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Review Article

COVID-19: a brief review

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ABSTRACT

In December 2019, Wuhan, in China, became the center of an outbreak of pneumonia of unknown cause. In January 2020, a novel coronavirus was identified. Later the whole genomic sequence of this novel virus was established. The World Health Organization named the disease "COVID-19" and marked it as a pandemic. The origin of the virus is still conjectural. Studies suggested markedly increased levels of several pro-inflammatory cytokines and chemokines in these patients, which lead to injury to several organs. The organ which is most commonly damaged is the lungs. On histopathology, lung shows diffuse alveolar damage with hyaline membrane formation. The incubation period ranges from 1-14 days. The clinical features vary widely, from asymptomatic to multi-organ failure and shock. The common clinical features are related to the respiratory system. For diagnosis, oropharyngeal/nasopharyngeal swabs should be collected by Dacron swabs under proper precaution and the samples should be collected in viral transport media. The viral ribonuclei acid is detected by Real Time-Polymerase Chain Reaction. Till now no definite therapy or vaccination is available and the main approach to manage the pandemic is by preventive measures like social distancing, hygiene maintenance, and contact tracing.

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INTRODUCTION

Human coronaviruses (HCoVs) have long been considered usual pathogens causing "common cold" in otherwise healthy people. However, in the 21st century two highly pathogenic HCoVs ; severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in 2003 and 2012 respectively from animal reservoirs to cause global epidemics with high morbidity and mortality.

Very recently, in December 2019, Wuhan, Hubei province, China, became the centre of an outbreak of pneumonia of

unknown cause, which raised alarm not only within China but internationally.[1] In January 2020, Chinese scientists had isolated a novel coronavirus from patients in Wuhan. It was identified as an enveloped RNA virus, belonging to family, betacoronavirus, and was called "2019-nCoV". Thereafter, Sanghai Public Health Clinical Centre and School of Public Health established the whole genomic sequence of this novel virus and the sequence pattern revealed that "2019-nCoV" had some amino acid homology to SARS-CoV of 2003.2 Thus, on 11th February 2020, the virus was named by the International Committee on Taxonomy of Viruses (ICTV) as "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" because of its phylogenetic similarity with SARS-CoV.

However, the World Health Organization (WHO) during the same time named the disease as "COVID-19" (CO=Corona, VI=virus, D=disease, 19 for 2019) and the agent causing "COVID-19" as the "COVID-19 virus", instead of "SARS-CoV-2" , in order to avoid reference to any specific geographical location or stigmatization on any place or group of people. The WHO has recently declared COVID-19 a public health emergency of international concern.[3]

ORIGIN AND SPREAD OF COVID-19 VIRUS

The virus is thought to have an animal origin. There had been a continuous common source of the outbreak in December 2019, which would imply that several animals to human zoonotic events would have occurred at the Huanan Seafood Wholesale Market, China. Among the cluster of pneumonia cases that occurred in December 2019 in Wuhan, majority had the history of exposure to the same seafood market selling many live animals.[4] Following this there could have been transmission from human to human via droplets and fomites, as hypothecated in January 2020.[4,5]

The origin of the virus is still conjectural. However, evidences in the past had shown that whole genome sequences of corona like viruses obtained from bats matched with those of SARS-CoV and MERS-CoV . Thus, it was proposed that bats could be the natural reservoirs of these two viruses. Since, SARS-CoV, MERS-CoV and the new COVID-19 virus all belong to the family of betacoronavirus, it is therefore believed that COVID-19 virus also might have originated from bats, and later on could have disseminated to other intermediary animals before making a leap to humans. Such zoonotic spill overs were documented recently for SARS-CoV and for MERS-CoV.[6,7] The 2002-2003 SARS outbreak, for example, was traced back to palm civets and other small mammals, while MERS sprang from camels to man. The origin for this zoonotic event could be bats, acting as natural hosts, as shown for many other viruses, such as Nipah, Hendra, Ebola, and Lyssa virus.

So far as COVID-19 virus is concerned, intermediate hosts are still under scrutiny, deserving more detailed field studies assessing infection and seroprevalence.[8] Nevertheless, as supported by current data and evidences, human infection in the whole sale wet market in Wuhan could have occurred because of intimate exposure to wild animals. Eventually human to human transmission could happen via droplets and fomites, albeit to a lesser extent via consumption of undercooked animal and sea food.

PATHOLOGY OF COVID-19

The organ, which faces the main brunt of injury, is lung. The pathological damage is initiated by damage to type I pneumocytes and endothelium of the pulmonary capillaries and activation of macrophages. Tumor necrosis factor alpha and interleukin 1 are secreted from damaged pneumocytes and activated macrophages and cause further damage to the endothelial cells. This leads to the secretion of chemotactic factors and adhesion molecules by the endothelial cells, which promotes accumulation of inflammatory cells including neutrophils at the site of injury. Degranulation of the neutrophils further releases inflammatory mediators, platelet activating factor, protease, reactive oxygen species that lead to aggravation of the tissue injury.[9] However, the exact mechanism of high pathogenicity of SARS, MERS and COVID-19 is not well understood. Studies revealed markedly increased levels of several pro-inflammatory cytokines and chemokines in these infections, which can be correlated with degree of pulmonary damage.[2,10,11] It is also suggested that T helper 1 (Th1) cell has a role in the pathogenesis of COVID 19. The levels and numbers of cytokines are also found to be related with the severity of the disease, which suggests that cytokine storm has a role in the pathogenicity[2]. Interestingly, unlike SARS, in COVID-19 infection, cytokines from Th2 cells are also increased which suppress inflammation.[10]

