

COVID-19: A REVIEW REPORT

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Abstract

COVID-19 may be a very contagion caused by a recently discovered called corona virus. Novel corona virus was found in December 2019 in Wuhan, China. World Health Organization has declared the COVID-19 as pandemic disease and outbreak as a health emergency globally. Novel Corona Virus is additionally referred to as severe acute respiratory syndrome corona virus- 2. The foremost infected people with corona virus show commonly respiratory illness like- fever, cold, sneezing, cough, pneumonia, upper respiratory illness, GIT disease like nausea, vomiting as symptoms. Recently published evidences stated that light Fever and cough within the 80 % patients, shortness of breath in 30-35% patients and 10-15% patients show Muscle ache and other ache. Novel Corona virus enters through the membrane ACE-2 receptor within the human cell. Corona virus is spherical or pleomorphic, single stranded, enveloped ribose macromolecule and included club shaped glycoprotein. SARS, Respiratory (breathing) infections are often transmission via droplets of various diameter like >5-10 micrometer. Molecular test administered with respiratory samples, like throat swab, sputum and bronchoalveolar lavage and in some severe cases it reported in stool and blood also. After the WHO and other diagnostic guideline said that the PCR and RT-PCR test reported for corona diagnosis.

Keyword: Corona Virus, Wuhan city, Covid-19, PCR, WHO, RT-PCR.

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INTRODUCTION

CORONA viruses are the largest group of the viruses which belongs to the Nidovirales order. The order includes four families which are Arteriviridae, Roniviridae, CORONAVIRIDAE and Mesoniviridae. CORONA viridae family is divided into two families, Torovirinae and CORONA virinae. Further CORONA virinae is categorized into- alpha, beta, gamma and delta CORONA virus [1]. Alpha-CORONA virus includes the human CORONA virus (HCoV)-229E and HCoV-NL63. Beta-CORONA virus includes Severe Acute Respiratory Syndrome Human Coronavirus

(SARS-CoV), Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) HCoV-OC43 and HCoV-HKU1. Viruses of birds and whales are included in Gamma-CORONA virus and virus of pigs belongs to Delta-CORONA virus [2]. There are lot of strains but limited are responsible for severe complications like SARS-CoV, which is responsible for SARS (Severe Acute Respiratory Syndrome), MERS-CoV is responsible for MERS (Middle East Respiratory Syndrome). Similarly a new strain is detected in December 2019 is called SARS-CoV-2. This strain is causing a new

disease is known as COVID-19 or CORONA virus which is emerged in Wuhan, China. SARS-CoV-2 is named by The International Committee on Taxonomy of Viruses (ICTV) [3].

Worldwide 215 countries and area are affecting with COVID-19. WHO has announced 3.27M confirmed cases and 230k deaths in the world till May 2, 2020 [11]. Government of India declared 28046 active cases, 10632 recovered cases, 1 migrated and 1301 fatalities (39,980 confirmed cases) till the time. In Uttar Pradesh (UP), India there are 2455 confirmed cases (1756 are active cases, 656 recovered and 43 deceased) [16].

History

Very first CORONA virus outbreak occurred in 2002 in Guangdong, China. This was a Severe Acute Respiratory Syndrome (SARS) epidemic caused by SARS-CoV. Before this outbreak these kind of virus were supposed to infect animals majorly [4]. Mild, self-limiting reparatory infections were found in humans. Spring season is the most favorable condition for transmission of this virus. Spring Festival was celebrated from January 17 to February 23, 2003. In 2003 around 1.82 billion people traveled to China [5]. This SARS epidemic resulted in 8,098 infected humans and 774 deaths in 37 countries [1][3]. All over mortality rate was 9%. This rate was approximately 50% in aged people (over the 60 years). People were quarantined during this outbreak. After June, 2003 no SARS case was found [1]. After 10 years a new virus was detected in Middle East. This virus was named as Middle East Respiratory Syndrome-CoV (MERS-CoV). First case of MERS-CoV was found in Saudi Arabia in 2012. This outbreak affected over 2000 people with 858 deaths [3]. In December 2019 a case of new CORONA virus were found in Wuhan, China. Soon China found several cases of pneumonia with unrecognized etiology. On February 11, 2020, WHO announced name of this new disease as 'COVID-19'. On March 11, 2020, the World Health Organization declared COVID-19 as a pandemic [2]. In India the

first confirmed case was found in Thrissur, Kerala on January 30, 2020. In Uttar Pradesh (UP), first infected person was found in Ghaziabad on March 5, 2020 [8].

