterogeneous, reflecting the immaturity of the disease knowledge. Most were treated with hydroxychloroquine and antibiotics (predominantly azithromycin), the recommendation at the time. Additionally, similar to another review [94], a reduced number of patients received no treatment for COVID-19, and intubation,
mechanical ventilator support, and mortality were higher than the general population, suggesting greater disease severity, which, again, may relate to the number of hospitalizations in this cohort. Furthermore, more patients than expected required ICU admission which may be explained by the association of AD complications.

Most cases had no previous AD and, ultimately, all developed one, which supports the causal relationship hypothesis. Furthermore, most patients with AD comorbidity exacerbations were previously in remission.

The majority presented with neurological affection. Neurological complications have been common in COVID-19 [95-98]. The dissemination to the nervous system through the cribriform plate, olfactory bulb [99] and virus damaged capillary endothelium [100] have been hypothesized for such association. When referring to a neurological AD, other mechanisms such as the hyperinflammatory state leading to blood-brain barrier disruption, extensive tissue damage, and epitome exposure, could instead contribute to its development, as only one case reported positive CSF rRT-PCR for SARS-CoV-2 and specific antibody driven subtypes of autoimmune encephalitis were found: anti-MOG associated encephalomyelitis and anti-NMDA receptor encephalitis. The most common neurological AD found was GBS, which is a typical post respiratory or gastrointestinal infection disorder [101, 102]. Among other pathogens [101], MERS-CoV was associated with GBS [18]. The median COVID-19 to De novo AD latency of 12 days and mean hospitalization time of 19.2 days resembles the 1–2 weeks latency and the 2–4 weeks peak clinical deficit reported in the literature [101, 102]. Although the preceding pathogen infection is usually connected with one clinical phenotype [101], three subtypes were found. Another neurological AD found, ADEM, is already associated with viral infections. Although more common in pediatric age, all cases found were adults [103]. Though few patients required supportive therapy for neurological AD, downplaying its severity, it should be noted that many required it for COVID-19.

The majority of vasculitis found were MIS-C, a disorder similar to Kawasaki disease that has been connected with the rise of SARS-CoV-2 cases [15]. As Kawasaki disease presumably develops in genetically susceptible hosts after exposure to a trigger, suspected to be an upper respiratory tract infection [104], a similar mechanism could be occurring here. Although predominantly having mild COVID-19, most cases required ICU admission and eight children (with MIS-C and Kawasaki disease) develop cardiogenic shock.

The most common blood-related AD was ITP. As secondary ITP has been associated with cross-reaction with HIV antigens, creating autoantibodies and immune complexes [105-107], the same might occur with SARS-CoV-2. However, although not always present [108], out of eight ITP cases, only two rendered positive antiplatelet antibodies, and COVID-19 has been associated with thrombocytopenia, the degree of which related to the severity of SARS-CoV-2 infection [109].

In the final major group, APS, four anti-beta-2-glycoprotein I and anti-cardiolipin antibody positive patients complicated with multiple thrombotic events. Though antiphospholipid antibodies can be present in acute infections, they usually present with low levels and are not associated with thrombotic events [110]. Infections are also suspected triggers as they preceded APS in many cases [111, 112].

**Limitations**

Even though good appraisal in several quality domains was seen across studies, key elements of good reporting were lacking, and 21 cases did not report an outcome. Likewise, other reviews shared the same findings [94]. A possible explanation might be the urgency to publish new information, as COVID-19 is a recently identified disease. This, however, may lead to a lack of important information that could further the knowledge of possible associations with ADs. Nevertheless, all cases were included as a way to find the most possible number of associations.

Although numerous associations between infections and ADs are described, the acute state of infection and hyperinflammatory state which occurs with COVID-19 could mimic the immunological findings of an AD. Since the reported autoimmune manifestations might encompass the immunological component of the infection, caution is warranted when interpreting the results. Nevertheless, a high suspicion rating is always necessary when considering an AD diagnosis.

Furthermore, milder AD cases might not be represented due to publication bias as more severe cases are more likely to be published and diagnosed.
Although a thorough search was done, using an expansive search query to be as inclusive as possible, methodological limitations are still present. First, only one database was used and, even though this review provides a look at the first image of the COVID-19 pandemic, it may have missed studies that were published since the search date. Additionally, despite using piloted forms and training to minimize inaccuracies, only one reviewer performed data extraction.

Conclusions

This systematic review provides a characterization and summarization of AD cases associated with SARS-CoV-2 infection. There are some findings that may suggest the existence of this relationship and although this study as a review of case reports cannot verify causality, it supports further studies and provides a resource for clinicians to be aware of possible AD complications of SARS-CoV-2 infected patients.

Declarations

Availability of Supporting Data

The data set supporting the results of this article is included within the article (and its additional files).

Competing interests

None of the authors have any financial or non-financial competing interests to disclose.

Funding

None.

Author’s contributions

NG performed the screening, study selection, data collection, analysis, and interpretation, conceptualized and drafted the manuscript. EM performed screening and study selection, analyzed data, and contributed to the writing of the manuscript. CC aided in data analysis and interpretation and performed critical revision of the article. PMT contributed to conception and design of the work. All authors have reviewed and approved the manuscript for submission.

Abbreviations

AD: Autoimmune disorder; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; COVID-19: Coronavirus disease 2019; MERS-CoV: Middle East respiratory syndrome coronavirus; MIS-C: Multisystem inflammatory syndrome in children; GBS: Guillain-Barré syndrome; ICU: Intensive care unit; JBI: Joanna Briggs Institute; SD: Standard deviations; rRT-PCR: Real-time reverse transcription polymerase chain reaction; IgG: Immunoglobulin G; CSF: Cerebrospinal fluid; LDH: Lactate dehydrogenase; CT: Computerized tomography; APS: Antiphospholipid syndrome; SLE: Systemic lupus erythematosus; ITP: Immune thrombocytopenic purpura; ADEM: Acute disseminated encephalomyelitis; AIHA: Autoimmune hemolytic anemia; IBD: Inflammatory bowel disease; MRI: Magnetic resonance imaging; IVIG: Intravenous immunoglobulin; HIV: Human Immunodeficiency Virus; ANA: Antinuclear antibodies; UC: Ulcerative colitis; ANCA: Anti-neutrophil cytoplasmic antibodies; MIS-A: Multisystem inflammatory syndrome in adults; IgA: Immunoglobulin A

Bibliography

1. Cooper GS, Bynum ML, Somers EC. *Joa: Recent insights in the epidemiology of autoimmune diseases: improved prevalence estimates and understanding of clustering of diseases.* 2009, 33(3-4):197-207.

2. Ercolini A, Miller SDJC, Immunology E. *The role of infections in autoimmune disease.* 2009, 155(1):1-15.
3. Marrack P, Kappler J, Kotzin BL. *Autoimmune disease: why and where it occurs*. 2001, 7(8):899-905.

4. Wang L, Wang FS, Gershwin ME. *Human autoimmune diseases: a comprehensive update*. 2015, 278(4):369-395.

5. Kamradt T, Göggel R, Erb K. *Induction, exacerbation and inhibition of allergic and autoimmune diseases by infection*. 2005, 26(5):260-267.

6. Pneumonia of unknown cause—China. 2020 [https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/]

7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X. *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China*. 2020, 395(10223):497-506.

8. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R. *A novel coronavirus from patients with pneumonia in China*. 2020.

9. Viruses CS. GotICoTo: The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. 2020, 5(4):536.

10. Organization WH: Naming the coronavirus disease (COVID-19) and the virus that causes it. In.; 2020.

11. Su S, Wong G, Shi W, Liu J, Lai AC, Zhou J, Liu W, Bi Y, Gao GF. *Epidemiology, genetic recombination, and pathogenesis of coronaviruses*. 2016, 24(6):490-502.

12. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, Lancet HASC. *COVID-19: consider cytokine storm syndromes and immunosuppression*. 2020, 395(10229):1033.

13. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X. *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study*. 2020.

14. Jones VG, Mills M, Suarez D, Hogan CA, Yeh D, Segal JB, Mathew RJ. *COVID-19 and Kawasaki disease: novel virus and novel case*. 2020, 10(6):537-540.

15. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis PJ. *Hyperinflammatory shock in children during COVID-19 pandemic*. 2020, 395(10237):1607-1608.

16. Lin Y-S, Lin C, Fang Y, Kuo Y-M, Liao P-C, Yeh T-M, Hwa K, Shieh C, Yen J, Wang HJ. *Antibody to severe acute respiratory syndrome (SARS)-associated coronavirus spike protein domain 2 cross-reacts with lung epithelial cells and causes cytotoxicity*. 2005, 141(3):500-508.

17. Lo AW, Tang NL, To KF. *How the SARS coronavirus causes disease: host or organism?* 2006, 208(2):142-151.

18. Kim J-E, Heo J-H, Kim H-o, Song S-h, Park S-S, Park T-H, Ahn J-Y, Kim M-K, Choi J-P. *Neurological complications during treatment of middle east respiratory syndrome*. 2017, 13(3):227-233.

19. Arabi YM, Arifi AA, Balkhy HH, Najm H, Aldawood AS, Ghabashi A, Hwa H, Alothman A, Khalidi A, Al Raiy B. *Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus*. 2014, 160(6):389-397.

20. Moher D, Liberati A, Tetzlaff J, Altman DG. *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement*. 2009, 6(7):e100097.

21. Sedaghat Z, Karimi N. *Guillain Barre syndrome associated with COVID-19 infection: A case report*. *Journal of Clinical Neuroscience* 2020.

22. Chiu JS, Lahoud-Rahme M, Schaffer D, Cohen A, Samuels-Kalow M. *Kawasaki Disease Features and Myocarditis in a Patient with COVID-19*. *Pediatric Cardiology* 2020.

