COVID-19 in Special Patient Groups

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ABSTRACT

At the end of 2019, a new coronavirus was identified as the cause of many pneumonia cases in Wuhan, a city in China’s Hubei Province. These cases spread rapidly, causing an epidemic throughout China, followed by increasing cases in other countries. In February 2020, the World Health Organization defined the definition of Coronavirus disease-2019 (COVID-19), which means 2019 coronavirus disease. The virus that causes COVID-19 is called severe acute respiratory syndrome-coronavirus-2. The rapidly expanding COVID-19 pandemic has affected all areas of daily life, including medical care. Although this epidemic significantly affected individuals from all parts of society, the clinical course, diagnosis, and treatment approaches may differ in some specific populations. The association of COVID-19 with various medical comorbidities and its impact on specific and vulnerable populations need to be addressed separately. This information will also assist in the management of COVID-19. The effects and the relationship of COVID-19 on comorbidities (chronic renal, diabetes mellitus, chronic liver, etc.) and special populations (pregnant, elderly, transplant patients, etc.) are comprehensively presented in the text.

Keywords: Chronic disease, comorbidity, COVID-19, special populations

Introduction

Pregnancy

The Coronavirus disease-2019 (COVID-19) pandemic has many unknowns in terms of consequences for pregnant women. Complications and adverse events in pregnant women in infections caused by other coronaviruses, such as severe acute respiratory syndrome (SARS) and middle east respiratory syndrome, have led to careful evaluation of pregnant women against serious SARS-coronavirus-2 (CoV-2) infection.

Many physiological changes occur in the immune system, respiratory system, cardiovascular system, and coagulation pathway during pregnancy. These changes can have positive or negative effects on the course of COVID-19. While the impact of SARS-CoV-2 on pregnancy is not yet clear, collaborative, global studies are needed to determine the effects on implantation, fetal growth and development, delivery, and neonatal health. In addition to the direct effects of the disease, the restrictions caused by the pandemic negatively affect pregnant and maternal health by blocking access to reproductive health services and causing increased pressure on mental health and socio-economic deprivation.

Prevention, clinical manifestations, and diagnosis of COVID-19 are the same for pregnant and non-pregnant people, but there are some special considerations during pregnancy.

Pregnancy does not increase susceptibility to SARS-CoV-2 infection; however, it appears to worsen the clinical course of COVID-19 compared with women of reproductive age.
who are not pregnant. The risk of severe COVID-19 during pregnancy may be higher than that in the general population.

Vertical transmission is possible. Although congenital infection rates have been reported to be about 2 percent of maternal infections, well-documented cases of possible intrauterine transmission are rare. Severe neonatal disease is rare. Antenatal corticosteroid use for the threat of preterm labor is safe for the mother, and corticosteroid use may be beneficial for severe maternal disease.

Clinicians should be cautious about thromboprophylaxis and possible thromboembolic events in mothers with COVID-19. Asymptomatic COVID-19 may be common during pregnancy. The risk of developing preeclampsia is high even if the infection is asymptomatic (2).

Clinicians should be alert to the wider effects of the pandemic and ensure screening for mental health problems (3).

Anyone planning a pregnancy or who is pregnant or newly pregnant should be offered the COVID-19 vaccine as soon as possible rather than delaying vaccination after birth or breastfeeding (Class 1B). According to all available data, current SARS-CoV-2 vaccinations are safe for use before, during, and after pregnancy. The vaccine reduces the risk of developing COVID-19 and the likelihood of severe transmission if the disease develops (4).

Compared with uninfected pregnancies, pregnant women infected with COVID-19 do not have an increased risk of miscarriage or congenital anomalies.

Although the risk of preterm birth, cesarean delivery, and stillbirth appears to be increased, this risk appears to be limited to patients with severe or critical illnesses and third-trimester infections (5).

### Geriatry

The susceptibility to infections increases in elderly individuals due to physiological and immunological disorders such as deterioration of mucosal barriers with aging, cellular and humoral immunity changes, and decreased antibody response to vaccines. Additionally, multiple chronic diseases in geriatric patients increase this susceptibility and cause infections to be more severe than those in young people.

Elderly individuals also have a high risk of mortality and morbidity in terms of COVID-19. Additionally, COVID-19 may present different symptoms and clinical findings in the elderly compared to young people. Although COVID-19 usually presents with symptoms such as fever, cough, weakness, anorexia, shortness of breath, myalgia, sore throat, loss of taste, and smell in young people, it has been reported that dyspnea is more common in the elderly (6,7). With aging, the fever response to infections decreases, and the cough reflex weakens (8). As in other infections, fever response may not be obtained in the elderly, symptoms may be milder, or non-specific findings may be seen in COVID-19. Symptoms and signs such as confusion, mental changes, decreased mobility, loss of appetite, and urinary/stool incontinence may be detected (9). Atypical presentation of COVID-19 in the elderly may cause a delay in diagnosis, detection at a later stage, and even death. Asymptomatic infection is also common in the elderly. The development of delirium in hospitalized elderly patients diagnosed with COVID-19 has been associated with increased mortality (10).

