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Review Article

From SARS-CoV to Coronavirus Disease 2019 (COVID-19) - A Brief Review

Mradul Kumar Daga[1], Naresh Kumar[2], J Aarthi[3], Govind Mawari[4], Sandeep Garg[5], Ishan Rohatgi[6]

[1]Director-Professor, Department of Internal Medicine & Centre for Occupational and environment Health, Maulana Azad Medical College, New Delhi, India.
[2]Professor of Medicine and Head, Department of Pulmonary Medicine, Maulana Azad Medical College, New Delhi, Inida.
[3]Resident, Department of Medicine, Maulana Azad Medical College, New Delhi, India.
[4]Scientist B, Centre for Occupational and Environment Health, Maulana Azad Medical College, New Delhi, India.
[5]Professor of Medicine, Maulana Azad Medical College, New Delhi, India.
[6]Senior Resident, Maulana Azad Medical College, New Delhi, India.
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Corresponding Author:
Mradul Kumar Daga, Department of Internal Medicine & Centre for Occupational and environment Health, Maulana Azad Medical College, New Delhi, India.
E-mail Id:
drmraduldaga@gmail.com
Orcid Id:
https://orcid.org/0000-0001-7774-7602
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A B S T R A C T

Emerging and reemerging pathogens are global challenges for public health. For the third time in as many decades, a zoonotic coronavirus has crossed species to infect human populations. Given the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) outbreak in 2002 and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) outbreak in 2012, 2019-nCoV is the third coronavirus to emerge in the human population in the past 18 years-an outbreak that has raised great hue and cry globally as it has sickened thousands of people across the world. This novel coronavirus was named as COVID-19 which stands for Corona Virus Disease 2019. The 2019-nCoV originated from Wuhan, Hubei Province, China beginning in December 2019. The World Health Organization declared it as a Public Health Emergency of International Concern. At that point, there were 9826 confirmed cases globally, with 213 deaths. Of these, 9720 cases were in China; outside of China, health authorities reported 106 confirmed cases in 19 countries. As of February 2, the WHO updated the count, reporting 14 557 confirmed cases from 24 countries-14 411 of them in China. In this review we focus our attention on Covid-19 and how different this epidemic is from the previous two outbreak caused by coronavirus.

Keywords: SARS-CoV, COVID-19, Respiratory Syndrome, Coronavirus

Introduction

Coronaviruses (CoV) belongs to a group of RNA viruses that causes disease in mammals and birds. Coronaviruses are common throughout the world, known to cause mild respiratory tract infections being the second most common cause of common cold among humans, until the emergence of SARS in 2002 and MERS in 2012 which caused major outbreak causing pneumonia like illness. Now, a novel coronavirus was identified in Wuhan, China, in December 2019 i.e. Covid-19. The World Health Organization declared

it as a Public Health Emergency of International Concern.[1] The impact of this outbreak is yet unclear as transmission of the disease is still persisting.

Structure

Coronaviruses (CoVs), of the family Coronaviridae, are enveloped viruses with a single-strand, positive-sense RNA genome approximately 26 to 32 kilobases in size, which is the largest known genome for an RNA virus.[2] It has "corona"-like or crown-like morphology observed in the electron microscope, hence named as coronavirus.[3] All corona viruses share similarities in the organization and expression of their genome, in which 16 non-structural proteins (nsp1 through nsp16), encoded by Open Reading Frame(ORF) 1a/b at the 50 end, are followed by the structural proteins Spike (S), Envelope (E), Membrane (M) and Nucleocapsid (N), which are encoded by other ORFs at the 30 end. CoVs are separated into four genera based on phylogeny: alpha-CoV (group 1), beta-CoV (group 2), gamma-CoV (group 3) and delta-CoV (group 4). Within the beta-CoV genus, four lineages (A, B, C and D) are recognized.

