

COVID 19-AN OVERVIEW ON EPIDEMIOLOGY, SYMPTOMS, PREVENTION, MANAGEMENT, TREATMENT AND ROLE OF HEALTH WORKERS

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ABSTRACT

With the first case of a highly infectious virus named Coronavirus in Wuhan, China in December 2019, this deadly virus was declared a pandemic by WHO. COVID-19 was found to be very similar to patients infected with MERS-CoV and SARS-CoV. The virus was transmitted from bats to humans through some unidentified intermediary. Since its introduction in humans, it has infected 118000 people, killing 3583 till last week of May 2020 in India. The reported route of transmission is inhalation or direct contact with the infected surface or patients. This symptomatic disease includes symptoms such as cough, fever, sore throat, fatigue, and in some severe patients, it may cause multiple organ failure, pneumonia, severe or acute respiratory diseases. In some cases people may be asymptomatic till 14 d of infection. The patients with mild illness are usually isolated and others are prevented with protective measures such as medical mask, hand hygiene. In the present article, the epidemiology, route of transmission, clinical symptoms, prevention, management, treatment and role and responsibility of health workers is overviewed on the basis of published research and review articles and current state of knowledge.

Keywords: Coronavirus, COVID 19, SARS-CoV 2, Anti-viral drugs, Symptoms, Prevention

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INTRODUCTION

A newly emergent virus SARS-CoV-2 caused respiratory tract infection in Wuhan, China in December, 2019. This was named as coronavirus disease 2019 or COVID 2019. It was declared as novel virus that caused the major pandemic [1, 2]. Although the first case of SARS-CoV occurred in November, 2002 in china and till that time this virus has infected more than a lakh of people worldwide, killing thousands of them [3]. In 2003, World Health Organization (WHO) issued a global alert regarding such cases in Hong Kong and Vietnam [4, 5]. In 2012, WHO announced the discovery of new virus, MERS-CoV that killed 2 patients in Middle East [1]. According to the reports of The Program for Monitoring Emerging Diseases, since 2012, 300 cases of pneumonia were reported due to unidentified causes in China [6, 7]. As per 2003 reports, during the epidemic in Southern China, it was discovered that very similar virus was found in horseshoe bat, Bat SARS-CoV [6, 8-11]. It was also suggested that SARS can return if conditions for virus in the form of mutation, amplification and transmission fit and it could be a potentially dangerous virus. Coronaviruses are known to have high mutation and recombination rates which allow the virus to cross species barrier and adapt to new host [4]. They cause intestinal and respiratory infection in humans and other animals. SARS-CoV and Bat SARS-CoV are together known as 2b-Coronaviruses. SARS-CoV 2 has found to be originated from bat however; there is no evidence so far that it has its origin from seafood market [6, 12]. The present review indicates the epidemiology, clinical symptoms, prevention, management, treatment and role of health care workers in COVID 19.

Genomic structure

CoVs are largest group of all viruses in Nidovirales order, which include Coronaviridae, Roniviridae, and Arteriviridae families. SARS-CoV is among the 36 coronaviruses of the family *Coronaviridae* [13]. The Coronaviridae is subdivided into two subfamilies named Coronavirinae and Torovirinae. Furthermore, the subfamily Coronavirinae is divided into four groups, the alpha, beta, gamma and delta coronaviruses. Coronavirinae is known to have the largest (approximately 30 kilobase) identified RNA genomes. Coronaviruses are enveloped, non-segmented positive-sense RNA viruses [14, 15]. The genome acts as a mRNA for translation of replicase polyprotein through 5'cap structure along with 3' poly (A) tail. About 2/3rd of the

genome is occupied by non-structural protein (20kbs) as compared to structural and accessory protein (10kbs). The RNA replication and transcription occurs through 5' end containing a leader sequence and untranslated region (UTR) that contain multiple stem loop structures. The 3'UTR also contains RNA structures required for replication and synthesis of viral RNA [16].

