Review Article

Novel coronavirus- A comprehensive review

Aparna M. Nair[1], Shilpa PH[2], Vijay Shekhar[3], Rahul V. C. Tiwari[4], Izaz Shaik[5], Bhargavi Dasari[5], Heena Tiwari[6]

[1]Department of Periodontics, PMS College of Dental Science and Research, Trivandrum, Kerala, [3]Government Dental Surgeon, PHC Sampatchak, Patna, Bihar, [4]CLOVE Dental and OMNI Hospitals, Visakhapatnam, Andhra Pradesh, [6]PGDHHM, Government Dental Surgeon, Kondagaon, Chhattisgarh, India, [2]Faculty of Dentistry, AIMST University, Bedong, Malaysia, [5]Rutgers School of Dental Medicine, Newark, New Jersey, USA

Abstract

Recently coronavirus outbreak which started in Wuhan, China, has caused international concern that has affected more than 29 lakh people worldwide and with no vaccine or specific antiviral drugs present as well as oblivious testing of carriers who are generally asymptomatic, the use of general health intervention techniques are failing to comply. As compared to other epidemics like severe acute respiratory syndrome-coronavirus (SARS-CoV) and the Middle-East respiratory syndrome (MERS-CoV), coronavirus (also named as COVID-19) exhibit mild symptoms in the majority of cases. But in the case of a vulnerable population, it can prove to be life-threatening. Relying on proper barrier technique, use of chest computed tomography scans, managing co-morbid conditions of susceptible patients, identifying the pattern of disease spread as well as the use of polymerase chain reaction to assess the specificity of cases will eventually prove to be efficacious since most of the positive cases are asymptomatic at the beginning which poses a challenge to the primary health care physicians. The development of vaccines will also take some time so it is better to know about COVID-19 better and also follow quarantine restrictions properly till then. In this review, we try to put forward all the relevant studies which have been published by the end of March 2020 so as to summarize the natural history, diagnosis as well as treatment strategies for eradicating COVID-19, which will help in managing this pandemic.

Keywords: Coronavirus, pandemic, respiratory distress

Introduction

All the subtypes of coronaviruses (CoV) come under the Coronaviridae family. They are pleomorphic RNA viruses which contain crown-shaped protein subunits with a size of 80–160 nm and polarity of 27–32 kb. Due to the enormous rate of recombination of coronavirus which in turn because of various transcription anomalies and changes in RNA dependent RNA polymerase enzyme, the mutation in CoV is higher.[1] From November–December 2019, severe acute respiratory syndrome (SARS-CoV-2) caused atypical pneumonia in a few cases which had a possible origin in the wet markets in the city of Wuhan, China.[2] Later on, when the spread increased many folds which resulted in the World Health Organization (WHO) acknowledging this coronavirus as a public health emergency of international interest (PHEIC).[3] It was found out that CoV was structurally related to the SARS virus which caused severe respiratory distress. Earlier epidemics, that is, SARS and the Middle-East respiratory syndrome (MERS) caused havoc and had caused a lot of fatalities as well as problems for the medical fraternity.[4] Since coronavirus has been stated as a PHEIC, it will prioritize the disease in all the countries wherein global effort will be put into place to halt this outbreak.[5] CoV has spread quickly throughout East Asia as well as Europe amidst strict lockdowns and quarantine.[6] As of April 25th, 2020, according to WHO,

Address for correspondence: Dr Aparna M. Nair, Department of Periodontics, PMS College of Dental Science and Research, Trivandrum, Kerala, India.
E-mail: draparnamnair87@gmail.com

Received: 29-03-2020 **Revised:** 25-04-2020
Accepted: 28-04-2020 **Published:** 30-07-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_496_20

How to cite this article: Nair AM, Shilpa PH, Shekhar V, Tiwari RV, Shaik I, Dasari B, *et al.* Novel coronavirus- A comprehensive review. J Family Med Prim Care 2020;9:3200-4.

almost 210 countries are affected, with close to 29 lakh people suffering from this viral disease and with 200,568 deaths, thus a pandemic has been declared with the United States of America being the current hotspot for this outbreak where more than 9 lakh people are CoV positive and there is around 52,000 deaths reported [Table 1].