The treatment approach for COVID-19 in the elderly is the same as in younger patients. In addition to drug therapy, supportive treatments such as nutrition, exercise, and respiratory rehabilitation should be applied when necessary.

### Human Immunodeficiency Virus Infection

The clinical features of COVID-19 appear the same in people with human immunodeficiency virus (HIV) as in the general population.

Among patients with well-controlled HIV infection under treatment, the majority remain asymptomatic (11). However, people with HIV are at risk for serious COVID-19 and complications. In several large observational studies, HIV infection has been associated with more severe COVID-19, higher hospitalization rates, higher rates of new infections after vaccination, and in some cases higher death rates from COVID-19 (12).

Among people with HIV, those who are older, have multiple comorbidities, have lower CD4-cell counts, and identify as Black or Hispanic are at the highest risk for adverse outcomes (13). Generally, the management of COVID-19 in patients with HIV is the same as in patients without HIV.

### Rheumatological Diseases

The presence of a rheumatic disease alone may be associated with an increased risk of facing further complications from COVID-19, although the evidence is mixed (14).

Additionally, patients with various rheumatic diseases have a higher prevalence of various comorbidities such as advanced age, chronic lung and kidney disease, heart disease, hypertension, obesity and diabetes, which are risk factors for serious disease in COVID-19.
The clinical features of COVID-19 in patients with systemic rheumatic diseases are variable and do not differ from patients without these underlying diseases.

However, various rheumatic diseases may have clinical features that can mimic COVID-19, such as weakness, muscle pain, and fatigue. For patients with a current diagnosis of rheumatic disease, the clinician may need to differentiate the signs and symptoms of a disease flare from those of possible COVID-19 infection; therefore, the suspicion of possible COVID-19 infection should always be kept in mind.

Adjustments to medication regimens in patients with documented or probable COVID-19 should be individualized, with particular attention to the severity of the infection. Approaches are largely expert judgment, and temporary discontinuation of biological agents (e.g., anti-TNF inhibitors, IL-6 receptor inhibitors) is recommended. For most patients with COVID-19, hydroxychloroquine/chloroquine, sulfasalazine, methotrexate, leflunomide, immunosuppressants (e.g., mycophenolate, AZA), JAK inhibitors. However, where patients have active or organ-threatening rheumatic disease, their immunosuppressive therapy may need to be continued based on an individualized assessment (15).

The decision to continue these agents should be made with rheumatology, infectious diseases, and intensive care specialists involved in managing the patient's acute illness. Another exception to discontinuation of a particular agent may be where an antirheumatic therapeutic is also used for treating COVID-19. Additionally, patients receiving glucocorticoids should maintain the prescribed dose to prevent acute rheumatic disease exacerbation and complications of adrenal insufficiency associated with abrupt discontinuation of this drug (16).

There is limited evidence that COVID-19 infection has poor outcomes and subsequently adversely affects rheumatic disease in patients with rheumatic disease. The use of the vaccine is recommended for patients with rheumatic diseases.

**Oncological Diseases**

While the data is mixed, most studies suggest a higher risk of serious COVID-19 in adult patients with active cancer (17,18).

Improvements during prognosis are seen with advances in treating COVID-19 and early diagnosis (19).

The risk likely varies with the type and stage of cancer and the treatment received. In particular, hematological malignancies or lung cancer, advanced and/or progressive cancer, active chemotherapy treatment, advanced age, and comorbid conditions are risk factors for severe COVID-19 (20).

Previous cancer is also a risk factor, but the risk is lower than that with active cancer (20).

Overall, COVID-19 disease management is similar to that in the general population. However, cancer is considered a risk factor for progression to severe COVID-19 infection, leading to faster and earlier initiation of available treatments.

For most cancer patients with COVID-19, chemotherapy, or immunotherapy should be discontinued, whether patients are symptomatic of COVID-19 or not. Generally, cancer treatment is continued when contagion-based measures can be discontinued. Institutional protocols usually determine the duration of such measures.

**Diabetes Mellitus**

People with diabetes are at high risk for COVID-19, and complications such as severe illness, need for hospitalization, need for intubation, and death may occur more frequently. Intensive care unit stays, long hospital stays, and death has been reported more frequently in patients with type 2 diabetes due to COVID-19 (21,22,23). Data on serious morbidity and mortality rates in patients with type 1 diabetes are less, but just as with other infections, patients with type 1 diabetes have an increased risk of COVID-19 compared with the healthy population.