23. Allez M, Denis B, Bouaziz JD, Battistella M, Zagdanski AM, Bayart J, Lazaridou I, Gatey C, Pillebout E, Chaix Baudier ML. *Covid-19 related IgA vasculitis*. *Arthritis & rheumatology* (Hoboken, NJ) 2020.

24. Dolinger MT, Person H, Smith R, Jarchin L, Pittman N, Dubinsky MC, Lai J. *Pediatric Crohn's Disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 Treated with Infliximab*. *Journal of pediatric gastroenterology and nutrition* 2020.

25. Ottaviani D, Boso F, Tranquilli E, Gapeni I, Pedrotti G, Cozzio S, Guerrera GM, Giometto B. *Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital*. *Neurological Sciences* 2020, 41(6):1351-
27. Scheidl E, Canseco DD, Hadji-Naumov A, Berezniak B: **Guillain-Barré syndrome during SARS-CoV-2 pandemic: A case report and review of recent literature.** Journal of the Peripheral Nervous System 2020, 25(2):204-207.

28. Parsons T, Banks S, Bae C, Gelber J, Alahmadi H, Tichauer M: **COVID-19-associated acute disseminated encephalomyelitis (ADEM).** Journal of Neurology 2020.

29. Zanin L, Saraceno G, Panciani PP, Renisi G, Signorini L, Migliorati K, Fontanella MM: **SARS-CoV-2 can induce brain and spine demyelinating lesions.** Acta Neurochirurgica 2020, 162(7):1491-1494.

30. Hanafi R, Roger PA, Perin B, Kuchinski G, Develal N, Dallery F, Michel D, Hacein-Bey L, Pruvo JP, Outteryck O et al.: **COVID-19 Neurologic Complication with CNS Vasculitis-Like Pattern.** AJNR American journal of neuroradiology 2020.

31. Patil NR, Herc ES, Girgis M: **Cold agglutinin disease and autoimmune hemolytic anemia with pulmonary embolism as a presentation of COVID-19 infection.** Hematology/ Oncology and Stem Cell Therapy 2020.

32. Moeinzadeh F, Dezfooli M, Naimi A, Shahidi S, Moradi H: **Newly Diagnosed Glomerulonephritis During COVID-19 Infection Undergoing Immunosuppression Therapy, a Case Report.** Iranian journal of kidney diseases 2020, 14(3):239-242.

33. Farzi MA, Ayromlou H, Jahanbakhsh N, Bavil PH, Janzadeh A, Shayan FK: **Guillain-Barré syndrome in a patient infected with SARS-CoV-2, a case report.** Journal of Neuroimmunology 2020, 346.

34. Webb S, Wallace VC, Martin-Lopez D, Yogarajah M: **Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication.** BMJ case reports 2020, 13(6).

35. Lantos JE, Strauss SB, Lin E: **COVID-19-Associated Miller Fisher Syndrome: MRI Findings.** AJNR American journal of neuroradiology 2020, 41(7):1184-1186.

36. Manganotti P, Pesavento V, Buote Stella A, Bonzi L, Campagnolo E, Bellavita G, Fabris B, Luzzati R: **Miller Fisher syndrome diagnosis and treatment in a patient with SARS-CoV-2.** Journal of NeuroVirology 2020.

37. Virani A, Rabold E, Hanson T, Haag A, Elrufay R, Cheema T, Balaan M, Bhanot N: **Guillain-Barré Syndrome associated with SARS-CoV-2 infection.** IDCases 2020, 20.

38. Rana S, Lima AA, Chandra R, Valeriano J, Desai T, Freiberg W, Small G: **Novel Coronavirus (COVID-19)-Associated Guillain-Barré Syndrome: Case Report.** Journal of clinical neuromuscular disease 2020, 21(4):240-242.

39. Artru F, Alberio L, Moradpour D, Stalder G: **Acute immune thrombocytopaenic purpura in a patient with COVID-19 and decompensated cirrhosis.** BMJ case reports 2020, 13(7).

40. Yang Y, Zhao J, Wu J, Teng Y, Xia X: **A Rare Case of Immune Thrombocytopenic Purpura Secondary to COVID-19.** Journal of Medical Virology 2020.

41. Bomhof G, Mutsaers PGNJ, Leebeek FWG, te Boekhorst PAW, Hofland J, Croles FN, Jansen AJG: **COVID-19-associated immune thrombocytopenia.** British Journal of Haematology 2020.

42. Lévesque V, Millaire É, Corsilli D, Rioux-Massé B, Carrier FM: **Severe immune thrombocytopenic purpura in critical COVID-19.** International Journal of Hematology 2020.

43. Hayden A, Vyas-Lahar A, Rella V, Rudinskaya A: **Severe refractory thrombocytopenia in a woman positive for coronavirus disease 2019 with lupus and antiphospholipid syndrome.** Lupus 2020.

44. Quintana-Castanedo L, Feito-Rodriguez M, Fernández-Alcalde C, Granados-Fernández M, Montero-Vega D, Mayor-Ibarguren A, de Lucas-Laguna R: **Concurrent chilblains and retinal vasculitis in a child with COVID-19.** Journal of the European Academy of Dermatology and Venereology : JEADV 2020.

45. Mayor-Ibarguren A, Feito-Rodriguez M, Quintana Castanedo L, Ruiz-Bravo E, Montero Vega D, Herranz-Pinto P: **Cutaneous small vessel vasculitis secondary to COVID-19 Infection: A case report.** Journal of the European Academy of Dermatology and Venereology : JEADV 2020.

46. Negrini S, Guadagno A, Greco M, Parodi A, Burlando M: **An unusual case of bullous haemorrhagic vasculitis in a COVID-19 patient.** Journal of the European Academy of Dermatology and Venereology 2020.

47. Del Giudice P, Boudoumi D, Le Guen B, Reverte M, Gunnecht J, Lacour JP, Kraemer JP, Motard A, Roa M: **Catastrophic acute bilateral lower limbs necrosis associated with COVID-19 as a likely consequence of both vasculitis and coagulopathy.** Journal of the European Academy of Dermatology and Venereology : JEADV 2020.
Fisher syndrome after SARS-CoV-2 infection
Reyes-Bueno JA, García-Trujillo L, Urbaneja P, Ciano-Petersen NL, Postigo-Pozo MJ, Martínez-Tomás C, Serrano-Castro PJ: report and review of the literature

Oriot P, Hermans MP: prominent clinical pulmonary symptoms

Abdi S, Ghorbani A, Fatehi F: British Journal of Haematology

Lopez C, Kim J, Pandey A, Huang T, DeLoughery TG: response to corticosteroid-based therapy—a case report

Hu Z, Chen W, Liang W, Xu C, Sun W, Yi Y: reducing cytokine storm as a late complication of critically ill COVID-19

Ma J, Xia P, Zhou Y, Liu J, Chen S: the literature

Nesr G, Garnett C, Bailey C, Arami S: ITP flare with mild COVID-19 infection in pregnancy: a case report

Capes A, Bailly S, Hantson R, Gerard L, Laterre PF: COVID-19 infection associated with autoimmune hemolytic anemia. Annals of Hematology 2020, 99(7):1679-1680.

Barzegar M, Mirmosayyeb O, Neshat N, Sarrafi R, Khovash F, Maghzi AH, Shaygannejad V: COVID-19 infection in a patient with multiple sclerosis treated with fingolimod. Neurology(R) neuroimmunology & neuroinflammation 2020, 7(4).

Singh S, Govindarajan R: COVID-19 and generalized Myasthenia Gravis exacerbation: A case report. Clinical Neurology and Neurosurgery 2020, 196.

Zhao H, Shen D, Zhou H, Liu J, Chen S: Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? The Lancet Neurology 2020, 19(5):383-384.

Padroni M, Mastrangelo V, Asioli GM, Pavolucci L, Abu-Rumeileh S, Piscaglia MG, Querzani P, Callegarini C, Foschi M: Guillain-Barré syndrome following COVID-19: new infection, old complication? Journal of Neurology 2020, 267(7):1877-1879.

Alberti P, Beretta S, Piatti M, Karantzoulis A, Piatti ML, Santoro P, Viganò M, Giovannelli G, Pirro F, Montisano DA et al.: Guillain-Barré syndrome related to COVID-19 infection. Neurology: Neuroimmunology and NeuroInflammation 2020, 7(4).

Zulfiqar AA, Lorenzo-Villalba N, Hassler P, Andrès E: Immune thrombocytopenic purpura in a patient with covid-19. New England Journal of Medicine 2020, 382(18):E43.

Nesr G, Garnett C, Bailey C, Arami S: ITP flare with mild COVID-19 infection in pregnancy: a case report. British Journal of Haematology 2020.

Arnaud S, Budowski C, Ng Wing Tin S, Degos B: Post SARS-CoV-2 Guillain-Barré syndrome. Clinical Neurophysiology 2020, 131(7):1652-1654.

Ma J, Xia P, Zhou Y, Liu J, Zhou X, Wang J, Li T, Yan X, Chen L, Zhang S et al.: Potential effect of blood purification therapy in reducing cytokine storm as a late complication of critically ill COVID-19. Clinical Immunology 2020, 214.

Hu Z, Chen W, Liang W, Xu C, Sun W, Yi Y: Severe exacerbation of immune thrombocytopenia and COVID-19: the favorable response to corticosteroid-based therapy—a case report. Annals of Hematology 2020.

Lopez C, Kim J, Pandey A, Huang T, DeLoughery TG: Simultaneous onset of COVID-19 and autoimmune haemolytic anaemia. British Journal of Haematology 2020, 190(1):31-32.

