

Novel Coronavirus-In the light of Epidemiological Findings

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ABSTRACT

Coronavirus Disease (COVID-19) caused by SARS-CoV-2/Novel Coronavirus (nCoV), a newly identified strain in 2019, with different strains (SARS-CoV-1 or SARS-CoV) coronavirus earlier had caused respiratory illnesses like Middle East Respiratory Syndrome (MERS) in 2012 and Severe Acute Respiratory Syndrome (SARS) in 2004. For COVID-19, initially virus was identified in Wuhan city of China when 27 Pneumonia cases of unknown origin were found. The number of confirmed cases was increased up to 9000 in Wuhan city and 98 people were also diagnosed positive in 18 different countries, including United States. On 30 January 2020, World Health Organisation (WHO) has declared the Coronavirus outbreak as a Public Health Emergency of International Concern (PHEIC). The case fatality rate is high (2%), as globally 376,320 deaths from 6,194,533 confirmed cases were reported and still it is increasing. This review describes about the current updates with regard to COVID-19 burden, history, transmission agent, host factors, environment, reservoir and source, routes of transmission, pathogenesis and clinical features, laboratory diagnosis and prevention and its management.

Keywords: Outbreak, Pandemic, Respiratory infection, Viral pneumonia

INTRODUCTION

Coronavirus is a re-emerging infectious disease belonging to coronaviridae family and Nidovirales order. Human coronavirus was first identified in the mid-1960s. Six types of corona viruses were already known to the world. The SARS-CoV-2 is a new virus and the seventh corona virus, never seen before in people. It is different than other human coronaviruses that causes the common cold [1]. In December 2019, infection was originated as series of pneumonia cases of unknown origin in Wuhan, Hubei, China with clinical presentation resembling viral pneumonia [2]. Those cases were linked with Huanan seafood wholesale market of Wuhan which was later identified as a coronavirus disease. It has been noted that the newly identified coronavirus is similar to bat coronavirus and SARS-CoV-1 [3]. From a study in China, researchers have found that there are two types of coronavirus strains called as “L” and “S” types [4]. Coronavirus was also the causative agent of SARS (with 774 deaths from 8094 confirmed cases) and MERS (with 858 deaths from 2494 confirmed cases), but case fatality rate was high as compared to COVID-19. On February 11, 2020, the World Health Organisation named the disease coronavirus disease 2019 (abbreviated “COVID-19” SARS-CoV-2).

TIMELINE OF COVID-19 DISEASE

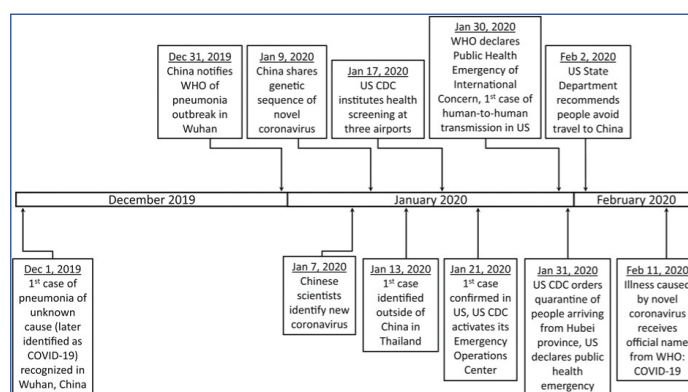
First case of the disease was reported in Wuhan City, Hubei Province, China [5] on 31st December, 2019. Then, the disease started spreading rapidly with the following timeline:

9th January 2020- WHO announced that a novel coronavirus that has not previously been identified in humans which was detected in samples taken from patients in Wuhan City [6].

11th January 2020- First death reported in Wuhan city because of Coronavirus disease 2019.

26th January 2020-Confirmed cases of COVID-19 have been reported in many countries, including China, Hong Kong, Macau, Taiwan, Australia, France, Japan, Malaysia, Nepal, Singapore, Thailand, The Republic of Korea, United States, Vietnam [Table/Fig-1] [7,8].

On 27th January 2020- 41 travel-related cases were identified and travelled back to their countries, 27 cases to Asia, six to North America, five to Oceania, and three to Europe [9].



[Table/Fig-1]: Timeline of early stages of COVID-19 outbreak.

On 30th January, 2020- United States reported the first confirmed case and on the same day, the International Health Regulations Emergency Committee of WHO declared the outbreak as a “PHEIC”

On 6th February, 2020-in 24 countries other than China, minimum of 216 cases have been confirmed: Germany, Australia, Cambodia, Vietnam, Canada, Finland, France, India, United Arab Emirates, Japan, Malaysia, Thailand, Nepal, The Philippines, Russia, Singapore, Belgium, South Korea, Spain, Sri Lanka, Sweden, Italy, United Kingdom and United States, . Two deaths have now been reported outside of mainland China (one in Hong Kong and one in Philippines) [10].