Human Coronavirus

Previous to the emergence of SARS CoV, there were two prototype human coronaviruses, OC43 and 229E, both being etiologic agents of the common cold.[4] Six coronavirus species were known to cause human disease.[2] Four viruses-229E, OC43, NL63, and HKU1 - are prevalent and typically cause common cold symptoms in immunocompetent individuals. The two other Strains-severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV)-are zoonotic in origin and have been linked to sometimes fatal illness.[5]

After the identification of SARS CoV, there have been two more human coronavirus that have been isolated and are known to cause respiratory illness. HKUI is a beta coronavirus lineage A identified in January, 2005, in a 71-year-old man who was hospitalized with an acute respiratory distress and radio-graphically confirmed bilateral pneumonia; the man had recently returned to Hong Kong from Shenzhen China.[6] HKU1 is most closely related to the Mouse Hepatitis Virus (MHV). CoV-HKU1 pneumonia, mainly affects old people with major underlying diseases and upper respiratory tract infection due to CoV-HKU1 affects mainly young children, with or without underlying diseases. This virus has been difficult to propagate in cell culture and there is little information available about the biology of this virus.

HCoV-NL63 is an alpha coronavirus isolated from a 7-month-old child in Netherlands who was suffering from bronchiolitis and conjunctivitis.[7] Subsequently, it has been reported in other parts of the world. HCoV-NL63 can cause a range of symptoms ranging from mild upper respiratory tract illness to bronchiolitis and pneumonia like illness. There has been an association seen with NL63 and croup in children.[8] While primarily associated with infections of children, NL63 has been also been detected in immunocompromised adults with respiratory tract infections.

HCoV-229E is an alphacoronavirus, it is among the viruses responsible for the common cold. It causes a range of respiratory symptoms from common cold to pneumonia and bronchiolitis and it is among the coronaviruses most frequently co-detected with other respiratory viruses, particularly with human respiratory syncytial virus. HCoV-OC43 is a beta coronavirus, lineage A with a worldwide distribution, causing 10% to15% of common cold cases. Four HCoV-OC43 genotypes (A to D) have been identified so far.

While little is known about the pathogenesis of any of the human coronaviruses, there have been detailed studies of the pathogenesis of some of the animal coronaviruses, which may contribute to the understanding of the human viruses. In humans, CoV infections primarily involve the upper respiratory tract and the gastrointestinal tract, and vary from mild, self-limiting disease, such as the common cold, to more severe manifestations, such as bronchitis and pneumonia with renal involvement.[9]

Another Decade Another Coronavirus-Novel Coronavirus

2019-nCoV (COVID-19):

For the third time in as many decades, a zoonotic coronavirus has crossed species to infect human populations. This virus, provisionally called 2019-nCoV- novel beta corona virus, was first identified in Wuhan, China, in persons exposed to a seafood or wet market. In late December 2019, several local health facilities reported clusters of patients with pneumonia of unknown cause that were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China.[10] On December 31, 2019, the Chinese Centre for Disease Control and Prevention (China CDC) dispatched a rapid response team to accompany Hubei provincial and Wuhan city health authorities and to conduct an epidemiologic and etiologic investigation.

The current corona virus outbreak in China is the third epidemic caused by corona virus in the 21st century, already surpassing SARS and MERS in the number of individuals infected. A cluster of pneumonia cases were reported in Wuhan, China on December 31, 2019, among which there were patients who had exposure to a large seafood market selling many species of live animals. Another human coronavirus had evolved, researchers from the Shanghai Public Health Clinical Centre and School of Public Health and their collaborators on January 10,2020, released a full genomic sequence of 2019-nCoV to public databases. According to the available analyses of novel coronavirus

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isolated from patients, there has been some similarity between some of the amino acids of COVID-19 and SARS-CoV and molecular analysis suggests that COVID-19 also binds to ACE2, like SARS-CoV. The situation is rapidly evolving as the number of cases is approaching a lakh. The transmissibility of COVID-19 from human to human is quite high accounting for such rapid increase in number of cases so far. Although the case fatality rate seems to be lower than SARS-CoV and MERS-CoV, the effect of this outbreak is still not predictable.