Abdi S, Ghorbani A, Fatehi F: The association of SARS-CoV-2 infection and acute disseminated encephalomyelitis without prominent clinical pulmonary symptoms. Journal of the Neurological Sciences 2020, 416.
71. Waltuch T, Gill P, Zinns LE, Whitney R, Tokarski J, Tsung JW, Sanders JE: Features of COVID-19 post-infectious cytokine release syndrome in children presenting to the emergency department. American Journal of Emergency Medicine 2020.

72. Sokolovsky S, Soni P, Hoffman T, Kahn P, Scheers-Masters J: COVID-19 associated Kawasaki-like multisystem inflammatory disease in an adult. American Journal of Hematology 2020.

73. Albiol N, Awol R, Martino R: Autoimmune thrombotic thrombocytopenic purpura (TTP) associated with COVID-19. Annals of Hematology 2020, 99(7):1673-1674.

74. Chiotos K, Bassiri H, Behrens EM, Blatz AM, Chang J, Diorio C, Fitzgerald JC, Topjian A, John ARO: Multisystem Inflammatory Syndrome in Children During the Coronavirus 2019 Pandemic: A Case Series. Journal of the Pediatric Infectious Diseases Society 2020, 9(3):393-398.

75. Kutlu Ö, Metin A: A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: Will cases of psoriasis increase after COVID-19 pandemic? Dermatologic Therapy 2020.

76. Beccuti G, Ghizzoni L, Cambria V, Codullo V, Sacchi P, Lovati E, Mongodi S, Iotti GA, Mojoli F: A COVID-19 pneumonia case report of autoimmune polyendocrine syndrome type 1 in Lombardy, Italy: letter to the editor. Journal of Endocrinological Investigation 2020, 43(8):1175-1177.

77. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, Chen H, Ding X, Zhao H, Zhang H et al: Coagulopathy and antiphospholipid antibodies in patients with covid-19. New England Journal of Medicine 2020, 382(17):E38.

78. Brun G, Hak JF, Coze S, Kaphan E, Carvelli J, Girard N, Stellmann JP: COVID-19-White matter and globus pallidum lesions: Demyelination or small-vessel vasculitis? Neurology(R) neuroimmunology & neuroinflammation 2020, 7(4).

79. Bruni A, Garofalo E, Zuccalà V, Currò G, Tartaglini C, Navarra G, De Sarro G, Navalesi P, Longhini F, Ammendola M: Histopathological findings in a COVID-19 patient affected by ischemic gangrenous cholecytitis. World journal of emergency surgery : WJES 2020, 15(1):43.

80. Reichard RR, Kashani KB, Boire NA, Constantopoulos E, Guo Y, Lucchinetti CF: Neuropathology of COVID-19: a spectrum of vascular and acute disseminated encephalomyelitis (ADEM)-like pathology. Acta Neuropathologica 2020, 140(1).

81. Verheyden M, Grosber M, Gutermuth J, Velkeniers B: Relapsing symmetric livedo reticularis in a patient with COVID-19 infection. Journal of the European Academy of Dermatology and Venereology : JEADV 2020.

82. Pilotto A, Odolini S, Stefano Masciocchi S, Comelli A, Volonghi I, Gazzina S, Nocivelli S, Pezzini A, Focà E, Caruso A: Relapsing symmetric livedo reticularis in a COVID-19 patient. Annals of Dermatology 2020.

83. Wei H, Yin H, Huang M, Guo Z: The 2019 novel coronoavirus pneumonia with onset of oculomotor nerve palsy: a case study. Journal of Neurology 2020, 267(5):1550-1553.

84. Rosen MH, Axelrad J, Hudesman D, Rubin DT, Chang S: Management of Acute Severe Ulcerative Colitis in a Pregnant Woman With COVID-19 Infection: A Case Report and Review of the Literature. Inflammatory bowel diseases 2020, 26(7):971-973.

85. Cerasti D, Ormitti F, Pardatscher S, Malchiodi L, Picetti E, Menozzi R, Rossi S: Multiple Acute Ischemic Strokes in a COVID-19 Patient: a Case Report. SN Comprehensive Clinical Medicine 2020.

86. Lee JM, Lee SJ: Olfactory and Gustatory Dysfunction in a COVID-19 Patient with Ankylosing Spondylitis Treated with Etanercept: Case Report. Journal of Korean medical science 2020, 35(21):e201.

87. Arca KN, Starling AJ: Treatment-Refractory Headache in the Setting of COVID-19 Pneumonia: Migraine or Meningoencephalitis? Case Report. SN Comprehensive Clinical Medicine 2020.

88. Zoghi A, Ramezani M, Roozbeh M, Darazam IA, Sahaerain MA: A case of possible atypical demyelinating event of the central nervous system following COVID-19. Multiple Sclerosis and Related Disorders 2020, 44.

89. Anand P, Slama MCC, Kaku M, Ong C, Cervantes-Arslanian AM, Zhou L, David WS, Guidon AC: COVID-19 in patients with myasthenia gravis. Muscle and Nerve 2020, 62(2):254-258.

90. Dogan L, Kaya D, Sarikaya T, Zengin R, Dincer A, Ozkan Akinci I, Afşar N: Plasmapheresis treatment in COVID-19-related autoimmune meningoencephalitis: Case series. Brain, behavior, and immunity 2020.

91. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C et al: Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine 2020, 180(7):934-943.
92. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X et al: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet 2020, 395(10229):1054-1062.

93. Ngo ST, Steyn FJ, McCombe PA: Gender differences in autoimmune disease. Frontiers in Neuroendocrinology 2014, 35(3):347-369.

94. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, Alvarado-Améz LE, Bonilla-Aldana DK, Franco-Paredes C, Henao-Martinez AF et al: Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Medicine and Infectious Disease 2020, 34:101623.

95. Correia AO, Feitosa PWG, de Sousa Moreira JL, Nogueira SÁR, Fonseca RB, Nobre MEPJN, Psychiatry, Research B: Neurological manifestations of COVID-19 and other coronaviruses: a systematic review. 2020.

96. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Faï-Kremer S, Ohana MJNEJoM: Neurologic features in severe SARS-CoV-2 infection. 2020.

97. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, Sánchez-Larsen Á, Layos-Romero A, García-García J, González E, Redondo-Peñas I, Perona-Moratalla AB, Del Valle-Pérez JAJN: Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. 2020.

98. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, Chang J, Hong C, Zhou Y, Wang DJJn: Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. 2020, 77(6):683-690.

99. Netland J, Meyerholz DK, Moore S, Cassell M, Perlman SJJov: Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. 2008, 82(15):7264-7275.

100. Baig AM, Khaleeq A, Ali U, Syeda HJAcn: Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host–virus interaction, and proposed neurotropic mechanisms. 2020, 11(7):995-998.

101. Hughes RA, Cornblath DRJTL: Guillain–barre syndrome. 2005, 366(9497):1653-1666.

102. Yuki N, Hartung HPJNEJoM: Guillain–Barré syndrome. 2012, 366(24):2294-2304.

103. Tenembaum S, Chitnis T, Ness J, Hahn JSJN: Acute disseminated encephalomyelitis. 2007, 68(16 suppl 2):S23-S36.

104. Rowley AHJArom: Kawasaki disease: novel insights into etiology and genetic susceptibility. 2011, 62:69-77.

105. Nardi M, Tomlinson S, Greco MA, Karpatkin SJC: Complement-independent, peroxide-induced antibody lysis of platelets in HIV-1-related immune thrombocytopenia. 2001, 106(5):551-561.

106. Rodeghiero F, Stasi R, Gensheimer T, Michel M, Provan D, Arnold DM, Bussel JB, Cines DB, Chong BH, Cooper NJB: Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. 2009, 113(11):2386-2393.

107. Scaradavou AJBr: HIV-related thrombocytopenia. 2002, 16(1):73-76.

108. McMillan RJJopho: Antiplatelet antibodies in chronic adult immune thrombocytopenic purpura: assays and epitopes. 2003, 25:S57-S61.

109. Lippi G, Plebani M, Henry BMJCCA: Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. 2020.

110. Levine JS, Branch DW, Rauch JJNEJoM: The antiphospholipid syndrome. 2002, 346(10):752-763.

111. Abdel-Wahab N, Lopez-Olivo MA, Pinto-Patarroyo GP, Suarez-Almazor ME: Systematic review of case reports of antiphospholipid syndrome following infection. 2016, 25(14):1520-1531.

112. Cervera R, Asherson RA, Acevedo ML, Gómez-Puerta JA, Espinosa G, de la Red G, Gil V, Ramos-Casals M, García-Carrasco M, Ingelmo M et al: Antiphospholipid syndrome associated with infections: clinical and microbiological characteristics of 100 patients. 2004, 63(10):1312-1317.

