

## TACKLING COMORBIDITIES AND CRITICAL CARE

### Editorial

#### Comorbidities and COVID-19

The current pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease (COVID-19) has posed enormous challenges to healthcare systems all around the world. While supportive therapy remains the backbone of the management of infected patients, the consensus seems to be a biphasic approach with possible antiviral therapy during the initial phase and immunosuppressive strategies in the later hyperinflammatory phase.

With the unprecedented explosion and propagation of both peer-reviewed and non-peer-reviewed research into and

information about the disease, while helping the physicians on the frontlines, has made it certain that any summary will be outdated by the time it is published, if not before. However, an attempt is made in this article to introduce some of the comorbidities and their interaction with COVID-19.

The disease has a number of interactions with a large number of comorbidities. A large China CDC case series<sup>[1]</sup> of 44,672 cases shows that the main risk factors of mortality include increasing age (8% in the 70–79 years age group, 14.8% in the  $\geq 80$  years age group), cardiovascular diseases (10.5%), diabetes (7.3%), chronic respiratory diseases (6.3%), hypertension (6%), and cancer (5.6%). A systematic review from China showed that critical illness/death is more

in patients with diabetes (OR = 3.68, 95% CI 2.68–5.03), hypertension (OR = 2.72, 95% CI 1.60–4.64), cardiovascular disease (OR = 5.19, 95% CI 3.25–8.29), and respiratory disease (OR = 5.15, 95% CI 2.51–10.57)<sup>[2]</sup> Similar findings have been published from other countries.<sup>[3]</sup>

## Cardiovascular diseases

Patients with cardiovascular diseases such as hypertension, cardiomyopathy, arrhythmias and coronary artery disease are more likely to be infected and to develop severe symptoms.<sup>[4]</sup> Risk factors for cardiovascular disease such as age, diabetes, and hyperlipidemia are themselves associated with impaired immune response and thus may predispose to COVID-19.<sup>[5]</sup> There may be an increased frequency of cardiovascular events after COVID-19 infection. This may occur with multifactorial and bidirectional mechanisms, as in other viral infections such as influenza.<sup>[6,7]</sup> COVID-19 specific mechanisms such as higher expression of Angiotensin Converting Enzyme-2 (ACE2) in patients with hypertension have been proposed. Post-COVID-19 cardiovascular sequelae include myocardial ischemia and non-ischemic myocarditis, evidenced by elevated serum troponins. The proposed mechanisms include direct damage to cardiomyocytes, systemic inflammation, interstitial fibrosis, immune dysregulation, exaggerated cytokine response and hypoxia.

## Diabetes

There is an association between diabetes and severe COVID-19.<sup>[8]</sup> Infection with SARS-CoV-2 probably triggers higher stress leading to release of glucocorticoids and catecholamines and thus to hyperglycemia and loss of glycemic control.<sup>[9]</sup> On the other hand, Zhou and Tan<sup>[10]</sup> point out that about 10% of type 2 diabetics with COVID-19 suffered at least one episode of hypoglycemia. Hypoglycemia may trigger a higher inflammatory response. Diabetes is associated with several defects of the immune system, including inhibition of lymphocyte proliferative response, impaired monocyte/macrophage and neutrophil functions, dysfunction of complement activation, and abnormal delayed type hypersensitivity response.<sup>[11]</sup>

## Cancer

The case fatality rate of COVID-19 in cancer patients in China is 28.6%, which is much higher than in the overall COVID-19 patients.<sup>[12]</sup> Cancer patients tend to be older, have a higher ACE expression, and have more comorbidities. After the initial innate immune response, a specific adaptive immune response is required to eliminate SARS-CoV-2. However,

lymphopenia is common in cancer patients and may impair this immune response. This suggests that immunoadjuvant therapies including convalescent plasma may be useful.<sup>[13]</sup>

## Kidney disease

Cheng *et al.*<sup>[14]</sup> found that Acute Kidney Injury (AKI) occurred in 5.1% of 701 patients and was associated with a high risk of in-hospital death with increasing hazard ratio (HR) of death with increasing stage of AKI (Stage 2: HR 3.51, 95% CI 1.49–8.26; Stage 3: HR 4.38, 95% CI 2.31–8.31). The proposed mechanisms include direct injury to kidney tissue by the virus, through an ACE2-dependent pathway, and by the deposition of immune complexes of viral antigens in the kidneys.