Genomic Characterisation and Epidemiology

Genetics: A novel coronavirus (2019-nCoV) has been identified from the genetic surveillance of clinical samples obtained from patients of viral pneumonia in Wuhan. Phylogenetic analysis of 2019-nCoV, sequenced from nine patients' samples, revealed that the virus belongs to beta coronavirus lineage A and subgenus *Sarbecovirus*. 2019-nCoV was found to be more similar to two bat-derived coronavirus strains, namely bat-SL-CoVZC45 and bat-SL-CoVZXC21, than to other well-known human-infecting coronaviruses, including the one that caused the SARS outbreak of 2003.[11] 2019-nCoV was found using next-generation sequencing of Bronchoalveolar Lavage (BAL) fluid samples and cultured isolates from these patients. COVID-19 infects a cell, creates long chains of proteins required by the virus to generate even more copies of itself and the viral proteins become functional when cut into smaller pieces by proteases. Its distinctive heart shape is the result of two identical protein subunits coming together to form a functional protease.

Reservoir

Phylogenetic analysis showed that bat-derived coronaviruses belongs to the genus Beta coronavirus and COVID-19 has resemblance to two viruses that were isolated from bats, bat-SL-CoVZC45 and bat-SL-CoVZXC21.[12] Bats acted as the natural reservoir in both SARS-CoV and MERS-CoV, whereas another animal (masked palm civet for SARS-CoV35 and dromedary camels for MERS-CoV) acted as intermediate host and the human were terminal hosts.[13] The available epidemiological data provides supporting evidence that, COVID-19 causing the Wuhan outbreak was initially nurtured by bats, and later on transmitted to humans probably via pangolin or some unknown wild animal which were being sold at Huanan seafood market.

Receptor Binding

Previous studies have uncovered several receptors that different coronaviruses bind to, such as ACE2 for SARS-CoV and CD26 for MERS-CoV.[14,15] Molecular modelling showed structural similarity between the receptor-binding domains of SARS-CoV and 2019-nCoV. Therefore, 2019-nCoV might use ACE2 as the receptor, despite the presence of amino acid mutations in the 2019-nCoV receptor-binding domain.

Epidemiology

Epidemiologically, eight of the nine patients in a study conducted by Lu R et al. had history of exposure to the Huanan seafood market in Wuhan, implying that they had an exposure to the infection source at the market.[11] However, one patient never visited that market, although he stayed in a hotel near the market before the onset of their illness. This finding suggested either droplet transmission as a possibility or the patient was infected by a currently unknown source. However, evidence of clusters of infected family members and healthcare workers has now confirmed the presence of human-to-human transmission.[16]

Current Statistics[17]

WHO has declared recent novel Corona virus outbreak as pandemic on11th of March 2020. As per WHO situation report on March 14, 2020, globally there are 1,42,539 confirmed cases, with China accounting for 81,021 confirmed cases and 3194 deaths. Outside of China there are 61,518 confirmed cases across 135 countries and 2199 deaths. On March 15, in India, total 82 confirmed cases have been reported, with 2 deaths and many suspected cases at surveillance as of now.

Clinical Features

A group of people affected by an acute respiratory illness in December 2019, now known as Novel Coronavirus-Infected Pneumonia (NCIP), was reported in Wuhan, Hubei Province, China. Huang et al., first observed 41cases of NCIP among which all of them had an exposure to Huanan Seafood Wholesale Market. The clinical manifestations included fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia. Organ dysfunction (e.g., shock, Acute Respiratory Distress Syndrome [ARDS], acute cardiac injury and acute kidney injury) and death can occur in severe cases.[18]

Clinical syndromes associated with 2019-nCoV infection:

Uncomplicated illness: Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache, muscle pain or malaise. The elderly and immunosuppressed may present with atypical symptoms. These patients do not have any signs of dehydration, sepsis or shortness of breath.

- **Mild Pneumonia**: Patient with pneumonia and no signs of severe pneumonia. Child with non-severe pneumonia has cough or difficulty breathing + fast breathing.
- **Severe Pneumonia (Adolescent or Adult):** Fever or suspected respiratory infection, plus one of respiratory

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rate >30 breaths/min, severe respiratory distress, or SpO2<90%

- **Acute Respiratory Distress Syndrome:** Onset-new or worsening respiratory symptoms within 1 week of known clinical insult. Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules. Origin of oedema-respiratory failure not fully explained by cardiac failure or fluid overload. Objective assessment (e.g. echocardiography) is needed to exclude hydrostatic cause of oedema if no risk factor is present.
- **Sepsis**: Adults-life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction.
- Children-suspected or proven infection and ≥2 SIRS criteria, of which one must be abnormal temperature or white blood cell count.
- **Septic Shock**: Adults-persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L.