Tables

Table 1. Summary of general population and case characteristics.
| Study | Patient’s characteristics | COVID-19 confirmation test | COVID-19 to AD latency | AD developed vs AD exacerbation | Main AD related laboratory findings | Treatment | Admission and outcomes |
|-------|---------------------------|-----------------------------|------------------------|---------------------------------|----------------------------------|-----------|------------------------|
| Sedaghat, Z. and N. Karimi [22] (2020) Iran Case report | Male 65 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: <14 days | De novo: Guillain–Barré syndrome (Acute motor and sensory axonal neuropathy) | - | AD: Immunoglobulin COVID-19: Hydroxychloroquine; Lopinavir/Ritonavir; Azithromycin | Hospitalization: >14 days Outcome: Not reported |
| Chiu, J. S., et al. [23] (2020) USA Case report | Male 10 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: 0 days | De novo: Kawasaki Disease | - | AD: Ibuprofen; Normal saline bolus; Dopamine | Hospitalization: unknown duration Outcome: Not reported |
| Allez, M., et al. [24] (2020) France Case report | Male 24 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: 0 days | De novo: IgA vasculitis Exacerbation: Crohn's disease (Previously in remission with: Ileocecal surgical resection; Adalimumab) | - | AD: Low molecular weight heparin; Methylprednisolone | Hospitalization: 7 days Outcome: Favorable |
| Dolinger, M. T., et al. [25] (2020) USA Case report | Male 14 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: Unclear | De novo: MIS-C Exacerbation: Crohn's disease (Previously active) | High serum IL-6; High serum IL-8; High serum TNF-α | AD: Enoxaparin; Intravenous fluid therapy; Infliximab; Piperacillin/tazobactam; Drainage of perianal abscess; Ciprofloxacin; Metronidazole COVID-19: Hydroxychloroquine; Azithromycin | Hospitalization: 13 days Outcome: Favorable |
| Ottaviani, D., et al. [26] (2020) Italy Case report | Female 66 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: 7 days | De novo: Guillain–Barré syndrome | - | AD: Immunoglobulin COVID-19: Lopinavir/Ritonavir; Hydroxychloroquine; Intubation | Hospitalization: >10 days ICU admission: Yes Outcome: Not reported |
| Scheidl, E., et al. [27] (2020) Germany Case report | Female 54 | COVID-19 confirmation test: Positive rRT-PCR COVID-19 to AD latency: 21 days | De novo: Guillain–Barré syndrome (Acute inflammatory demyelinating polyneuropathy) | CSF high protein level | AD: Immunoglobulin | Hospitalization: >7 days Outcome: Favorable |
| Parsons, T., et al. [28] (2020) | Female 51 | COVID-19 confirmation | De novo: Acute disseminated CSF high protein level | AD: Methylprednisolone; Immunoglobulin | Hospitalization: ≥59 days |
| Country | Case report | Gender | Age | Diagnosis | COVID-19 test | COVID-19 latency | De novo | AD | Hospitalization | ICU admission | Outcome |
|---------|-------------|--------|-----|-----------|---------------|----------------|---------|-----|-----------------|--------------|---------|
| USA | Zanin, L., et al. [29] (2020) | Female | 54 | COVID-19 confirmation test | Positive rRT-PCR | 0-18 days | De novo: Acute disseminated encephalomyelitis | AD: Acosamide; Levetiracetam; Phenytoin; COVID-19: Antiretroviral; Hydroxychloroquine; Dexamethasone; Intubation; Tracheostomy | ≥34 days | Favorable |
| Italy | Zanin, L., et al. [29] (2020) | Male | 65 | COVID-19 confirmation test | Positive rRT-PCR | COVID-19 to AD latency: >1 day | Thrombocytopenia | COVID-19: Oxygen therapy (high-concentration mask (15L/min)); Spiramycin; Amoxicillin and clavulanic acid | ICU admission: Yes | Outcome: Favorable |
| USA | Hanafi, R., et al. [30] (2020) | Female | 51 | COVID-19 confirmation test | Positive rRT-PCR | 0 days | De novo: CNS Vasculitis | AD: Red blood cell transfusion; Folic acid; Recommended use of warm intravenous fluids and blood products; Unfractionated heparin | Hospitalization: <4 days | Favorable |
| USA | Patil, N. R., et al. [31] (2020) | Male | 41 | COVID-19 confirmation test | Positive rRT-PCR | COVID-19 to AD latency: 10 days | Exacerbation: ANCA-associated vasculitis - Glomerulonephritis (Previously active with: Hydroxychloroquine) | AD: Methylprednisolone; Plasmapheresis; Immunoglobulin; Cyclophosphamide | COVID-19: Hydroxychloroquine; Levofloxacin | Hospitalization: 15 days | Favorable |
| USA | Webb, S., et al. [34] (2020) | Male | 57 | COVID-19 confirmation test | Positive rRT-PCR | COVID-19 to AD latency: 7 days | De novo: Guillian-Barré syndrome (Acute inflammatory demyelinating polyneuropathy) | CSF high protein level | ICU admission: Yes | Outcome: Not reported |
| Iran | Farzi, M. A., et al. [33] (2020) | Male | 25 | COVID-19 confirmation test | Positive rRT-PCR | COVID-19 to AD latency: 6 days | Exacerbation: Psoriasis (Status not specified) | AD: Immunoglobulin | Hospitalization: >17 days | Favorable |
| USA | Lantos, J. E., et al. [29] (2020) | Male | 31 | COVID-19 confirmation test | Positive rRT-PCR | COVID-19 to AD latency: 14 days | De novo: Guillain-Barré syndrome | AD: Immunoglobulin | Hospitalization: >7 days | ICU admission: Yes | Outcome: Not reported |
| authors | country | age | gender | comorbidities | COVID-19 confirmation test | COVID-19 to AD latency | De novo: | AD | COVID-19 | Hospitalization | Outcome |
|---------|---------|-----|--------|---------------|---------------------------|-----------------------|----------|----|----------|-----------------|---------|
| al. [35] (2020). USA | Case report | 36 | - | Strabismus | Positive rRT-PCR | 4 days | Barré syndrome (Miller Fisher syndrome) | COVID-19: Hydroxychloroquine | 2 days | Favorable |
| Manganotti, P., et al. [36] (2020) Italy | Case report | Female | 50 | - | COVID-19 confirmation test: Unclear | to AD latency: 16 days | De novo: Guillain–Barré syndrome (Miller Fisher syndrome) | CSF high protein level | AD: Immunoglobulin | Hospitalization: 24 days | Outcome: Favorable |
| Virani, A., et al. [37] (2020) USA | Case report | Male | 54 | Hypertension; Dyslipidemia; Restless leg syndrome; Chronic back pain | Positive rRT-PCR | 7 days | De novo: Guillain–Barré syndrome (Acute inflammatory demyelinating polyneuropathy) | - | AD: Mechanical ventilator support; Immunoglobulin | Hospitalization: 7 days | ICU admission: 7 days |
| Artru, F., et al. [39] (2020) Switzerland | Case report | Male | 38 | Obesity; Cirrhosis (alcoholic liver disease); Chronic thrombocytopenia | Positive rRT-PCR | 10 days | De novo: Immune thrombocytopenic purpura | Exacerbation: IgA nephropathy | AD: Platelet transfusions; Immunoglobulin; Dexamethasone | Hospitalization: 36 days | Outcome: Favorable |
| Yang, Y., et al. [40] (2020) China | Case report | Female | 32 | - | COVID-19 confirmation test: | to AD latency: 10 days | De novo: Immune thrombocytopenic purpura | Thrombocytopenia | AD: Methylprednisolone; Platelet injection | Hospitalization: 27 days | Outcome: Favorable |
| Bomhof, G., et al. [41] (2020) Netherlands | Case series | Male | 59 | Neuroendocrine tumour of the small bowel | Positive rRT-PCR | to AD latency: 10 days | De novo: Immune thrombocytopenic purpura | High serum IL-6; Thrombocytopenia; Positive antiplatelet antibodies | AD: Platelet transfusion; Dexamethasone | Hospitalization: ≥27 days | Outcome: Favorable |
| Female | 66 | Hypertension | COVID-19 confirmation test: | Positive rRT-PCR | to AD latency: 7 days | De novo: Immune thrombocytopenic purpura | Thrombocytopenia | AD: Platelet transfusion; Dexamethasone; Immunoglobulin | Hospitalization: ≥22 days | Outcome: Favorable |
| Male 67 | COVID-19 confirmation test: Positive rRT-PCR | De novo: Immune thrombocytopenic purpura | High serum IL-6; Thrombocytopenia | AD: Platelet transfusions; COVID-19: Intubation; Unfractionated heparin | Hospitalization: 13 days | ICU admission: Yes | Outcome: Death |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertension; DM | COVID-19 to AD latency: 17 days | | | | |
| Male 53 | COVID-19 confirmation test: Positive rRT-PCR | De novo: Immune thrombocytopenic purpura | Thrombocytopenia; Positive anti-PF4 | AD: Immunoglobulin; Dexamethasone; Platelet transfusions; Red blood cell transfusions; Tranexamic acid; Endobronchial clot removal; Romiplostim; Vincristine; Methylprednisolone (pulse doses) COVID-19: Intubation; Mechanical ventilator support; Prone positioning; Propofol; Fentanyl; Cisatracurium; Ceftriaxone; Azithromycin; Unfractionated heparin | Hospitalization: ≥39 days | ICU admission: Yes | Outcome: Favorable |
| Hypertension; Dyslipidemia; DM (Type 2) | COVID-19 to AD latency: 23 days | | | | |
| Female 51 | COVID-19 confirmation test: Positive rRT-PCR | Exacerbation: Systemic lupus erythematosus, Antiphospholipid syndrome (Previously in remission with: Hydroxychloroquine; Azathioprine; Belimumab; Warfarin) | Thrombocytopenia | AD: Platelet transfusions; Immunoglobulin; Prednisone; Eltrombopag | Hospitalization: 12 days | Outcome: Favorable |
| - | COVID-19 to AD latency: Unclear | | | | |
| Male 11 | COVID-19 confirmation test: Negative rRT-PCR; Positive IgG | De novo: Retinal vasculitis | - | - | Outcome: Not reported |
| Hypertension; Transient ischaemic attack; Atrial fibrillation; Chronic kidney disease | COVID-19 to AD latency: Unclear | | | | |
| Female 83 | COVID-19 confirmation test: Negative rRT-PCR; Positive IgM and IgG | De novo: Cutaneous small vessel vasculitis | Positive anti-cardiolipin antibodies | AD: Prednisone | Hospitalization: 10 days | Outcome: Favorable |
| Hypertension; Myocardial infarction; COPD; | COVID-19 to AD latency: 30 days | | | | |
| Male 79 | COVID-19 confirmation test: Positive rRT-PCR | De novo: Cutaneous small vessel vasculitis | - | COVID-19: Hydroxychloroquine; Enoxaparin; ceftaroline; Methylprednisolone; Oxygen therapy (8 L/min; FiO2: 40%) | Hospitalization: >25 days | ICU admission: Yes | Outcome: Death |
| Hypertension; | COVID-19 | | | | | | |
| Case report | Country | Gender | Age | Conditions | COVID-19 confirmation test: | De novo: | CSF high protein level | AD: | Hospitalization: | Outcome: |
|-------------|---------|--------|-----|------------|-------------------|---------|---------------------|-----|----------------|---------|
| Del Giudice, P., et al. [47] (2020) | France | Male | 83 | Obesity; DM (Type 2); Hypertension; Mesenteric ischemia; Distal arteriopathy; Myocardial infarction | COVID-19 confirmation test: Positive rRT-PCR | Thrombocytopenia | - | - | >1 days | Death |
| Nasiri, S., et al. [48] (2020) | Iran | Male | 73 | COVID-19 confirmation test: Positive rRT-PCR | Exacerbation: Psoriasis (Status not specified; treated with: Prednisolone) | - | COVID-19: Hydroxychloroquine; Lopinavir/Ritonavir; Acetaminophen | Favorable |
| Novi, G., et al. [49] (2020) | Italy | Female | 64 | Hypertension; MGUS | COVID-19: Hydroxychloroquine; Lopinavir/Ritonavir; Acetaminophen | Favorable |
| Pfefferkorn, T., et al. [50] (2020) | Germany | Male | 51 | COVID-19 confirmation test: Positive rRT-PCR; Positive IgG | CSF high protein level | AD: Methylprednisolone; Immunoglobulin; Prednisone | Favorable |
| Panariello, A., et al. [51] (2020) | Italy | Male | 23 | Substance Use Disorder (THC; cocaine and phencyclidine) | COVID-19 confirmation test: Positive rRT-PCR | CSF high protein level; Pleocytosis | AD: Hyaluronidase; Plasma exchange; Midazolam; Aripiprazole; Quetiapine; Antibiotic prophylactic therapy; Valproate; Dexamethasone; Immunoglobulin; COVID-19: Oxygen therapy; Hydroxychloroquine; Darunavir/cobicistat | Not reported |
| Vega Hernández, P., et al. [52] (2020) | Spain | Female | 13 | COVID-19 confirmation test: Positive rRT-PCR | Anemia; Positive direct Coombs test | AD: Methylprednisolone (pulse doses); Prednisone | Favorable |
| Yokogawa, N., et al. [53] (2020) | Male | 57 | | COVID-19 confirmation test: Positive rRT-PCR | De novo: Acute arthritis | - | - | 27 days | Favorable |
Japan
Case report
Hypertension; Hyperlipidemia
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency:
20 days
De novo: Anti-MOG associated encephalomyelitis
CSF high protein level; Pleocytosis; Positive anti-MOG antibody
AD: Methylprednisolone; Prednisolone; Plasma exchange
Hospitalization: 18 days
Outcome: Favorable

