Type of article : Review

Corona Virus- An Overview

N. Aravindha Babu[1], E.P. Sridevi Anjuga[2], N.Anitha[3], L.Malathi[3],

[1]Professor, [2]Post Graduate Student, [3]Reader, Department of Oral Pathology and MicrobiologySree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Pallikaranai, Chennai

Abstract

Coronavirus disease 19 (COVID-19) is a highly communicable and pathogenic viral infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that has developed in Wuhan, China and spread all over the world.Genomic analysis revealed that SARS-CoV-2 is phylogenetically associated with severe, acute respiratory syndrome-like (SARS-like) bat viruses, so bats could be the primary reservoir possible. The intermediate source of origin and human transfer is unknown, but the accelerated human to human transmission has been widely confirmed.Maximal precautionary steps and resources have also been put forwardby most nations to mitigate transmission and decrease mortality rates.

Key Words: *Corona virus, China, COVID 19, SARS-coV2, Pandemic*

Introduction

Today the world is standing together to battle against coronavirus disease 2019 (COVID-19)[1].With its roots in WuhanCity (China), COVID19 is an emerging viral pandemic that demands a massive human impact[1]. It started as a group of pneumonia cases with unknown etiology, soon recognized to be caused by aNovel coronavirus strain (CoV), now known as severe acute respiratory syndrome CoV-2 (SARS-CoV-2), which mainly spreads through droplets, respiratory secretions and direct contact[1].

Coronaviruses belong to the order of Nidoviralesin the family Coronaviridae. Corona depicts crown-like spikes on the external surface of virus; thus, it has been called a coronavirus[2].COVID-19 presents as an asymptomatic or mild infection in the majority of the population (80 percent)[1].Multiple protocols and management strategies are being developed around the world to overcome this problem[1].Pandemic infections have been accompanied by a significant number of unavoidable deaths and high mortality increase all around the world[1]. Besides, human-to - human transmission of newly emerging pandemic pathogens regularly creates fear, with a negative impact on the economy and overall well-being of large human populations[2]. As of mid- June 2020, the infection has spread over the world 87,08,008 and mortality rate of 4,61,715[1].

ORIGIN:

On 31 December 2019, the WHO China Country Office was reported 44 cases of pneumonia with unidentified etiology in Wuhan City[3].The infection was started from the Hunan seafood market in China's Wuhan city and quickly infecting over 50 peoples. Live animals such as bats, frogs, snakes, birds, marmots and rabbits are frequently sold at the Hunan seafood market[2].

