

Covid-19

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Introduction

Coronaviruses infect both humans and animals. Since the 1960s, globally endemic human coronaviruses have been identified as frequent causes of respiratory infections such as the common cold and responsible for all 10-20% of respiratory tract infection in adults.

A novel coronavirus, designated 2019-nCoV, was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei province of China, at the end of 2019. Epidemiologic investigation in Wuhan identified an initial association with a seafood market where most patients had worked or visited.(1) On January 30, 2020, the World Health Organization declared the outbreak a “public health emergency of international concern” (PHEIC). The current outbreak of this novel coronavirus researched an unfortunate milestone record with the death count officially exceeding that of the SARS outbreak. As of Monday (09.02.2020), latest data indicate this novel coronavirus has killed 910 people in about a month and a half, with 40573 cases worldwide. As number of confirmed cases and deaths have been raising continuously, details of the novel coronavirus in several aspects are still not very clear. Very recently, WHO has named the disease COVID-19, short for “coronavirus disease 2019.”

Epidemiology

Currently, it has been reported in all provinces in China and 25 countries worldwide.

Virology

Coronaviruses are large enveloped, positive single-stranded RNA viruses that can be divided into four genera, namely alpha, beta, delta and gamma. A host-derived membrane surrounds the genome, which is encased in a helical nucleocapsid. As

they are positive-sense single-stranded RNA viruses, they do not need to carry enzymes to initiate infection.(2) The virus genome has been sequenced and these results in conjunction with other reports show that it is 75-80% identical to the SARS-CoV and even more closely related to several bat coronaviruses.(3)

Alpha and beta coronaviruses are found in both humans and animals. Gamma and delta coronaviruses have only been identified in animals. Coronaviruses are widespread among birds and mammals, with bats being host to the largest variety of genotypes.

Human Coronaviruses

Following four viruses have been identified as common causes for respiratory tract diseases in human after initial detection coronavirus in 1960.

- 229E (alpha coronavirus)
- NL63 (alpha coronavirus)
- OC43 (beta coronavirus)
- HKU1 (beta coronavirus)

As a result of genetic recombination occurs between members of the same or different coronavirus groups, new viruses emerge from the animal reservoirs and subsequently jump to human. There are three new coronaviruses have been emerged as a result of this genetic recombination up to now.

- MERS-CoV (beta coronavirus) - Middle East Respiratory Syndrome (MERS)
- SARS-CoV (beta coronavirus) - severe acute respiratory syndrome (SARS)
- 2019-nCoV (beta coronavirus) - 2019 novel coronavirus acute respiratory disease

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Experience learnt from SARS and MERS

SARS

SARS was first reported in 2003, when it emerged in China. The illness spread by close person-to-person contact to countries in North America, South America, Europe, and greater Asia before the global outbreak was contained later in 2003. Common symptoms of SARS included fever, cough, dyspnea, and occasionally watery diarrhea. A viral pneumonia that rapidly progresses to respiratory failure. Of infected patients, 20% to 30% required mechanical ventilation and 9.6% died, with higher fatality rates in older patients and those with medical comorbidities. 8098 individuals were infected and 774 died. There have been no reported cases since 2004.(4,5,6)

MERS

An acute viral respiratory tract infection caused by the novel beta coronavirus MERS-CoV, first identified in Jordan and Saudi Arabia in 2012. Cases have been limited to the Arabian Peninsula and its surrounding countries, and to travelers from the Middle East or their contacts. MERS shares many clinical features with SARS such as severe atypical pneumonia. Patients with MERS have prominent gastrointestinal symptoms and often acute kidney failure. November 2019, MERS-CoV has caused a total of 2494 cases and 858 deaths, the majority in Saudi Arabia. MERS necessitates mechanical ventilation in 50% to 89% of patients with a case fatality rate of 36%.(7,8,9)

Transmission and incubation period of 2019-nCoV

Coronaviruses are zoonotic and rarely, animal coronaviruses can infect people and then spread between people such as with MERS, SAR and now with 2019-nCoV. Human-to-human transmission has been confirmed and transmission from asymptomatic individuals during the incubation period may occur. Ro (reproduction number) estimate is 1.4 to 2.5, meaning that every person infected could infect between 1.4 and 2.5 people. In comparison, measles has an RO of 12-18 and SARS had a similar RO as the 2019-nCoV. The viral incubation period is estimated at ~5 days (95% confidence interval, 4 to 7 days). Chinese authorities have reported that the incubation period may be longer (up to 14 days).(8)

Routes of transmission

It is transmitted by the direct contact with infected secretions or large aerosol droplets.