Singh, S. and R. Govindarajan [55] (2020).
USA
Case report
Female 36
Thymic hyperplasia
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency: 0 days
Exacerbation:
Myasthenia Gravis (seronegative generalized)
(Previously in remission with:
Prednisone; Mycophenolate Mofetil; Pyridostigmine; Immunoglobulin)
AD: Plasmapheresis; Stress dose IV steroids; Intubation
COVID-19: Supportive care
Hospitalization: 24 days
Outcome: Favorable

Capes, A., et al. [56] (2020).
Belgium
Case report
Male 62
Hypertension; Oropharyngeal squamous cell carcinoma
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency: 16 days
De novo: Autoimmune hemolytic anemia
Thrombocytopenia; Anemia; Positive ANA; Positive direct Coombs test
AD: Red blood cell transfusion
COVID-19: Intubation
Hospitalization: >19 days
ICU admission: Yes
Outcome: Not reported

Barzegar, M., et al. [57] (2020).
Iran
Case report
Female 42
Major depression disorder; Hypothyroidism; Pulmonary embolism
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency: Unclear
Exacerbation:
Multiple sclerosis (relapsing-remitting), Myasthenia gravis, (Previously in remission with:
Fingolimod)
AD: Methylprednisolone; Glatiramer acetate
COVID-19: Azithromycin; Ceftriaxone; Oxygen therapy;
Hydroxychloroquine; Osellamivir; Piperacillin/tazobactam
Hospitalization: 13 days
Outcome: Favorable

Murt, A., et al. [58] (2020). Turkey
Case report
Male 41
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency: 15 days
De novo: Immune thrombocytopenic purpura
Thrombocytopenia
AD: Dexamethasone; Immunoglobulin
COVID-19: Favipiravir
Hospitalization: ≥9 days
Outcome: Favorable

Zhao, H., et al. [59] (2020). China
Case report
Female 61
COVID-19 confirmation test:
Positive rRT-PCR
COVID-19 to AD latency: ≤3 days
De novo: Guillain-Barré syndrome
CSF high protein level
AD: Immunoglobulin
COVID-19: Supportive care; Umifenovir; Lopinavir/Ritonavir
Hospitalization: 30 days
Outcome: Favorable
| Authors          | Gender | Age | Diagnosis                                                                 | Test Results         | AD Treatments                                                                 | Outcomes                                                                 | Hospitalization                      |
|------------------|--------|-----|---------------------------------------------------------------------------|----------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------|
| Padroni, M., et al. [60] (2020) Italy Case report | Female | 70  | COVID-19 confirmation test: Positive rRT-PCR to AD latency: 23 days        | De novo: Guillain-Barré syndrome (Acute motor and sensory axonal neuropathy) | CSF high protein level                                                    | AD: Immunoglobulin; Intubation; Mechanical ventilator support               | Hospitalization: >8 days Outcome: Not reported |
| Alberti, P., et al. [61] (2020) Italy Case report | Male   | 71  | COVID-19 confirmation test: Positive rRT-PCR to AD latency: 4 days         | De novo: Guillain-Barré syndrome (Acute motor and sensory axonal neuropathy) | CSF high protein level; Pleocytosis                                       | AD: COVID-19: Oxygen therapy (FiO2: 60-80%); Lopinavir/Ritonavir; Hydroxychloroquine; Mechanical ventilator support (CPAP); Prone positioning | Hospitalization: 1 day Outcome: Death |
| Zulfiqar, A. A., et al. [62] (2020) France Case report | Female | 65  | COVID-19 confirmation test: Positive rRT-PCR to AD latency: 8 days         | De novo: Immune thrombocytopenic purpura | Exacerbation: Autoimmune hypothyroidism (Status not specified)           | AD: Immunoglobulin; Platelet transfusions; Prednisolone; Eltrombopag       | Hospitalization: 14 days Outcome: Favorable |
| Nesr, G., et al. [63] (2020) UK Case report | Female | 34  | COVID-19 confirmation test: Positive rRT-PCR to AD latency: 0 days         | Exacerbation: Immune thrombocytopenic purpura (Previously in remission)    | Thrombocytopenia                                                         | AD: Immunoglobulin; Prednisolone                                         | Hospitalization: 2 days Outcome: Favorable |
| Arnaud, S., et al. [64] (2020) France Case report | Male   | 64  | COVID-19 confirmation test: Positive rRT-PCR to AD latency: 23 days        | De novo: Guillain-Barré syndrome                                           | CSF high protein level                                                   | AD: Immunoglobulin; COVID-19: Cefotaxime; Azithromycin; Hydroxychloroquine | Hospitalization: ≥27 days Outcome: Favorable |
| Ma, J., et al. [65] (2020). China Case report | Male   | 69  | COVID-19 confirmation test: Positive IgM and IgG to AD latency: 49 days    | De novo: Antiphospholipid syndrome                                          | High serum IL-6; Thrombocytopenia; Positive anti-beta-2-glycoprotein I; Positive anti-cardiolipin antibodies | AD: Low molecular weight heparin; Aspirin; Plasma exchange; COVID-19: Antibiotic therapy; Ribavirin; Intubation; Mechanical ventilator support (pressure control (PC) mode; FiO2: 40%; PEEP: 8 cmH2O); Immunoglobulin; Supportive care | Hospitalization: >61 days ICU admission: Yes Outcome: Not reported |
| Hu, Z., et al. [66] (2020) China Case report | Female | 72  | COVID-19 confirmation test: Positive rRT-PCR to AD latency:                | Thrombocytopenia                                                      | Exacerbation: Immune thrombocytopenic purpura (Previously in remission with: Prednisone; | AD: Immunoglobulin; Platelet transfusions; Methylprednisolone; COVID-19: Umifenovir; Darunavir/cobicistat | Hospitalization: 29 days Outcome: Favorable |
| Lopez, C., et al. [67] (2020). USA Case report | Female | 46 | COVID-19 confirmation test: Positive rRT-PCR; COVID-19 to AD latency: 4 days | De novo: Congenital thrombocytopenia | Thrombocytopenia; Anemia; Positive direct Coombs test (Warm agglutinin disease) | AD: Immunglobulin; Red blood cell transfusions; Prednisone | COVID-19: Azithromycin; Hydroxychloroquine | Hospitalization: 9 days | Outcome: Favorable |
|-----------------------------------------------|--------|-----|-----------------------------------------------------------------|--------------------------------|-----------------------------------------------------|---------------------------------|---------------------------------|-----------------|-----------------|
| Abdi, S., et al. [68] (2020). Iran Case report | Male | 58 | COVID-19 confirmation test: Positive rRT-PCR; COVID-19 to AD latency: 4 days | De novo: Acute disseminated encephalomyelitis | - | AD: Dexamethasone | Hospitalization: 13 days | ICU admission: Yes | Outcome: Death |
| Ortot, P. and M. P. Hermans [69] (2020) Belgium Case report | Male | 60 | COVID-19 confirmation test: Positive rRT-PCR; COVID-19 to AD latency: 5 days | Exacerbation: Type 1 diabetes mellitus (Treated with: Gargine; Glulisine; Empagliflozin) | - | AD: Intraavenous fluid therapy; Insulin | COVID-19: Mechanical ventilator support | Hospitalization: >43 days | ICU admission: Yes | Outcome: Favorable |
| Reyes-Bueno, J. A., et al. [70] (2020). Spain Case report | Female | 51 | COVID-19 confirmation test: Negative rRT-PCR; Positive IgG | De novo: Guillain–Barré syndrome (Miller Fisher syndrome) | CSF high protein level | AD: Immunglobulin; Gabapentin | Hospitalization: ≥19 days | Outcome: Favorable |
| Waltuch, T., et al. [71] (2020). USA Case series | Male | 13 | COVID-19 confirmation test: Negative rRT-PCR; Positive IgG | De novo: MIS-C | High serum IL-6; High serum IL-8; High serum TNF-α | AD: Intravenous fluid therapy; Meropenem; Linezolid; Immunglobulin; Tocilizumab; Anakinra | COVID-19: Intubation; Enoxaparin | Hospitalization: >2 days | ICU admission: Yes | Outcome: Not reported |
| Male | 10 | Asthma | COVID-19 confirmation test: Positive rRT-PCR; COVID-19 to AD latency: 12 days | De novo: MIS-C | High serum IL-6; High serum IL-8; High serum TNF-α | AD: Intravenous fluid therapy; Cefepime; Clindamycin; Dopamine; Immunoglobin; Tocilizumab; Linezolid | Hospitalization: unknown duration | ICU admission: Yes | Outcome: Not reported |
| Male | 5 | COVID-19 confirmation test: Negative | De novo: MIS-C | High serum IL-6; High serum IL-8; High serum TNF-α | AD: Intravenous fluid therapy; Ceftriaxone; Clindamycin; Enoxaparin; Dopamine; Immunoglobulin; Tocilizumab | Hospitalization: >3 days | ICU admission: Yes | | |

