REVIEW ARTICLE - MICROBIOLGY

Pandora's box – Another Novel Coronavirus

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ABSTRACT

The pandemic of COVID -19 is causing increased number of infected patients' worldwide. This review summarizes about Morphology of SARS COV 2 which is the etiological agent of COVID-19, pathogenesis, Epidemiology, available diagnostics, and proposed infection prevention; Control measures. With so much uncertainties still prevailing, every health care facilities should adhere the national; International guideline to contain the spread of COVID-19.

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https://dx.doi.org/10.31975/NJBMS.2020.10033

INTRODUCTION:

The 1918 Influenza pandemic is the most severe pandemic in the past history. For more than a century it was used as a bench mark against which all other pandemics have been measured.(1) We should remember 1918 pandemic as we come across the infectious disease emergency- The pandemic of Novel corona virus disease (COVID19). This virus has been spreading throughout China for the past 2 months and involving 76 countries till date.

MORPHOLOGY:

Corona viruses belongs to a family within the Nidovirales order, it will replicate by using a nested set of mRNAs ("nido-" for "nest"). The corona virus subfamily is further classified into four genera: alpha, beta, gamma, and delta corona viruses. The human corona viruses (HCoVs) are in two of these genera: alpha corona viruses (HCoV-229E and HCoV-NL63) and beta corona viruses (HCoV-HKU1, HCoV-OC43, Middle East respiratory syndrome corona virus [MERS-CoV], and SARS CoV

2 (The novel corona virus that causes corona virus disease 19-COVID 19). [2,3]

Corona virus virions are spherical to pleomorphic enveloped particles. The envelope is surrounded with club shaped glycoprotein spikes and a core consisting of matrix protein.

Within the matrix there is a single strand of positive-sense RNA associated with nucleoprotein. The envelope glycoprotein's are responsible for attachment to the host cell and also carry the main antigenic epitomes, particularly the epitomes recognized by neutralizing antibodies.[4]

The length of the viral genome is 27 to 32 kb. Replication of viral RNA occurs in the host cytoplasm. By a unique mechanism in which RNA polymerase binds to a leader sequence and then detaches and reattaches at multiple locations, allowing for the production of a nested set of mRNA molecules.

The genome encodes four or five structural proteins, S (spike), M (membrane), N (nucleocapsid), HE, and E (envelope). HCoV-229E, HCoV-NL63, and the SARS corona virus possess four genes that encode the S, M, N, and E proteins, respectively, whereas HCoV-OC43 and HCoV-HKU1 encodes the HE protein. The *ACE2* gene encodes the angiotensin-converting enzyme-2, which has been proved to be the receptor for both the SARS-CoV-1 and SARS – CoV2.[5]

The virus enters the host cell, and the uncoated genome is transcribed and translated. The mRNAs form a unique "nested set" sharing a common 3′ end. New virions form by budding from host cell membranes.

PATHOGENESIS:

Corona viruses grow well in differentiated respiratory epithelial cells. Infected cells become vacuolated and the cilia will be damaged. And produce syncytial formation. Release of inflammatory mediators leads to increase nasal secretion and cause local inflammation and swelling. These responses will stimulate sneezing, obstruct the airway, and raise the temperature of the mucosa.[4] Transmission is via airborne droplets to the nasal mucosa.

The cytokines and chemokines released in patients with COVID-19 are IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Also IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α,

and TNFα are released in some severe cases.[5]

EPIDEMIOLOGY:

Until 2002, the virus was considered a relatively simple, nonfatal virus. An outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002–2003 in Guangdong province in China, caused an eventual spread to 17 countries. Since then scientists became deeply concerned about the pathogenesis of coronaviruses.[6] In 2012, again another novel coronavirus MERS- CoV caused an outbreak in Saudi Arabia with case fatality rate of 37%.

And now a new strain of coronavirus which differs considerably in genetic structure from previously recognized coronavirus called SARS CoV-2 causing COVID 19 disease has been identified. The virus isolated from the sample is in the same family of viruses namely SARS-CoV and MERS-CoV. Genetic homology is about 75-80% with SARS-CoV. COVID-19 has 96% homology with Bat corona viruses

Coronavirus is a zoonotic disease. SARS-CoV was transmitted from civet cats to humans. However, studies in the field suggested that masked palm civets functioned as intermediate hosts between an unknown animal reservoir and humans. In agreement, several CoVs sequences, some of them related to SARS-CoV, were detected in bat species. These findings support the hypothesis that bats represent the main viral reservoir for CoVs and that SARS-CoVs originated from bats.

MERS-CoV transmits from dromedary camels to humans. Several known coronaviruses are circulating in animals that have not yet infected humans. Epidemiological studies have suggested that MERS is due to a CoV transmitted by the contact with dromedary camels or camel products (Chan *et al.*2015). The origin of human infections through the camelids is demonstrated by virus neutralization experiments and by the viral genomic sequence analyses. Interestingly, MERS-CoV- like viruses have been identified in different bat species suggesting that bats functioned as the source of this new human CoV as well [7.]