Epidemiology of Covid-19

The local outbreak from exposure to the above wholesale food market marks the first phase. From the first case in December 2019 the epidemiological analysis showed that already at this early stage, the person-to-person transmission had taken place through close contact. The second phase began on 13 January, characterized by the rapid expansion and spread of the virus within hospitals (nosocomial infection) and by family transmission (transmission by close contact). As of January 23, 29 provinces of China, plus six foreign countries, had reported a total of 846 confirmed cases, an increase of about 20 times since the first phase. The third phase started on January 26, which is characterized by the rapid increase in cases of conglomerates.[7] Li and his colleagues described the first 425 cases found in Wuhan, which was the epicenter of this outbreak and defined the earliest known detailed clinical and epidemiological description about the spread of COVID-19. In this study, it was found that the elderly population who are above 60 years of age and had other comorbid conditions were more seriously affected than the younger and healthier population with severe breathlessness being most common. Surprisingly children who were less than 14 years of age were less affected with only mild symptoms which would, later on, affect the balance ratio of population between young and old people in a community.[4] Italy suffered from significant mortality with a rate of not less than 8–9% due to this disease, and another reason is that it has the second largest population of older people, who generally have weaker immunity and others associated pathological conditions, such as heart disease, hypertension, diabetes, cerebrovascular disease, etc., While in comparison, China, where the disease actually started, suffered only 2–3% of mortality. Most countries suffer from the shortage of medical staff, ventilators, and personal protective equipment, which also contributes to the increased mortality and morbidity of this viral disease. The countries affected by it suffer a total block; therefore stage III (person-to-person contact) is controlled to interrupt the viral load chain in their population.

Natural history and clinical features of Covid-19

Mostly coronavirus causes respiratory and enteric diseases in human beings. SARS and MERS caused major outbreaks in the human population in the years 2003 and 2012 respectively which had mortality rates between 10 and 40%. Current coronavirus (SARS-CoV-2) has a lot of genomic similarity with the main SARS virus but the former has a higher spread.[8] The disease starts when a human inhales the viral particles through infected droplets or fomites and the virus travels down to lower respiratory airways. In the respiratory system in order to enter the alveolar epithelial cell, the virus binds to the cell through ACE2 enzyme receptors.[9] Virus alters the normal respiratory cell and induces a massive cytokine release which induces inflammatory damage and it also activates other inflammatory chemokines from surrounding vascular endothelial cells of the alveolar capillaries, which then continue this inflammatory damage cycle. This excess of inflammation causes lung damage through severe pneumonia and spreading to involve other organs with time leading to multi-organ failure.[2] Researchers also found out that the novel coronavirus originated from wild bats, which was also responsible for the SARS epidemic. Modes of transmission include a person-to-person transmission especially respiratory droplets due to sneezing or coughing by an infected individual as well as fomites where coronavirus can persist for a few hours to few days.[10] Even in hospitals, person-to-person transmission can occur easily leading to the spread of this infection.[11] Social distancing as well as washing hands with soap or using hand sanitizers having around 70% concentration of alcohol prove to be effective in controlling the spread of this infection. For health professionals; adequate masks, gloves as well as personal protective equipment are essential.[12] Researchers like Huang *et al.* conducted a study on 41 confirmed COVID patients. The major clinical features which were visible in patients were fever, myalgia, dyspnea, dry cough. The uncommon symptoms noticed were anosmia, cough with sputum production, headache, and diarrhea. Chest X-ray showed opacities bilaterally in the lung region which could be further persuaded in computed tomography (CT scan). CT scan was also helpful in detecting early cases which were not evident in chest X-ray. The serious cases ended up in septic shock, acute respiratory distress syndrome, kidney damage, etc.[13] Therefore, the categorization of COVID-19 was based on the severity of infection from asymptomatic, mild, moderate, and severe viral infection.[5] It was also dependent on CT scan findings which denoted the level of severity of spread in the lungs resulting in mild to severe pneumonia cases [Table 2]. Another study carried out by Chen *et al.* inferred that older people with other co-debilitating conditions like diabetes, hypertension, cardiovascular diseases, etc., were more susceptible to a serious form of COVID-19 disease due to less immunity.[14]