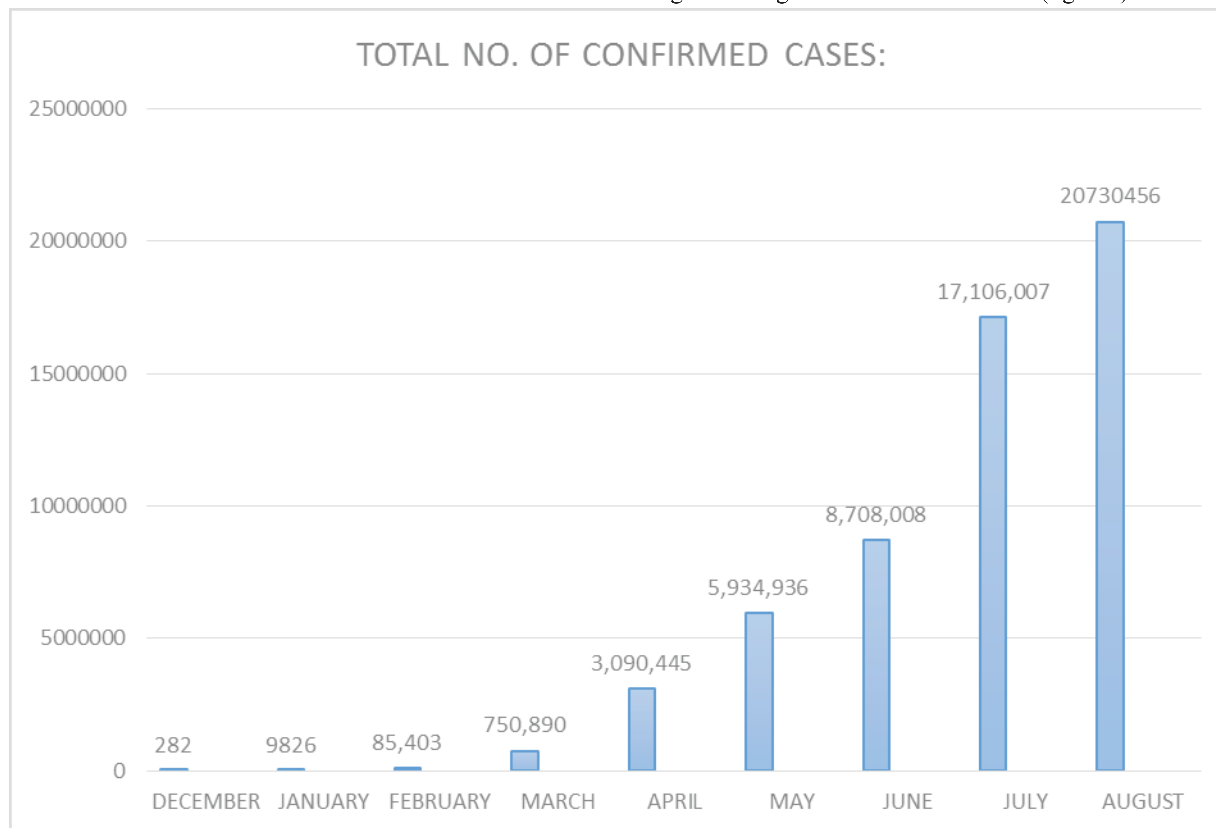
On 12th January 2020, the National Health Commission of China released further details stating that this pandemic is due to viral pneumonia[2].The virus was identified as a novel coronavirus by the sequence-based analysis of the isolated patients[2].Also, the genetic sequence was also provided for the viral diagnosis[2]. It was initially suggested that patients infected in Wuhan was coronavirus caused pneumonia in China could have visited the seafood market where live animals were sold or used as food source infected animals or birds[2]. Further studies, however, showed that some people contracted the infection even with no record of visiting the seafood market[2].Such findings suggested a human to human spreadability of this virus[2]. This virus was later identified in more than 100 countries worldwide[2]. Owing to close contact with an infected person, exposed

to coughing, sneezing, respiratory droplets or aerosols, the human transmission of the virus occurs[2]. Aerosols may enter the human body (lungs) through nose or mouth inhalation[2].

OUTBREAKS:

On 31 December 2019, the WHO China Country Office was notified with cases of unidentified etiology (unknown cause) of pneumonia reported in Wuhan City, China Province of Hubei[3].

Number of confirmed cases from December 2019 to august 2020 given below[3,4,5,6,7,8,9.10,11] (figure1)



CLASSIFICATION:

NIDOVIRALES

CORONAVIRIDIAE ARTERIVIRIDIAE MESONIVIRIDIAE RONIVIRIDIAE

TOROVIRINAE **CORONAVIRINAE**

ALPHA **BETA** DELTA GAMMA

SARS-coV MERS- coV**SARS- coV2**

All viruses in the order of Nidovirales are enveloped, non-segmented RNA viruses with positive sense. They all contain large RNA virus genomes, with some viruses having the largest RNA genomes,consists 33.5 kilobase (kb) genomes[12].

Other common characteristics within the order Nidovirales entail:

· A highly conserved genomic structure, with a broad replicase gene preceding structural genes and accessory genes[12].

· Many non-structural genes expressed through ribosomal frameshifting[12].

· Numerous unique or abnormal enzymatic activities encoded within the large replicase – transcriptase polyprotein[12].

· Downstream gene expression by synthesis of 3′nested subgenomic mRNAs[12].