Origin and Spread

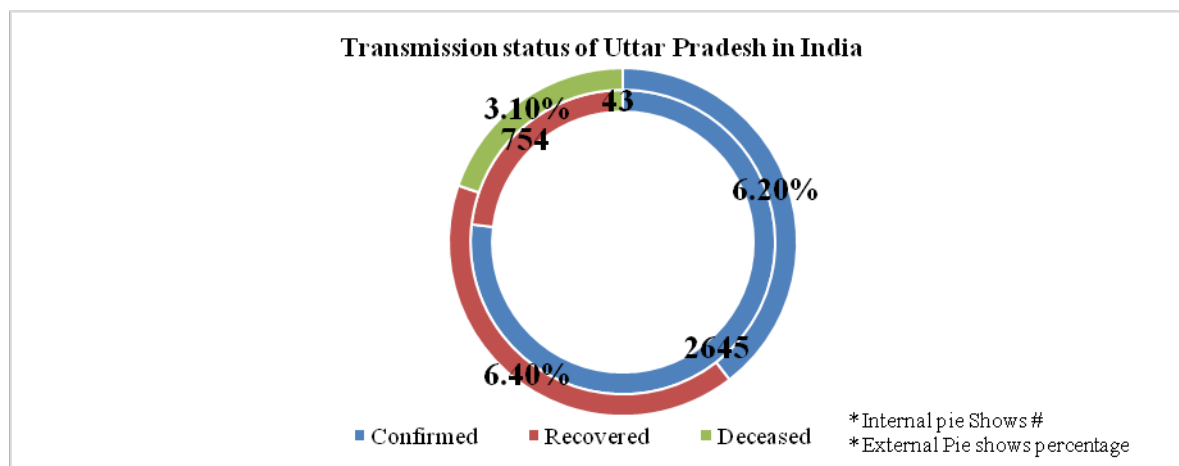
According to WHO CORONA virus are a large family of viruses which are responsible for many infectious in humans and animals Bats and birds (warm blooded flying vertebrates) are ideal natural host for CORONA virus gene. Bats are the host for alpha-CORONA virus and beta-CORONA virus. Birds are host for gamma CORONA virus and delta CORONA virus. Only alpha and beta CORONA virus can cause disease in human.

Bats and Chinese horseshoe bats are natural host for MERS-CoV and SARS CoV respectively. Camel and civets are intermediate host for MERS-CoV and SARS-CoV respectively. Then these two CORONA viruses come into the contact with humans [7].

SARS-CoV has similar genomic organization with SARS-like CORONA virus (bat-SL-CoV ZC45 and bat-SL-CoV-ZXC21) derived in bats (88% similarity). It's strain is genetically different from MERS-CoV and SARS-CoV (with approximate 79% genomic similarity). Thus, the virus name as SARS-CoV-2 [6]. COVID-19 spreads mainly by droplet produced as a result of coughing or sneezing of a COVID-19 infected person. This can happen in two way-

Direct close contact: one can get the infection by being in close contact with COVID-19 patients (within one meter of the infected person), especially if they do not cover their face when coughing or sneezing. Indirect contact: the droplet survive on surfaces and clothes for many days. Therefore, touching any such infected surface or cloth and then touching one's mouth, nose, or eyes can transmit the disease. The incubation period of COVID-19 (time between getting infection and showing symptoms) is 1-14 days. Some people with the infection, but without any serious symptoms can also spread the disease.

Spread in Uttar Pradesh in India is shown in given graph (Fig.1) [17].



Microbiology Structure

CORONA viruses are single-stranded, non-segmented, positive sense, enveloped, RNA [1, 3]. CORONA viruses virions are spherical (or pleomorphic) in shape (65-125nm in diameter) with spike [4, 8]. These club-shaped spikes projected from surface of the virion, create an image like solar CORONA, thus it was named as CORONA virus. CORONA virus particles carry four types of proteins, are spike(S), membrane (M), envelope (E) and nucleocapsid (N). The S protein (~150kDa) form distinct spikes on the surface of virion. The M protein (~25-3kDa) contains three transmembrane domains. It is smaller than the S protein but present in large quantity in virion. The E protein (~8-12kDa) is not only small in size and also present in small numbers as transmembrane in the virion. This protein contains an N-terminal ectodomain and a C-terminal endodom. The E and M proteins are responsible for virion's shape and maintaining its shape. Single protein is present in nucleocapsid is the N protein. It is made from two domains are, N-terminal domain (NTD) and C-terminal domain (CTD). Both domains bind RNA but use different procedure [1, 8].

Genome

CORONA virus has the largest RNA genome among all the viruses. Its genome ranges from 26.4 to 31.7kbs in length. The RNA genome contain 5'cap with 3'poly tail.