Where did it start?

Both SARS and MERS are thought to have originated from bats, then spread through civets and camel respectively, to humans. Even though the initial source of 2019-nCoV is still not known, but first cases were linked to a seafood or wet market in the city of Wuhan, capital of the central Hubei province.(10)

Case definitions for surveillance

The case definitions are based on the information currently available and might be revised as new information accumulates. Countries may need to adapt case definitions depending on their own epidemiologic situation.(11)

Suspect case

A. Patient with severe acute respiratory infection (fever, cough, and requiring admission to hospital), **AND** with no other etiology that fully explains the clinical presentation **AND** a

history of travel to or residence in China during the 14 days prior to symptom onset,

OR

B. Patient with any acute respiratory illness **AND** at least one of the following during the 14 days prior to symptom onset:

- a. a) contact with a confirmed or probable case of 2019-nCoV infection, or
- b. b) worked in or attended a health care facility where patients with confirmed or probable 2019-nCoV acute respiratory disease patients were being treated.

Probable case

Probable case: A suspect case for whom testing for 2019-nCoV is inconclusive or is tested positive using a pan-coronavirus assay and without laboratory evidence of other respiratory pathogens.

Confirmed case

A person with laboratory confirmation of 2019-nCoV infection, irrespective of clinical signs and symptoms. (11)

Clinical features of Covid-2019

The 2019 coronavirus (2019-nCoV) infection may be asymptomatic or may result in an acute respiratory disease. Covid-19 may present with mild, moderate, or severe illness; the latter includes severe pneumonia, ARDS, sepsis and septic shock. Early recognition of suspected patients allows for timely initiation of infection prevention and control. Males are more commonly affected, and the median age range of patients is 49 to 59 years. Nearly all reported cases have occurred in adults (median age 59 years).

Frequently reported signs and symptoms at the illness onset include fever (83-98%), cough (76-82%), and myalgia or fatigue (11-44%). Less commonly reported symptoms include sputum production, headache, haemoptysis and diarrhea. The fever course among the patients with 2019-nCoV infection is not fully understood. It could be prolonged and intermittent. There are no specific signs or symptoms that would suggest Covid-19 compared symptoms and signs of respiratory illnesses caused by other viruses.(12,13)

Investigations and confirmation of the diagnosis

In the FBC, lymphopenia (63%) appears as a prominent laboratory abnormality along with leukopenia in 9-25% , leukocytosis in 24-30% and thrombocytopenia in 12%. Elevated transaminases were noted in 37% of whom extreme elevations are rare. Inflammatory markers are elevated in majorly (CRP- 68%, ESR-84%) and procalcitonin is normal in most. Chest X-ray and CT findings show bilateral infiltrate in 75% and unilateral involvement in 25%.

2019-nCoV is not detected by standard respiratory viral panels. Lower respiratory specimens likely have a higher diagnostic value than upper respiratory tract specimens for detecting 2019-nCoV infection. WHO recommends that lower respiratory specimens such as sputum, endotracheal aspirate, or bronchoalveolar lavage be collected for 2019-nCoV testing where possible. If it is not possible, upper respiratory tract specimens such as a nasopharyngeal aspirate or combined nasopharyngeal and oropharyngeal swabs should be collected. Specimen testing is performed using a real time reverse transcription PCR (rRT-PCR) assay for 2019-nCoV. Turnaround time for the PCR assay testing is about 24-48 hours.

Treatment

There is no specific anti-viral treatment recommended. Main stay of treatment consists of promptly implement infection control measures, supportive care to relieve symptoms and support organ function.

