

CHAPTER 6

COPD AND COVID-19

Burcu Akkok

*(Asst. Prof. Dr.); Department of Pulmonary Medicine,
Sutcu Imam University Faculty of Medicine, Kahramanmaras, Turkey
e-mail: bkaraokur@hotmail.com
ORCID ID:0000-0002-4924-1636*

INTRODUCTION

As Coronavirus Disease 2019 (COVID-19) appeared in December 2019 in China, it began to spread rapidly throughout the world and as a result of this, it has been announced as a pandemic in March 2020 by World Health Organization (WHO). COVID-19 having a broad clinical spectrum can occur with clinical conditions ranging from asymptomatic cases to cases with severe respiratory failure requiring intensive care. As cases continued to increase, preliminary information relating with COVID-19 began to come from China, being the place of origin of disease. In a multi-center epidemiological study conducted with 1099 patients, the average age was reported to be 47 years, it was stated that it was seen more in men with ratio of 52.1%, and in 23.7% of patients at least one chronic disease such as Chronic Obstructive Pulmonary Disease (COPD), Hypertension (HT), Diabetes Mellitus (DM) accompanied it. In another study conducted with different case numbers, it was determined that COPD prevalence varied in the range of 1.1 and 2.9%.

Chronic diseases are defined as diseases that continue for three months or more, having slow progress, being caused by more than one risk factor, being complicated and that generally impairing life quality of a person. As it

is the case with Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) pandemics, in COVID-19 pandemic, in the increase of death incidents, these diseases constituting risk factor have been leading factors in causes of death in developed and developing countries throughout the world. COPD is a leading cause of death and disability worldwide, with persistent respiratory symptoms and characterized by airflow restriction due to airway inflammation and / or alveolar abnormalities. Attacks during the disease both increase the progression of the disease and cause an increase in mortality. As hospitalizations increase during an attack, there is also an increase in health expenditures. As it is known, the most important cause of COPD attacks is respiratory tract infections and it is seen that most of these infections are viral infections.

It is estimated that COPD patients will be more affected by this pandemic since the possibility of protection of these patients from COVID-19 infection may decrease due to the fact that COPD patients are older than the normal healthy population, they also have other comorbid diseases caused by age, and the cognitive functions related to the disease may decrease. At the same time, since the symptoms of COPD and viral infection are similar, patients may hesitate to apply to a healthcare institution. This situation may cause delays in diagnosis and treatment in both diseases.

RISK FACTORS, COPD AND COVID-19 PREVALENCE

COPD has been found to be associated with an increased risk of mortality and morbidity in community-acquired pneumonia. Altered local / systemic inflammatory response, impaired host immunity, microbiome imbalance, persistent mucus production, structural damage, and inhaled corticosteroid use have been suggested to contribute to such risks. Most of the risk factors mentioned are also considered as risk factors for COVID-19. With the spread of the pandemic around the world, it has been predicted that COVID-19 will be more common in patients with COPD and will be severely affected. However, according to currently available data, COPD does not appear to be a common comorbidity in COVID-19 patients. Different results were obtained from studies conducted in different countries. While the prevalence of COPD was reported to be 2-3% among patients with COVID-19 pneumonia in the first publications conducted in Wuhan, the first place of pandemic, in an article published in Italy in April 2020, COPD was among the comorbidities accompanying patients with COVID-19 with a rate of 18.3%. It has been shown to

