IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Impact Factor: 6.252
Volume 2, Issue 2, June 2022

A Review : Covid – 19 Multidisciplinary

Akshada D Dhobale[1], Shraddha M. Khaladkar[2], Nutan S. Wakale[3]
Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India[1,3]
Department of Pharmaceutics (QAT), Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India[2]

Abstract: *Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has provoked an ongoing global pandemic of coronavirus disease 2019 (COVID-19), which has affected 130 million people worldwide and caused nearly 3 million deaths in just over 1 year. In 2020, COVID-19 has represented the third highest cause of death in the US after heart disease and cancer. and this outbreak has led to the largest drop in life expectancy since World War II Several studies have reported the diversity of long-term complications of COVID-19 with a variety of symptoms and organ-related injuries, which has been referred to as "long COVID" or "post-acute COVID-19 syndrome" Even if the frequency of these complications is not high, the massive number of people who have been infected with SARS-CoV-2 suggests that this will represent a public health issue leading to a major consumption of healthcare resources. However, the exploration of patients with post-acute COVID-19 syndrome requires a multidisciplinary approach, as complications far exceed the problem of dyspnea, and it appears that pulmonary and systemic complications can be intimately entangled.*

Keywords: COVID-19, Complication, Multidisciplinary, Dyspnea

I. INTRODUCTION

If there is one thing that we as healthcare professionals have realised even more during the COVID-19 pandemic, it is that we need our team members from other disciplines, and we need to work together to provide the best possible outcome for our patients. With regards to the various impairments that patients may have to deal with and the rehabilitation aspects of these impairments, the multidisciplinary approach in the management and rehabilitation of patients are key SARS-CoV-2 is the seventh coronavirus to date that is known to infect humans. This has been possible by frequent cross-species infections and occasional spillover events (1). Two of these previously identified coronaviruses were responsible for major epidemics in the past two decades; Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) also originating from China in 2002–2003 and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) originating from the Middle East in 2012 (2, 3). All three of these coronaviruses are considered zoonotic in origin and have the ability to cause severe and fatal illness in humans (3, 4). Unfortunately, given their large genetic diversity and the frequent recombination of their genomes coupled with the increase in human-animal interface activities due to modern agricultural practices, novel coronaviruses are likely to continue to develop and cause periodic seasonal spreads (3).

II. MODE OF TRANSMISSION

According to current evidence, the WHO reports that SARS-CoV-2 transmission occurs via respiratory droplets and contact Routes. Droplet transmission occurs through direct contact When a person is exposed to infective respiratory droplets When they are within 1 m of someone with respiratory Symptoms including coughing and sneezing. Being within this Distance puts the individual at risk of having their mucous Membranes, including their mouth, nose and eyes, exposed To the droplets. Transmission can also occur through indirect Contact by way of fomites on surfaces in the immediate Environment around the infected person. Airborne transmission May be possible when aerosol-generating procedures are Performed including endotracheal intubation, cardiopulmonary Resuscitation, administration of nebulized treatments, and Others (5). Transmission of the virus can occur in the pre-symptomatic Incubation period. A study in a nursing home showed that more Than half of the residents with positive test results for SARS-CoV-2 infection were pre-symptomatic and most likely contributed to Transmission (6).

III. PATHOGENESIS

Although the pathogenesis of SARS-CoV-2 is not clearly Understood, information regarding viral replication and Pathogenesis can be extracted from what we know about other Beta-coronaviruses (SARS-CoV and MERS-CoV) due to their Similarities to SARS-CoV-2. Direct Viral Injury SARS-CoV-2 binds to epithelial cells in the oral and nasal cavities And can also migrate further down the respiratory tract into the Conducting airways. SARS-CoV has been shown to infect primary Ciliated cells in the conducting airway and therefore, it has been Hypothesized that the same occurs with SARS-CoV-2. About 80% Of the infected patients will have a mild course limited to the Upper and conducting airways (7). They produce surfactant, which is responsible for the Maintenance of surface tension in alveolar walls. These cells are Also responsible for maintaining the lung epithelium after injury Through epithelial regeneration (8). Therefore, as replicated Viral particles are released from the cell and move on to infect More type II pneumocytes, the resulting apoptosis eventually Causes diffuse alveolar damage and impaired gas exchange, which Is hypothesized to lead to acute respiratory distress syndrome (ARDS). A similar mechanism is postulated for SARS-CoV-2 (7)(Figure 1).

