



COVID-19 Severity in Different Group of Population: A Review Article

Khadija A.M. Glal

Demonstrator of Clinical Pharmacy, Department of Clinical Pharmacy, Faculty of Pharmacy, Tanta University, Tanta, Egypt.

Abstract – COVID-19 is a new virus first appear in Wuhan city and belongs to coronaviridae family with close similarity to severe acute respiratory syndrome virus (SARS-CoV) appearing in 2003. the disease severity differs from mild self-control symptoms as fever, malaise, and sore throat to severe diseases as respiratory distress syndrome, cardiac injury, and even death. the virus has high incidence rate and high prevalence around the world especially. until now there is no definite proven therapy, so the prevention strategy is the solution.

Method: This paper provides information on COVID-19 progress in different group of population with focusing on population at risk COVID-19 complication and mortality and extracting the most common feature shared between them to predict the probable mechanism of pathogenesis.

Keywords: COVID-19- respiratory distress syndrome- cardiac injury-prevention-mortality.

1. INTRODUCTION

COVID-19 epidemic is the main global health catastrophe today. SARS-CoV-2 is an enveloped, ssRNA virus and the phylogenetic analysis of its genome which consists of 29,903 nucleotides revealed that the virus was most closely related (89.1% nucleotide similarity) to SARS-CoV virus that caused the outbreak of Severe Acute Respiratory Syndrome in 2003 so the International Committee on Taxonomy of Viruses referred to as the SARS-CoV-2 virus(1). COVID-19 belongs to the genera Beta coronaviridae which are known to have frequent cross-species transmission and coronaviruses name was driven from their envelope-embedded crown like-spike proteins that determine the viral host/cell type specificity, receptor recognition and cell membrane fusion process(2). several coronaviruses can infect humans and the disease can range from mild condition as common cold (HCoV-229E, HCoV-NL63, HCoV-HKU1, and HCoV-OC43) to severe disease or even death (MERS-CoV, SARS-CoV and COVID-19)(3). The SARS-CoV-2 disease pathogenesis may be due to direct viral infection, cytokine dysregulation, or coagulopathy. In SARS, antibody to S-protein is protective but CD8+ T-cell mediated damage is responsible for Acute respiratory distress syndrome, multi-organ failure, and cardiac injury(4). ACE2 and dipeptidyl peptidase 4 are two COVID-19 receptors that also transducers involved in normal physiological processes as maintaining glucose homeostasis, renal and cardiovascular physiology, and regulating inflammation so any disturbance in these receptor lead to many physiological disturbances in many organs(4). This disease has 15% - 49% case fatality rate in patient > age 80 and critically ill patients respectively and the disease severity correlates with increased viral load and shedding and this put the concept of isolation to avoid virus spread(5). coronaviruses can impair the host innate immune system response in different ways as by avoiding the triggering and amplification of the host type I IFN response(6). older age, obesity, co-morbidity (high blood pressure, heart problems, respiratory problem, or diabetes), high sequential organ failure assessment (SOFA score), and d-dimer greater than 1 µg/mL are indicator of poor prognosis(7).



2. EPIDEMIOLOGY

The SARS-CoV-2 virus emerged in December 2019 and then spread rapidly worldwide. Wuhan City in China is the center of COVID-19 outbreak. The virus can affect all age groups with both sexes, with a higher number of COVID-19 in men may be because ACE 2 expression in females is attenuated or because the female immune system might detect pathogens just a little earlier. Black and South Asian people in England are more likely to die or to be hospitalized than white people. In December 2020, the WHO announced that there are about 66 million confirmed cases with 1.53 million deaths in 220 different countries with more prevalence in the United States (14.7M), India (9.7M), and Brazil (6.6M) and that implies a high incidence rate of infection with 2.31% of death (8).

3. TRANSMISSION

COVID-19 has a zoonotic origin and has its reservoir in bats, so infected animals have transmitted the virus to humans. COVID-19 is highly contagious and can be transmitted by respiratory droplets (cough/exhale), direct contact of mucous membranes, the fecal-oral route, or contact with any excreta containing the living virus. Vertical transmission of SARS-CoV-2 is also reported. In addition, people can catch COVID-19 by touching contaminated objects or surfaces, then touching their eyes, nose, or mouth as COVID-19 may persist on surfaces for a few hours or up to several days. There is also awareness that pets can spread the disease, or consuming raw or uncooked animal products may be a source of infection. The median incubation period of COVID-19 is five days, and most patients will develop symptoms in 11th to 15th day after infection. Therefore, it has been recommended to quarantine those exposed to infection for 14 days (9–11).