Presenting Characteristics

In a single-center retrospective study by Wang, et al., 138 consecutively hospitalized patients in Wuhan with confirmed NCIP was observed.[19] The median age was 56 years (22-92 years) and 54.3% of patients were male. Out of these, 102 (73.9%) patients were admitted in isolation ward and 36 (26.1%) patients required ICU admission because of development of organ dysfunction. The median durations from start of symptoms to dyspnoea, hospital admission and development of ARDS were 5 (range 1-10) days, 7 (range 4-8) days and 8 (range 6-12) days respectively. Sixty four (46%) patients had one or more coexisting medical illness with hypertension in 43 (31.2%), cardiovascular disease in 20 (14.5%), diabetes in 14 (10.1%) and malignancy in 10 (7.2%) being the most common. Less common conditions include cerebrovascular accident, COPD, chronic kidney disease, chronic liver disease and HIV.[19] While comparing the patients who required ICU care to non-ICU care, it was observed that the patients requiring ICU care were significantly older and had more underlying co-morbidities. Presenting signs and symptoms included fever (98.6%), fatigue (69.6%), dry cough (59.4%), anorexia (39.9%), myalgia (34.8%), dyspnoea (31.2%), expectoration (26.8%), pharyngeal pain (17.4%), diarrhea (10.1%), nausea (10.1%) dizziness (9.4%), headache (6.5%), vomiting (3.6%) and abdominal pain (2.2%).[19] Occurrence of pharyngeal pain, dyspnoea, dizziness, abdominal pain and anorexia was more in ICU patients. Respiratory rate, heart rate and Mean Arterial Pressure (MAP) were similar between the patients receiving ICU care and non ICU patient.

In another study conducted by Guan W et al., clinical profile of 1099 patients with laboratory confirmed Covid-19 from 552 hospitals of China was observed.[20] The median incubation period observed in this study was 4 (range 2-7) days. However, its reliability is limited by the fact that data on incubation period was derived from only quarter of these cases and might have been affected by recall bias. The median age of the patients was 47 years (range, 35-58 years), and 41.9% were female. On admission, the patients were categorized into nonsevere and severe disease category. 926 (84.2%) patients were in non-severe disease category and remaining 173 patients were in severe disease category. The patients with severe disease were significantly older than patients with non-severe disease. Patients with severe disease had more coexisting illness (38.7%) than that of non-severe disease group patients (21%). Most common coexisting disease was hypertension (15%) followed by diabetes (7.4%). Most common symptoms observed were fever followed by dry cough. Fever was present in 43.8% cases at admission and total of 88.7% patients developed fever during hospital stay and cough was present in 67.8% patients. Fatigue, dyspnoea and sputum production were observed in 38.1%, 18,7% and 33.7% cases, respectively. This means Covid-19 infection can occur without fever also and dry cough is a predominant complaint present in 2/3rd of patients. Other symptoms included headache, myalgia or arthralgia, sore throat, nasal congestion, chills, nausea or vomiting, and diarrhea. Though, sneezing is very common symptom in common cold, it has not been observed in any of the above two studies. Further, running nose is common in common cold but rare in Covid-19 infection. Interestingly, the most common co-morbidity in these patients was found to be hypertension followed by diabetes in one study and cardiovascular disease in another study. It is known that coronaviruses bind to their target cells through ACE2. Hypertension, diabetes and cardiac illnesses are frequently treated with ACE inhibitors or ARBs which can increase the expression of ACE2; hence, facilitating infection with coronavirus and be responsible for increased severity of the disease in these group of patients.