A report from Brescia, Italy showed that 5 of 20 kidney transplant recipients with COVID-19, and 2 of 5 patients with Chronic Kidney Disease died. Immunosuppression, elderly age, and multiple comorbidities have been considered to have contributed to this high mortality.<sup>[15]</sup>

## Inflammatory bowel disease (IBD)

Bezzio *et al.*<sup>[16]</sup> have seen that patients with IBD are at an increased risk of COVID-19, especially when they have active disease and are taking immunosuppressive therapy. They also have a higher risk of death (OR 8.45, 95% CI 1.26–56.56). The authors were not able to confirm any higher incidence of gastrointestinal symptoms. The mechanism of high mortality remains unclear.

## Conclusion

A number of comorbidities are associated with increased incidence of infection with SARS-CoV-2 and increased severity of the disease and death. These include cardiovascular disease, diabetes, cancer, kidney disease and inflammatory bowel disease. In addition, aging, obesity, and chronic pulmonary diseases also seem to be associated with increased disease severity and mortality. The interaction of SARS-CoV-2 with the renin-angiotensin-aldosterone system through ACE2 is a key factor in its infectivity and pathogenesis. High ACE2 expression is one of the common threads of the comorbidities that we have discussed.

**Lakshmi Narayana Yaddanapudi**

Department of Anaesthesia and Intensive Care, PGIMER, Chandigarh, India

Address for correspondence: Prof. Lakshmi Narayana Yaddanapudi, Department of Anaesthesia and Intensive Care, PGIMER, Sector 12, Chandigarh, India. E-mail: narayana.yaddanapudi@gmail.com

## References

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, *et al.* Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infection. J Infect* 2020;S0163-4453(20)30234-6. doi: 10.1016/j.jinf.2020.04.021.
- Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; and the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. *JAMA* 2020; 323:2052-9. doi: 10.1001/jama.2020.6775.
- Babapoor-Farrokhran S, Gill D, Walker J, Rakeshi RT, Bozorgnia B, Amanullah A. Myocardial injury and COVID-19: Possible mechanisms. *Life Sci* 2020;253:117723. doi: 10.1016/j.lfs. 2020.117723.
- Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Bondi-Zoccai G, *et al.* Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. *J Am Coll Cardiol* 2020;75:2352-71.
- Kwong JC, Schwartz KL, Campitelli MA, Chung H, Crowcroft NS, Karnachow T, *et al.* Acute myocardial infarction after laboratory-confirmed influenza infection. *N Engl J Med* 2018;378:345-53.
- Davis MM, Taubert K, Benin AL, Brown DW, Mensah GA, Baddour LM, *et al.* Influenza vaccination as secondary prevention for cardiovascular disease: A science advisory from the American Heart Association/American College of Cardiology. *J Am Coll Cardiol* 2006;48:1498-502.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA* 2020;323:1239. doi: 10.1001/jama.2020.2648.
- Wang A, Zhao W, Xu Z, Gu J. Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. *Diabetes Res Clin Pract* 2020;162:108118.
- Zhou J, Tan J. Diabetes patients with COVID-19 need better blood glucose management in Wuhan, China. *Metabolism* 2020;107:154216. doi: 10.1016/j.metabol.2020.154216.
- Hussain A, Bhowmik B, Moreira NC. COVID-19 and diabetes: Knowledge in progress. *Diab Res Clin Pract* 2020;1162:108142.
- Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, *et al.* Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020. doi: 10.1016/j.annonc.2020.03.296.
- Gosain R, Abdou Y, Singh A, Rana N, Puzanov I, Ernstoff MS. COVID-19 and cancer: A comprehensive review. *Curr Oncol Rep* 2020;22:53. doi: 10.1007/s11912-020-00934-7.
- Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, *et al.* Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* 2020;97:829-38. doi: 10.1016/j.kint. 2020.03.005.
- Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A, *et al.*, on behalf of the "Brescia Renal COVID Task Force. Management of patients on dialysis and with kidney transplant during SARS-COV-2 (COVID-19) pandemic in Brescia, Italy. *Kidney Int Rep* 2020;5:580-5.
- Bezzio C, Saibeni S, Variola A, Allocca M, Massari A, Gerardi V, *et al.* Outcomes of COVID-19 in 79 patients with IBD in Italy: An IG-IBD study. 2020;gutjnl-2020-321411. doi: 10.1136/gutjnl-2020-321411.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/joacp.JOACP_305_20

**How to cite this article:** Yaddanapudi LN. Comorbidities and COVID-19. *J Anaesthesiol Clin Pharmacol* 2020;36:S18-20.

**Submitted:** 31-May-2020 **Accepted:** 01-Jun-2020 **Published:** 31-Jul-2020