4. PATHOPHYSIOLOGY

The inhaled virus binds to ciliated epithelial cells ACE2 receptor in the nasal cavity and multiplies and this binding is mediated by virus S protein and facilitated by the cellular transmembrane serine protease 2 (TMPRSS2 protease) and upon this binding the anti-inflammatory process is weakened, and the angiotensin II function is exaggerated. At this stage, the person is asymptomatic but infectious and the virus can be detected by nasal swabs. Next few days the virus migrates down the respiratory tract and triggers proinflammatory cytokines (interleukin IL-6, IL-10 and TNF- α , granulocyte colony stimulating factor), accumulation of free radicals, changes in intracellular pH, and accumulation of lactic acid with subsequent hypoxia and cardiopulmonary changes (12). Clinical symptoms can be mild in about 80% of the infected patients as the virus was restricted to the upper respiratory airway and the initial inflammatory response attracts virus-specific T cells to the site of infection and clear the infected cells but unfortunately, 20% of the infected patients elicit an aberrant host immune response resulting in bilateral diffuse alveolar damage, hyaline-membrane formation, and ultimately acute respiratory distress syndrome (13–15). As ACE 2 receptor also exists in the cytoplasm of GI epithelial cells, the same pathogenesis scenario of lung infection can occur in the digestive system. COVID-19 can affect any part of the digestive tract primarily terminal ileum as ACE 2 expression in the terminal ileum was higher especially in IBD patients causing GIT related symptoms as diarrhoea (6).

5. CLINICAL PICTURE

Symptoms may differ according to the patient, the time after infection and the site of virus binding. Symptoms develop 2 days to 2 weeks following exposure of virus and most of the infected cases are



asymptomatic or have only mild nonspecific symptoms as fever, myalgia, headache, and respiratory symptoms. A distinctive feature of covid-19 is the presence of mucus plugs with fibrinous exudate because of pro-inflammatory cytokines overproduction. the virus causes transient damage to the olfactory epithelium cell, leading to temporary loss of taste and smell. the virus can develop gastrointestinal symptoms like diarrhea in addition to cardiovascular complications. Lymphocytic endotheliitis, liver cell necrosis, myocardial infarction, hypokalemia, and vasoconstriction may also be observed(12,16,17)

The Course of virus progression differs from one person to another depending on the infected subject and his overall health

Hypertensive patients: Nearly two-thirds of people > 60 years old have high blood pressure and the risk of hypertensive patients to catch COVID-19 infection is twice as compared to the overall population. about 30% to 50% of the hospitalized patients from COVID-19 infection shared high blood pressure and 76% patient who had died from the virus had high blood pressure and thus may be due to a weaker immune system of hypertensive people to fight virus or via using of certain drugs antihypertensive medication as ACEI and ARBs that can raise levels of an ACE2 enzyme and increase infection risk(18–22)

Diabetic patients: people with uncontrolled diabetes are at higher risk not to getting the virus but to get complications if they catch the virus as hyperglycemia modulate immune and inflammatory responses, and RAAS system, thus predisposing patients to severe COVID-19 complication and possible lethal outcomes and having another co-morbidity as heart disease or infection along with diabetes make the condition worser. insulin and dipeptidyl peptidase 4 inhibitors can be used safely in patients with diabetes mellitus and COVID-19 however, patients might need to stop taking metformin and sodium–glucose cotransporter 2 inhibitors. patients with diabetes mellitus should follow general preventive rules rigorously and monitor glucose levels closely, and eat healthily(23,24).

Immunocompromised patients: immunocompromised patients are often affected by a variety of diseases and requiring especial care. the biological response to SARS-CoV-2 infection requires the activation of the innate and acquired immunity. the overactivation and lung sequestration of hyperactivated T cells act as a driver for pulmonary damage and are related with the severe lung immune injury and death, immunosuppression may be protective against these severe complication owing to its anti-inflammatory effect that can mitigating the cytokine storm related to COVID-19 so COVID-19 course in immunocompromised patients is asymptomatic with low fatality rate such as children under anticancer therapy, immunosuppressive chronic drugs users, transplant recipients and AIDS patients(25–28).