≤5 days Cyclosporine; Interferon alfa)
| | De novo: MIS-C | High serum IL-6; High serum IL-8; High serum TNF-α | AD: Intravenous fluid therapy; Cefepime; Vancomycin; Metronidazole |
| | | | Hospitalization: unknown duration |
| | De novo: MIS-A | Positive ANA; Positive anti-Ro/SSA; Low complement C3 and C4 | AD: Intravenous fluid therapy; Aspirin; Immunglobulin; Methylprednisolone; Prednisone |
| | | | Hospitalization: 6 days |
| | De novo: Autoimmune thrombotic thrombocytopenic purpura | Thrombocytopenia; Anemia; Positive ADAMTS-13 inhibitor | AD: Methylprednisolone; Immunoglobulin; Plasma infusion; Plasma exchange |
| | | | Hospitalization: 17 days |
| | De novo: MIS-C | - | AD: Epinephrine; Norepinephrine; Vancomycin; Cefepime; Clindamycin; Doxycycline; Immunoglobulin; Methylprednisolone; Aspirin; COVID-19: Intubation; Mechanical ventilator support |
| | | | Hospitalization: 17 days |
| | De novo: MIS-C | - | AD: Milrinone; Epinephrine; Vasopressin; Methylprednisolone (pulse dose); Immunoglobulin; Vancomycin; Cefepime; Clindamycin; COVID-19: Mechanical ventilator support |
| | | | Hospitalization: 12 days |
| | De novo: MIS-C | - | AD: Intravenous fluid therapy; Immunoglobulin; Methylprednisolone; Aspirin; Mechanical ventilator support; Furosemide; Piperacillin/tazobactam; Ciprofloxacin; Vancomycin |
| | | | Hospitalization: 8 days |
| Gender | Age | COVID-19 confirmation test: | COVID-19 to AD latency: | De novo: MIS-C | Pleocytosis | AD: | Hospitalization: | ICU admission: | Outcome: |
|--------|-----|-----------------------------|-------------------------|----------------|-------------|-----|------------------|----------------|---------|
| Female | 5   | COVID-19 confirmation test: | 0 days                  | De novo: MIS-C | -           | AD: Epinephrine; Methylprednisolone; Vancomycin; Ceftriaxone; COVID-19: Intubation; Mechanical ventilator support | 11 days        | Yes     | Favorable        |
| Female | 6   | COVID-19 confirmation test: | 0 days                  | De novo: MIS-C | -           | AD: Norepinephrine; Dopamine; Epinephrine; Methylprednisolone; Aspirin; Vancomycin; Ceftriaxone; Metronidazole; COVID-19: Intubation; Mechanical ventilator support | >7 days        | Yes     | Outcome: Not reported |
| Female | 71  | COVID-19 confirmation test: | 4 days                  | Exacerbation: | Psoriasis (Previously in remission) | | Hospitalization: | >4 days | Outcome: Not reported |
| Female | 32  | COVID-19 confirmation test: | 18 days                 | Exacerbation: | Autoimmune polyglandular syndrome type 1 (hypoparathyroidism) | | Hospitalization: | 37 days | Yes | Favorable |
| Male   | 69  | COVID-19 confirmation test: | 18 days                 | | | | Hospitalization: | >24 days | Yes | Outcome: Not reported |
| Female | 65  | COVID-19 confirmation test: | Unclear                 | | | | Hospitalization: | >33 days | ICU admission: | Yes |

Kutlu, Ö. and A. Metin [75] (2020) Turkey Case report

Beccuti, G., et al. [76] (2020) Italy Case report

Zhang, Y., et al. [77] (2020) China Case series
| Name, et al. [Ref] (Year) | Country | Diagnosis | Age | Clinical Features | Laboratory Features | Treatment | Outcome | Notes |
|---------------------------|---------|-----------|-----|------------------|---------------------|-----------|---------|-------|
| Brun, G. et al. [78] (2020) | France | Coronary artery disease | Male 70 | COVID-19 to AD latency: 33 days | Positive anti-cardiolipin antibodies | COVID-19: Antibiotic therapy; Ribavirin | Hospitalization: >24 days ICU admission: Yes | Outcome: Not reported |
| Brun, A., et al. [79] (2020) | Italy | Hypertension; Emphysema; Nasopharyngeal carcinoma; Stroke | Male 59 | COVID-19 to AD latency: 10 days | Positive anti-beta-2-glycoprotein I; Positive anti-cardiolipin antibodies | COVID-19: Antibiotic therapy; Ribavirin | Hospitalization: >12 days ICU admission: Yes | Outcome: Not reported |
| Reichard, R. R., et al. [80] (2020) | USA | Myocardial infarction | Male 71 | COVID-19 to AD latency: Unclear | - | COVID-19: Oxygen therapy; Intubation; Prone positioning; Mechanical ventilator support; Sedation/paralysis; Vasopressor support; Stress dose IV steroids | Hospitalization: >44 days ICU admission: Yes | Outcome: Favorable |
| Verheyden, M., et al. [81] (2020) | Belgium | Hypertension; | Male 57 | COVID-19 to AD latency: 8 days | High serum IL-6; Thrombocytopenia | COVID-19: Oxygen therapy; Paracetamol; Hydroxychloroquine | Hospitalization: 8 days ICU admission: Yes | Outcome: Favorable |
| Pilotto, A., et al. [82] (2020) | Italy | Hypertension; | Male 60 | COVID-19 to AD latency: 8 days | CSF high protein level; High CSF IL-6; High CSF IL-8; High CSF TNF-α; High CSF β2-microglobulin | COVID-19: Lopinavir/Ritonavir; Hydroxychloroquine | Hospitalization: 11 days ICU admission: Yes | Outcome: Favorable |
| Wei, H., et al. [83] (2020) | China | DM (Type 2); | Male 62 | COVID-19 to AD latency: 0 days | - | COVID-19: Oxygen therapy; Moxifloxacin; Oseltamivir; | Hospitalization: 12 days ICU admission: Yes | Outcome: Death |
| Author(s) | Country | Gender | Age | Confirmation Test | AD Latency | Exacerbation | Antiviral Treatment | Hospitalization Duration | Outcome |
|-----------|---------|--------|-----|-------------------|------------|--------------|---------------------|--------------------------|---------|
| Rosen, M. H., et al. [84] (2020) USA | Female | 26 | COVID-19 | Unclear | Ulcerative colitis (pancolitis) | - | Ribavirin; Lopinavir; Paracetamol; Ibuprofen | 16 days | Hospitalization: |
| Cerasti, D., et al. [85] (2020) Italy | Female | 47 | COVID-19 | Obesity | Antiphospholipid syndrome (Status not specified) | - | COVID-19: Ganciclovir; Oseltamivir; Darunavir; Cobicistat; Meropenem; Linezolid; Supportive care; Intubation | 9 days | Outcome: Death |
| Lee, J. M. and S. J. Lee [86] (2020) South Korea | Female | 53 | COVID-19 | Chronic migraine; Stroke; Restless leg syndrome | Ankylosing spondylitis exacerbaton (Previously in remission with: Etanercept; Methotrexate) | - | AD: Etanercept | No admission | Outcome: Favorable |
| Arca, K. N. and A. J. Starling [87] (2020) USA | Female | 58 | COVID-19 | De novo: Acute disseminated encephalomyelitis | Multiple sclerosis (Previously in remission with: Fingolimod) | - | COVID-19: Hydroxychloroquine; Azithromycin; Intubation | unknown duration | Hospitalization: |
| Zoghi, A., et al. [88] (2020) Iran | Male | 21 | COVID-19 | De novo: Acute disseminated encephalomyelitis | CSF high protein level; Pleocytosis | - | AD: Plasma exchange; Vancomycin; Meropenem; Acyclovir | 14 days | Hospitalization: |
| Anand, P., et al. [89] (2020) USA | Female | 42 | COVID-19 | De novo: Myasthenia Gravis (MuSK+) | Mysasthenia Gravis (MuSK+) (Previously in remission with: Prednisone) | - | AD: Prednisone; Immunoglobulin | 5 days | Hospitalization: |
| Dogan, L., et al. [90] (2020) Turkey | Male | 49 | COVID-19 | De novo: Autoimmune meningoencephalitis | High serum IL-6 | - | AD: Plasmapheresis | 34 days | Hospitalization: |