The studies of cryo-electron microscopy and cryo-electron tomography depicted that coronavirus virions are spherical in shape with 125nm of diameter. The surface of the virion show club-shaped spike-like projections, that give them the appearance of solar corona hence named Corona Virus [17, 18]. The virion envelop consist nucleocapsid. Coronavirus contain 4 structural proteins. The S protein (150kDa) makes up the distinctive spikes like structure on surface of the virus [19, 20]. It is Class I fusion protein involved in the attachment with the host cell [21, 22]. This makes S-protein the main target for neutralizing antibody and antiviral peptides [23-27]. The M protein (25-30 kDa) is the small protein and the most abundant structural protein in virion [28]. The E protein (08-12 kDa) is found in small quantities within virion. The E protein is required for pathogenesis in SARS-CoV [29-31]. The N protein is present in nucleocapsid and composed of two separate domains, C-terminal domain and N-terminal domain. Both domains are capable of binding RNA but by different mechanisms [32, 33]. Apart from four types of proteins, a fifth type of structural protein is the hemagglutinin-esterase (HE), is present in a subset of beta-coronaviruses and enhance the S-protein mediated cell entry and spread through the mucosa [34, 35]. The genome also consist of open reading frames (ORFs) out of which ORF1a and ORF1b are involved in encoding with 16 non-structural proteins and 7 of them are predicted to be involved in transcription and replication of largest genome. ORF1b is also the molecular target for the design of clinical diagnostic tests [36-45].

Route of transmission

The rapid economic growth and urbanization has led to higher demand for animal proteins and moreover, the frequent mixing of various animals in densely populated areas with lack of biosafety measures have resulted in the transmission of virus from animal to humans [6, 46-48]. The consumption of wild animals for animal proteins and direct contact with other host animals is the major

route of coronavirus transmission. Furthermore, the human to human transmission because of lack of awareness and hospital infection control and lack of control of such infections in public places has facilitated the rapid growth of such kind of virus. SARS-CoV 2 usually transmit human to human i.e., between family members including friends, neighbours and relatives who contacted the patients or incubation carriers. It transmits through the respiratory tract by Respiratory secretions, respiratory droplets (>5-10 µm in diameter) and direct contact [49-57]. An analysis on 75,465 coronavirus cases showed no airborne transmission [58]. As per the March 2020 reports by WHO, the airborne transmission may be possible under certain circumstances of endotracheal intubation, manual ventilation, bronchoscopy, open suctioning etc. Some evidence showed that COVID can lead to intestinal infection and be present in faeces but no such fecal-oral transmission has been reported yet [49]. SARS-CoV has 2-3 d of stability in the environment or on dry surface at room temperature, which is higher as compared to other known virus and 2-4 d of survival in stool [59]. However, source and transmission is still elusive. In February 2020, it was reported by National Health Commission, China that approximately 3.8% of COVID 19 patients transmitted infection to healthcare workers. As COVID-19 is contagious, it is highly transmissible in humans, especially in children and elderly. The most vulnerable age group of patients is 47-59 y out of which 41.9-45.7% was females. Wuhan, China being the origin of COVID 19 infected 31.3% of the patients who travelled to Wuhan and 72.3% of patients that although had no travel history of Wuhan but contacted the people from Wuhan [57]. WHO reported total 5,197,776 confirmed cases of COVID 19 with 334,675 deaths till last week of May 2020 worldwide. In India, 30% of elderly people aged above 60 y got infected with COVID-19 and 5% above 80 y of age.

Clinical characteristics

SARS being severe acute respiratory syndrome show mild or uncomplicated illness and approximately 14% require hospitalization and oxygen support and 5% required admission to an Intensive Care Unit [60]. Most people who suffered from COVID 19 experienced mild to moderate illness and other symptoms include fever, malaise, cough, and mild flu like symptoms. A study conducted by Prof. Nan-Shan Zhong's team, on 1099 confirmed cases found that most common symptoms of coronavirus included fever, cough, fatigue, headache, sputum production, shortness of breath, sore throat, diarrhea and vomiting [61-64]. Less common symptoms may include dyspnea, anorexia and nasal congestion [65]. The elderly people with underlying diseases such as diabetes, hypertension, cardiovascular diseases, chronic obstructive pulmonary diseases etc. developed rapidly into acute respiratory distress syndrome, coagulation dysfunction and even death [54]. Patients with heart disease showed an increase in ACE2 and possibility of heart attack and severe infection [71]. The laboratory examination reports depicted the normal or decreased white blood cells, lymphocytopenia. The neutrophil count, blood urea, D-dimer, inflammatory factors (interleukins, tumor necrosis factor) and creatinine level showed a significant increase [54, 64, 67]. People rapidly developed multiple organ failure, respiratory failure, shock, arrhythmia, acute heart injury, acute respiratory distress syndrome and even deaths [54]. As with elderly, children also get easily infected with the virus because of immature or weak immune system. Therefore, the necessary care and attention is always needed for both age groups [68].

