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# Impact of COVID-19 on autoimmune diseases

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**Abstract**

Autoimmune diseases are characterized by the existence of autoantibodies and perpetuated inflammatory reactions due to the loss of immune tolerance and dysregulated immune system, leading to target organ damage and malfunction. Autoimmune diseases which are occurred as a result of COVID-19 is a new phenomenon that was attract a lot of attention globally. Autoantibodies are frequently detected in patients with COVID-19 possibly reflecting a pathogenic role of immune dysregulation. The relative role(s) played by the immune response to SARS-CoV-2 versus direct viral effects in the respiratory system and other organ systems has been questioned, with the possibility of immunopathogenesis being a major causal component of severe COVID-19. According to the evidence of COVID-19-mediated autoimmunity, it might be fair to think of autoimmunity as a serious complication of COVID-19.

**Keywords:** COVID-19 – autoimmune diseases - SARS-CoV-2

## Introduction

Emerging and reemerging pathogens are global challenges for public health. In late December 2019, several local health facilities reported clusters of patients with pneumonia of unknown cause that were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China. On December 31, 2019 [1]. This new coronavirus disease was termed Coronavirus Disease 19 (COVID-19) by the World Health Organization (WHO) on February 11, 2020, and it was declared a pandemic on March 11, 2020. The International committee on Taxonomy of Viruses renamed the virus from 2019 novel coronavirus (2019-nCoV) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2].

Studies show that some people with COVID-19 have responded to certain medications used to treat rheumatic autoimmune diseases, drawing attention to the relationship between COVID-19 and autoimmune diseases [3].

## Role of immune system in pathogenesis

Covid 19 patients exhibited heterogeneous signs and symptoms, varying from influenza like and respiratory, to systemic symptoms that affect multiple organs [4, 5]. Autoantibodies are frequently detected in patients with COVID-19 possibly reflecting a pathogenic role of immune dysregulation [6]. Viral effects and immune-mediated mechanisms are the two pathogeneses of severe acute respiratory syndrome–associated coronavirus (SARS-CoV) infection, and autoimmune responses have been found in SARS-CoV infection. One study suggested that the SARS-CoV antigen can cross-react with autoantibodies in autoimmune diseases [3], therefore, autoimmune phenomena exist in SARS subjects [7]. Autoimmune diseases are characterized by the existence of autoantibodies and perpetuated inflammatory reactions due to the loss of immune tolerance and dysregulated immune system, leading to target organ damage and malfunction [3]. The relative role(s) played by the immune response to SARS-CoV-2 versus direct viral effects in the respiratory system and other organ systems has been questioned, with the possibility of immunopathogenesis being a major causal component of severe COVID-19. Elevated innate immune cytokines detected in peripheral blood including interleukin (IL)-1, IL-6, IL-8, or C-X-C Motif Chemokine Ligand 10 (CXCL10) have been associated with severe or fatal COVID-19 [8].

## Autoimmune complications of COVID-19

### Sub-acute thyroiditis

Subacute thyroiditis (SAT) is a self-limiting inflammatory disorder of the thyroid and a relatively uncommon cause of thyrotoxicosis linked to a viral infection. SARS-COV- was responsible for follicular cell destruction and dysfunction and fibrosis following the acute phase, representing the histopathological hallmarks of destructive thyroiditis [9]. The thyroid gland and the virus infection with its associated inflammatory-immune responses are known to be engaged in complex interplay. SARS-CoV-2 uses ACE2 combined with the transmembrane protease serine 2 (TMPRSS2) as the key molecular complex to infect the host cells. Interestingly, ACE2 and TMPRSS2 expression levels are high in the thyroid gland and more than in the lungs [10]. COVID-19-associated SAT is likely to present with the classic clinical features of

fever and neck pain, hyperthyroid TFTs (low TSH, high free T4), and suggestive ultrasound findings [11].

**Autoimmune hypothyroidism**

The term "hyperthyroidism" defines a syndrome associated with excess thyroid hormone production. Graves' disease is an autoimmune disease, and a leading cause of hyperthyroidism. Hyperthyroidism is considered [12]. A case of Graves' disease, which developed following SARS-CoV2 infection was presented in a 43-year-old man with no prior history of thyroid disease [13].

**Kawasaki disease (KD)**

Kawasaki disease (KD) is an acute inflammatory disease characterized by medium-sized vasculitis with predilection for coronary arteries, predominantly affecting children <5 years of age [14]. A possible correlation between Kawasaki disease (KD), as an autoimmune disorder with mucocutaneous-lymph node involvement, and COVID-19 in pediatrics has been raised [15]. Children diagnosed after the SARS-CoV-2 epidemic began showed evidence of immune response to the virus, were older, had a higher rate of cardiac involvement, and features of MAS. The SARS-CoV-2 epidemic was associated with high incidence of a severe form of Kawasaki disease [16].

**Immune Thrombocytopenia Purpura (ITP)**

Thrombotic complications seem to emerge as an important issue in patients infected with COVID19. Preliminary reports on COVID-19 patients' clinical and laboratory findings include thrombocytopenia, elevated D-dimer, prolonged prothrombin time, and disseminated intravascular coagulation [17]. ITP can often be unmasked or exacerbated by viral syndromes. While molecular mimicry is common with several viruses, it is possible that COVID-19 can induce a similar physiologic response [18]. It is important for practitioners to be vigilant and aware of this phenomenon as case reports suggests that Covid-19 was a causal factor in immune thrombocytopenia [19].

**Autoimmune hemolytic anemia (AIHA)**

Red blood cell (RBC) autoantibodies are a relatively uncommon cause of anemia. However, autoimmune hemolytic anemia (AIHA) must be considered in the differential diagnosis of hemolytic anemias, especially if the patient has a concomitant lymphoproliferative disorder, autoimmune disease, or viral or mycoplasmal infection. Classifications of AIHA include warm AIHA, cold agglutinin syndrome, paroxysmal cold hemoglobinuria, mixed-type AIHA, and drug-induced AIHA [20]. Autoimmune hemolytic anemia (AIHA) is a rare autoimmune disorder characterized by autoantibodies against red blood cells (RBCs), and it can be triggered by various viral infections. In COVID-19, both cold agglutinin disease (CAD) and warm AIHA have been reported [21].

**Guillain–Barré syndrome (GBS)**

Guillain-Barré syndrome (GBS) is a heterogeneous disorder which often follows viral infections such as influenza virus, campylobacter jejuni, and zika virus, and commonly presents with a prolonged clinical course leading to increased morbidity among affected patients [22, 23]. On MRI, typical findings in Guillain–Barré syndrome are surface thickening and contrast enhancement on the conus medullaris and the nerve roots of the cauda equina. The facial nerve is the most affected cranial nerve [24]. Overlap of respiratory paralysis in GBS and COVID-19 infection makes it critically important for the physicians to diagnose and manage GBS early in all patients of COVID-19, recognizing that respiratory compromise due to GBS may be rapidly progressive but treatable with a high success rate in COVID-19 patients [25]. Several published reports have described a possible association between Guillain-Barré syndrome (GBS) and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection [26].

**Conclusion**

Autoimmune diseases are chronic disabling conditions that negatively affect individuals, families, society, and the healthcare system. Besides this, pandemics are always associated with different concurrent complications and challenges, as well as potential sequelae that may emerge either early or late after the pandemics. According to the evidence of COVID-19-mediated autoimmunity, it might be fair to think of autoimmunity as a serious complication of COVID-19. A more precise understanding of the involved mechanisms potentially helps to monitor and prevent the incidence or exacerbation of autoimmune manifestations [27].

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