The relationship between COVID-19 and diabetes is bilateral. COVID-19 can damage the pancreatic endocrine and exocrine systems with a cytokine storm. The observation of higher amylase levels in patients with severe COVID-19 infection than in mild cases supports this (24). It also stimulates hyperglycemia cytokine storm. COVID-19 cases with diabetes had higher levels of IL-6, C-reactive protein, and D-dimer than those without (25).

The role of hyperglycemia in severe disease in diabetic individuals is not fully understood. It is unclear whether hyperglycemia is a cause or consequence, as COVID-19 triggers an intense inflammatory response. As a matter of fact, there are studies reporting patients who develop newly diagnosed diabetes after COVID-19 (26). Newly diagnosed hyperglycemia may be due to critical illness or directly associated with beta cell damage from the virus or with the inflammatory response to the virus (27).

Whatever the cause, hyperglycemia indicates a poor prognosis. It has been determined that glycemic control and fluctuations in the first days of hospitalization determine the length of stay, need for intensive care, and mortality (28). Last previous HbA1c is associated with outcomes in both type 1 and type 2 diabetes and mortality, especially when HbA1c is >10% in COVID-19 disease (29).
Diabetic ketoacidosis, hyperosmolar coma, and severe insulin resistance can be seen in COVID-19 in people with known diabetes. The approach in managing patients should aim to prevent hypoglycemia, significant hyperglycemia, and ketoacidosis. Although using corticosteroids in addition to oxygen therapy reduces mortality, it can increase hyperglycemia, the need for insulin therapy, diabetic ketoacidosis, and hyperosmolar coma by increasing existing insulin resistance. The continuation of current insulin treatments, frequent blood glucose, and ketone monitoring are recommended in diabetic COVID-19 cases (30).

**Chronic Lung Disease**

Chronic lung diseases such as chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, interstitial lung disease, lung cancer, and sarcoidosis are associated with poor outcomes of COVID-19.

**COPD:** A meta-analysis stated that a previous history of COPD increases the risk of severe COVID-19 4-fold, and active smoking increases the risk of severe COVID-19 (31). COPD has been associated with a higher need for intensive care, invasive ventilation, and a higher risk of death in patients with COVID-19 (32,33). Patients with COPD presenting with new or increased respiratory symptoms, fever, or other COVID-19 symptoms should be tested for COVID-19, even if they are mild (34). It is recommended that patients with COPD continue to take all maintenance medications, such as bronchodilators and inhaled glucocorticoids, throughout the COVID-19 pandemic. There is insufficient evidence that inhaled glucocorticoids have an adverse effect on the course of COVID-19. Because of the risk of aerosolizing SARS-CoV-2 and increasing the spread of disease in patients receiving nebulized therapy, the risk of transmission should be minimized by avoiding using nebulizers in the presence of other people (34).

**Asthma:** In studies on the risk of COVID-19 in asthma patients, no increased risk of severe COVID-19 has been demonstrated in patients with well-controlled mild-to-moderate asthma. These patients are also not at risk for death associated with COVID-19. However, hospitalized people with severe asthma who have recently required oral corticosteroids are at an increased risk of death from COVID-19 (35). Patients with asthma are advised to continue taking the drugs they used during the pandemic, particularly inhaled corticosteroids.

**Bronchiectasis:** Patients with bronchiectasis may be more susceptible to COVID-19 than those without. COVID-19 patients with bronchiectasis have seen worse clinical outcomes, such as more severe clinical manifestations and death (36).

**Interstitial lung disease:** People with interstitial lung disease are at an increased risk of death from COVID-19, particularly if they are fibrotic. There is also an increased risk in older men and those with obesity or low lung function. For this reason, a diet is recommended for those who are overweight and have interstitial lung disease (34).

**Sarcoidosis:** Studies on patients with sarcoidosis have reported that the rate of COVID-19 is higher than that in the general population. It has been determined that sarcoidosis patients, especially those with lung and neurological involvement, are at a high risk for COVID-19 (37). The use of rituximab, especially in sarcoidosis patients, has been associated with an increased risk of COVID-19.

**Chronic Renal Disease**

In patients with chronic kidney disease, the susceptibility to infections is generally increased due to the deterioration of the immune system. Chronic kidney disease is also an independent risk factor for COVID-19-related mortality (38). High mortality in these patients may also be associated with advanced age and a high number of comorbidities. COVID-19 mortality has also increased in patients undergoing hemodialysis. The necessity of going to the dialysis center 3 times a week for hemodialysis patients, close contact with other patients and healthcare professionals increases the likelihood of having COVID-19 (39).