New viral diseases typically emerge because of human activity that brings people into contact with wildlife. Mutations occurring within viral genome also make it transmissible to humans. We must realize that in our crowded world of 7.8 billion people, a combination of altered human

behaviors, environmental changes, and inadequate global public health mechanisms now easily turn obscure animal viruses into existential human threats. We have created a global, human-dominated ecosystem that serves as a playground for the emergence and host-switching of animal viruses, especially genetically error-prone RNA viruses, whose high mutation rates have, for millions of years, provided opportunities to switch to new hosts in new ecosystems.

COVID 19 is thought to be a zoonotic virus, as most of the first group of patients were workers or customers of a local whole sale seafood market which also sold live consumable animals, including poultry, donkey, sheep, pig, camels, hedgehogs, snakes.

MODE OF SPREAD:

The coronavirus causing COVID-19 - spreads from person to person in close proximity, similar to other respiratory illnesses, such as the flu. Droplets of body fluids - such as saliva or mucus - from an infected person are dispersed in the air or on surfaces by coughing or sneezing. These droplets can come into direct contact with other people or can infect those who pick them up by touching infected surfaces and then their face [8.] According to scientists, coughs and sneezes can travel several feet and stay suspended in the air for up to 10 minutes. It is not yet known how long the virus can survive outside a host but, in other viruses, it ranges from a few hours to months. Transmission is of particular concern on transport, where droplets containing the coronavirus could pass between passengers or via surfaces like aeroplane seats and armrests. The incubation period of the coronavirus, the length of time before symptoms appear, is between one and 14 days. As the virus is an entirely new strain, it is believed that there is no existing immunity in anyone it will encounter. Some level of immunity will naturally develop over time, but this means that those with compromised immune systems, such as the elderly or sick, are most at risk of becoming severely ill or dying from the coronavirus. [9]

LAB DIAGNOSIS:

Specimen types, method of collection, storage and transport plays an important role in laboratory diagnosis and guidelines for the same are provided by WHO, CDC & ICMR [10-16]. Acceptable clinical specimens are respiratory specimens like nasopharyngeal or oropharyngeal aspirates or washes, nasopharyngeal or oropharyngeal swabs, broncheoalveolar lavage, tracheal

aspirates, and sputum [10,11,13,15].Swab specimens should be collected only on swabs with a synthetic tip (such as polyester or Dacron) with aluminum or plastic shafts. Swabs with calcium alginate or cotton tips with wooden shafts are not acceptable [10-16].

Specimen handling and Storage: Specimens can be stored at 4^{o}C for up to 72 hours after collection. If a delay in extraction is expected, store specimens at -70^{o}C or lower. Extracted nucleic acids should be stored at -70^{o}C or lower [11-15].

Specimen Rejection criteria: Specimens not kept at 2-4°C (≤4 days) or frozen at -70°C or below are rejected. Other criteria include incomplete specimen labeling or documentation, inappropriate specimen type, insufficient specimen volume [13].

DIAGNOSTIC METHODS:

Available diagnostic methods are mainly molecular methods - Quantitative Real Time reverse-transcription PCR assays to detect only the novel virus and some may also detect other strains (e.g. SARS-CoV) that are genetically similar. Initial work to develop a serology test for SARS-CoV-2 is underway at CDC and many other reputed laboratories worldwide. [12-15]

BIOSAFETY PRECAUTIONS:

Recommendations to wear appropriate personal protective equipment (e.g. gowns, gloves, eye protection) when working with clinical specimens. Specimen processing should be performed in a certified class II biological safety cabinet following biosafety level 2 or higher guidelines [13, 15].

INFECTION PREVENTION & CONTROL MEASURES AT HEALTH CARE SETTINGSs:

Guidance to Health care facilities, Health care providers on infection prevention and control measures during management of suspected and confirmed case of novel Corona virus is issued by WHO [8-11], ministry of health-India [12] and many other organizations globally. The Principle strategies to follow are given in BOX-1.

BOX-1: Strategies for Infection prevention & Control

1. Ensuring **triage**, early recognition, and source control ;
2. Applying **standard precautions** for all patients;
3. Implementing empiric **additional precautions** for suspected cases ;
4. Implementing **administrative controls**;
5. Using **environmental** and engineering **controls**.

clinical suspicion; well-equipped triage station at the entrance, presence of screening questionnaires, availability of signs in public areas reminding symptomatic patients to

alert HCWs. And most importantly emphasis on hand hygiene and respiratory hygiene

FOLLOWING STANDARD PRECAUTIONS FOR ALL PATIENTS: The HCW needs to follow hand and respiratory hygiene, appropriate personal protective equipment (PPE) according to risk assessment, follow injection safety practices & safe waste management, proper linen disposal, environmental cleaning and sterilization of patient-care equipment.