Laboratory and Radiological Findings

Patients of Covid-19 infection has leucopenia and lymphopenia. However, ICU patients had raised white blood cell and neutrophil counts as well as higher levels of D-dimer, blood urea nitrogen, LFT, LDH and creatine kinase-MB as compared to non-ICU patients.[19] Median leukocytes, lymphocyte and platelet counts were lesser in severe cases than nonsevere cases.[20]

Almost 60% of patients showed abnormalities on chest radiograph. The most common pattern being bilateral patchy shadowing (36.5%) followed by local patchy shadowing (28.1%), ground-glass opacity (20.1%) and

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interstitial abnormalities (4.4%).[20] 86.2% patients showed abnormalities on chest CT. Most common abnormality on chest CT was ground glass opacity (56.4%) followed by bilateral patchy shadowing (51.8%), local patchy shadowing (41.9%) and interstitial abnormalities (14.7%).[20] These radiological abnormalities were more commonly found in patients with severe disease. This also means that 13.8% of laboratory-confirmed cases did not have any radiological abnormality even on CT.

Organ Dysfunctions and Main Treatment Given

Common complications observed were ARDS (19.6%), arrhythmia (16.7%), septic shock (8.7%), acute cardiac injury (7.2%) and acute kidney injury (3.6%).[19] Patients who required ICU care were more frequently had these complications. Other complications like DIC and rhabdomyolysis were noted in another study.[20]

Almost all patients received empirical therapy in the form of antiviral treatment, antibiotics and steroids: 35.8% of the study population received antivirals (oseltamivir), 58.0% patients received antibacterial drugs (Moxifloxacin, Ceftriaxone or Azithromycin) and 18.6% patients received systemic glucocorticoids. Oxygen therapy was given in 41.3% more so in severe disease. Mechanical ventilation was required in 6.1% of total patients exclusively in severe disease. Less than one percent patients required even extracorporeal membrane oxygenation (ECMO) and Continuous Renal-Replacement Therapy (CRRT).[20] Death occurred in 1.4% of total patients studied. The death rate was 0.1% in nonsevere disease and 8.1% in severe disease.[20]

Sample Collection and Testing

- Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. However, do not delay antimicrobial therapy to collect blood cultures.
- Collect specimens from both the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) and lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage) for 2019-nCoV testing by RT-PCR. Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients).
- Serology for diagnostic purposes is recommended only when RT-PCR is not available.
- To demonstrate viral clearance in a hospitalized patient repeat upper respiratory tract and lower respiratory tract samples should be collected.

Laboratory Testing: The 2019-nCoV laboratory test assays were based on the previous WHO recommendation. Upper and lower respiratory tract specimens were obtained from patients. RNA was extracted and tested by real-time RT-PCR with 2019-nCoV-specific primers and probes. Tests were carried out in biosafety level 2 facilities at the Hubei (provincial) CDC and then at the National Institute for Viral Disease Control at China CDC. If two targets (open reading frame 1a or 1b, nucleocapsid protein) tested positive by specific real-time RT-PCR, the case would be considered to be laboratory-confirmed. A cycle threshold value (Ct-value) less than 37 was defined as a positive test, and a Ct-value of 40 or more was defined as a negative test. A medium load, defined as a Ct-value of 37 to less than 40, required confirmation by retesting. If the repeated Ct-value was less than 40 and an obvious peak was observed, or if the repeated Ct-value was less than 37, the retest was deemed positive.

The genome was identified in samples of bronchoalveolar-lavage fluid from the patient by one of three methods: Sanger sequencing, Illumina sequencing, or nanopore sequencing. Respiratory specimens were inoculated in cells for viral isolation in enhanced biosafety laboratory 3 facilities at the China CDC.[21]

Transmission Pattern: Many domestic and wild animals, including camels, cattle, cats and bats, may serve as hosts for coronaviruses. It is considered that, generally, animal coronaviruses do not spread among human beings. However, there are exceptions, such as SARS and MERS, which mainly spread though close contact with infected people via respiratory droplets from cough or sneezing.

