

A review of COVID-19

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Abstract

The Covid-19 (Novel corona virus) continues to wreak havoc across China, European countries, USA and now seems to gain a strong foothold in India. Corona virus causes respiratory infection including pneumonia, cold, sneezing and coughing. Corona virus transmitted human to human via airborne droplets. Corona virus enters in human cell through membrane ACE-2 exopeptidase receptor. COVID-19 is a new disease and there is limited information regarding risk factors for severe illness. Based on currently available information older adults and people of any age who have serious underlying medical conditions might be at higher risk for severe illness from COVID-19. WHO and IJCMR advised to avoid public place and close contact to infected persons.

Keywords: Corona virus, COVID-19, SARS-CoV, Novel corona virus

Introduction

Severe acute respiratory syndrome (SARS) was first recognized as a global threat in mid-March 2003. The first known cases of SARS occurred in Guangdong province, China, in November 2002 and WHO reported that the last human chain of transmission of SARS in that epidemic had been broken on 5 July 2003. The etiological agent, the SARS coronavirus (SARSCoV) is believed to be an animal virus that crossed the species barrier to humans recently when ecological changes or changes in human behaviour increased opportunities for human exposure to the virus and virus adaptation, enabling human-to-human transmission. By July 2003, the international spread of SARS-CoV resulted in 8098 SARS cases in 26 countries, with 774 deaths. The epidemic caused significant social and economic disruption in areas with sustained local transmission of SARS and on the travel industry internationally in addition to the impact on health services directly [1].

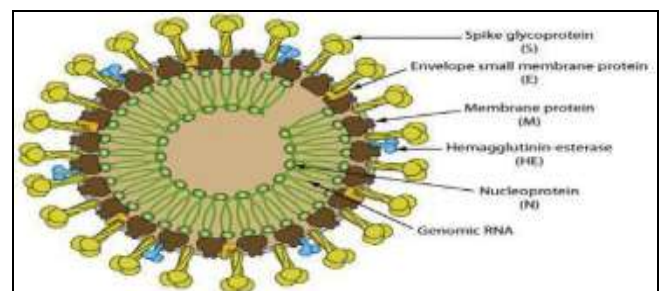
On December 31, 2019, the China Health Authority alerted the World Health Organization (WHO) to several cases of pneumonia of unknown aetiology in Wuhan City in Hubei Province in central China. The cases had been reported since December 8, 2019, and many patients worked at or lived around the local Huanan Seafood Wholesale Market although other early cases had no exposure to this market. On January 7, a novel coronavirus, originally abbreviated as 2019-nCoV by WHO, was identified from the throat swab sample of a patient. This pathogen was later renamed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronavirus Study Group and the disease was named coronavirus disease 2019 (COVID-19) by the WHO. As of January 30, 7736 confirmed and 12,167 suspected cases had been reported in China and 82 confirmed cases had been detected in 18 other countries. In

the same day, WHO declared the SARS-CoV-2 outbreak as a Public Health Emergency of International Concern (PHEIC) [2].

Microbiology

COVID-19 is a spherical or pleomorphic enveloped particle containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections. Some coronaviruses also contain a hemagglutinin-esterase protein (HE) [3].

Coronaviruses possess the largest genomes (26.4–31.7 kb) among all known RNA viruses, with G + C contents varying from 32% to 43%. Variable numbers of small ORFs are present between the various conserved genes (ORF1ab, spike, envelope, membrane and nucleocapsid) and, downstream to the nucleocapsid gene in different coronavirus lineages. The viral genome contains distinctive features, including a unique N-terminal fragment within the spike protein. Genes for the major structural proteins in all coronaviruses occur in the 5'–3' order as S, E, M, and N [4].



(<https://www.google.com/imgres?imgurl=https%3A%2F%2Fars.el>)

Fig 1: Schematic of a coronavirus.

Mode of Transmission

Respiratory infections can be transmitted through droplets of different sizes: when the droplet particles are $>5-10 \mu\text{m}$ in diameter they are referred to as respiratory droplets, and when they are $<5 \mu\text{m}$ in diameter, they are referred to as droplet nuclei^[5]. According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes. In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported^[6].

Droplet transmission occurs when a person is in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is therefore at risk of having his/her mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets. Transmission may also occur through fomites in the immediate environment around the infected person. Therefore, transmission of the COVID-19 virus can occur by direct contact with infected people and indirect contact with surfaces in the immediate environment or with objects used on the infected person (e.g., stethoscope or thermometer)^[5].