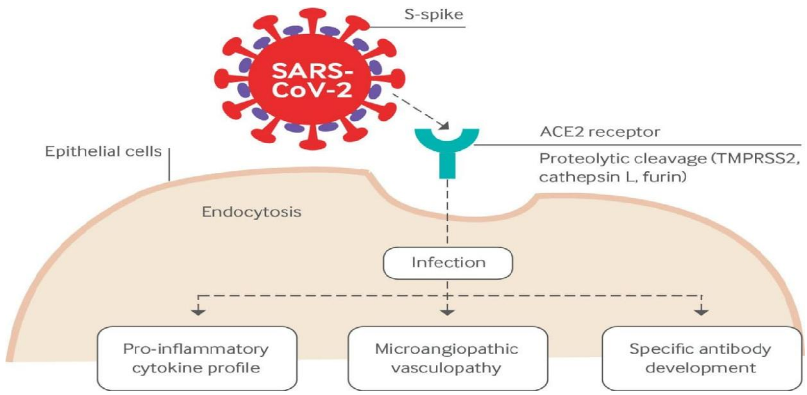

Figure no. 1 Pathogenesis of Covid-19

Viral Replication Cycle SARS-CoV-2 has been shown to use the angiotensin-converting Enzyme 2 (ACE2) receptor for cell entry, similar to SARS-CoV (2). Through the examination of human tissue specimens, ACE2 Receptors have been found in various organs and cells including The nasopharynx, nasal and oral mucosa, small intestine, colon, Kidney, liver, vascular endothelium, and epithelial cells of lung Alveoli (mainly type II pneumocytes) (9). The RBD in the S protein of SARS-CoV-2 specifically Recognizes its host ACE2 receptor. The viral RBD region is made Of 394 glutamine residues and is recognized by 31 lysine residues Of the human ACE2 receptor. Previous studies revealed that host Susceptibility to SARS-CoV infection is mainly determined by the Affinity between the host ACE2 receptor and the viral RBD in the Early viral attachment phase. It is thought that this mechanism is Likely similar in SARS-CoV-2 and that a genetic recombination Event in the RBD region of SARS-CoV-2 may be the cause of its Higher transmission rate as compared to SARS-CoV (10).

3.1 Clinical Symptoms

Clinical symptoms have been shown to occur most commonly Between days 4 and 5 from exposure; however, studies have Shown that the incubation period can last up to 14 days (5). The most common symptoms reported in the literature so Include fever, cough, fatigue and shortness of breath, which Are similar to other viral infections including the seasonal flu. One study identified 24 critically ill patients from nine Seattle-Area hospitals with laboratory-confirmed COVID-19 infection With symptoms beginning 7 ± 4 days before admission. The Most commonly reported symptoms were cough and shortness Of breath and around 50% of patients had fever on admission. (11).

IV. DIAGNOSIS

SARS-CoV-2 RNA is detected via reverse-transcription Polymerase chain reaction (RT-PCR) most commonly collected From nasopharyngeal (NP) swabs. In the United States, the CDC recommends the collection of NP swabs for asymptomatic Individuals. Instead, specimens from symptomatic patients Should be collected from bilateral anterior nares and mid- Turbinate. An oropharyngeal (OP) swab could be collected If an NP swab is not possible. The CDC also recommends Collecting sputum in patients with a productive cough, however Sputum induction is not recommended.

Also, when (i.e., patients who are mechanically intubated), a lower Respiratory tract sample via a bronchioalveolar lavage (BAL) Should be collected (12).

4.1 Risk Factors Associated with Severe Disease

Many studies have shown that severe illness and death occur In patients with certain risk factors including older age and Underlying medical comorbidities. A study done by Wu et al.Showed that among 44,672 cases of COVID-19 in Wuhan, China, The majority of patients were 30 to 79 years of age (87%) followed By those aged 80 years and older (3%) while only 1% were aged 9 Years and younger (13). Older age was one of the identified risk Factors associated with poor prognosis and death (14). A study by Guan et al. showed that those with severe disease were older by a Mean of 7 years compared to those with mild disease (15). It remains unclear whether gender is an independent risk Factor for more severe disease. A retrospective case series done in New York, showed that among the 393 patients with confirmed COVID-19, 60.6% were males. Also, males were more likely to Receive mechanical ventilation (16). However, this correlation Does not imply causation since this study did not adjust for other Medical comorbidities.