CANTACT AND DROPLET PRECAUTIONS: Adequately ventilated single patient rooms. For general ward rooms with natural ventilation, adequate ventilation is considered to be 60 L/s per patient (20% of side floor to have opening)**,** Cohorting – 1m apart, Team of HCWs designated for exclusive care of suspected or confirmed cases, HCWs should use a medical mask, eye protection (googles) or facial protection (face shield), clean, non-sterile, long-sleeved gown; gloves.The use of boots, coverall and apron is not required during routine care; new set of PPE's is needed, when care is given to a different patient. Single use disposable equipments are recommended; if shared – disinfect with 70% ethyl alcohol. Refrain from touching eyes, nose or mouth with potentially contaminated gloved or bare hands. Avoid moving and transporting patients out of their room or area unless medically necessary. HCWs transporting patients should perform hand hygiene and wear appropriate PPE and they have to notify the area receiving the patient .Routinely clean and disinfect surfaces with patient contact. Limit the number of visitors; maintain a record of all persons entering the patient's room, including all staff and visitors.

AIR BORNE PRECAUTIONS FOR AEROSOL-GENERATING PROCEDURES:

- Aerosol-generating procedures leading to increased risk of transmission of coronaviruses are tracheal intubation, non-invasive ventilation, tracheotomy, cardiopulmonary resuscitation, manual ventilation before intubation, and bronchoscopy.
- Procedures only in an adequately ventilated room using full PPE (N 95 mask)that is, natural ventilation with air flow of at least 160 L/s per patient or in negative pressure rooms with at least 12 air changes per hour

and controlled direction of air flow when using mechanical ventilation

- Use eye protection (i.e., goggles or a face shield), wear a clean, non-sterile, long-sleeved gown and gloves. If gowns are not fluid resistant, HCWs should use a waterproof apron for Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected

Limit the number of persons present in the room to the absolute minimum required for the patient's care and support.

ADMINISTRATIVE MEASURES: adequate training for HCWs; adequate patient-to-staff ratio; establishing a surveillance process for acute respiratory infections potentially caused by novel CoV among HCWs; ensuring that HCWs and the public understand the importance of promptly seeking medical care; and finally monitoring compliance .

ENVIRONMENTAL CONTROLS: Cleaning and disinfection procedures should be done consistently and correctly. Recommendations to Clean environmental surfaces with water and detergent, applying commonly used hospital disinfectants (such as sodium hypochlorite), Cleaning from "clean" areas to "dirty" areas. Manage laundry, food service utensils and medical waste in accordance with safe routine procedures.

CLEANING AND DISINFECTION OF THE ENVIRONMENT: Floors and horizontal work surfaces - cleaned at least once/twice a day. Dry sweeping with a broom should never be done - Cleaning with a moistened cloth. Cleaning of the environment before disinfection is always recommended. Change cleaning solutions and equipment frequently; as these items will get contaminated quickly (follow your hospital protocols).

USE OF DISINFECTANTS: 1% Bleach (sodium hypochlorite) for disinfection of material contaminated with body fluids [30g/l of regular bleaching powder with 33% available chlorine]. Clean and disinfect patient areas daily, with particular attention to frequently touched surfaces – counter tops, door handles and medical equipment. Use bleaching powder (15g/1L water regular bleaching powder - 33%available chlorine) for disinfection of toilets/bathrooms.

INFECTION PREVENTION & CONTROL AT COMMUNITY LEVEL: Everyone should follow everyday all the following Preventive Actions like Hand

hygiene & Cough etiquette. One should Avoid close contact with symptomatic persons. Avoid Spitting in Public Places. Practise food safety & eat thoroughly cooked food. Avoid unprotected contact with live wild/domestic/ farm animals. Wear protective gowns, gloves, mask and facial protection while handling animal and animal products .Remove protective clothing after work, wash aprons daily and leave at work site. Avoid exposing family members to soiled work clothing and shoes. One should seek early medical care for fever, cough and difficulty in breathing.Avoid touching your eyes, nose, and mouth with unwashed hands. Avoidance of unnecessary travel is advised by WHO, CDC and other organisations.

VACCINE TRIALS:

Researchers are trying to develop a vaccine against 2019-nCoV, and WHO is supporting their efforts. The researchers are currently working on vaccine candidates targeting the SARS-CoV-2 spike protein. They also hope to use the spike protein to isolate antibodies from people who have recovered from infection by the new coronavirus. If produced in large quantities, such antibodies could potentially be used to treat new infections before a vaccine is available. Candidate vaccine for COVID 19 from Moderna therapeutics is under Phase 1 trial. The following vaccine trials are under preclinical phase from CureVac, GlaxoSmithKline, Inovio Pharmaceuticals, Johnson & Johnson, Regeneron Pharmaceuticals, Sanofi & Vir Biotechnology.

CONCLUSION:

It is a challenging time on many fronts. The new virus represents the unprecended public health threat & aggressive action is being taken globally to contain the virus spread. There are still many epidemiological Uncertainties' regarding the reservoir, period of infection and transmission dynamics. Being aware that the epidemiological situation is still evolving, every nation should continue to act decisively in coordination to tackle the threat caused by COVID-19 and to prevent further transmission of the 2019 novel CoV virus.

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Received on: 27.02.2020 Revised on: 02.03.2020 Accepted on: 05.03.2020