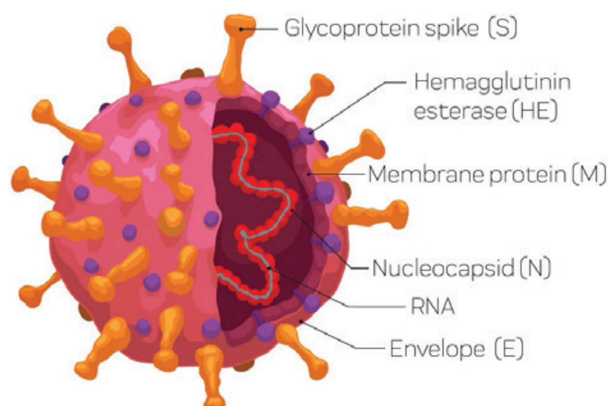
· The significant distinction within the families

of Nidovirusis in number, type and structural protein Sizes. Such variations cause significant alterations in nucleocapsid and virion structure and morphology[12].

VIRION STRUCTURE:

Coronaviruses are minute in size (65–125 nm in diameter) and contain a single stranded RNA as a nucleic material, varying in length from 26 to 32 kbs[2].

Coronavirus virions are spherical with a diameter of about 125 nm as shown by cryo-electron tomography and cryo-electron microscopy in recent studies[12].The most striking feature of coronaviruses is the club-shaped spike projections originating from the virion surface[12]. These spikes are a characteristic of the virion, giving them the appearance of a solar corona, prompting the name, coronaviruses[12].Nucleocapsid is inside the envelope of the virion[12].Coronaviruses possess helically symmetric nucleocapsids, which is infrequent among positive-sense RNA viruses, but far more common in RNA viruses with negative-sense[12].



Particles of the coronavirus contain four major structural proteins.Those are the proteins spike (S), membrane (M), envelope (E), and nucleocapside (N), all encoded inside the 3′ end of the viral genome[12].

The S protein (~150 kDa) uses an N-terminal signal sequence to obtain entry to the endoplasmic reticulum and heavily glycosylated[12].Homotrimers of the virus encoded S protein make up the characteristic spike structure on the virus surface[12]. The glycoprotein trimeric S is a class I fusion protein and mediates binding to the host receptor[12]. S is cleaved into two different polypeptides noted S1 and S2 by a host cell furin-like protease[12]. S1 constitutes the broad S-protein receptor-binding domain while S2 constitutes the stalk of the spike molecule[12].

The M-protein is the structural protein most abundant in the virion[12]. This is a small protein (~25–30 kDa) with three transmembrane domainsand it is thought to give form to the virion[12].Recent data indicate M protein is present in the virion as a dimer, and can incorporate two different configurations, allowing the membrane to curve and bind to the nucleocapsid[12].

Within the virion, the E protein (~8–12 kDa) is present in small quantities. The E proteins of coronavirus are strongly divergent but have a similar architecture[12]. The E protein membrane topology is not entirely resolved although most results indicate it is a transmembrane protein[12]. The E protein has an ectodomain N-terminal and an endodomain C-terminal and has activity on the ion channel[12].

The N protein is the only protein found in nucleocapsid[12].This consists of two distinct domains, an N-terminal domain (NTD) and a C-terminal domain (CTD), both capable of in vitro binding RNA still, each domain uses various mechanisms to bind RNA[12].

Hemagglutinin-esterase (HE) is a fifth structural protein present in a subset of β-coronaviruses[12]. The protein functions as hemagglutinin, binds sialic acids to surface glycoproteins and it includes the action of acetyl-esterase[12].

TRANSMISSION:

The source of origination and transmission are essential to be established to improve preventive strategies to contain the infection[2].