Obese patients: there are high rates of obesity around the world and high percentage of the population of BMI > 30 are at risk of catching infection. And the infected obese patient become critically ill and require intensive care and by increasing the obesity degree the mortality become higher as patient of BMI of 35 to 40 have chances of dying from covid-19 by 40%, while people with BMI > 40 could increase the risk by 90%. the possible explanation of obesity–COVID-19 correlation is based on accumulation of fats in wrong places as the liver and skeletal muscles or even lung with subsequent disturbance in insulin level, metabolic function, and inflammatory cytokines. obesity also can deteriorate the adiponectin that directly protect the lung(29–31).

Geriatric: old age alone is strongest predictor of the infection fatality ratio (IFR). for every 1,000 people infected with the coronavirus >50 and <65 about five will die, and for people in their mid-seventies or older 116 will die. for old people infected with COVID-19 are more likely to be associated with a ramped-up



immune response as by geriatric process body can develop low level of inflammation so COVID-19 could be pushing the already overworked immune system over the edge and worse the condition(32,33).

Patient with cardiac disease: pulmonary system is the main site of Covid-19 pathogenesis. but ACE 2 protein also expressed on multiple human cells including myocardial cells and the risk of heart damage increases in patients with already existing cardiac problems. cardiac injury may be a result of direct viral invasion, pro-inflammatory mediator release, or used treatment medication. COVID-19 associated cardiac issues can range from myocarditis secondary to pulmonary infection to heart failure as systemic inflammatory response to infection elevates lung pressure(18).

Patients with liver disease: in cases of severe COVID-19 infection, mild liver injury may occur, but acute liver failure seems to be very rare and may be seen only in critically ill/ICU patients. in the liver, ACE2 is expressed mainly on cholangiocytes. COVID-19 may cause liver injury in different ways as direct viral entry could lead to increasing in liver enzymes, cytokine storm might be associated with disease severity and mortality, and Immune dysfunction or immune system overreaction can lead to liver derangement. furthermore, Pneumonia-associated hypoxia and hypotension might also contribute to liver injury(34).

Patients with kidney disease: hospitalized patients with COVID-19 are at significant risk of acute kidney injury which appears to be a sign of COVID-19 infection severity and the mortality rate is higher for these patients. AKI may originate from acute tubular necrosis, microinflammation, increased blood clotting, or through direct infection of the kidney. Most patients with COVID-19-related AKI continue to have low kidney function after discharge from the hospital(35).

Pregnant and lactating mother: no evidence suggests that pregnant women are at greater risk of becoming seriously ill or for miscarriage than other adults if they develop coronavirus. however, people who are in their third trimester of pregnancy, pregnant women > 35 years old, who had a BMI of 30 or more, and those who had pre-existing medical problems (high blood pressure and diabetes) are at higher risk of developing severe illness and requiring hospital hospitalization(35). WHO recommendation encourage mothers with suspected or confirmed COVID-19 to maintain breastfeeding as breastfeeding substantially offset the potential risks for transmission(36).

Children: Children appear to be at low risk of COVID-19 and most children cases are asymptomatic or have only mild illness as the case with other zoonotic coronaviruses (SARS-CoV and MERS-CoV)(36).

6. PREVENTION

As until now no definite treatment for COVID-19 so cooperating with disease control efforts will reduce your risk of catching or spreading COVID-19. the most prevention tools against COVID-19 is to stay home, allow sunlight and proper ventilation at home, eat healthy, avoid eating uncooked food, do not smoke, regularly clean the hands, maintain at least 1meter (3 feet) distance from infected person, avoid touching eyes, nose, and mouth, covering your mouth and nose with your bent elbow or tissue when you cough, or sneeze then dispose of the used tissue immediately, seek medical attention if you have difficulty breathing or fever, avoid traveling to places especially if you are an older person or have diabetes, heart, or lung disease and if you recently visited (past 14 days) areas where COVID-19 is spreading you must self-isolate by staying at home if you begin to feel unwell, even with mild symptom such as headache, low grade fever (37.3 C or above) and slight runny nose, until recovery. The mask should primarily be used by health workers, care takers, and individuals with respiratory symptoms, such as fever and cough(37).



7. CONCLUSION

COVID-19 outbreak is argued and comprise a threat to public health due to its wide propagation all over the world causing millions of infections and deaths. Profoundly, no proven medicine has been existed. patients can be categorized into two groups: group 1 (population with high risk) as patients of old age, hypertension, diabetes, cardiomyopathy, liver disease, kidney problem, and that of lung disease which shared the same modulating in immunity and inflammatory process. group2 (population with low risk) as children, and immunocompromised patients which shared the decreased immunity. as a result, we could say that the mechanism of virus pathology is immune mediated and the effectiveness of chloroquine, immunomodulator therapy, and cortisone in COVID-19 disease supported. finally, the preventive measures such as proper ventilation, hand hygiene and use of surgical masks to safeguard themselves from the disease.