be in 6th place. Later, in a study conducted in Europe, it is seen that the rate of COPD, which is one of the comorbidities accompanying COVID-19 cases, has changed. In a review by Lippi et al., It was reported that COPD carries a 5-fold higher risk for severe COVID-19 infection. Again, in this review, it is especially emphasized that patients with a history of COPD should pay attention to restrictive measures in order to minimize the possible exposure to COVID-19 and show necessary care to avoid contact with COVID-19 cases. Close and careful monitoring of all COPD patients with suspected COVID-19 is recommended for clinicians. In another publication where 1590 cases from different regions were examined, all diseases accompanying COVID-19 were investigated and accordingly it was determined that the most obvious differences of COPD cases compared to non-COPD cases at the time of application were older age, higher fever, less dry cough, but more sputum, shortness of breath, and loss of consciousness. Again, considering the course of the disease in this study, it was reported that the rate of development of respiratory failure, intensive care requirement, intubation and ultimately mortality rates were higher in COPD patients. Although more than 97 genetic factors have been identified in the pathophysiology of COPD, smoking is the most important environmental risk factor for COPD. While 15% to 50% of smokers develop COPD, 80% to 90% of COPD patients are smokers or ex-smokers. Although there is no definitive evidence that smokers are at increased risk of COVID-19 in studies conducted to date, WHO argues that smokers are at risk for COVID-19 infection. In a study conducted on 1099 COVID-19 patients supporting WHO, it was stated that while 4.7% of non-smokers died, 12.7% of smokers have died or were subject to a serious clinical situation and 16.9% of severe cases were smoking while 11.8% of milder cases were smoking. On the other hand, in a meta-analysis conducted in China, it has been shown that active smoking is not significantly associated with COVID-19 severity. In another review that included 2002 patients in which eleven case series were examined, it was reported that the risk of serious disease was quadrupled in COVID-19 patients accompanied by COPD, and this risk was approximately 2 times in active smokers. In the same study, it was calculated that mechanical ventilation and intensive care need and mortality were statistically significantly higher in patients with COPD. Apart from smoking, other risk factors that play a role in the development of COPD are also predicted to affect the incidence and prognosis of COVID-19. Biomass resulting from biomass combustion is considered to be the main risk factor especially in non-smoking COPD patients. Biomass has been shown to alter the pulmonary defense like tobacco smoke,

and this effect has been emphasized to increase and accelerate the progression of COPD. The effect of biomass on the lungs is supported by several epidemiological studies that report an increased risk of acute respiratory infections in people exposed to this environmental pollutant. While there are no studies on COVID-19 infection with biomass exposure yet, a report by Harvard University researchers reported an increased mortality rate with COVID-19 associated with long-term exposure to fine particulate matter (PM 2.5), one of the main components of biomass. The reason for the relatively low prevalence of COPD in COVID-19 patients compared to other comorbidities is thought to be due to the difference in data from different countries, as well as the length of time since the beginning of the pandemic. Another reason for low prevalence can be attributed to the avoidance of close contact by COPD patients, strict observance of quarantine and general hygiene rules and therefore not being infected.

THE RELATIONSHIP BETWEEN COVID-19 PATHOGENESIS AND COPD

In the pathogenesis of COVID-19, lung epithelial cells are the main target for the virus. Coronaviruses attach to host cells through the spike (S) protein on their outer surface and enter the cell. The life cycle of the virus in humans begins with the binding of the S protein to angiotensin-converting enzyme 2 (ACE2) receptors on the host cell surface. Therefore, increased ACE2 receptor level in a host affects the prognosis and mortality of COVID-19. In the studies conducted, increased ACE2 expression was found in the lower respiratory tract bronchial epithelial cells of patients with COPD and smokers. This explains the possibility of having COVID-19 severe in the population with COPD.

CLINICAL COURSE OF COVID-19 IN COPD

COVID-19 pneumonia and COPD attack symptoms are similar in clinical practice. At this point, the question that comes to mind is whether we will accept COVID-19 as a cause of COPD attack. Although corona viruses are accepted as the cause of COPD attack, imaging and postmortem studies in COVID-19 show that the pathophysiology is different from COPD exacerbation pathology. In this case, the need for a rapid differential diagnosis by the clinician arises. Some tips for the differentiation of this situation may provide

convenience to physicians. One of them is fever which is a common finding in COVID-19 cases, but which is not a common finding in COPD exacerbations. Similarly, while cough is dry in COVID-19, it is more productive in COPD. Cough with sputum is also in the foreground in patients with COVID-19 and COPD. Studies have shown that exposure to viral infection may increase bacterial colonization in the lower respiratory tract and even increase the risk of bacterial infection in the period after COPD. Therefore, it can be predicted that the clinical course of the infection with COPD and COVID-19 may be poor. The most important auxiliary tests in differential diagnosis are of course the patient's laboratory data and radiological images. The most commonly used method for COVID-19 pneumonia in radiological imaging is lung computer tomography (CT). Radiological findings were classified for COVID-19 pneumonia as the CT images accumulated with the increase of cases. Typical CT findings are specified. (Table I) Emphysema, bronchiectasis, peribronchial thickening and possible cardiac pulmonary edema findings can be seen on CT during COPD attack. Although these images contribute to us in the differential diagnosis, the possible cause of the COPD attack may be COVID-19 pneumonia, and signs of viral pneumonia can also be added to these images. Comparison with the previous radiological images of the patient, if any, may be helpful in differential diagnosis. Definitive diagnosis can be reached by Polymerase chain reaction (PCR) and other blood parameters.