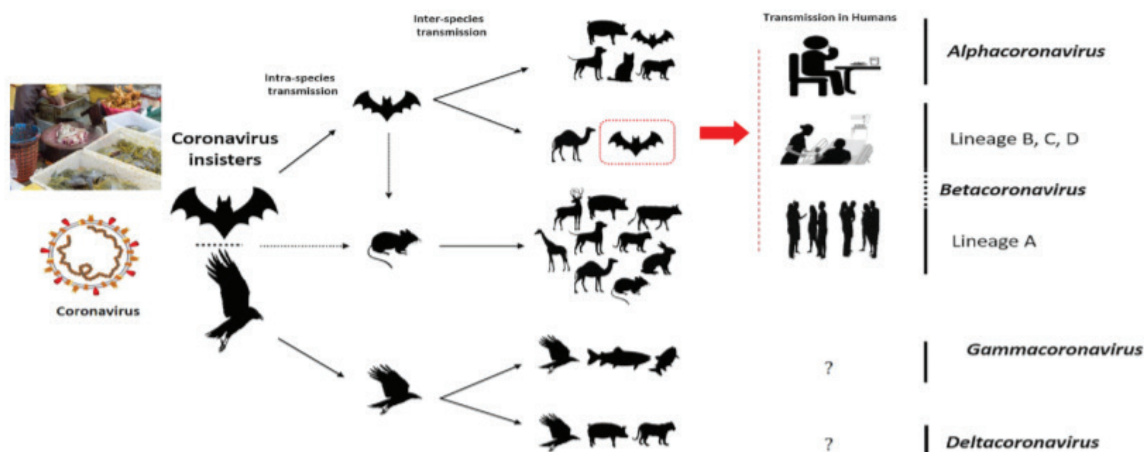
While patients with symptomatic COVID-19 were the key source of transmission, recent findings indicate that asymptomatic patients and patients are also carriers of SARS-CoV-2 during their incubation time[13]. This epidemiological function of COVID-19 has made its monitoring highly challenging, because these patients are difficult to classify and quarantine these patients in time, that can cause SARS-CoV-2 to build up in communities[13].

The common routes of novel coronavirus transmission includeDirect transmission (inhalation

of droplets, cough, sneeze) and indirect Transmission (contact to oral,nasal and eye mucous membranes)[14]. Though typical clinical manifestations of a novel coronavirus infection do not involve eye symptoms, the study of conjunctival samples from confirmed disease and the suspected 2019-nCoV cases indicate that the 2019-nCoV transmission is not restricted to the respiratory tract and that eye contact may provide an effective way for the virus to enter the body[14]. Studies have indicated airborne 2019-nCoV via aerosols produced during medical procedures[14]. It is important that RT-PCR testing could also detect the 2019-nCoV RNA in a stool specimen obtained on day 7 of the patient's illness[14].

When individual coughs, sneezes, laughs or speaks, large droplets or aerosols are produced (> 5 µm diameter) and small (5 µm diameter). Through gravity,Larger droplets easily fall to the ground; transmission of droplets involves close physical contact between an infected person and a susceptible person[15].On the other side, tiny droplets or small particle fragments of evaporated droplets have a low settling velocity so that they can stay in the air for longperiods of time and travel higher before reaching the respiratory tract or contaminating surfaces[15].

The schematic diagram of transmission of corona virus given below[2]:



INCUBATION:

The incubation period of COVID-19 has been estimated at 5 to 6 d on average.However there is evidence that it may be as extended upto 14 days, which is now the widely adopted duration for medical observation and quarantine of exposed persons[13].

HIGH RISK POPULATION:

Current findings indicate this present infectious disease is typically vulnerable to people of all ages[13]. However, those who are in close contact. The risk of SARS-CoV-2 infection is higher for patients with symptomatic and asymptomatic COVID-19, particularly healthcare professionals and other hospital patients[13]. The maximum mortality rates were 14.8 per cent among people over 80 years of age[1]. These results were reported in one of the largest data analyzes of 72,314 patient records conducted in China[1].Although patients with no prior comorbid conditions had a case fatality rate of 0.9%, it was substantially higher for those with serious underlying comorbidities, making these population groups more vulnerable to extreme COVID-19[1].