5'-leader-UTR-transcriptase-S (Spike) - M (Membrane)-E (Envelope) - N (Nucleocapsid)-3'UTR-poly (A) tail is the organization of CORONA virus genome. Number of proteins and their unique functions depends on the type of CORONA virus.

Replication Cycle

Infection begins with the attachment of viral spike(S) with host cell receptor. Non-covered particle enters into the host cell then its genome penetrates to the cell cytoplasm. The RNA attaches to host cell's ribosome for the translation of open reading frame of genome and create a long polypeptide. The polypeptide sunder into multiple nonstructural proteins because of its own proteinase. Some nonstructural proteins form a multi-protein replicase-transcriptase complex (RTC). The RNA-dependent RNA polymerase (RdRp) is the main replicase – transcriptase protein. Other nonstructural proteins assist in the replication and transcription process. The exo-ribonuclease nonstructural protein provides extra fidelity to replication.

Transmission

In India cases are reached at 42,533 of COVID-19, a new study by Indian Council of Medical Research (ICMR) hints at early community transmission in India, ICMR, studied on patients of SARI (Severe Acute Respiratory Illness) who were undergone

COVID-19 tested and laboratory confirmed cases of 52 district of 21 states and union territories, out of them 39% patients did not report a history of foreign travel or contact with infected person [9]. Transmission is examined by the relationship between confirmed cases and their infected and uninfected close contacts. Household transmission can be characterize by the household contacts (those sharing room, apartment, or other sleeping arrangement) who were later confirmed to have SARS-CoV-2 infection. The distribution of serial interval (time between symptoms arise in confirmed case and their infected contacts) is calculated by fitting parametric distribution to the time of symptom onset in clear case-contact pair. The distribution of individual reproductive number (the number of secondary infections caused by each case) were calculated from the number of secondary infections observed among close contacts of each index case [10]. India expand its testing strategy include all hospitals for all suspected patients. Currently India has 42,533 confirmed case; 11,707 recovered cases and 1373 deceased. In Uttar Pradesh context, currently 2645 confirmed cases, 754 cases are recovered and 43 cases are deceased till first week of May 2020 [17].

Symptoms

COVID-19 affects different people in different way. Most infected people have mild to moderate moderate illness and recover without hospitalization. Most common symptoms are fever, dry cough, and tiredness. Less common symptoms are aches-pains, sore throat, diarrhea, conjunctivitis, head-ach, loss of taste or smell, Rash on skin or discoloration of fingers and toes. Serious Symptoms are – Difficulty in breathing or shortness of breath, chest pain or pressure, loss of speech or movement.

Seek immediate medical attention if you have serious symptoms. Always call visiting your doctor or health facility. People with mild symptoms who are otherwise healthy should manage their symptoms at home. On average it take 5-6 days from when someone is infected with the virus for symptoms to show, however it can take 14 days. To prevent transmission and slow transmission of COVID-19, WHO has recommended

some preventive measure Wash hand regularly with soap and water, or clean them with alcohol –based hand rub.; maintain at-least one meter distance from people have any of symptoms of having sneezing and cough.; avoid touching face, nose, mouth and eyes.; Cover mouth and nose with mask or cloth.; advised to stay home if unwell.; Refrain from smoking and other activity that weaken the lungs.; practice physical distancing by avoiding unnecessary travelling and staying away from large group of people [11].

Diagnosis and Prevention

Indian Ministry of Health and Family welfare has develop a guideline for person who are under COVID-19 investigation[a]. If any of person has any travel history (Outside District / State /Country) within one month. Clinical factors are also used to assess the requirement of testing. These includes Symptoms related with cold, cough, difficulty in breathing; travel history in affected area, region, state, continent and country; close contact with any laboratory confirmed patient; family members and spouse of any confirmed patient. Test RT-PCR (Real Time- Polymerase Chain Reaction) and RT-PCR (Reverse Transcription- Polymerase Chain Reaction) is recommends collecting sample expectorated sputum from upper and lower respiratory tract and mucous from nostrils. Sample is diagnosis under the (RT-LAMP) Reverse transcription Loop mediated isothermal amplification. Its time consuming process and science behind test is RT-PCR act on RNA dependent RNA polymerase / helicase / Spikes / Nucleoside [12]. During this pandemic, the current laboratory test is time consuming it took around 24-48 hours to give response and also due to shortage of commercial diagnostic kits delay diagnosis. In some of countries outside India, COVID-19 infection is diagnosis with typical chest computerized tomography (CT) which is quite fast and give response at same time. In order to prevent the COVID-19 Infection, “Hydroxychloroquine”- is used it as prophylactic use for prevention and control of Patient have confirmed laboratory test. Staff who are working at laboratories, Quarantine Centers, isolation centers and ward staff for prevention and control.