With regard to 2019-nCoV, early patients were reported to have some link to the Huanan Seafood Market in Wuhan, China, suggesting that these early infections were due to animal-to-person transmission. Soon, more cases were reported among medical staff and others with no history of exposure to that market or visiting Wuhan, which was taken as an indication for human-to-human transmission.[22] The latest guidelines from Chinese health authorities, described three main transmission routes for the 2019-nCoV:[23]

- Direct transmission are reported to occur when respiratory droplets (as produced when an infected person coughs or sneezes) are ingested or inhaled by individuals nearby in close proximity.
- Aerosol transmission may occur when respiratory droplets mix into the air, forming aerosols and causing infection when inhaled into the lungs.
- Contact transmission may occur when a subject touches a surface or object contaminated with the virus.

According to the literature, individuals could be infected when they subsequently touch their mouth, nose, or possibly eyes. In addition to these three routes, one study also indicated the digestive system as a potential transmission route for 2019-nCoV infection. Since patients had abdominal discomfort and diarrhoea symptoms, researchers analysed 4

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datasets with single-cell transcriptomes of digestive system and found that ACE2 was highly expressed in absorptive enterocytes from ileum and colon.[23]

Management

The management of patients with Covid-19 infection need to be individualized as the patient may present with a wide spectrum of disease manifestation ranging from uncomplicated illness to ARDS and septic shock.

Early supportive therapy and monitoring:

- **Give supplemental oxygen therapy immediately to patients with SARI and respiratory distress, hypoxaemia, or shock**: Initiate oxygen therapy at 5 L/ min and titrate flow rates in non-pregnant adults to reach target SpO2 ≥90% and in pregnant patients to maintain SpO2 ≥92-95 %. Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive oxygen therapy during resuscitation to target SpO2 ≥94%; otherwise, the target SpO2 is ≥90%.
- **Conservative fluid management in patients with SARI without shock**. Cautious intravenous fluid management is warrantied in patients with SARI as aggressive fluid resuscitation might hamper oxygenation, especially in resource limited set up with reduced availability of mechanical ventilation.
- **Give empiric antimicrobials to treat all likely pathogens causing SARI**. Empirical antimicrobials should be initiated within 1 hour of initial patient assessment for patients with sepsis. Remarks: do not delay antimicrobials even in suspect case of COVID-19, administer appropriate empiric antimicrobials within one hour of identification of sepsis. Empiric antibiotic treatment should be based on the clinical diagnosis (community-acquired pneumonia, health care-associated pneumonia [if infection was acquired in healthcare setting], or sepsis), local epidemiology and susceptibility data, and treatment guidelines. When there is local circulation or other risk factors for influenza, including travel history or exposure to animal influenza viruses, a neuraminidase inhibitor for treatment of influenza should be included in empiric therapy. Empiric therapy should be de-escalated on the basis of microbiology results and clinical judgment.
- **Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately**: Application of timely, effective, and safe supportive therapies is the cornerstone of therapy for patients that develop severe manifestations of 2019-nCoV.
- **Understand the patient's co-morbid condition (s) to tailor the management of critical illness and appreciate the prognosis**. Communicate early with patient and family. During intensive care management of SARI, determine which chronic therapies should be continued and which therapies should be withheld temporarily.
- **Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason**: No survival benefit was seen with systemic corticosteroids as perceived in a systematic review of observational studies of corticosteroids administered to patients with SARS. Possible side effects that were discerned were avascular necrosis, psychosis, diabetes, and delayed viral clearance. Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason.
- **Management of hypoxemic respiratory failure and ARDS**: High-Flow Nasal Oxygen (HFNO) or Non-Invasive Ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure and they should be closely monitored for clinical deterioration. Endotracheal intubation should be performed by a trained and experienced person using airborne precautions. Implement mechanical ventilation using lower tidal volumes (4-8 ml/ kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure <30cm H2O) In patients with severe ARDS, prone ventilation for >12 hours per day is recommended. Use a conservative fluid management strategy for ARDS patients without causing tissue hypoperfusion.
- **Management of septic shock:** Recognize septic shock in adults when infection is suspected or confirmed and vasopressors are needed to maintain mean arterial pressure (MAP) ≥65 mmHg and lactate is ≥ 2 mmol/L, in absence of hypovolemia. In resuscitation from septic shock in adults, give at least 30 ml/kg of isotonic crystalloid in adults in the first 3 hours. Administer vasopressors when shock persists during or after fluid resuscitation.
- **Specific anti-Novel-CoV treatments and clinical research**: Favilavir, an anti-viral drug, has been approved by the National Medical Products Administration of China for treatment for coronavirus.[24] In a clinical trial that is being operated in Shenzhen, Guangdong province involving 70 patients, favorable result with very few side effects was observed. Remdesivir (GS-5734), an ebola drug developed by Gilead Sciences that was found to be ineffective is now being tested in phase III randomized clinical trial in partnership with China.[25] The trials are being performed on 761 patients in a randomized, placebo-controlled, double-blind study at multiple hospitals in epicentre Wuhan, the of the novel coronavirus outbreak. According to a