Prevention in case of COVID 19

- A healthy person should maintain 1m away from the infective person or who has respiratory symptoms such as sneezing, coughing.
- Washing hands frequently
- Sanitizing hands with alcohol-based hand rub when dirt is not visible
- Wearing a medical mask to limit the spread of certain respiratory diseases
- Avoiding over-crowded places, group of people and enclosed spaces

- Covering nose and mouth with an elbow while coughing and sneezing
- Disposing the mask or tissue immediately after use
- Appropriate ventilation/air flow in the living space of patient by opening windows and doors as much as possible
- Replacing mask with a newer one, as soon as it becomes damp
- Discarding used mask and disposing immediately upon removal
- Maintaining a balanced diet, keeping yourself hydrated, exercising regularly and sleeping well [69, 70]

Management in case of COVID 19

People with mild illness and no risk factors can be:

- Isolated in non-traditional facilities such as hotels, stadiums, gymnasiums where they can remain till recovery or till laboratory test for COVID 19 are negative
- Isolated in a well-ventilated single room
- The movement should be limited in the house
- Patient's family members should stay in different rooms
- Number of caregivers should be limited and if possible only a person with good health should be assigned
- Relatives or other visitors should not be allowed to enter
- Hand hygiene should be performed
- Surfaces should be cleaned frequently using disinfectants containing 0.1% sodium hypochlorite
- Clean the clothes, towels of the patients daily with regular detergent and water or machine wash at 60-90 °C and dry thoroughly
- Mask and other medical waste should be disposed of properly at a sanitary landfill
- Surfaces touched or came in contact with infected patients or with their respiratory secretion or other body fluids should be disinfected with regular disinfectants containing a 0.5% diluted bleach solution [71]

Myth busters in corona virus

With the rise in the cases of the Corona virus, the myths related to treatment and spread of diseases also increased. The WHO has advised public to not believe in such myths are given instructions to all worldwide. Following advices were given by WHO:

- No Licensed drug for treatment and prevention of COVID-19: Many reports have shown that hydroxychloroquine has been successful in treatment of Covid 19 but no proof is reported yet. The use of hydroxychloroquine can cause serious side effects and can even lead to death.
- Peppers in soup and other meals do not prevent or cure COVID-19: Hot peppers cannot prevent or cure COVID-19. The only way to protect yourself against the disease is Social distancing maintaining atleast 1m distance and taking all the precautions.
- Houseflies and Mosquito bites do not transmit Covid 19: COVID 19 spreads only through droplets of an infected person when the patient cough, sneeze or speak. The disease may also spread by touching a contaminated surface and then touching eyes, nose or mouth.
- Spraying, introducing and drinking methanol, ethanol, bleach or another disinfectant will never protect you against COVID-19 and can be dangerous: Use of bleach for spraying on body or drinking is very dangerous and poisonous, it can cause irritation and damage to skin and body.
- Mobile networks (5G) or any Radiowaves do not spread COVID 19. Virus cannot travel through radio waves or mobile networks.