PATHOGENESIS:

Before the outbreak of SARS-CoV, coronaviruses were thought to cause only mild, self-limiting respiratory infections in humans[12].Such viruses are common in humans, causing 15-30 per cent of infections of the respiratory tract per year[12].They cause more serious disease in neonates, the elderly and people with underlying diseases, with an increased incidence of lower respiratory tract infection in these populations[12]. SARS-CoV, group 2b β-coronavirus, has been reported as the causative agent of the outbreak of Severe Acute

Respiratory Syndrome (SARS) in the Guangdong Province of China in 2002–2003[12]. This is the most severe of all human diseases caused by coronavirus[12]. It is widelyaccepted that SARS-CoV originated in bats as a huge number of Chinese horseshoe bats carry SARS-related CoV sequences and provide serological evidence of previous CoV infection[12].SARS-CoV mainly infects pulmonary epithelial cells. The virus can penetrate macrophages and dendritic cells but causes only abortive infection[12].Despite this, inducing infection of these types of cells may be necessaryProinflammatory cytokines which can lead to the illness[12].These types of cells produce many cytokines and chemokines and are elevated in the serum of patients infected with SARS-CoV[12].The precise mechanism of lung disease and the human cause of serious illness remains undetermined[12].

The ability to infect humans is primarily due to peridomestic animal infection, which is considered to be intermediate hosts, sustaining recombination and mutation events, as well as developing genetic diversity among coronavirus[16].Studies have indicated that the glycoprotein spike (S glycoprotein) plays an important role in restricting the host range by adding virions to the host cell membrane[16]. Coronaviruses typically replicate mainly in the respiratory and intestinal epithelial cells and then induce cytopathic alterations[16].

SIGNS AND SYMPTOMS:

COVID-19 incubation time is from 1-14 days(Mean 5-7 day period), with peak viraemia occurring until symptoms begin[1]. This highlights the capacity for transmission of asymptomatic or minimally symptomatic patients[1].Most COVID-19 patients account for relatively mild cases[13].

The most common features of COVID-19 infection are listed below with its frequency:

Fever (80%-90%), Cough (60%-80%), Breathlessness (18%-46%), Fatigue (38%), Body ache/joint pain (15%), Sore throat (11%-14%), Headache (6%-14%), Chills (12%), Body ache/joint pain (15%), Running nose (5%), Nausea/vomiting (5%), Diarrhoea (2%-10%)[1].

SIGNS need hospitalization are:

Fever and upper respiratorysymptoms lasting for more than 5 daysand any of the following signs[1]:

- Breathlessness/respiratoryrate more than 24/min[1],
- Oxygen saturation (SpO2) less than 95% in room air[1].
- Fatigue with heart rate of greater than 110/bpm[1].
- Systolic blood pressure less than 90 mmHg[1].

COMORBID ILLNESS AND FATALITY RATES IN HIGH RISK GROUPS:

Cardiovascular disease (10.5%), diabetes mellitus (7.3%), chronic respiratory disease (6.3%), hypertension(6%), cancer (5.3%)[1].

CATEGORIZATION OF DISEASE:

MILD:

- Fever, upper respiratory symptoms, mild sore throat and gastro-intestinal symptoms.
- Testing may be considered in select individualsin the high-risk group.
- Testing: NOT ESSENTIAL
- Level of care: HOME CARE

MODERATE:

- Breathlessness/respiratory rate greater than 24/min, Oxygen saturation (SpO2) less than 95% in room temperature, Fatigue with heart rate of greater than 110/bpm, Systolic blood pressure <90 mmHg.
- Testing: HIGH PRIORITY
- Level of care: INPATIENT CARE

SEVERE:

- SpO2 less than 90% in room temperature, Hypotension requiring ionotropic support, Acute Respiratory Distress Syndrome /myocarditis.
- Testing: MANDATORY
- Level of care: INPATIENT CARE

INVESTIGATIONS:

TESTS:

SARS-COV-2 DETECTION BY POLYMERASE CHAIN REACTION:

SARS-CoV-2 is an enveloped positive-stranded RNA virus that contains approximately 30,000 nucleotides and 15 genes[17].Some of these genes were used for diagnostic reverse-transcription polymerase chain reaction (RT-PCR) study, including E (envelope), N (nucleocapsid), RdRp (RNA-dependent RNA polymerase), nsp10. Genes (nonstructural protein 10), and genes nsp14 (nonstructural protein 14, exoribonuclease)[17].Unlike other RNA viruses, SARSCoV-2 is subject to mutation, while Nsp14's profreading role limits nucleotide miscorporation levels. Sequence variants can lead to reduced recognition of the individual primary samples used in PCR-based assays[17]. RT-PCR is highly accurate[17].The suggested diagnostic test on the respiratory samples is the reverse transcription-polymerase chain reaction (RT-PCR). Even though initial studies showed low sensitivities of 30-60%, the new studies show better results[1].

NUCLEIC ACID AMPLIFICATION TEST:

Routine confirmation of cases of COVID-19 is based on the identification of specific sequences of virus RNA by NAAT such as real-time reverse transcription polymerase chain reaction (RT-PCR) with confirmation by nucleic acid sequencing. The target viral genes to date include the genes N, E, S and RdRP[18].

SEROLOGY:

Coronaviruses consistof 4 structural proteins: theimmunodominant receptor-binding spike (S) protein, the nucleocapsid (N) protein, the envelope (E) protein, and the membrane (M) protein[17].Diagnostic methods used to identify specific antibodies to SARS-CoV-2 proteins include rapid diagnostic tests, such as lateral flow tests, enzyme-linked immunosorbent assays, neutralization assays and chemiluminescent immunoassays[17].Only neutralization assays may provide information on antibodies reported to suppress viral growth[17].Although the primary use of serological tests is to assess the previous exposure to SARS-CoV-2 can promote the diagnosis of COVID-19 in patients with high clinical suspicion but with negative PCR tests[17].Serological surveys may assist with an ongoing outbreak investigation and a retrospective evaluation of the attack rate or severity of an outbreak[18].In situations where NAAT assays are negative and there is a strong epidemiological link to COVID-19 infection, paired serum samples (in both the acute and convalescent phases) may support diagnosis once validated.Serology tests are given[18].

VIRAL SEQUENCING:

In addition to verifying the existence of the virus, routine sampling of a percentage of specimens from clinical cases may be useful for monitoring mutations in viral genomes that may impact medical countermeasures, including diagnostic tests[18].

BIOMARKERS:

Several biomarkers including lymphocyte counts, neutrophil-to-lymphocyte ratios, C-reactive protein, troponin T, D-dimer, lactate dehydrogenase, procalcitonin, interleukin-6, and ferritin, predict disease progression and COVID-19 mortality[17].

Biomarkers are :

- Hematology – ↓ lymphocyte count,↑ neutrophil and ↓ platelet count.
- Biochemical - ↓ Albumin, ↑Creatinine, ↑Lactate dehydrogenase, ↑ Cardiac troponin,

↑ B-type natriuretic peptide, ↓Oxygen saturation.

- Inflammatory - ↑ C-reactive protein, ↑ Ferritin, ↑ Procalcitonin, ↑Interleukin-6
- Coagulation - ↑ D-dimer

GENERAL TREATMENT MEASURES:

Patients are classified for further decisions on hospitalization and treatment choices based on disease severity[1].The therapy involves antiviral drugs or specific therapy and support management for complications[1]. The theoretical concern of the NSAIDs is worsening outcomes in COVID-19 infections as these levels of angiotensin-converting enzyme 2 in the lung, the virus entrance receptor, remain to be proven[1].Small studies have also found that exposure to NSAID is significantly

correlated with pleuro-pulmonary complications in patients with community-acquired pneumonia[1]. Paracetamol may be favored in COVID19 management over NSAIDs for the above reasons[1].