4.2 Investigational Approaches and Adjunctive Therapies

Unfortunately, up until this point, there has yet to be a vaccine Or proven effective therapy against SARS-CoV-2 infection. While many trials, including much needed randomized controlled trials (RCTs), are currently underway, the mainstay of therapy remains Supportive care. This ranges from symptomatic treatment to ventilator support for patients with ARDS depending on Illness severity. This also includes recognizing and treating Superimposed bacterial infections and/or sepsis early on. Many of the current clinical trials are investigating drugs that were Previously used to treat SARS-CoV and MERS-CoV. These will be discussed further below.

4.3 Azithromycin

Azithromycin is a macrolide antibiotic that has been widely Used in patients with chronic pulmonary inflammatory Disorders and/or community acquired pneumonia for its Anti-inflammatory effect (17). However, there is limited data Suggesting the beneficial effect of azithromycin in combination With chloroquine/hydroxychloroquine in the treatment of ARDS In patients with SARS-CoV-2 infection

4.4 Remdesivir

Remdesivir is a novel nucleotide analog that incorporates into Nascent viral RNA chains and causes premature termination Inhibiting viral replication. Remdesivir has been shown to be An effective antiviral agent against beta-coronaviruses such as SARS-CoV and SARS-MERS in mice, non-human primates and In vitro, and is currently in clinical trials for the treatment of Ebola virus (18). A study in China showed that Remdesivir is highly effective In controlling SARS-CoV-2 infection in vitro . Another Study that was recently published involving compassionate-use Of Remdesivir showed clinical improvement in 68% of patient (36 out of 53) who had severe SARS-CoV-2 infection; 57% were Extubated and 47% were discharged (19).

4.5 Ivermectin

Ivermectin is an FDA-approved medication for the treatment of Various parasites and has an established safety profile in humans. Ivermectin has been shown to inhibit in vitro replication of Various positive single stranded RNA viruses such as dengue and West Nile (20, 21). This drug has recently demonstrated in Vitro activity against SARS-CoV-2 when a single dose was able To control viral replication within 24–48 h. It is hypothesized that This is likely through the inhibition of importin α/β1 heterodimer,Which mediates nuclear import of viral proteins, a process that Many RNA viruses rely on during infection (22)

4.6 Convalescent Plasma

Convalescent plasma (CP) therapy is a classic adaptive Immunotherapy that has been used for decades in the prevention And treatment of various diseases. CP was used in prior epidemics Including SARS-CoV, MERS-CoV, and H1N1 in 2009 and It showed successful results with a safe profile . Given The similarity between SARS-CoV-2, SARS-CoV, and

MERS- CoV, CP may have potential efficacy in this current pandemic. However, no RCTs involving CP in SARS-CoV-2 infection have Been completed as of yet, and hence the risks and benefits Remain unclear. In an uncontrolled case series, the treatment of five patients With severe SARS-CoV-2 infection and ARDS with CP showed Clinical improvement in all five cases

4.7 Corticosteroids

The use of glucocorticoids in patients with SARS-CoV-2 Infection, especially in those with severe disease, was a point of Major controversy. The rationale behind their use is to decrease Lung inflammation as seen in ARDS. However, this comes with Adverse effects such as inhibiting the immune response and thus Increasing the risk of secondary infections as well as delaying Viral clearance . A Cochran review published in July 2019 That included 48 RCTs found insufficient evidence to determine if Corticosteroids were effective at reducing mortality and duration Of mechanical ventilation in patients with ARDS (23, 24)

4.8 Chloroquine/Hydroxychloroquine

Chloroquine and hydroxychloroquine are widely used anti-Malarial drugs. Hydroxychloroquine is a chloroquine analog with Less drug to drug interaction and a better safety profile. Both chloroquine and hydroxychloroquine are shown To inhibit the growth of SARS-CoV-2 in vitro and decrease Viral replication in a concentration-dependent manner. Hydroxychloroquine was found to be more potent. It has been Hypothesized that both chloroquine and hydroxychloroquine May inhibit SARS-CoV-2 replication. They may do this By changing the pH at the surface of the cell membrane Thereby inhibiting fusion in addition to inhibiting nucleic acid Replication, glycosylation, and viral assembly and release

4.9 Vitamin C

Vitamin C, also known as ascorbic acid, has antioxidant Properties and plays a significant role in reducing inflammatory Response. Studies have shown that ascorbic acid down-regulates.the production of pro-inflammatory cytokines . These Concepts have generated interest in the use of ascorbic Acid in the management of inflammatory conditions. In a Recent randomized clinical trial involving 167 patients in the Intensive care unit, intravenous infusion of high-dose ascorbic Acid compared to placebo did not significantly reduce organ Dysfunction scores or improve levels of biomarkers indicating Inflammation among patients with sepsis and ARDS, two Disease processes heavily associated with inflammation

4.10 Zinc

It has been shown that increased zinc concentration inside the Cell can effectively impair replication of a number of RNA viruses Such as influenza and polioviruses. A study showed that zinc in Combination with zinc-ionophores like pyrithione inhibited the Replication of SARS-CoV in cell cultures . Therefore, zinc Supplementation may be of potential benefit for prophylaxis and Treatment of COVID-19 and it is currently under investigation In multiple clinical trials in combination with other agents Including hydroxychloroquine, vitamin C, and vitamin D .