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report, Remdesivir, when administered to a coronavirus patient in the US, appeared to have improved the clinical condition. An HIV protease inhibitor, Lopinavir is being studied along with ritonavir for the treatment of nCovid-19.[26] Lopinavir/Ritonavir in combination with ribavirin showed reduced fatality rate and milder disease course during an open clinical trial in patients in the 2003 SARS outbreak.[27]

A number of experimental vaccines for 2019-nCoV are undergoing trials, though it is unlikely that they will be available to halt the current situation. Some medical experts believe that it might become endemic in humans, so the search for vaccines should be however be pursued.

Surveillance: WHO Recommendation for Surveillance of the Novel Coronavirus. (Covid-19)

The primary objectives of surveillance are to:

- Detect cases/clusters of nCoV infection and any evidence of amplified or sustained human-to-human transmission;
- Determine risk factors and the geographic risk area for infection with the virus.

The following people should be investigated and tested for COVID-19 infection.

Case Definitions for Surveillance[28]

As per WHO, the following people should be under surveillance:

Suspected Case:

- A case of Severe Acute Respiratory Infection (SARI), who present to the hospital with fever and cough like symptoms to the severity that requires admission and the clinical presentation has no other alternative diagnosis.
- AND has a history of travel to or residence in a country, area or territory that has reported local transmission of COVID-19 disease during the 14 days prior to symptom onset.
- A patient with any acute respiratory illness AND who has been a contact of a confirmed or probable case of COVID-19 disease during the 14 days prior to the onset of symptoms.
- A patient with severe acute respiratory infection (that is, fever and at least one sign or symptom of respiratory disease, for example, cough or shortness breath) AND who requires hospitalization AND who has no other etiology that fully explains the clinical presentation.

Probable Case

A suspected case for whom the report from laboratory testing for the COVID-19 virus is inconclusive is a probable case.

Confirmed Case

A person with laboratory confirmation of infection with the COVID-19 virus, irrespective of clinical signs and symptoms is a confirmed case. A case with respiratory specimens that tested positive for the 2019-nCoV by at least one of the following three methods: isolation of 2019-nCoV or at least two positive results by real-time reverse-transcription-polymerase chain-reaction (RT-PCR) assay for 2019-nCoV or a genetic sequence that matches 2019-nCoV.

Prevention and Control

There is no definite treatment or vaccine available for general population. The best prevention is to avoid being exposed to the virus. Airborne precautions and other protective measures have been discussed and proposed for prevention. Infection Preventive and Control (IPC) measures that may reduce the risk of exposure include:

Preventive Measures that may reduce the Risk of Exposure include the following

- Use of face masks, covering coughs and sneezes with tissues (or flexed elbow) that are then safely disposed of;
- Regular hand washing with soap or disinfection with hand sanitizer containing at least 60% alcohol (if soap and water is not available);
- Avoidance of contact with infected people and keeping the distance as much as possible (at least 1 meter); and the refrain from touching the eyes, nose, and mouth with unwashed hands health care workers are recommended to use the particulate respirator such as certified N95 or FFP2 when performing aerosols generating procedures, and to use medical masks while providing any care to suspected or confirmed cases.
- Individuals with respiratory symptoms are advised to use medical masks both at the health care settings and home care properly following the infection prevention guidelines.