Table 1. Radiological Findings That May Be Seen in COVID-19 Pneumonia

Typical findings	Atypical findings
<ul style="list-style-type: none"> • Frosted glass opacity • Consolidation • Paving stone • Air bronchogram • Airway changes, air cyst • Reticular appearance • Nodules (with halo and inverted halo sign) 	<ul style="list-style-type: none"> • Pleural fluid • Lymphadenopathy • Pericardial fluid • Cavitation

PARTICULARS TO PAY ATTENTION TO DURING TREATMENT AND FOLLOW-UP OF COPD DURING PANDEMIC PERIOD

A stable course of the disease is important in the follow-up of the patient with COPD. The continuity of the treatment they receive during the follow-up of these patients has been the main strategy of COPD patient management during the pandemic. An interim report was published separately by the Goyal

Initiative for Chronic Obstructive Lung Disease (GOLD), which is the COPD Global Initiative, and the National Institute for Health and Care Excellence (NICE), mentioning the management of COPD and emphasizing the importance of continuity of treatment. General preventive measures in stable COPD management can be listed as keeping the general body resistance high, paying attention to nutrition and sleep patterns, wearing masks in case of contact with the external environment and paying attention to general hygiene recommendations, not to ignore the possibility that the disinfectants used may cause bronchospasm and have a worse course of COVID-19 pneumonia as it increases the risk of COPD attacks. It is considered to quit smoking because it increases the risk. If we need to emphasize the nutrition of COPD patients again, especially poor nutritional status causes the risk of skeletal muscle loss or sarcopenia in these patients. Physical therapy and adequate nutritional supplementation are extremely important in helping COPD patients during recovery from severe illnesses, as neuro-muscular blockade will be required in both those with COVID-19-induced Acute Respiratory Distress Syndrome (ARDS) and the group that needs mechanical ventilation due to acute exacerbation of COPD. It is also stated in these reports that these patients should not come to the hospital for routine control, face-to-face contact should be minimized as much as possible. In this context, it is recommended to communicate with patients by phone, online interview or e-mail. Another important point that should not be forgotten is that while trying to physically protect patients with COPD, we should not ignore their emotional states. Even under normal conditions, approximately 40% of patients with COPD exhibit clinically depressive symptoms such as extreme fatigue, loss of interest in activities enjoyed, and 36% show anxiety symptoms such as nervousness, fear, and panic. It is thought that these symptoms will increase even more due to the pandemic. For this reason, COPD patients should be evaluated as multidisciplinary in face-to-face doctor interviews or online interviews, and necessary support should be given in terms of mental health.

It was also emphasized in the report that the stable COPD patients should continue their treatment regularly. In the same report, the view that inhaled corticosteroids (ICS) or oral corticosteroids used in COPD maintenance treatment are inappropriate during the COVID-19 pandemic does not constitute scientific evidence. In recent studies, it has been reported that dexamethasone will likely become the standard care treatment for COVID-19 patients, including patients with COPD. Although there are studies showing that the use of ICS increases the risk of pneumonia, published reports emphasize that patients using ICS should continue to use their medications and the current state of

the disease should not deteriorate during the pandemic period. Again in the GOLD report, it is said that even if the discontinuation of ICS was planned before, it should be postponed. The same is true for patients on long-term oral corticosteroids. These patients should continue to take their medication at the same dose. Prophylactic antibiotic use recommended for selected patients should continue as it was before the pandemic; however, prophylactic antibiotics should not be used to reduce the risk of COVID-19 pneumonia. Pulmonary rehabilitation programs recommended for COPD patients in groups B, C and D in a routine way should be continued using online resources. Patients who receive long-term oxygen therapy should continue their treatment without any change. Another important point is that COPD patients who smoke should be encouraged to quit smoking both to protect the bad prognosis of COVID-19 and to reduce the risks of acute exacerbation.