Comorbidities such as immunosuppressive drugs, advanced age, diabetes mellitus (DM), hypertension, and cardiovascular disease increase the risk of developing COVID-19 complications in kidney transplant patients (40). It has been reported that acute kidney injury may develop in almost half of the hospitalized kidney transplant patients with COVID-19 (41). Simultaneously, the risk of mortality in kidney transplant COVID-19 patients has increased compared with the general population. It may be necessary to adjust the immunosuppressive agents used in kidney transplantation patients with COVID-19.

**Chronic Liver Disease**

It is unclear whether those with chronic liver disease are more susceptible to COVID-19. However, patients with chronic liver disease or those receiving immunosuppressive therapy may be at higher risk of serious illness for COVID-19.

**Chronic hepatitis B (HBV) and hepatitis C (HCV):** It is not known whether patients with chronic HBV and HCV are at a high risk of serious COVID-19. However, patients with chronic HBV or HCV-related cirrhosis have a poor prognosis (42).
There is no evidence that antiviral drugs used in chronic HBV or HCV have a negative effect on COVID-19. Therefore, patients with COVID-19, while using antiviral medication should not discontinue their antiviral therapy. HBV reactivation has been observed with glucocorticoids and tocilizumab are used for treating COVID-19. Therefore, when these treatments are to be administered, patients should be evaluated for HBV prophylaxis.

**Non-alcoholic fatty liver disease:** These patients have many risk factors, such as obesity and DM and therefore have increased mortality in COVID-19 and other respiratory diseases (43). These patients should be encouraged to change their lifestyle.

**Alcoholic liver disease:** Those with alcoholic liver disease are immunocompromised and more prone to infections. Additionally, most of these patients are accompanied by comorbidities such as obesity and metabolic syndrome. The restrictions and isolation applied during the pandemic period may also increase alcohol intake in these patients. For all these reasons, patients in this group are among the groups most affected by the COVID-19 pandemic and have a high risk of serious illness (43,44).

**Autoimmune hepatitis:** There is no need for discontinuation or dose adjustment of maintenance immunosuppressive therapy during the pandemic period in patients with autoimmune hepatitis. Medication adjustments may be necessary for patients with autoimmune hepatitis who experience COVID-19. There is no need to discontinue or adjust the dose of the immunosuppressive agent used in asymptomatic or mild COVID-19. In moderate or severe COVID-19, patients’ previous history of relapse and risk of exacerbation should be evaluated. The dose of immunosuppressive drugs (e.g., azathioprine) can be reduced by 25-50%. Symptoms and daily liver enzymes should be monitored in hospitalized patients. If hospitalization is not required, liver enzymes need to be checked every 1-2 weeks, and if symptoms and enzymes are stable, follow-up needs to be done every 2-4 weeks. In cases of COVID-19-related neutropenia or lymphopenia, the dose of azathioprine or mycophenolate mofetil should be reduced and blood counts should be checked every 1-2 weeks (45).

**Solid Organ Transplant**

Solid organ transplant recipients may be at increased risk for coronavirus disease as they are immunocompromised and less likely to respond an adequate immune response to the vaccine. COVID-19 poses challenges for individuals who are solid organ transplant candidates or recipients and for the transplant process.

Donor-derived SARS-CoV-2 infection has been reported through lung transplantation, but not through non-lung transplantation (46).

Considering the risk of progression to severe disease and the potential to transmit SARS-CoV-2 to healthcare workers, all solid organ donors, and transplant candidates should be screened for COVID-19 with history, lung imaging, and microbiological testing.

After solid organ transplant, transplant recipients may be at risk of contracting infection, progressing to symptomatic infection, and/or developing more severe COVID-19.

The clinical manifestations of COVID-19 in solid organ transplant recipients are variable and generally similar to those observed in non-immunosuppressed patients. However, fever is less common.

The approach to diagnosis is similar to that in the general population. Clinicians are more sensitive to assessing and testing transplant recipients as transplant recipients may be missing signs and symptoms of COVID-19 and disease progression can be rapid (47).

The treatment approach (e.g., use of antivirals, supportive care) is similar to that for the general population. Attention should be paid to potential drug-drug interactions and their effects on the immunosuppressive regimen.

Adjustments for treating the immunosuppressive regimen must be individualized depending on the severity of the disease, the specific regimen used, the type of organ transplant, the post-transplant time, and the risk of acute allograft rejection. Some transplant recipients recover by reducing their dose of immunosuppressive therapy. Conversely, continued immunosuppression in some patients may increase the risk of uncontrolled infections.

**Ethics**

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**Authorship Contributions**


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