4.11 Montelukast

Montelukast has been shown to suppress oxidative stress and Have anti-inflammatory effects. Use of high dose montelukast has Been effective in the treatment of acute asthma. Because much of The morbidity and mortality from COVID-19 infection is due to Excessive inflammatory processes, it is thought that montelukast May play a role in limiting the progression of disease . One of the protein complexes involved in cytokine production And inflammatory responses is NF-B (nuclear factor kappa-light- Chain-enhancer of activated B cells). Therefore, inhibition of the NF-B signalizing pathway has been investigated for potential Therapeutic options in inflammatory (25)

V. COVID-19 RESPONSE

Many have criticized the global response to COVID-19 due to the rapidly increasing number of cases and deaths worldwide . It is important to highlight the sequence of events in this response in order to recognize areas of concern and associated consequences, and to extract potential lessons and improvements for future pandemics.As previously mentioned, the cluster of cases identified in Wuhan were reported to the WHO by Chinese authorities on December 31, 2019 and confirmed to be associated with a novel coronavirus, later termed COVID-19, on January 8, 2020 .There have been multiple reports of suspected intimidation of clinicians who initially identified cases linked to COVID-19, which likely led to a delay in the release of information and a lack of transparency

5.1 Second Wave

As seen in multiple previous pandemics including the influenza Pandemic of 1918, the first wave is often followed several months Later by a second wave of infections that could potentially be Even worse than the first. A second wave can be caused by a Region being re-exposed to infection by an influx of infected People from another. The degree of the resulting new outbreak Will depend on the level of immunity in the first region from the initial wave.

VI. CONCLUSION

Pandemics propose an immense challenge to public health, Health care systems, and global economic security. Due to Modern agricultural practices that increase human-animal Interface, new zoonotic coronaviruses are likely to continue to Spillover from animals to humans causing future outbreaks. Gaining insight into every aspect of coronaviruses is crucial To implement proper control measures to help prevent these Outbreaks or lessen their impact on humans and society if they were to still happen. Special focus should be placed on Understanding their pathophysiology to help better tailor and Generate effective drug therapies and vaccinations.

ACKNOWLEDGMENT

We would like to thank Samarth Institute of pharmacy, Belhe principle Dr. Subhash Kumbhar And also most thanks to Mrs. Shraddha Khaladkar mam for their valuable guidance Time to Time and consistent support. we would like thanks to our friends especially Mr. Rupesh kurhade for his valuable suggestions.

REFERENCES

[1]. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbial. (2019) 17:181–92. Doi: 10.1038/s41579-018-0118-9

[2]. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia Outbreak associated with a new coronavirus of probable bat origin. Nature.(2020) 579:270–3. Doi: 10.1038/s41586-020-2012-7

[3]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus From patients with pneumonia in China, 2019. N Engl J Med. (2020) 382:727–33. Doi: 10.1056/NEJMoa2001017

[4]. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF.The proximal origin of SARS-CoV-2. Nat Med. (2020) 26:450–2.Doi: 10.1038/s41591-020-0820-9

[5]. World Health Organization. Modes of Transmission of Virus Causing COVID-19: Implications for IPC Precaution Recommendations. (2020).Available online at: https://www.who.int/news-room/commentaries/detail/ Modes-of-transmission-of-virus-causing-covid-19-implications-for-ipcprecaution-recommendations (accessed June 11, 2020)

[6]. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. N Engl J Med. (2020) 382:2081–90. doi: 10.1056/NEJMoa2008457

[7]. Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. Eur Respir J. (2020) 55:2000607. Doi: 10.1183/13993003.00607-2020

[8]. Mossel EC, Wang J, Jeffers S, Edeen KE, Wang S, Cosgrove GP, et al. SARSCoV replicates in primary human alveolar type II cell cultures but not in type I-like cells. Virology. (2008) 372:127–35. Doi: 10.1016/j.virol.2007.09.045

[9]. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, Van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus.A first step in understanding SARS pathogenesis. J Pathol. (2004) 203:631–7.doi: 10.1002/path.1570