CONSIDERATIONS ON THE USE OF INHALERS AND DEVICES USED IN TREATMENT

The equipment used by patients in treatment is also of great importance in the pandemic process. Face masks and spacers used should be cleaned regularly in accordance with the cleaning instructions, inhaler devices should not be used with others. Some patients receive their inhaler therapy with a nebulizer. In another report published by NICE, it is stated that the use of nebulizers by patients will not pose an additional risk in terms of contamination, since the aerosol comes from the liquid in the nebulizer compartment and does not carry virus particles from the patient. However, if the patient has COVID-19 infection, the possibility of infecting others may increase. For this reason, patients should not be prescribed a nebulizer unless necessary, and if they do, it should be stated that they should be used in a well ventilated separate room. Likewise, patients using non-invasive mechanical ventilation (NIMV) at home should be instructed to use the device alone, if possible, in a well-ventilated room by taking appropriate precautions. Whether nebulizer or NIMV interconnections, both equipment should be disinfected frequently and regularly.

MANAGEMENT OF COPD PATIENTS DURING PANDEMIC PERIOD

As the epidemic spread, its effect was felt particularly in COPD patients. Pulmonary rehabilitation and face-to-face doctor meetings had to be post-

poned in most patients. This situation has created anxiety and worry in most COPD patients. Therefore, a written action plan should be prepared for all COPD patients. With this plan, it is planned to reduce the anxiety and worry of the patients and to provide information about the situation in which they should apply to the hospital. Pandemic prevention methods do not differ in COPD patients.

Hand hygiene and other preventive cleaning recommendations for these patients are no different from the normal population. Patients should be warned to use only substances that are used for disinfection and that they may cause bronchospasm. Regular nutrition, adequate hydration, regular sleep are recommended and exercise at home is also recommended for preventing COPD patients from COVID-19 and other infections.

Since coexistence of chronic diseases such as cardiovascular disease, hypertension and diabetes mellitus is common in patients with COPD, as the presence of these diseases may increase the possibility of having COVID-19 and the possibility of having a more mortal course if COVID-19 pneumonia develops, treatment of accompanying diseases should be followed regularly.

COPD patients should pay attention to daily changes in themselves, if there are symptoms such as high fever, cough, increase in sputum or shortness of breath, weakness, muscle pain, if the present symptoms do not disappear after symptomatic treatment at home, especially in the presence of high fever, shortness of breath and cough that does not decrease despite symptomatic treatment. They should apply to the nearest health institution. In order to reduce the risk of COVID-19 transmission while going to the healthcare institution, if possible he should go alone and if it is not possible, he should be accompanied by a maximum of one person. In addition to the precautions to be followed in the pandemic in polyclinics, routine respiratory function tests should not be requested from these patients.

Whether the cause of COPD attacks is COVID-19 or other reasons, different methods are not recommended for exacerbation treatment. If these patients are clinically indicated, oral steroids and / or antibiotics should be given. If the patient needs to be hospitalized due to an attack, the use of an inhaler intermediate device (such as spacer, aerochamber) should be prioritized, as far as possible, in terms of contamination risk. Continuation of routine oxygen therapy is recommended in COPD patients during an attack. Again, in the recommendations, it is stated that oxygen support should be given with oxygen mask in possible or definite COVID-19 patients, and high flow nasal oxygen should be avoided as much as possible in COPD patients

with COVID-19. Again, procedures such as sputum induction and nasotracheal aspiration, which are applied from time to time in hospitalized or advanced COPD patients, which may produce high amounts of infectious aerosols and pose a high risk for COVID-19 transmission, should be avoided, and if it is required, the necessary precautions should be taken.