**Notes:**
- AD: Methylprednisolone; Prednisone; Cyclosporine COVID-19: Azithromycin; Hydroxychloroquine
- Hospitalization: 16 days, Outcome: Favorable
- Hospitalization: 9 days, Outcome: Death
- Hospitalization: unknown duration, ICU admission: Yes, Outcome: Favorable
- Hospitalization: 14 days, ICU admission: Yes, Outcome: Favorable
- Hospitalization: 5 days, Outcome: Favorable
| Gender | Age | Comorbidities | COVID-19 confirmation test | COVID-19 to AD latency | De novo: | CSF high protein level | AD: | COVID-19: | Hospitalization: | ICU admission: | Outcome: |
|--------|-----|---------------|----------------------------|-----------------------|---------|------------------------|-----|------------|----------------|----------------|----------|
| Male   | 59  | Hypertension  | Positive rRT-PCR          | 15 days               | Autoimmune meningoencephalitis |                      | AD: Plasmapheresis | COVID-19: Intubation; | Mechanical ventilator support; | Prone positioning; Azithromycin; Hydroxychloroquine; Favipiravir | 39 days | Favorable |
| Female | 51  | Hypertension; DM; Obesity | Positive rRT-PCR | 15 days               | Autoimmune meningoencephalitis |                      | AD: Plasmapheresis | COVID-19: Intubation; | Mechanical ventilator support; | Prone positioning; Azithromycin; Hydroxychloroquine; Favipiravir | 33 days | Favorable |
| Male   | 55  | Hypertension  | Positive rRT-PCR          | 12 days               | Autoimmune meningoencephalitis |                      | AD: Plasmapheresis | COVID-19: Intubation; | Mechanical ventilator support; | Prone positioning; Azithromycin; Hydroxychloroquine; Favipiravir | >39 days | Not reported |
| Male   | 22  | Autism        | Positive rRT-PCR          | 14 days               | Autoimmune meningoencephalitis |                      | AD: Plasmapheresis | COVID-19: Intubation; | Mechanical ventilator support; | Prone positioning; Azithromycin; Hydroxychloroquine; Favipiravir | 31 days | Favorable |

**Abbreviations:** A Disintegrin And Metalloproteinase with a Thrombospondin Type 1 Motif, Member 13 (ADAMTS-13); Anti-Neutrophil Cytoplasmic Antibodies (ANCA); Antinuclear antibody (ANA); Antiphospholipid Syndrome (APS); Autoimmune Disease (AD); Brain natriuretic peptide (BNP); Central Nervous System (CNS); Cerebrospinal fluid (CSF); Chronic Obstructive Pulmonary Disease (COPD); Coronavirus Disease 2019 (COVID-19); Diabetes Mellitus (DM); Fraction of Inspired Oxygen (FiO2); Immunoglobulin A (IgA); Immunoglobulin G (IgG); Immunoglobulin M (IgM); Intensive Care Unit (ICU); Interleukin 6 (IL-6); Interleukin 8 (IL-8); Monoclonal Gammapathy Of Undetermined Significance (MGUS); Multisystem Inflammatory Syndrome in Adults (MIS-A); Multisystem Inflammatory Syndrome in Children (MIS-C); Myelin Oligodendrocyte Glycoprotein (MOG); N-methyl-D-aspartate (NMDA); Platelet Factor 4 (PF4); Positive End-Expiratory Pressure (PEEP); Real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR); Recombinant Human Parathyroid Hormone (rhPTH); Systemic Lupus Erythematosus (SLE); Tumor necrosis factor α (TNF-α)
Table 2. **Total and by group summary of findings.** General population and case characteristics, laboratory findings divided by areas, COVID-19 related radiologic findings and treatment, and AD-related treatment summarized with frequencies and descriptive statistics for the total and all major groups.
| General (N (%))            | Total | Neurologic AD | Blood AD | Vasculitis AD | Connectivitis/ SLE/APS AD |
|---------------------------|-------|---------------|----------|---------------|--------------------------|
| N*                        | 85 (100%) | 36 (42.4%) | 15       | 19            | 6 (7.1%)                 |
| Age (Median)              | 53 (32-63 IQR) | 54 (45.25-61.75 IQR) | 53 (38-65 IQR) | 13 (9-36 IQR) | 67 (50-69.25 IQR) |
| Sex (N (% Female))        | 40 (47.1%) | 16 (44.4%) | 9 (60.0%) | 8 (42.1%) | 3 (50.0%)               |
| AD comorbidity            | 23 (27.1%) | 6 (16.7%) | 5 (33.3%) | 4 (21.1%) | 2 (33.3%)               |
| De novo AD                | 18 (21.2%) | 12 (7-15 IQR) | 10 (6.25-15.75 IQR) | 5 (0-13 IQR) | 25.5 (12-45 IQR) |
| Exacerbation of AD       | 1 (1.2%) | 1 (2.8%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%)               |

| Outcome                  | Favorable | 55 (64.7%) | 13 | 11 | 1 (16.7%) |
| Death                    | 9 (10.6%) | 5 (13.9%) | 1 (6.7%) | 2 (10.5%) | 1 (16.7%) |

| Laboratory findings (N (%)) | CSF high protein level | CSF pleocytosis | CSF albumin-cytological dissociation | CSF high IgG |
|-----------------------------|------------------------|-----------------|-------------------------------------|--------------|
| N                           | 20 (23.5%)             | 6 (7.1%)       | 5 (5.9%)                            | 5 (5.9%)     |

| Immune markers             | Anti-MOG antibodies | Anti-NMDA receptor antibodies | Anti-ganglioside antibodies (Asialo GM1) | Anti-cardiolipin antibodies | Anti-beta-2-glycoprotein I antibodies | Direct Coombs Test | High cold agglutinin titers | Anti-ADAMTS-13 inhibitory antibodies | Anti-platelet antibodies | Anti-platelet factor 4/heparin antibodies | ANA | High Complement | Low complement | High IgA serum levels | ANCA | Anti-Ro/SSA |
|----------------------------|---------------------|-----------------------------|------------------------------------------|---------------------------|---------------------------------------|-------------------|-----------------------------|------------------------------------------|-------------------------|-------------------------------------------|-----|----------------|----------------|----------------------|------|-------------|
| N                          | 1 (1.2%)             | 1 (1.2%)                    | 1 (1.2%)                                 | 6 (7.1%)                  | 4 (4.7%)                              | 4 (4.7%)          | 2 (2.4%)                    | 1 (1.2%)                                 | 1 (1.2%)                | 1 (1.2%)                                  | 3 (3.5%) | 1 (1.2%) | 1 (1.2%) | 1 (1.2%)               |      | 1 (1.2%)   |

| Hemostasis system markers | High d-dimers | |
|--------------------------|---------------|-----|
| N                        | 32 (37.6%)    | 10 (27.8%) | 5 (33.3%) | 13 (68.4%) |

Page 29/33
### Inflammatory markers

| Marker                        | N (%)            | Normal | Bilateral ground-glass opacities | Bilateral pulmonary infiltrates | Diffused consolidations |
|-------------------------------|------------------|--------|----------------------------------|--------------------------------|------------------------|
| High c-reactive protein       | 49 (57.6%)       | 18 (50.0%) | 5 (33.3%)                        | 17 (89.5%)                     | 4 (66.7%)              |
| High procalcitonin           | 12 (14.1%)       | 0 (0.0%)   | 0 (0.0%)                         | 12 (63.2%)                     | 0 (0.0%)               |
| High ferritin                | 25 (29.4%)       | 10 (27.8%) | 3 (20.0%)                        | 10 (52.6%)                     | 1 (16.7%)              |
| High lactate dehydrogenase   | 23 (27.1%)       | 7 (19.4%)  | 5 (33.3%)                        | 9 (47.4%)                      | 2 (33.3%)              |
| High erythrocyte sedimentation rate | 14 (16.5%)   | 5 (13.9%)  | 0 (0.0%)                         | 8 (42.1%)                      | 0 (0.0%)               |
| High serum IL-6              | 14 (16.5%)       | 5 (13.9%)  | 2 (13.3%)                        | 6 (31.6%)                      | 1 (16.7%)              |
| High serum IL-8              | 5 (5.9%)         | 0 (0.0%)   | 0 (0.0%)                         | 5 (26.3%)                      | 0 (0.0%)               |
| High serum TNF-α             | 5 (5.9%)         | 0 (0.0%)   | 0 (0.0%)                         | 5 (26.3%)                      | 0 (0.0%)               |
| High troponins levels         | 9 (10.6%)        | 0 (0.0%)   | 0 (0.0%)                         | 7 (36.8%)                      | 2 (33.3%)              |
| High myoglobin level          | 1 (1.2%)         | 0 (0.0%)   | 0 (0.0%)                         | 1 (5.3%)                       | 0 (0.0%)               |

