

## COVID-19 and Comorbidities

### REVIEW

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#### ÖZET:

Aralık 2019'da Wuhan'da tespit edilen yeni bir koronavirüs hızla Çin'e, ardından diğer ülkelere yayılmıştır. Bu çalışmanın amacı, eşlik eden hastalıkların COVID-19 hastaları üzerindeki etkilerini araştırmak ve bu hastaların yönetimi hakkında bilgi vermektir. PubMed ve Google Akademik elektronik veritabanları kullanılarak COVID-19'un klinik özellikleri ve eşlik eden hastalıklar değerlendirilmiştir. Altta yatan hastalıkları bulunan ve ileri yaşta olan bireylerde hastalık daha şiddetli seyretmektedir. Morbidite ve mortalite ile ilişkili hastalıklar ve diğer durumlar arasında hipertansiyon, diabetes mellitus, kardiyovasküler hastalık, kronik akciğer hastalığı, kanser (özellikle metastatik hastalık, akciğer kanseri ve hematolojik maligniteler) ve kronik böbrek hastalığı bulunmaktadır. Komorbidite sayısı arttıkça, hastaların klinik seyri daha ciddi olmaktadır. Eşlik eden hastalıkların kapsamlı olarak değerlendirilmesi ve iyi bir şekilde yönetilmesi, COVID-19 hastalarının daha iyi bir sonuç almasına yardımcı olabilir.

**Anahtar Sözcükler:** COVID-19, Komorbidite, Diabetes Mellitus, Kronik Böbrek Hastalığı, Kanser

#### ABSTRACT:

A novel coronavirus was identified in Wuhan in December 2019 and it rapidly spread throughout China, followed by in other countries. The aim of this study is to investigate the effects of comorbidities on patients with COVID-19 and to give information about their management. The electronic databases PubMed and Google Scholar have been used to assess comorbidities and clinical characteristics of COVID-19. Severe disease predominantly occurs in adults with underlying medical comorbidities or advanced age. Comorbidities and other conditions that associated with morbidity and mortality include hypertension, diabetes mellitus, cardiovascular disease, chronic lung disease, cancer (particularly metastatic disease, lung cancer, and hematologic malignancies) and chronic kidney disease. As the number of comorbidity increases, patients' clinic progresses more severely. A comprehensive assessment and good management of comorbidities can help patients with COVID-19 achieve a better outcome.

**Keywords:** COVID-19, Comorbidities, Diabetes Mellitus, Chronic Kidney Disease, Cancer

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## 1. INTRODUCTION

A novel coronavirus was identified in Wuhan in December 2019 and it rapidly spread throughout China, followed by in other countries. In February 2020, the World Health Organization defined the disease COVID-19, which infers coronavirus disease 2019 (1).

COVID-19 has a heterogeneous clinical spectrum, ranging from mild flu-like symptoms to multiple organ failure, acute respiratory distress syndrome and death. In a report from China that included approximately 44,500 confirmed infections with an estimation of disease severity (2):

- 81% of patients was reported as mild (no or mild pneumonia)
- 14% of patients was reported as severe disease (eg, with hypoxia, dyspnea, or >50% lung involvement on imaging within 24-48 hours)
- 5% of patients was reported as critical disease (eg, with shock, respiratory failure, or multiorgan dysfunction)
- The overall mortality rate was 2.3%; all deaths were reported among critical cases.

Critical or fatal disease proportion is higher among hospitalized patients. In a research that included 2741 patients in a

health care system of New York City, who were hospitalized for COVID-19, 665 patients (24%) died or were discharged to hospice, 749 patients (27.3%) received intensive care, and 647 (23.6%) received invasive mechanical ventilation (3).

### *1.1. Risk factors for severe illness*

Severe disease predominantly occurs in adults with underlying medical comorbidities or advanced age. Comorbidities and other conditions that associated with morbidity and mortality include (table 1)(4):

- Hypertension
- Diabetes mellitus
- Cardiovascular disease
- Chronic lung disease
- Cancer (particularly metastatic disease, lung cancer, and hematologic malignancies)
- Chronic kidney disease
- Obesity
- Smoking

Since cardiovascular and pulmonary diseases are the subject of separate articles, we will deal with other internal medicine problems; diabetes mellitus, chronic kidney failure and cancer.

**Table 1. Risk factors for severe COVID-19**

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|--|
| ▪ Age >65 years  |
| ▪ Hypertension   |
| ▪ Cardiovascular disease   |
| ▪ Diabetes mellitus  |
| ▪ Pulmonary disease  |
| ▪ Chronic kidney disease   |
| ▪ Obesity (BMI $\geq$ 30)  |
| ▪ Use of biologics agents (eg, TNF inhibitors, interleukin inhibitors) |
| ▪ Transplant or other immunosuppression                                |
| ▪ HIV, CD4 cell count <200 cells/microL or unknown CD4 count           |

## 1. DIABETES MELLITUS

### *1.1 Diabetes and Infection: Pathophysiology*

Diabetes is a chronic inflammatory situation characterized by multiple metabolic and vascular disorders that affects the response against microorganisms. Insulin resistance and hyperglycemia increase synthesis of pro-inflammatory cytokines, glycosylation end products (AGEs) and adhesion molecules (5-6). This inflammatory process may be the underlying mechanism that leads to infections in patients with diabetes.

Immunity defects have been linked with hyperglycemia, even though still not fully understood. Poorly controlled diabetes has been associated to inhibited lymphocyte proliferative response, impaired neutrophil and monocyte/macrophage functions. Complement activation dysfunction and abnormal hypersensitivity reaction have also been defined in diabetic patients (7-9). Reduction in forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) is associated with hyperglycaemia(10). Infections, particularly pneumonia and influenza, are common and more serious in older patients with type 2 diabetes mellitus.