Radiology of lesions in Covid-19

Chest CT scan usually gives a much better visualization of the lung pneumonia and its spread. Initially, it is diffuse opacities affecting different airways.[14] Later on, ground-glass opacities were noticed in mild cases whereas bilateral lung involvement with consolidation was seen in the intensive care unit patients.[13] Another study in 21 patients revealed, that initial chest CT showed bilateral lung involvement in 86% of patients.[15] Predominantly ground-glass opacity was seen in 58% cases whereas consolidation is seen in 28% cases.[16] The major differences in the chest CT findings between COVID-19 and other epidemics like SARS and MERS, was the bilateral lung involvement in the former as compared to later cases had unilateral involvement [Table 3]. Other features of pneumonia-like pleural effusion, lymphadenopathy, or alveolar space cavitation was not seen in CVID-19 affected patients.[14]

Table 1: Stages of pandemic

Stage 1	When cases of infection are imported into a country which wasn't the source of the infection.
Stage 2	The second stage of an epidemic is when there are cases of local transmission within the country.
Stage 3	Community transmission where it becomes hard to track the chain of transmission of the virus in a large number of cases.
Stage 4	When an infection becomes endemic in some countries and keeps resurfacing round the year.

Table 2: The severity of COVID-19 with their diagnostic criteria[5]

Asymptomatic infection	Chest X-ray is normal but the RT-PCR shows positive viral infection.
Mild	Cases show low-grade fever, cough, pharyngitis, sneezing. Few cases also show nausea, diarrhea, etc. pharyngeal congestion is noted on physical examination of the suspected case.
Moderate	Productive cough with developing pneumonia and increased episodes of fever and cough. At this stage, the CT image of the lungs starts showing opacities.
Severe	Respiratory distress is evident with full-blown pneumonia, hypoxia, cyanosis along with fever, cough, and diarrhea. Oxygen saturation is also affected.
Critical	Acute respiratory distress syndrome, septic shock, heart failure, kidney failure can occur in end-stage cases.

Table 3: Patterns seen in CT scan of the lungs in COVID-19 affected patients who were diagnosed with pneumonia[3]

Ground-glass opacities +/-consolidation	Prominent
Pure consolidation	Rare
Multiple lesions	Prominent
Bilateral involvement	Prominent
Posterior part/lower lobe predilection	Prominent
Peripheral/subpleural distribution	Prominent
Ground-glass opacity with superimposed thickening of interlobular septa	Can be present
Air-filled bronchi on a background of airless lung	Can be present
Atoll sign with dense crescent formation on high-resolution CT	Rare
Pleural effusion	Rare
Cavitation, calcification, lymphadenopathy	Absent