### Other general laboratory measurements

| Marker                        | N (%)            | Normal | Bilateral ground-glass opacities | Bilateral pulmonary infiltrates | Diffused consolidations |
|-------------------------------|------------------|--------|----------------------------------|--------------------------------|------------------------|
| Anemia                        | 22 (25.9%)       | 3 (8.3%) | 8 (53.3%)                        | 8 (42.1%)                      | 3 (50.0%)              |
| Reticulocytosis               | 4 (4.7%)         | 0 (0.0%) | 4 (26.7%)                        | 0 (0.0%)                       | 0 (0.0%)               |
| Leukocytosis                  | 29 (34.1%)       | 11 (30.6%) | 4 (26.7%)                        | 11 (57.9%)                     | 3 (50.0%)              |
| Leukopenia                    | 2 (2.4%)         | 0 (0.0%) | 0 (0.0%)                         | 0 (0.0%)                       | 2 (33.3%)              |
| Lymphocytopenia               | 36 (42.4%)       | 7 (19.4%) | 9 (60.0%)                        | 14 (73.7%)                     | 4 (66.7%)              |
| Thrombocytopenia              | 31 (36.5%)       | 6 (16.7%) | 12 (80.0%)                       | 9 (47.4%)                      | 4 (66.7%)              |
| Thrombocytosis                | 3 (3.5%)         | 3 (8.3%)  | 0 (0.0%)                         | 0 (0.0%)                       | 0 (0.0%)               |
| Hyponatremia                  | 8 (9.4%)         | 1 (2.8%)  | 0 (0.0%)                         | 7 (36.8%)                      | 0 (0.0%)               |
| High alanine aminotransferase (ALT) | 17 (20.0%)   | 5 (13.9%) | 1 (6.7%)                         | 10 (52.6%)                     | 0 (0.0%)               |
| High aspartate aminotransferase (AST) | 13 (15.3%)  | 6 (16.7%) | 1 (6.7%)                         | 5 (26.3%)                      | 0 (0.0%)               |
| High gamma-glutamyl transferase | 2 (2.4%)        | 1 (2.8%)  | 0 (0.0%)                         | 1 (5.3%)                       | 0 (0.0%)               |
| Direct hyperbilirubinemia     | 2 (2.4%)         | 0 (0.0%) | 0 (0.0%)                         | 2 (10.5%)                      | 0 (0.0%)               |
| Indirect hyperbilirubinemia   | 3 (3.5%)         | 0 (0.0%)  | 3 (20.0%)                        | 0 (0.0%)                       | 0 (0.0%)               |
| Hypoalbuminemia               | 12 (14.1%)       | 1 (2.8%)  | 0 (0.0%)                         | 8 (42.1%)                      | 3 (50.0%)              |

### COVID-19 related radiologic findings (N (%))

| Finding                        | N (%)            | Normal | Bilateral ground-glass opacities | Bilateral pulmonary infiltrates | Diffused consolidations |
|-------------------------------|------------------|--------|----------------------------------|--------------------------------|------------------------|
| Normal                        | 9 (10.6%)        | 2 (5.6%) | 2 (13.3%)                        | 3 (15.8%)                      | 0 (0.0%)               |
| Bilateral ground-glass opacities | 34 (40.0%)     | 17 (47.2%) | 4 (26.7%)                        | 3 (15.8%)                      | 4 (66.7%)              |
| Bilateral pulmonary infiltrates | 12 (14.1%)     | 3 (8.3%)  | 3 (20.0%)                        | 2 (10.5%)                      | 3 (50.0%)              |
| Diffused consolidations       | 11 (12.4%)       | 8 (22.2%) | 2 (13.3%)                        | 0 (0.0%)                       | 1 (16.7%)              |
| Other tests                  | N     | (N)               | (N)     | (N)    | (N)     | (N)     |
|-----------------------------|-------|-------------------|---------|--------|---------|---------|
| Nerve conduction studies - GBS | 12    | (14.1%)           | 12 (33.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Skin biopsy - leukocytoclastic vasculitis | 3     | (3.5%)            | 0 (0.0%) | 0 (0.0%) | 3 (15.8%) | 0 (0.0%) |
| Bone marrow aspirate - normal cellularity with an increased megakaryocyte count | 2     | (2.4%)            | 0 (0.0%) | 2 (13.3%) | 0 (0.0%) | 0 (0.0%) |

| AD treatment                  | N (%) | (N)               | (N)    | (N)     | (N)     | (N)     |
|-------------------------------|-------|-------------------|--------|---------|---------|---------|
| None                          | 13    | (15.3%)           | 3 (8.3%) | 0 (0.0%) | 2 (10.5%) | 3 (50.0%) |
| Immunoglobulin                | 42    | (49.4%)           | 19 (52.8%) | 10 (66.7%) | 11 (57.9%) |
| Corticosteroids               | 35    | (41.2%)           | 11 (30.6%) | 12 (80.0%) | 10 (52.6%) |
| Antibiotic prophylaxis        | 16    | (18.8%)           | 3 (8.3%) | 0 (0.0%) | 13 (68.4%) |
| Plasma exchange therapies     | 13    | (15.3%)           | 10 (27.8%) | 1 (6.7%) | 1 (5.3%) |
| Supportive therapy            | 12    | (14.1%)           | 4 (11.1%) | 0 (0.0%) | 7 (36.8%) | 0 (0.0%) |
| Transfusion                   | 12    | (14.1%)           | 0 (0.0%) | 11 (73.2%) | 0 (0.0%) | 1 (16.7%) |
| Immunomodulator               | 9     | (10.6%)           | 1 (2.8%) | 1 (6.7%) | 5 (26.3%) | 0 (0.0%) |
| Shock therapy                 | 8     | (9.4%)            | 0 (0.0%) | 0 (0.0%) | 8 (42.1%) | 0 (0.0%) |
| Anticoagulant                 | 6     | (7.1%)            | 0 (0.0%) | 1 (6.7%) | 3 (15.8%) | 1 (16.7%) |
| Other                         | 5     | (5.9%)            | 1 (2.8%) | 1 (6.7%) | 3 (15.8%) | 0 (0.0%) |
| Acetylsalicylic acid          | 5     | (5.9%)            | 0 (0.0%) | 0 (0.0%) | 4 (21.1%) | 1 (16.7%) |
| Anticonvulsant                | 3     | (3.5%)            | 3 (8.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Thrombopoietin pathway therapy| 3     | (3.5%)            | 0 (0.0%) | 2 (13.3%) | 0 (0.0%) | 1 (16.7%) |
| Cirurgy                       | 3     | (3.5%)            | 0 (0.0%) | 1 (6.7%) | 2 (10.5%) | 0 (0.0%) |
| Antiviric prophylaxis         | 2     | (2.4%)            | 2 (5.6%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Antipsychotic                 | 1     | (1.2%)            | 1 (2.8%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Antifibrinolytic              | 1     | (1.2%)            | 0 (0.0%) | 1 (6.7%) | 0 (0.0%) | 0 (0.0%) |
| NSAID                         | 1     | (1.2%)            | 0 (0.0%) | 0 (0.0%) | 1 (5.3%) | 0 (0.0%) |

| COVID-19 treatment           | N (%) | (N)               | (N)   | (N)    | (N)     | (N)     |
|-------------------------------|-------|-------------------|-------|--------|---------|---------|
| None                          | 26    | (30.6%)           | 8 (22.2%) | 4 (26.7%) | 10 (52.6%) | 1 (16.7%) |
| Supportive therapy            | 40    | (47.1%)           | 21 (58.3%) | 6 (40.0%) | 7 (36.8%) | 3 (50.0%) |
| Hydroxychloroquine           | 33    | (38.8%)           | 20 (55.6%) | 4 (26.7%) | 4 (21.1%) | 0 (0.0%) |
| Antiviric therapy             | 28    | (32.9%)           | 17 (47.2%) | 4 (26.7%) | 0 (0.0%) | 4 (66.7%) |
| Antibiotic therapy            | 31    | (36.5%)           | 16 (44.4%) | 5 (33.3%) | 4 (21.1%) | 4 (66.7%) |
| Other                         | 16    | (18.8%)           | 4 (11.1%) | 5 (33.3%) | 3 (15.8%) | 1 (16.7%) |

Abbreviations: A Disintegrin And Metalloproteinase with a Thrombospondin Type 1 Motif, Member 13 (ADAMTS-13); Anti-Neutrophil Cytoplasmic Antibodies (ANCA); Antinuclear antibody (ANA); Antiphospholipid Syndrome (APS); Autoimmune Disease (AD); Cerebrospinal fluid (CSF); Coronavirus Disease 2019 (COVID-19); Immunoglobulin A (IgA); Immunoglobulin G (IgG); Immunoglobulin M (IgM); Intensive Care Unit (ICU); Interleukin 6 (IL-6); Interleukin 8 (IL-8); Interquartile range (IQR); Myelin Oligodendrocyte Glycoprotein (MOG); N-methyl-D-aspartate (NMDA); Nonsteroidal anti-inflammatory drug (NSAID); Systemic Lupus Erythematosus (SLE); Tumor necrosis factor α (TNF-α)

*In this case percentages refer to the 85 total population.*
Figure 1

PRISMA flowchart. Search results and study selection process by stage according to the PRISMA statement guidelines.
Figure 2

JBI Critical Appraisal Checklist. Summary of results for each of the JBI Critical Appraisal Checklist for Case Reports quality domains.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.docx