CONCLUSION

COPD is one of the risk factors that increase mortality for COVID-19, both because of the elderly patients' age and its prevalence with other comorbid diseases. This risk is further increased as most COPD patients are smokers and / or ex-smokers. For this reason, COPD patients should have a written action plan that informs the methods of protection from COVID-19, the status of the treatments they are using, and how they will behave if they become infected with COVID-19. In order to avoid contact with patients with COPD, online and telephone calls should be organized even if there is no face-to-face meeting, and patients should be interviewed in a way that supports both medical support and mental health. Patients should continue their current treatment without any change. Even if hospitalization is required, they should receive their treatments in line with the recommendations without risking both themselves and healthcare professionals in terms of contamination. Again, pulmonary rehabilitation becomes important in these patients as it helps both functional and psycho-social recovery. In addition to COPD, patients should be encouraged to quit smoking as smoking affects the course of the disease negatively.

REFERENCES

- World Health Organization (WHO). Available from: <https://www.who.int/csr/don/12-january-2020-novel-corona-virus-china/en/>. Accessed on 31 March, 2020. 2020.
- Guan WJ, Ni ZY, Hu Y, et al. China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Apr 30;382(18):1708-1720. doi: 10.1056/NEJMoa2002032. Epub 2020 Feb 28. PMID: 32109013; PMCID: PMC7092819.
- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020 Mar 17;323(11):1061-1069. doi: 10.1001/jama.2020.1585. PMID: 32031570; PMCID: PMC7042881.

- Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*. 2020 Jul;75(7):1730-1741. doi: 10.1111/all.14238. Epub 2020 Feb 27. PMID: 32077115.
- WHO (2012-2013) World Health Organization. Global Alert and Response. Coronavirus Infections. Available at: http://www.who.int/csr/disease/coronavirus_infections/en/
- Assiri A, Al-Tawfiq JA, Al-Rabeeh AA, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet Infect Dis*. 2013 Sep;13(9):752-61.
- Organization WH. Noncommunicable diseases (Available from: <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>
- Global Strategy for Diagnosis, Management and Prevention of COPD. The Global Initiative for Chronic Obstructive Lung Diseases (GOLD). 2020 report. Available from: <https://goldcopd.org/gold-reports/> [Access: 01.01.2020].
- Restrepo M.I., Mortensen E.M., Pugh J.A., et al. COPD is associated with increased mortality in patients with community-acquired pneumonia. *Eur. Respir. J*. 2006;28:346–351.
- Restrepo M.I., Sibila O., Anzueto A. Pneumonia in patients with chronic obstructive pulmonary disease. *Tuberc. Respir. Dis*. 2018;81:187–197.
- Lupia T, Scabini S, Mornese Pinna S, et al. 2019 novel coronavirus (2019-nCoV) outbreak: A new challenge. *J Glob Antimicrob Resist*. 2020 Jun;21:22-27. doi: 10.1016/j.jgar.2020.02.021. Epub 2020 Mar 7. PMID: 32156648; PMCID: PMC7102618.
- Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA*. 2020 May 12;323(18):1775-1776. doi: 10.1001/jama.2020.4683. Erratum in: *JAMA*. 2020 Apr 28;323(16):1619. PMID: 32203977.
- Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med*. 2020 Jun;167:105941. doi: 10.1016/j.rmed.2020.105941. Epub 2020 Mar 24. PMID: 32421537; PMCID: PMC7154502.
- Guan WJ, Liang WH, Zhao Y, et al. China Medical Treatment Expert Group for COVID-19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020 May 14;55(5):2000547. doi:10.1183/13993003.00547-2020. PMID: 32217650; PMCID: PMC7098485.
- Olloquequi J. COVID-19 Susceptibility in chronic obstructive pulmonary disease. *Eur J Clin Invest*. 2020 Oct;50(10):e13382. doi: 10.1111/eci.13382. Epub 2020 Sep 2. PMID: 32780415; PMCID: PMC7435530.
- (WHO) WHO. Q&A on smoking and COVID-19. In: 2020
- Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Intern Med*. 2020 May;75:107-108. doi:

- 10.1016/j.ejim.2020.03.014. Epub 2020 Mar 16. PMID: 32192856; PMCID: PMC7118593.
- Leung JM, Yang CX, Sin DD. COVID-19 and nicotine as a mediator of ACE-2. *Eur Respir J*. 2020 Jun 4;55(6):2001261. doi: 10.1183/13993003.01261-2020. PMID: 32350104; PMCID: PMC7191112.
- Olloquequi J, Silva O R. Biomass smoke as a risk factor for chronic obstructive pulmonary disease: effects on innate immunity. *Innate Immun*. 2016 Jul;22(5):373-81. doi: 10.1177/1753425916650272. Epub 2016 May 25. PMID: 27226464.
- Dherani M, Pope D, Mascarenhas M, et al. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ*. 2008 May;86(5):390-398C. doi: 10.2471/blt.07.044529. PMID: 18545742; PMCID: PMC2647443.
- Smith KR, McCracken JP, Weber MW, et al. Effect of reduction in household air pollution on childhood pneumonia in Guatemala (RESPIRE): a randomised controlled trial. *Lancet*. 2011 Nov 12;378(9804):1717-26. doi: 10.1016/S0140-6736(11)60921-5. PMID: 22078686.
- Xiao Wu, RachelC Nethery, MBenjamin Sabath, et al. Exposure to air pollution and COVID-19 mortality in the United States: A nationwide cross-sectional study. *MedRxiv* doi: 2020.04.05.20054502
- Shereen MA, Khan S, Kazmi A, et al. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *J Adv Res*. 2020;24:91-98.
- Leung JM, Yang CX, Tam A, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. *Eur Respir J*. 2020 May 14;55(5):2000688. doi: 10.1183/13993003.00688-2020. PMID: 32269089; PMCID: PMC7144263.
- Simons SO, Hurst JR, Miravittles M, et al. Caring for patients with COPD and COVID-19: a viewpoint to spark discussion. *Thorax*. 2020 Dec;75(12):1035-1039. doi: 10.1136/thoraxjnl-2020-215095. Epub 2020 Sep 2. PMID: 32878969; PMCID: PMC7474898.
- Wilkinson TMA, Hurst JR, Perera WR, et al. Effect of interactions between lower airway bacterial and rhinoviral infection in exacerbations of COPD. *Chest*. 2006 Feb;129(2):317-324. doi: 10.1378/chest.129.2.317. PMID: 16478847; PMCID: PMC7094441.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5. Epub 2020 Jan 24. Erratum in: *Lancet*. 2020 Jan 30;: PMID: 31986264; PMCID: PMC7159299.
- Bernheim A, Mei X, Huang M, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. *Radiology*. 2020 Jun;295(3):200463. doi: 10.1148/radiol.2020200463. Epub 2020 Feb 20. PMID: 32077789; PMCID: PMC7233369.

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) COVID-19 Guidance, 2020. <https://goldcopd.org/gold-covid-19-guidance/>
- NICE guideline (NG168). Covid-19 rapid guideline :community-based care of patients with chronic obstructive pulmonary disease (COPD). Published date :09 April 2020. Available at: <https://www.nice.org.uk/guidance/ng168>
- Nguyen HT, Collins PF, Pavey TG, et al. Nutritional status, dietary intake, and health-related quality of life in outpatients with COPD. *Int J Chron Obstruct Pulmon Dis.* 2019 Jan 14;14:215-226. doi: 10.2147/COPD.S181322. PMID: 30666102; PMCID: PMC6336029.
- Yohannes, Abebaw M. and Baldwin, Robert C. et al. (2000) Mood disorders in elderly patients with chronic obstructive pulmonary disease. *Reviews in clinical gerontology*, 10 (2). pp. 193-202. ISSN 0959-2598
- Abewaw Mengistu Yohannes (2021) COPD patients in a COVID-19 society: depression and anxiety, *Expert Review of Respiratory Medicine*, 15:1, 5-7, DOI: 10.1080/17476348.2020.1787835
- RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med.* 2021 Feb 25;384(8):693-704. doi: 10.1056/NEJMoa2021436. Epub 2020 Jul 17. PMID: 32678530; PMCID: PMC7383595.35- Wedzicha JA, Banerji D, Chapman KR, Vestbo J, Roche N, Ayers RT, et al. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. *N Engl J Med* 2016;374:2222-2234.
- NICE guideline. COVID-19 rapid guideline: managing suspected or confirmed pneumonia in adults in the community. Published date: 03 April 2020.