DECLARATIONS

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable

Availability of data and materials: Not applicable

Competing interest: Not competing interest

Funding: Not funding

REFERENCES

- [1] Coronavirus disease 2019 [Internet]. [cited 2020 Apr 14]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- [2] Huang Y, Yang C, Xu X feng, Xu W, Liu S wen. Structural and functional properties of SARS-CoV-2 spike protein: potential antiviral drug development for COVID-19. *Acta Pharmacol Sin* [Internet]. 2020;41(9):1141–9. Available from: <http://dx.doi.org/10.1038/s41401-020-0485-4>
- [3] Coronavirus | Human Coronavirus Types | CDC [Internet]. [cited 2020 Dec 7]. Available from: <https://www.cdc.gov/coronavirus/types.html>
- [4] Channappanavar R, Zhao J, Perlman S. T cell-mediated immune response to respiratory coronaviruses [Internet]. Vol. 59, *Immunologic Research*. Humana Press Inc.; 2014 [cited 2020 Dec 8]. p. 118–28. Available from: <https://pubmed.ncbi.nlm.nih.gov/255530/>
- [5] Gold JAW, Wong KK, Szablewski CM, Patel PR, Rossow J, da Silva J, et al. Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 – Georgia, March 2020. *MMWR Morb Mortal Wkly Rep* [Internet]. 2020 May 8 [cited 2020 Dec 8];69(18):545–50. Available from: http://www.cdc.gov/mmwr/volumes/69/wr/mm6918e1.htm?s_cid=mm6918e1_w
- [6] Hunt RH, East JE, Lanas A, Malfertheiner P, Satsangi J, Scarpignato C, et al. COVID-19 and Gastrointestinal Disease. *Implications for the Gastroenterologist*. *Dig Dis*. 2020;8.
- [7] Cheng S, Wu D, Li J, Zou Y, Wan Y, Shen L, et al. Risk factors for the critical illness in SARS-CoV-2 infection: a multicenter retrospective cohort study. *Respir Res* [Internet]. 2020 Dec 1 [cited 2020 Dec 8];21(1):1–12. Available from: <https://doi.org/10.1186/s12931-020-01492-z>
- [8] Coronavirus disease (COVID-19) [Internet]. [cited 2020 Dec 8]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019?adgroupsurvey=%7Badgroupsurvey%7D&gclid=Cj0KCQiA5bz-BRD-ARIsABJT4nhvLDnZJdK__NTG7hfOCBcr7xhAh7Y9plcPCwmaRdgPvbzR0pSqEK4aAvTtEALw_wcB
- [9] van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N Engl J Med*. 2020 Apr 16;382(16):1564–7.
- [10] Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations [Internet]. [cited 2020 Dec 8]. Available from: <https://www.who.int/news->