Control Measures by Governments Worldwide

Most of the countries have executed border screening as number of cases of COVID-19 associated with travel has surged. Travel to and from Hubei Province has been curbed by China. Governments curtailed travel and trade, during previous outbreaks like SARS (severe acute respiratory syndrome) and Ebola, so such containment measures is anticipated. Temperature screening, symptom screening, and or questionnaires for passengers arriving from China have been initiated by multiple countries (e.g., Australia, Thailand, South Korea, Japan, India, Italy, Singapore, Malaysia, and Nigeria). Public gatherings, major conferences and schools and theatres have been shut down to curtail the spread of COVID-19. US State Department issued its

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highest-level travel advisory for Hubei Province: level 4, "do not travel."

Comparison with Previous Epidemics

Transmissibility and severity are the two most critical factors that determine the effect of an epidemic. Neither the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) nor the Middle East respiratory syndrome corona virus (MERS-CoV) epidemics had the combination of both high transmissibility and severity. Control strategies are driven by this combination. SARS-CoV (2003) and MERS-CoV (2012-current) cause severe disease, but despite the initial R0 estimations of greater than 2.0 for SARS-CoV and some large outbreaks, neither were as transmissible as initial concerns suggested. SARS-CoV caused 8098 reported cases and 774 deaths (case-fatality rate, 9.6%) in 37 countries before the epidemic was controlled. Control was thought to have been possible because a high proportion of cases were severe, making it easier to rapidly identify and isolate infected individuals. In addition, the virus was present at lower levels in upper airway secretions. There was no secondary transmission in the United States from the 8 imported cases, although in Toronto, Canada, a single importation is thought to have led to about 400 cases and 44 deaths. Later estimates of R0 were less than 1, indicating that SARS-CoV may not have been capable of sustained transmission, especially in the setting of control measures.[29]

Similarly, MERS-CoV appears to have high severity and low transmissibility. Since 2012, MERS-CoV has caused 2494 reported cases and 858 deaths (case fatality rate, 34%) in 27 countries. MERS-CoV has also caused some rapid outbreaks, mainly in hospitals in Saudi Arabia, Jordan, and South Korea, but estimates of MERS-CoV R0 are less than 1, and thus far it has been contained.[30]

IS 2019-nCoV Infection Severe?

WHO has reported to date approximately 14% of cases of COVID-19 as severe, with a case-fatality rate approaching 2.1%. Estimates of severity can vary as the time progresses during an epidemic/ pandemic. Due to the identification of the most severely affected cases in the beginning, the severity of an outbreak is usually reported higher. However, the case-fatality rate and severity could be underestimated as many cases are still under recovery and may die during the course of illness as well.

COVID-19 was officially declared as a Public Health Emergency of International Concern, on January 30, 2020, by WHO. On 11th March, 2020 it was declared as a pandemic by the WHO. Earlier in course, it was restricted to mostly Asian countries (China, Iran and South Korea) but gradually it has spread to the European and North American continent. It is difficult to predict how it is going to spread from now on. It will be dependent on several factors including individual country's response, mutation of the virus etc. It is imperative to be decisive and act diligently to control the spread quickly. The outbreak has brought forth the inadequacies in the early detection of epidemic and containment of disease. The economic and the social ramification of the pandemic have been severe with laying off of jobs with financial loss. The pandemic will serve as a learning lesson for future preparedness.

Summary

Covid-19 has caused a great threat to global health. It was found to be structurally similar to SARS after extensive study regarding Covid-19. As compared to previous two outbreaks caused by coronavirus namely SARS CoV and MERS CoV, Covid-19 outbreak has surpassed the number of people affected by this novel coronavirus and the international community is scrambling to keep up. The impact that Covid-19 has created so far resembles more of a severe seasonal influenza or a pandemic influenza as the case fatality rate observed with SARS and MERS is much higher than Covid-19 as of now. The current epidemiological studies indicate an estimated basic reproduction number (R_0) of 2.2, until this number falls below 1.0, it is likely that the outbreak will continue to spread. Scientists are rushing to develop a vaccine against this novel coronavirus, policymakers are debating over the most effective containment methods and healthcare system globally are straining to accommodate the growing number of sick individuals. The Covid-19 outbreak is threatening to become a global pandemic of the time not seen before a century.

Conflicts of Interest: None

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