Pathogenesis of Covid-19

Virus entry to the human cells is initiated by binding of the viral spike protein to the affected human cell particularly alveolar epithelial cells. After entering the cell, the viral genome causes an alteration in the genetic expression of the host cell so as to generate accessory proteins which help the coronavirus to further develop and spread to other host cells. Earlier similar viral epidemics like SARS and MERS affected the cells by binding to their Angiotensin-converting enzyme receptor-2 on the cellular membrane in case of SARS infection and dipeptidyl peptidase -4 enzyme receptor in case of MERS, which facilitated the entry as well as the propagation of the viral particles.[13] Viral RNA after entering the cell starts using host machinery in the cytoplasm to make new viral proteins. Genomic RNA is encapsulated and polyadenylated and encrypts various structural and non-structural polypeptide genes. These polyproteins are fragmented by proteases that display chymotrypsin-like activity.[15] The resulting complex drives (-) RNA production through both replication and transcription to encoding structural proteins.[16] Virions are formed by the combination of the viral nucleocapsid as well proteins which are synthesized by the host cell (which in COVID-19 is the alveolar epithelial cell). They enter the endoplasmic reticulum from where the virions bud off the cytoplasm of the host cell by exocytosis and are released into the bloodstream. These virion particles later infect other organs like the liver, kidney, intestine, and other parts of the respiratory tract.[1] COVID-19 has a higher rate of transmission as compared to the MERS and SARS infections as the former shows a higher replication rate (R0) which leads to its faster spread in the human population.[7] Recently, it has been suggested that a spillover of the viral particles from Bats with Pangolin as an intermediate host has led to the viral outbreak in the human population. This depends upon the ACE2 receptor similarity in these animals and some resemblance to the human population.[7]

Diagnosis of Covid-19

Various tests have been in place to diagnose COVID-19 with precision. Serological tests usually comprise enzyme-linked immunoassay or in some cases, western blot can also be used. The clinical samples which are taken from the suspected cases are Nasal secretions, oral swabs, sputum, bronchoalveolar lavage, blood, etc., Pool testing is also being considered as an alternative method for assessing community spread easily and cost-effectively. But as of now, the researchers have shown that the gold standard for identifying the COVID-19 viral particles is real-time polymerase chain reaction (RT-PCR) which is specific for the viral RNA. Northern blot hybridization, as well as immunofluorescent assay, has also been used to detect viral RNA and other viral antigenic components.[17] Many countries are in the process of developing rapid detection kits that detect viral exposure after around 7–10 days after viral contact. But they are less reliable as compared to RT-PCR.

Treatment options and strategies

There is no specific treatment as of now for the novel coronavirus infection. Usually, the symptomatic patients are given supportive care with adequate hydration as well as the use of antipyretics for fever. Severe cases need mechanical intubation and ventilation so that the regular supply of oxygen is maintained in debilitated lungs affected by the coronavirus. Clinical trials for the possible drugs have also begun in many countries for regulatory approval. Some researchers also link to a promising co-relation between Bacillus Calmette-Guérin vaccine and its beneficial effect on increasing immunity against coronavirus however, WHO has yet to verify this claim. Research is going on related to many antivirals that can prove effective in tackling coronavirus like- remdesivir, lopinavir, ritonavir, favipiravir, etc.,

Trials are also going on regarding hydroxychloroquine in the treatment of coronavirus affected patients. Recently in China, a randomized human trial was carried out in relation to remdesivir, which failed to improve the condition in many patients.[18] FDA, as well as other regulatory agencies, are still working on the development of a vaccine for the general public against this virus.[19] Plasmapheresis is also being carried out for using the convalescent serum antibodies of the coronavirus healed patients and providing it to serious patients, which has met with some success rate in a few nations.[20] It is extremely important that different types of pneumonia as well as respiratory distress, for example, associated with influenza, bacteria's as well mycoplasma, etc., are also differentiated from coronavirus acute respiratory distress syndrome since the treatment for them will be entirely different which is vital for the physicians especially working in intensive care units. For handling coronavirus epidemic all the medical health professionals should be aware of proper barrier technique as well they should be equipped with rapid diagnostic methods which have high specificity as well as sensitivity since it has been reported that around 40% of cases are asymptomatic who turn out to be positive later on but are infectious in the early stages also. It is imperative to understand the importance of pathogenesis and modes of transmission of coronavirus before treatment is devised. This review presented important points that will help in diagnosing and in turn handling serious as well as susceptible patients in a better manner by our primary health care officials who are facing this crisis in the frontline. As of now human trials for a vaccine for COVID-19 is still in progress, it will be all the more critical to reduce the morbidity as well as mortality associated with this disease by early diagnosis and quarantine. It is also important to keep in mind about the comorbid conditions of the elderly since those make them vulnerable to the viral attack and subsequent mortality. This article also provides a clue to the replication rate as well as genomic know-how of this particular virus which is important in assessing the community spread of the outbreak as well as the importance of polymerase chain reaction, which currently is the only technique that is providing a specific result using CoV genomic sequences and describes the relation between other similar outbreaks of SARS and MERS, which will help the frontline medical professionals in developing treatment strategies in similar lines to these epidemics which happened in the past.