room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations

- [11] Liu J, Liao X, Qian S, Yuan J, Wang F, Liu Y, et al. Community transmission of severe acute respiratory syndrome Coronavirus 2, Shenzhen, China, 2020. *Emerg Infect Dis.* 2020 Jun 1;26(6):1320–3.
- [12] Azer SA. COVID-19: pathophysiology, diagnosis, complications and investigational therapeutics. *New Microbes New Infect* [Internet]. 2020;37(M):100738. Available from: <https://doi.org/10.1016/j.nmni.2020.100738>
- [13] World Health Organization. Coronavirus Disease Situation Report-43. *World Heal Organ* [Internet]. 2020;2019(March):2633. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- [14] Patel A, Jernigan DB, Abdirizak F, Abedi G, Aggarwal S, Albina D, et al. Initial Public Health Response and Interim Clinical Guidance for the 2019 Novel Coronavirus Outbreak – United States, December 31, 2019–February 4, 2020. *MMWR Morb Mortal Wkly Rep* [Internet]. 2020 Feb 7 [cited 2020 Apr 14];69(5):140–6. Available from: http://www.cdc.gov/mmwr/volumes/69/wr/mm6905e1.htm?s_cid=mm6905e1_w
- [15] Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. *Nature.* 2020 Mar 12;579(7798):265–9.
- [16] symptoms of covid - Google Search [Internet]. [cited 2020 Dec 8]. Available from: <https://www.google.com/search?q=symptoms+of+covid&oq=symptoms+of+covid&aqs=chrome..69l57.7099j0j7&sourceid=chrome&ie=UTF-8>
- [17] Symptoms of Coronavirus: Early Signs, Serious Symptoms and More [Internet]. [cited 2020 Dec 8]. Available from: <https://www.webmd.com/lung/covid-19-symptoms#1>
- [18] How does COVID-19 affect the heart? – Mayo Clinic News Network [Internet]. [cited 2020 Dec 8]. Available from: <https://newsnetwork.mayoclinic.org/discussion/how-does-covid-19-affect-the-heart/>
- [19] Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): A pooled analysis. *Polish Arch Intern Med.* 2020 Apr 30;130(4):304–9.
- [20] High Blood Pressure & Coronavirus (Higher-Risk People): Symptoms, Complications, Treatments [Internet]. [cited 2020 Dec 8]. Available from: <https://www.webmd.com/lung/coronavirus-high-blood-pressure#1>
- [21] COVID-19 and high blood pressure: Am I at risk? – Mayo Clinic [Internet]. [cited 2020 Dec 8]. Available from: <https://www.mayoclinic.org/diseases-conditions/coronavirus/expert-answers/coronavirus-high-blood-pressure/faq-20487663>
- [22] Zhang J, Wu J, Sun X, Xue H, Shao J, Cai W, et al. Associations of hypertension with the severity and fatality of SARS-CoV-2 infection: A meta-Analysis. *Epidemiol Infect.* 2020;
- [23] Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol* [Internet]. 2020;17(January). Available from: <http://dx.doi.org/10.1038/s41574-020-00435-4>
- [24] Frequently Asked Questions: COVID-19 and Diabetes | ADA [Internet]. [cited 2020 Dec 8]. Available from: <https://www.diabetes.org/coronavirus-covid-19/how-coronavirus-impacts-people-with-diabetes>
- [25] Cheng W, Li Y, Cui L, Chen Y, Shan S, Xiao D, et al. Efficacy and Safety of Corticosteroid Treatment in Patients With COVID-19: A Systematic Review and Meta-Analysis. Vol. 11, *Frontiers in Pharmacology*. Frontiers Media S.A.; 2020.
- [26] Romanelli A, Mascolo S. Immunosuppression drug-related and clinical manifestation of Coronavirus disease 2019: A therapeutical hypothesis. Vol. 20, *American Journal of Transplantation*. Blackwell Publishing Ltd; 2020. p. 1947–8.
- [27] Gori A, Dondossola D, Antonelli B, Mangioni D, Alagna L, Reggiani P, et al. Coronavirus disease 2019 and transplantation: A view from the inside. Vol. 20, *American Journal of Transplantation*. Blackwell Publishing Ltd; 2020. p. 1939–40.
- [28] Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol* [Internet]. 2020 Jul 1 [cited 2020 Dec 9];146(1):110–8. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0091674920304954>
- [29] Unknown. Covid-19: Why are age and obesity risk factors for serious disease? Available from: <http://dx.doi.org/10.1136/bmj.m4130>
- [30] Jackson Leach R, Powis J, Baur LA, Caterson ID, Dietz W, Logue J, et al. Clinical care for obesity: A preliminary survey of sixty-eight countries. *Clin Obes.* 2020 Apr;10(2).
- [31] Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, et al. Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obes Rev.* 2020 Nov 1;21(11).



- [32] (No Title) [Internet]. [cited 2020 Dec 9]. Available from: <https://media.nature.com/original/magazine-assets/d41586-020-02483-2/d41586-020-02483-2.pdf>
- [33] Daoust J-F. Elderly people and responses to COVID-19 in 27 Countries. Tu W-J, editor. PLoS One [Internet]. 2020 Jul 2 [cited 2020 Dec 9];15(7):e0235590. Available from: <https://dx.plos.org/10.1371/journal.pone.0235590>
- [34] Ghoda A, Ghoda M. Liver Injury in COVID-19 Infection: A Systematic Review. *Cureus*. 2020;12(7):9487.
- [35] Kidney disease & COVID-19 | National Kidney Foundation [Internet]. [cited 2020 Dec 8]. Available from: <https://www.kidney.org/coronavirus/kidney-disease-covid-19>
- [36] Fox A, Marino J, Amanat F, Krammer F, Hahn-Holbrook J, Zolla-Pazner S, et al. Evidence of a significant secretory-IgA-dominant SARS-CoV-2 immune response in human milk following recovery from COVID-19. 2020;
- [37] Q&A on coronaviruses (COVID-19) [Internet]. [cited 2020 Apr 14]. Available from: <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>