Airborne transmission is different from droplet transmission as it refers to the presence of microbes within droplet nuclei, which are generally considered to be particles $<5 \mu\text{m}$ in diameter, can remain in the air for long periods of time and be transmitted to others over distances greater than 1 m.

In the context of COVID-19, airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed; i.e., endotracheal intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation^[5].

There is some evidence that COVID-19 infection may lead to intestinal infection and be present in faeces. However, to date only one study has cultured the COVID-19 virus from a single stool specimen^[7].

Clinical feature

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset of patients, by the end of the first week the disease can progress to pneumonia, respiratory failure and death. This progression is associated with extreme rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF α ^[8]. The median time from onset of symptoms to dyspnea was 5 days, hospitalization 7 days and acute respiratory distress syndrome (ARDS) 8 days. The need for intensive care admission was in 25–30% of affected patients in published series. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2nd or 3rd wk. The median duration of hospital stay in those who recovered was 10 days. Adverse outcomes and death are more common in the elderly and those with underlying comorbidities (50–75% of fatal cases). Fatality rate in

hospitalized adult patients ranged from 4 to 11%. The overall case fatality rate is estimated to range between 2 and 3%^[9].

Guan *et al.* published a report on 1099 patients with laboratory confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 29, 2020. The most common symptoms reported were fever (43.8% on admission, and 88.7% during hospitalization) and cough (67.8%), diarrhoea (3.8%) was uncommon. A severe form of the disease was reported in elderly and in patients with comorbidities. Overall reported cases of death in this study were 15 (1.4%)^[10]. The case reported from the United States was virus-positive in respiratory and faecal specimens; he had respiratory failure requiring oxygen supplementation. The patient was treated with intravenous Remdesivir (a novel nucleotide analogue prodrug under development) and reported to be afebrile and stable^[11].

In India a study conducted by Gupta N *et al* was found that the mean age of participants was 40.3 years (range 16-73 years). There was a male preponderance (66.7%). Seven were from Delhi, eight from Agra, two from Kolkata, and the remaining four were from Noida, Ghaziabad, Gurgaon, and Rajasthan, respectively. The average length of stay in hospital was 11.54 days and the mean duration of symptoms was 2.1 days. Eleven (52.4%) patients had a history of contact with a lab-confirmed COVID-19 patient. More than half of the patients, 13 (61.9%), had a travel history outside India. The majority of patients 8 (38.1%) visited Italy, followed by 2 (9.5%) who travelled to London, and other 3 patients (4.8%) who had been to Iran, Saudi Arabia, and Malaysia, respectively. The common presentation and symptoms experienced by nine patients were cough and fever. Sore throat, breathlessness, and headache were present in 5(23.8%), 1(4.8%), 3 (13.6%), respectively. Six patients (28.6%) had comorbidities. The most common comorbidity was hypertension (5 patients) and diabetes mellitus (3 patients) adequately controlled with drugs. One (4.8%) patient with hypertension and one with diabetes mellitus also showed anxiety disorder and hypothyroidism. Another patient had an underlying migraine and obstructive sleep apnoea. Chest roentgenogram was performed in all patients at initial presentation, and in 20 cases (95.2%), it showed no abnormality^[12].

In Rajasthan a study conducted by Bhandari S *et al* was found that male patients constituted 66.66% of total patients and majority of the patients (80.90%) were below 60 years of age. Most of the patients (71.40%) were either foreigners or had a history of foreign travel suggesting that these cases were not community acquired except for 4 cases from textile producing district Bhilwara (known as Manchester of India), an first epicenter of North India. Approximately 33.33% patients were completely asymptomatic and of those who were symptomatic cough was the most common symptom (85.71%) followed by fever (78.57%), myalgia (64.28%), headache (28.57%) and dyspnea (28.57%). Three patients (14.28%) had underlying co morbidity in the form of hypertension, diabetes mellitus, hypothyroidism, chronic kidney disease or coronary artery disease. 11 patients (52.38%) had lymphopenia in their hemogram during the course of admission. 3 patients (14.28%) had leucocytosis and 4 patients (19.04%) presented with thrombocytopenia. All 4 patients in the severe category had raised FDP, D-Dimer levels and they needed oxygen support. These