Uncontrolled glycaemia and diabetes were noticed as significant predictors of morbidity and mortality in patients who infected with various viruses, including the SARS-CoV, MERS-CoV and 2009 pandemic influenza A (H1N1)(11-13). In the current SARS-CoV-2 pandemic, studies from China (14-15) and Italy (16) reported that older patients with comorbidities, including diabetes, were at higher risk for mortality and severe COVID-19.

### *1.2. Clinical Management of Patients with COVID-19 and Diabetes*

There is insufficient data on optimal management of diabetics infected with

SARS-CoV-2 and COVID-19 patients with glycemic decompensation. Careful evaluation of drug interactions and glucose monitoring can reduce symptoms worsening and negative outcomes. In addition to hyperglycemia, the possibility of hypoglycemic attack should not be ignored. Patient-specific therapeutic strategies and optimal glucose control targets should be formulated according to disease severity, age, comorbidity and diabetic complications (17).

For the treatment of COVID-19, no drug or vaccine has been formally approved yet. The efficacy and safety of potential treatment alternatives, such as chloroquine phosphate, lopinavir/ritonavir, tocilizumab, remdesivir, ribavirin, being investigated by various clinical studies (18). Although the mechanism remains unclear, hydroxychloroquine improves glycemic control in treatment-refractory diabetic patients (19-20).

## 2. CHRONIC KIDNEY DISEASE

COVID-19 also affects patients with various kidney diseases, like other comorbidities. Patients with end-stage renal failure are particularly vulnerable to COVID-19 in this population due to advanced age and comorbidity such as diabetes and hypertension (21).

To guide nephrology clinicians, the International Society of Nephrology (ISN), American Society of Nephrology (ASN), and Centers for Disease Control (CDC) have published several guidelines. These resources include guidance about the following: early recognition and isolation of patients; separation and cohorting of patients within the dialysis unit and waiting areas; use of personal protective equipment (PPE) in the dialysis unit; and other measures for patients with suspected or confirmed COVID-19 (22-23).

Continuous renal replacement therapy (CRRT) is preferred if critical patients in the intensive care unit have end-stage renal failure or acute kidney injury (AKI). Depending on staff and machine availability, in patients who are able to tolerate intermittent hemodialysis (IHD) and hemodynamically stable, continuous low-efficiency dialysis (SLED), also called CRRT or long-term intermittent kidney replacement therapy (PIRRT), should be performed. This will potentially help limit exposure among hemodialysis nurses and minimize wastage of PPE (21).

COVID-19 patients without critical disease should be dialyzed in their isolation rooms instead of being transferred to the inpatient dialysis unit. To reduce the need for the nephrologist or the dialysis nurse to enter

an isolation room, audio streams and video should be used (24).

In patients with COVID-19 who develop AKI, should be avoided hypervolemia and be optimized volume status. Ultrasound and physical examination evaluations should be coordinated with the consulting teams to minimize contact, as much as possible.

### 3. CANCER

Cancer patients are at higher risk for COVID-19-related serious events (need for intensive care and mechanical ventilation, or death) compared to the general population, because they are immunocompromised. Even during a pandemic, cancer patients require timely evaluation, diagnosis, and treatment. It is difficult to treat cancer patients without compromising their care, and pragmatic approaches are needed to deal with this challenge (25).

Cancer patients who have respiratory symptoms and signs (eg cough, fever, dyspnea, and hypoxia) or who have been exposed to somebody with confirmed COVID-19 should be tested for SARS-CoV-2. If the test is positive, immunosuppressive cancer therapies should be delayed until the symptoms of COVID-19 improve. Some oral non-immunosuppressive treatments can be

continued depending on the patient's condition (26).

To assist oncology clinicians, oncology societies, namely the European Society of Medical Oncology (ESMO), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology, and many more, have issued guidelines. Recommendations of the ESMO (table 2) should be used as a guide to prioritize different aspects of cancer care to reduce the negative effects of COVID-19 pandemic on the follow-up of cancer patients (27).

### CONCLUSION

COVID-19 cases with any comorbidities give worse clinical results than those without. As the number of comorbidity increases, patients' clinic progresses more severely. A comprehensive assessment and good management of comorbidities can help patients with COVID-19 achieve a better outcome.

**Table 2.** COVID-19 and Cancer Patient Guide of ESMO

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|---|
| <ul style="list-style-type: none"> <li>▪ During the COVID-19 pandemic, the Benefit/Risk ratio of cancer treatment may need to be reconsidered.</li> </ul>   |
| <ul style="list-style-type: none"> <li>▪ Two groups of patients have been identified: “patients off therapy” (A); and patients under treatment (B) <ul style="list-style-type: none"> <li>(A) who have completed a treatment or have disease under control (off therapy)</li> <li>(B) neoadjuvant or adjuvant curative treatment or treatment for metastatic disease</li> </ul> </li> </ul>   |
| <ul style="list-style-type: none"> <li>▪ Patients with “active disease” can be eligible for surgery, chemotherapy and/or radiotherapy, biological therapy, endocrine therapy and immunotherapy (either in the adjuvant or in the metastatic setting)</li> </ul>   |
| <ul style="list-style-type: none"> <li>▪ For all patients (A and B) it is mandatory to provide health education: <ul style="list-style-type: none"> <li>a) Avoid crowded places</li> <li>b) Wear PPE when you attend hospital for visits and treatments</li> <li>c) Correctly wash your hands according to World Health Organization (WHO) indications</li> <li>d) Do not have contacts with friends and relatives with COVID-19 symptoms or living in endemic zones</li> <li>e) Guarantee social distancing with all people: protect yourself to protect others</li> </ul> </li> </ul> |

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