Conclusion

This coronavirus pandemic has posed a great threat to mankind and worldwide more than 29 lakh people have been affected by this viral disease and the numbers are still increasing every day. Therefore, it is the need of the hour, for rapid diagnosis and constant surveillance as well as social distancing to halt the progression of this deadly virus spread in the near future especially in developing countries where there are insufficient medical facilities and personnel as well as promote pool testing which is more cost-effective approach. It is vital to understand the biology of this virus so that vaccine or treatment strategies can be developed at the earliest so that further community spread is averted.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sahin AR, Erdogan A, Mutlu Agaoglu P, Dineri Y, Cakirci AY, Senel ME, *et al.* 2019 novel coronavirus (COVID- 19) outbreak: A review of the current literature. EJMO 2020;4:1-7.
2. Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). J Gen Intern Med 2020. doi: 10.1007/s11606-020-05762-w.
3. Zu ZY, Jiang MD, Xu PP, Chen W, Ni QQ, Lu GM, *et al.* Coronavirus disease 2019 (COVID-19): A perspective from China. Radiology 2020:200490. doi: 10.1148/radiol.2020200490.
4. Fauci AS, Lane HC, Redfield RR. Covid-19 — Navigating the uncharted. N Engl J Med 2020;382:1268-9.
5. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, *et al.* Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics 2020. doi: 10.1542/peds. 2020-0702.
6. Hosseiny M, Kooraki S, Gholamrezanezhad A, Reddy S, Myers L. Radiology perspective of coronavirus disease 2019 (COVID-19): Lessons from severe acute respiratory syndrome and Middle East respiratory syndrome. AJR Am J Roentgenol 2020;214:1078-82.
7. Sun J, He W-T, Wang L, Lai A, Ji X, Zhai X, *et al.* COVID-19: Epidemiology, evolution, and cross-disciplinary perspectives. Trends Mol Med 2020;26:483-95.
8. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, *et al.* Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet 2020;395:565-74.
9. 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.
10. Gralinski LE, Menachery VD. Return of the Coronavirus: 2019-nCoV. Viruses 2020;12:E135.
11. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, *et al.* Importation and human-to-human transmission of a novel coronavirus in Vietnam. N Engl J Med 2020;382:872-4.
12. Lu CW, Liu XF, Jia ZF. 2019-nCoV transmission through the ocular surface must not be ignored. Lancet 2020;395:e39.
13. 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.
14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 2020;395:507-13.
15. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, *et al.* CT imaging features of 2019 novel coronavirus (2019-nCoV).

Radiology 2020;295:202-7.

16. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al.* A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. Lancet 2020;395:514-23.
17. Coronavirinae in Viral Zone. Available from: https://viralzone.expasy.org/785.
18. Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P, *et al. In vitro* antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin Infect Dis 2020. doi: 10.1093/cid/ciaa237.
19. DRAFT landscape of COVID-19 candidate vaccines — 18 February 2020. Geneva: World Health Organization. Available from: https://www.who.int/blueprint/priority-diseases/key-ac tion/list-of-candidate-vaccines-developed-against-ncov.pdf.
20. WHO R&D blueprint: Informal consultation on prioritization of candidate therapeutic agents for use in novel coronavirus 2019 infection. Geneva: World Health Organization, January 24, 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/330680/WHO-HEO-RDBlueprint%28nCoV%29-2020.1-eng.pdf.