[10]. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res.(2020) 24:91–8. Doi: 10.1016/j.jare.2020.03.005

[11]. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al.Covid-19 in critically ill patients in the Seattle region - case series. N Engl J Med. (2020) 382:2012–22. doi: 10.1056/NEJMoa2004500

[12]. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19). (2020). Available online at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html (accessed April 13, 2020)

[13]. Wu Z, Mcgoogan JM. Characteristics of important lessons from the Coronavirus disease 2019 (COVID-19) outbreak in China: summary of A report of 72314 cases from the Chinese Center for Disease Control Prevention. JAMA. (2020) 323:1239–42. Doi: 10.1001/jama.2020.2648

[14]. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course And risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. (2020) 395:1054–62. Doi: 10.1016/S0140-6736(20)30566-3

[15]. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of coronavirus disease 2019 in China. N Engl J Med. (2020) 382:1708–20. Doi: 10.1056/NEJMoa2002032

[16]. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. N Engl J Med. (2020) 382:2372–4. Doi: 10.1056/NEJMc2010419

[17]. Amsden GW. Anti-inflammatory effects of macrolides–an underappreciated Benefit in the treatment of community-acquired respiratory tract infections And chronic inflammatory pulmonary conditions? J Antimicrob Chemother.(2005) 55:10–21. Doi: 10.1093/jac/dkh519

[18]. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir And chloroquine effectively inhibit the recently emerged novel Coronavirus (2019-nCoV) In vitro.Cell Res. (2020) 30:269–71.Doi: 10.1038/s41422-020-0282-0

[19]. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al.Compassionate use of remdesivir for patients with severe Covid-19. N Engl JMed. (2020) 382:2327–36. Doi: 10.1056/NEJMoa2007016

[20]. Tay MYF, Fraser JE, Chan WKK, Moreland NJ, Rathore AP, Wang C, et al. localization of dengue virus (DENV) 1-4 non-structural protein 5; protection against all 4 DENV serotypes by the inhibitor Ivermectin. Antiviral Res. (2013) 99:301–6. Doi: 10.1016/j.antiviral.2013.06.002

[21]. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved Drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res. (2020) 178:104787. Doi: 10.1016/j.antiviral.2020.104787

[22]. Yang SNY, Atkinson SC, Wang C, Lee A, Bogoyevitch MA, Borg NA, et al. The broad spectrum antiviral ivermectin targets the host Nuclear transport importin alpha/beta1 heterodimer. Antiviral Res. (2020) 177:104760. Doi: 10.1016/j.antiviral.2020.104760

[23]. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support Corticosteroid treatment for 2019-nCoV lung injury. Lancet. (2020) 395:473–5. Doi: 10.1016/S0140-6736(20)30317-2

[24]. Lewis SR, Pritchard MW, Thomas CM, Smith AF. Pharmacological agents For adults with acute respiratory distress syndrome. Cochrane Database Syst Rev. (2019) 7:CD004477. Doi: 10.1002/14651858.CD004477.pub3

[25]. Fidan C, Aydogdu A. As a potential treatment of COVID-19: montelukast.Med Hypotheses. (2020) 142:109828. Doi: 10.1016/j.mehy.2020.109828

[26]. ClinicalTrials.gov. Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) for Prophylaxis SARS CoV-2 Infection (COVID-19). (2020).Available online at: https://clinicaltrials.gov/ct2/show/NCT04283461(accessed April 16, 2020).

[27]. Phelan AL, Katz R, Gostin LO. The novel coronavirus originating in Wuhan,China: challenges for global health governance. JAMA. (2020) 323:709–10.Doi: 10.1001/jama.2020.1097

[28]. Friston KJ, Parr T, Zeidman P, Razi A, Flandin G, Daunizeau J, et al.Second Waves, Social Distancing, and the Spread of COVID-19 Across America. (2020). Available at: https://wellcomeopenresearch.org/articles/5-103/v1 (accessed June 27, 2020)

[29]. Aleta A, Martin-Corral D, Piontti AP, Ajelli M, Litvinova M, Chinazzi M,Et al. Modeling the Impact of Social Distancing, Testing, Contact Tracinng And Household Quarantine on Second-Wave Scenarios of the COVID-

19 Pandemic. (2020). Available at: https://www.medrxiv.org/content/10.1101/2020.05.06.20092841v1 (accessed June 27, 2020)

[30]. Hick JL, Biddinger PD. Novel coronavirus and old lessons – preparinng The health system for the pandemic. N Engl J Med. (2020) 382:e55.Doi: 10.1056/NEJMp2005118