Infection prevention and control (IPC) measures is a critical and integral part of clinical management of patients and should be initiated at the point of entry of the patient to hospital. Standard precautions should always be routinely applied in all areas of health care facilities. Standard precautions include hand hygiene; use of PPE to avoid direct contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Standard precautions also include prevention of needle-stick or sharps injury; safe waste management; cleaning and disinfection of equipment; and cleaning of the environment. (see table 1)(14)

Table 1: IPC measures

At triage	<ul style="list-style-type: none"> • Give suspect patient a medical mask • Direct patient to separate area, an isolation room if available • Keep at least 1meter distance between suspected patients and other patients. • Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others. • Perform hand hygiene after contact with respiratory secretions
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<p>Apply droplet precautions</p>	<ul style="list-style-type: none"> • Use a medical mask if working within 1-2 meters of the patient. • Place patients in single rooms, or group together those with the same etiological diagnosis. • If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation. • When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection (face-mask or goggles) • Limit patient movement within the institution
<p>Apply contact precautions</p>	<ul style="list-style-type: none"> • Use PPE (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving. • If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers). • If equipment needs to be shared among patients, clean and disinfect between each patient use. • Ensure that health care workers refrain from touching their eyes, nose, and mouth with potentially contaminated gloved or ungloved hands. • Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). • Ensure adequate room ventilation. Avoid movement of patients or transport. Perform hand hygiene.
<p>Apply airborne precautions during aerosol generation procedures</p>	<ul style="list-style-type: none"> • Ensure that healthcare workers performing aerosol-generating procedures (i.e. open suctioning of respiratory tract, intubation, bronchoscopy, cardiopulmonary resuscitation) use PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). • Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with minimum of 12 air changes per hour or at least 160 litres/second/patient in facilities with natural ventilation. • Avoid the presence of unnecessary individuals in the room. • Care for the patient in the same type of room after mechanical ventilation commences.

Provide standard supportive management for respiratory disease and complications, including advanced organ support if indicated.(14)

- Supplementary Oxygen Therapy (target SpO₂ ≥90% in non-pregnant adults and SpO₂ ≥92-95 % in pregnant patients)
- Conservative fluid management
- Antipyretics and /or Analgesics
- Administer appropriate empiric antimicrobials within ONE hour of identification of sepsis
- Empiric therapy includes a neuraminidase inhibitor for treatment of influenza when there is local circulation or other risk factors
- Other supportive care such as intubation, mechanical ventilation, non-invasive ventilation etc)
- Close monitoring for signs of deterioration.
- Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason septic shock or other disease processes (acute exacerbation of COPD, etc).(13)
- Managing sepsis and septic shock – follow surviving sepsis guideline

Anti-viral drugs

Potential treatments against the novel coronavirus include remdesivir, which was tested against Ebola, and Kaletra, a combination of the antivirals lopinavir and ritonavir. First case of covid-19 in USA was treated with intravenous remdesivir with favorable outcome.(15) However, it needs further studies to recommend these drugs to prescribe routinely for this condition.

Prognosis

At present, it is difficult to predict the mortality of Covid-19 as it has been fluctuating due to information come in. However, WHO estimated it between 2-3%. (see table 2)

Table 2: Case fatality rate of selected viral diseases

Disease	Case fatality rate
pH1N1	0.02-0.4%
Cocid-19	2-3%
SARS	10%
MERS	37%
Ebola virus	63%

Prevention

There is no vaccine available currently. It has begun developing a vaccine and hope to begin a phase 1 trial within 3 months. So, spread of 2019-nCoV infection can be controlled or reduced from person-to-person by doing the following

- Wash hands often with soap and water for at least 20 seconds. If soap and water are not available, use alcohol-based hand sanitizer containing at least 60% alcohol.
- Avoid touching your eyes, nose, or mouth with unwashed hands.
- Avoid close contact with people who are sick.
- Stay home when you are sick.
- Cover your cough or sneeze with a tissue, then throw the tissue in the trash.
- Clean and disinfect frequently touched objects and surfaces.(16,17)

Masks are Not Routinely Advised for public

for a healthy person, routinely wearing a mask while out in public is unlikely to be helpful. In addition, masks have to be changed every 20 minutes and they become moist and ineffective when worn through the day. Masks should instead be reserved to be worn if you have symptoms of respiratory tract infection to reduce transmission of virus.

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