patients had deranged liver functions and had elevated procalcitonin levels, serum ferritin levels and LDH levels. 1 out of the these 4 cases went into ARDS during the course of treatment. 10 patients yielded negative results for Covid-19. The mean duration from admission to getting 1st Covid-19 sample negative was 8.3 days. 18 patients (85.71%) are still under treatment. Conclusion: Clinical investigations in initial Covid-19 patients in the Indian subcontinent reveal lymphopenia as predominant finding in hemogram. Patients with older age and associated comorbid conditions (COPD and diabetes) seem to have greater risk for lung injury thereby requiring oxygen support during the course of disease and these patients also had greater derangement in their biochemical profile [13].

Diagnosis

The decision to test should be based on clinical and epidemiological factors and linked to an assessment of the likelihood of infection. PCR testing of asymptomatic or mildly symptomatic contacts can be considered in the assessment of individuals who have had contact with a COVID-19 case. Screening protocols should be adapted to the local situation. The case definitions are being regularly reviewed and updated.

Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and bronchoalveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India. This diagnostic criterion was based on the recommendation by the National Institute of Virology (Pune).

The COVID-19 RT-PCR Test is a real-time reverse transcription polymerase chain reaction (rRT -PCR) test. The test can be run in a singleplex format (three individual assays) or multiplexed into a single reaction and amplification set up. In a singleplex format, the test uses three primer and probe sets to detect three regions in the SARS-CoV-2 nucleocapsid (N) gene and one primer and probe set to detect human RNase P (RP) in a clinical sample. When multiplexed into a single reaction, the test uses two primer and probe sets to detect two regions in the SARS-CoV-2 N gene and one primer and probe set to detect RP. RNA isolated from upper and lower respiratory specimens (such as nasal, nasopharyngeal or oropharyngeal swabs, sputum, lower respiratory tract aspirates, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal aspirate) is reverse transcribed to cDNA and subsequently amplified using Applied Biosystems QuantStudio7 Flex (QS7) instrument with software version 1.3. During the amplification process, the probe anneals to a specific target sequence located between the forward and reverse primers. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades the bound probe, causing the reporter dye to separate from the quencher dye, generating a fluorescent signal. Fluorescence intensity is monitored at each PCR cycle by QS7 [14].

Differential diagnosis

The differential diagnosis includes all types of respiratory viral infections [influenza, parainfluenza, respiratory

syncytial virus (RSV), adenovirus, human metapneumovirus, non-COVID-19 coronavirus], atypical organisms (mycoplasma, chlamydia) and bacterial infections. It is not possible to differentiate COVID-19 from these infections clinically or through routine lab tests. Therefore, travel history becomes important [15].

Prevention

Since at this time there are no approved treatments for this infection, prevention is crucial. Several properties of this virus make prevention difficult because non-specific features of the disease, the infectivity even before onset of symptoms in the incubation period, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery.

The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak (2002), 21% of those affected were healthcare workers [16]. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. Patients should be placed in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19. Patients can be discharged from isolation once they are afebrile for at least 3 day and have two consecutive negative molecular tests at 1-day sampling interval. This recommendation is different from pandemic flu where patients were asked to resume work/school once afebrile for 24 h or by day 7 of illness. Negative molecular tests were not a prerequisite for discharge [15].

At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/ tissue rather than hands and practice hand hygiene frequently every 15–20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of mask by healthy people in public places has not shown to protect against respiratory viral infections and is currently not recommended by WHO [15].

There is no special vaccine for this yet. Only supportive therapy is the treatment strategy followed by health professionals. Supportive therapy includes administration of antipyretic and analgesic, maintenance of hydration, mechanical ventilation as respiratory support and uses of antibiotic in bacterial infections.

Some research studies claimed that ribavirin and interferon alpha have offered synergetic effect in early stage. While other studies reported mycophenolic acid as monotherapy. Still health professionals were not fully satisfied with any therapy so further clinical research needed [17, 19].

Conclusion

Corona virus was spreading human to human to transmission by close contact via airborne droplets

generating by coughing, sneezing and smooching. So, avoid these activities with infected partners, family members and relative. As per WHO and CDC guideline avoid the contact with sick person and also avoid the market or public place as per possible. There are no anti corona virus vaccine to prevent or treatment but some supporting therapy work. Future research needed to fight with corona virus. Till only 'Social distance is rescue'.

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