TREATMENT:

Initially, interferons-a nebulization, antibiotics of wide spectrum and anti-viral drugs were used to reduce the viral load[2]. Only remdesivir, however, has shown promising effect against the virus[2]. Remdesivir alone and significantly blocked the replication of SARSCoV-2 in combination with chloroquine or interferon beta, and patients were declared clinically recovered[2].There are actually several other anti-virals tested against infection[2]. Once tested against infection, Nafamostat, Nitazoxanide, Ribavirin, Penciclovir, Favipiravir, Ritonavir, AAK1, Baricitinib and Arbidol showed intermediate results inPatients and clinical isolates at in vitro[2]. Recentlyblood plasmaadministered into infected patients from clinically treated COVID-19 patients shows promising results with rapid recovery[2].There is no COVID-19 vaccine available while previous vaccines or techniques used to develop a SARS-CoV vaccine may be successful[2].Due to the lack of appropriate therapeutics or vaccines, the best methods to monitor human coronaviruses remain a strong program of public health surveillance, combined with rapid diagnostic testing and quarantine whenever necessary[10].

INFECTION CONTROL:

In SARS-COV-2 infection the prevailing mode of person-to - person transmission is through close contact with infected individuals that produce respiratory droplets[1]. The virus will remain active on inanimate surfaces for several hours and is likely to cause fomite transmission[1]. It seems unlikely that these particles would spread far enough to create secondary infection[1]. The most important factor for reducing the risk of transmitting microorganisms to patients was hand hygiene[2]. Depending on the type of surface, temperature or humidity of the atmosphere, SARS-CoV-2 can persist on surfaces for a few hours or up to several days[13].This enhances the need for good hygiene of the hands and the value of thorough disinfection of all surfaces[13].Since respiratory droplets are the main route of SARS-CoV-2 transmission, high-quality face masks are recommended for particulate respirators[13].

Conclusion

COVID-19 has emerged as a major public health threat in the last nine months.Due to its multiple variants and mutation, a detailed study and analysis is required to arrive for conclusive treatment. This takes a multifaceted approach for tackling the emerging COVID-19 pandemic. Until then the government, the health sector, community and individual person have a vital role to in preventing transmission as “PREVENTION IS BETTER THAN CURE”.

Ethical Clearance – Not required since it is a review article

Source of Funding – Nil

Conflict of Interest – Nil

References

1. Varghese GM, John R, Manesh A, Karthik R, Abraham O C. Clinical management of COVID-19. Indian J Med Res 2020;151:401-10
2. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 2020 Mar 16.
3. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 1.
4. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 11.
5. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 40.
6. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 71.
7. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 101.
8. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 132.
9. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 153.
10. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 193.
11. World Health Organization. Novel Coronavirus (2019-nCoV): situation report, 207.
12. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. InCoronaviruses 2015 (pp. 1-23). Humana Press, New York, NY.

13. Meng L, Hua F, Bian Z. Coronavirus disease 2019 (COVID-19): emerging and future challenges for dental and oral medicine. Journal of Dental Research. 2020 May;99(5):481-7.
14. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. International Journal of Oral Science. 2020 Mar 3;12(1):1-6.
15. Ge ZY, Yang LM, Xia JJ, Fu XH, Zhang YZ. Possible aerosol transmission of COVID-19 and special precautions in dentistry. Journal of Zhejiang University-SCIENCE B. 2020 Mar 16:1-8.
16. Fallahi HR, Keyhan SO, Zandian D, Kim SG, Cheshmi B. Being a front-line dentist during the Covid-19 pandemic: A literature review. Maxillofacial Plastic and Reconstructive Surgery. 2020 Dec;42:1-9.
17. Fang FC, Naccache SN, Greninger AL. The Laboratory Diagnosis of COVID-19--Frequently-Asked Questions. Clinical Infectious Diseases. 2020 Jun 8.
18. World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases: interim guidance, 19 March 2020. World Health Organization; 2020.