The main histopathological feature in lung is diffuse alveolar damage (DAD), pulmonary edema and hyaline membrane formation. Hyaline membrane formation is the characteristic of exudative phase. Fibrosis of different grade may be seen which is a part of the proliferative phase of DAD. Other features that may be found are granulation tissue, sparse inflammation, histiocytic collection, multinucleated histiocytes, atypical pneumocytes, hemorrhage. Superimposed bacterial pneumonia has also been documented.[12,13] The liver exhibits mild lymphocytic infiltration, centrilobular sinusoidal dilation and patchy necrosis. The heart shows only focal mild fibrosis and mild myocardial hypertrophy.[13]

CLINICAL CHARACTERISTICS OF COVID-19

According to the WHO estimation, the incubation period ranges from 1-14 days with a median incubation period of 5.2 days.[11] Those infected may be either asymptomatic or

may develop various symptoms. The commonest clinical manifestations include fever, dry cough, and fatigue.2 Upper respiratory symptoms such as sneezing, runny nose, sore throat are less frequently observed.[2,3,11] There may be other features like shortness of breath, hypoxemia, hemoptysis, myalgia, headache, diarrhea, lymphopenia and RNAemia.[11] CT scan of lung shows characteristic but nonspecific bilateral ground glass opacity.[2] WHO has classified the clinical syndromes associated with COVID-19 into 5 categories viz., mild illness, pneumonia, severe pneumonia, acute respiratory distress syndrome, sepsis , septic shock.[14] Major complications include acute respiratory distress syndrome, pneumonias, acute cardiac injury, acute kidney injury, secondary bacterial infections, septic shock and multi-organ failure.[2,11,14,15] Prognosis is poor in those with underlying conditions like diabetes, hypertension, or cardiovascular diseases. Median time from the onset of symptoms to death was found to be 14 days, and death rate in men was estimated to be 2.8%; in females 1.7%.[2,3,15]

LABORATORY DIAGNOSIS

Patient under Investigation (PUI)

- In order to categorize an individual as PUI, the clinician should ask the individual the following questions
- Does the person have fever or symptoms of lower respiratory infection, such as cough or shortness of breath?
- Has the individual travelled within 14 days of the onset of symptoms?
- Has the individual had close contact with a person confirmed with COVID-19?

Specimens to be collected

Once the person has been identified as PUI, he/she should be provided with a mask, and taken to an examination room, which should be located away from the crowded areas of the hospital (minimum 6 feet apart)

The doctor examining the patient should wear personal protection equipment (PEE) to prevent direct contact to body and eye and to prevent air borne transmission.

Specimen from the upper respiratory tract

- Nasopharyngeal swab
- Oropharyngeal swab

Synthetic fibre swabs with plastic shafts are preferred over calcium alginate swabs or cotton tipped swabs with wooden shafts, as cotton and calcium alginate may inactivate the virus and may interfere with the PCR test result. The swabs should immediately be placed in sterile tubes containing 2-3 ml of viral transport media.[16]

For collecting in ideal nasopharyngeal swab, insert a sterile swab into the nostril parallel to the palate until the swab touches the nasopharyngeal area. Place the swab for a few seconds to absorb secretions. Oropharyngeal swabs are collected by swabbing the posterior pharyngeal wall and both tonsillar fossae, avoiding touching the tongue and other oral mucosal parts.

The above two specimens are the most frequently collected ones which are recommended for the molecular identification of the pathogen. However, it is recommended to maintain the cold chain for the transport of the specimens in viral transport media before processing.

The details of collection storage and transport of all possible samples for the diagnosis of COVID-19 have been shown in table 1.

Tests performed in expert laboratories for patients meeting the case definition[16,17]

Upper respiratory samples such as nasopharyngeal aspirate, oropharyngeal aspirate, nasopharyngeal wash, nasal wash or lower respiratory specimen such as sputum and bronchoalveolar lavage are collected according to the standard protocol.[16]

Nucleic acid amplification technique i.e. RT PCR (reverse transcriptase Polymerase Chain Reaction) assay or real time RT PCR assay is performed from specimens collected and transported in an ideal manner.[17] To confirm clearance of virus, sample collection is to be repeated until the results are negative on two consecutive samples. Whole genome sequencing from the afore mentioned samples is performed only by reference laboratories in order to ascertain if the genomic configuration of present local isolate matches with that of COVID-19 virus.

The main approach to control COVID-19 is social distancing in general population and quarantine in

Table 1: Specimen collection guideline. Source: WHO 2018 protocol to investigate nonseasonal influenza and other emerging acute respiratory diseases

Specimen type	Collection material	Temperature
Sputum	Sterile container	4 ^{0} C
Biopsy/Autopsy tissue	Sterile container	4 ^{0} C
Serum	Serum separator tube	4 ^{0} C
Whole blood	Collection tube	4 ^{0} C

exposed or suspected individual. Clinical management of COVID-19 cases depends on the severity of the disease. While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit. Patients with mild illness and mild pneumonia may be cured by supportive care only. Those who develop severe pneumonia and ARDS require more aggressive patient care with oxygen therapy. Life threatening multiorgan failure due to a dysregulated host response is seen in patients with sepsis and septic shock.[14] Different trials with various therapeutic agents (e.g., antiviral drugs, antimalarial drugs) as well as attempts at developing a vaccine are underway.

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