- Exposing yourself to high temperature or sun does not prevent COVID 19: Even many cases are reported in areas with high temperature or hot weather.
- Holding Breathe for 10 seconds or without cough or feeling discomfort does not mean you are free from disease. The only method to test the disease is laboratory test.
- Alcohol consumption cannot protect you from disease but it would increase the risk of other health problems.
- COVID 19 cannot spread through hot, humid and cold weather.
- Hot bath does not protect from disease
- Ultra-Violet (UV) radiations should not be used to disinfect hands or skin, it only causes skin irritation and damage.
- Eating garlic cannot prevent infection: Although Garlic is a healthy food and it has anti-microbial properties but there is no evidence that it can prevent infection
- Corona virus affect all age groups. Although older age group with existing medical diseases are more vulnerable to disease but all age groups gets affected and all need to stay protected
- Antibiotics are not effective against prevention of COVID 19 [72]

Treatment in case of COVID 19

Remdesivir

Remdesivir has been reported to show broad-spectrum antiviral activity against several RNA viruses. Remdesivir is a 1'-cyano-substituted adenosine nucleotide analog prodrug used to treat the first case of COVID 19 in US successfully. It interferes with the NSP 12 polymerase as studied through *in vitro* cell line and mouse model [63, 73].

Chloroquine

Chloroquine is an anti-malarial drug that was reported with great potential to treat COVID 19 although, the mechanism against such viral infections was not well understood. Several studies found that chloroquine can interfere with glycosylation of cellular receptors of SARS-CoV. It can inhibit pH-dependent steps of virus replication, an immunomodulatory effect that suppress the production/release of TNF- α and IL-6. It can also interfere with viral infection and replication being novel class of autophagy inhibitor [74-77].

Ribavirin

Ribavirin is another antiviral drug that was used for the treatment of SARS. It markedly improves symptoms such as fever and improvement in oxygenation and radiographic appearance [78-82]. Although other reports failed to identify the treatment with Ribavirin as most patients received corticosteroids alongwith [83, 84].

IFNs

Oxygenation and radiographic appearance showed improvement with IFNs specifically IFN- α and high dose of methyl prednisolone that inhibit SARS-CoV *in vitro* [85-87].

Corticosteroids

Corticosteroids were found to be effective in SARS therapy and results demonstrated the decrease in virus load. But another report associated with corticosteroid therapy demonstrated that it may worsen the disease. Corticosteroids increase the susceptibility to pathogens, particularly fungal infections [88].

IVIg

IVIg has been demonstrated to have immunomodulatory properties and downregulate cytokine expression. Convalescent-phase plasma samples containing high levels of anti-SAR CoV antibodies have been used to treat SARS CoV in Hong Kong and China. Plasma exchange was reported as salvage therapy in Hong Kong, but no data of efficacy exist [89, 90].

Apart from single and prodrugs, combinational drugs has also shown potential in treatment of COVID 19. *In vitro* repors suggested that combination of Remdesivir and Chloroquine was effective in inhibiting SARS-CoV 2. Combination of Lopinavir and Ritonavir (protease inhibitor) was conformed to treat HIV and has potential to improve MERS-CoV and SARS-CoV [91-94]. Korean reports showed that this combination significantly decreased the β -corona virus viral loads of COVID 19. Another combination of Chinese and western medicines included Lopinavir/Ritonavir, arbidol and Shufeng Jiedu significantly improved the pneumonia symptoms in China [95].

Role and responsibility of health workers

Health workers should:

- Follow all the protective and preventive measures to minimize occupational health and safety risk
- Follow all the information, training and instructions provided on occupational health and safety risk
- Provide appropriate training on infection prevention control (IPC)
- Provide or ensure that all suspected or confirmed cases of COVID 19 have adequate protective personnel equipment (PPE) such as medical mask, gloves, gowns, sanitizers, soaps and gown etc.
- Provide safety measures to all suspected or confirmed cases of COVID 19
- Self-monitoring the signs and symptoms of COVID 19 and report the illness to managers
- Ensure that workplace and all the surfaces exposed to patients are cleaned and disinfected properly
- Search for the travel history of all the National and International travellers in past few months who came to them with respiratory symptoms
- If the patient is suspected with the disease in OPD they should be provided with masks immediately
- Examiners should use surgical masks and practice hand hygiene frequently
- Suspected cases should be isolated immediately and informed to diagnostic centres of respective state [96-98]

CONCLUSION

The novel virus outbreak has challenged every country in terms of their economy, medical and public health services. The increased urbanization and people's dependency on animal proteins have the potential that threat of such virus or other deadly infections may likely to continue. Therefore, apart from tackling the current situation globally, the need of the hour is to take comprehensive measures to prevent such outbreak in future.

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All the author have contributed equally.

CONFLICT OF INTERESTS

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