Dose as prescribe day one HCQ 400mg BD weekly dose till 7 week – one 400mg table in a week. Why Hydroxychloroquine, because it has prophylactic property and can be effective in auto Immune disease other use may be Rheumatoid, Rheumatic, inflammatory myopathy [13]. In India - ICMR is working R&D of vaccine of COVID-19, but clinical-trials are pending and claiming to launce in the end of 2020.

Vaccination and Management

Currently no vaccine is available at the time of pandemic outbreak. Vaccine development is long process it starts from research & Development and designing stable form (dry/wet) than it undergo clinical-trials which is time taking and precise process. There are four phases of clinical studies. In India - ICMR is working R&D of vaccine of COVID-19, but clinical-trials are pending and appealing to lunch in November 2020. US MLE suggested that Remdesivir is an experimental antiviral drug originally meant to treat Ebola but it is currently being explored as a potential therapeutic treatment for COVID-19. The drug is administered into the body via daily infusion for about 10 days. It worked by inhibiting the activity of a key enzyme that belongs to the CORONA Virus. This enzyme is called RNA-dependent RNA polymerase, it allows the virus to make more copies of itself inside the host cell. By inhibiting the activity of this enzyme, the virus can't replicate inside the cell. The drug gained attention after showing efficacy against MERS-CoV in monkeys. MERS-CoV is also a CORONA virus which caused on outbreak in 2012. MERS-CoV shares genetic similarity to the new CORONA virus SARS-CoV-2 which meant if Remdesivir worked against MERS-CoV, it could also worked against SARS-CoV-2. The clinical studies on the use of Remdesivir began following the COVID-19 pandemic [14]. Two Studies released their finding: one in US and another in china. *The US study was funded by the national Institute of Allergy and Infectious Diseases. It was conducted on more than 1,000 patients in a randomized clinical-trail, it showed that patient who were given Remdesivir had faster recovery instead of the average 15 days recovery time, they recovered in 11 days. The patient were given the treatment at an advanced stage of

COVID-19. Two groups didn't show statistically significant improvement in survival rate. *The second study was conducted in Wuhan, china, the birthplace of COVID-19 pandemic, It showed no major improvement in health or mortality for COVID-19 patients, The Chinese study was limited by its small sample size: just over 200. The researchers concluded their findings would require confirmation from larger studies. The Chinese study was terminated because of difficulty recruiting patients. It's still difficult to draw concrete conclusion from these two studies. As studies continue, new results will reveal whether Remdesivir is safe or effective in treating patients with mild or advance COVID-19 symptoms. The US is currently exploring Emergency-Use-Approval of Remdesivir for COVID-19 patients. Gilead Science, which company behind the drug said it can produce upto one million Remdesivir treatment courses by 2021[15].

At village set-ups where community is unable to reach public or private registered health facilities they prefer to go to local practitioner or quacks which resides within their reach. Here, the local Practitioner and quacks are use to identify the patients who are approach to them for general illment including Cold, Cough and Respiratory distress and related. A format is shared to all Local Practitioners and Quacks on which they update the information of suspected symptomatic cases, a block level supervisor will asked daily from local Practitioner and quacks about the symptomatic cases on daily basis. List of local Practitioner and quacks is obtained from marketing representatives by District Chief Medical Officer (CMO) than block wise list has been shared to Block Medical Officer further Block medical officer appoint around 10 supervisors and distribute their area to get update of suspected symptomatic cases on phone.

Conclusion

Outbreak of COVID-19 has become critical for community and it is invisible threat for India as well as for whole world. India has reported 42,533 cases till first week of May 2020. Still the knowledge about novel CORONA virus is limited. In last couple of months, India has tries to prevent third stage

of transmission and Nation is on the path of success to prevent third stage of transmission. Other activities like Lockdown, Strengthening health facility and capacity building of healthcare staff and Arogya Setu application is proved fruitful. In respect of Uttar Pradesh, along with all the activities, involvement of local practitioners and quacks to get patients having symptoms of cold and cold related symptoms. It really helped and at very first day one migrant villager was sampled and found CORONA positive (laboratory confirmed) who was reported by a quack of that block. Then after, we are rigorously collecting data and tracking symptomatic patients from quacks and local practitioners thus implementing strategy with more better way. Government Health, NHM and Technical Support Unit authorities is monitoring each step and as the more we learn about this COVID-19 virus and its associated breakout, the better we can respond.

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