On 11th March 2020- WHO declares COVID-19, a pandemic.

On 30th March 2020- Globally total confirmed cases were 638,146; total deaths were 30,039 in 203 countries/areas/territories. Majority of cases were from United States of America (103,321 confirmed cases and 1,668 deaths), Italy (92,472 confirmed cases and 10,023 deaths) and China (82,356 confirmed cases and 3,306 deaths) [11].

PROGRESSION OF CORONAVIRUS DISEASE IN INDIA

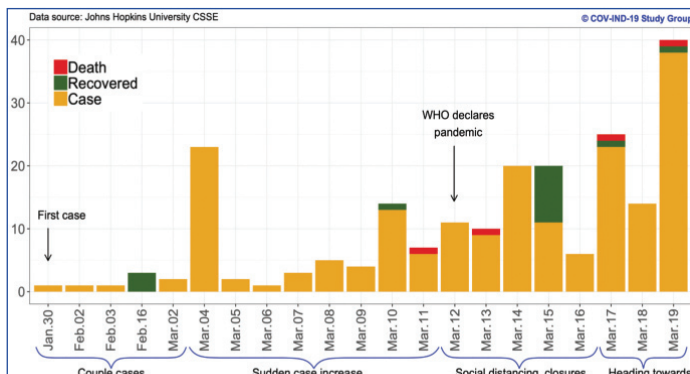
On 30th January 2020- A student returned to Kerala, India from Wuhan, China on 24 January, who later found to be positive after testing. Subsequently, two more cases of COVID-19 were reported

in the same city [12].

On 27th February 2020- One hundred and twenty four Indian passengers were evacuated from Japan and they were quarantined for 14 days [13].

On 14th March 2020- Total confirmed cases reached to 84 (67 Indian nationals and 17 foreign nationals) and two deaths (76-year-old male from Karnataka and 68-year-old female from Delhi). Till 22nd March, confirmed cases increased upto 360 and seven deaths in cities like Maharashtra (two deaths), Delhi (one death), Bihar (one death), Gujrat (one death), Karnataka (one death) and Punjab (one death) [14].

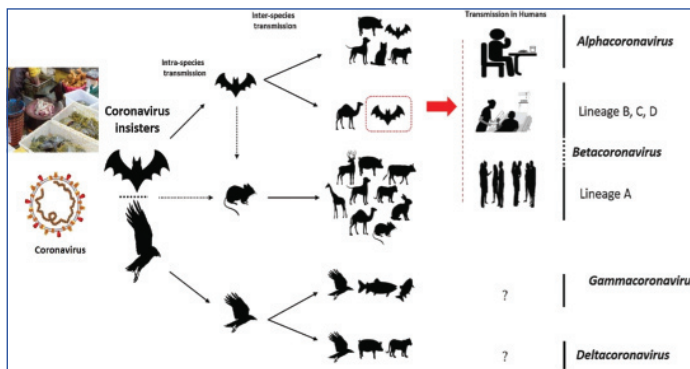
On 22nd March 2020- Hon'ble Prime Minister made a public appeal to encourage community participation in the response towards COVID-19 by observing a 'Janta curfew' on 22nd March from 7 am to 9 pm, later on 25th March 2020 he issued an order for all states/UTs prescribing a lockdown for containment of COVID-19 epidemic in the country for 21 days starting from 25th March [Table/Fig-2] [15].



[Table/Fig-2]: Confirmed new cases/recovered/ deaths because of COVID-19 in India.

As of 3rd June, according to the Ministry of Health and Family Welfare (MOHFW), a total of 101,497 cases were confirmed, 100,302 recovered and 5,815 reported deaths [16].

The outbreak of SARS-CoV in 2002-2003 in Guangdong province, China and then 10 years later in 2012, MERS-Cov was identified. In both the cases, bats were considered as a natural host of these viruses. They transmit the infection to humans by using camels and civet cats as an intermediate host [Table/Fig-3] [17,18].



[Table/Fig-3]: Potential animal origin of human coronaviruses [17,18].

HISTORICAL PERSPECTIVE

According to recent data, bats, fish, shellfish, porcupines and snakes are the most probable initial source of the current SARS-CoV-2 outbreak, that begun in December 2019 in Wuhan, China, apparently spreading from a "wet market/ Huanan Sea food market" to multiple cities and provinces in China [19-21].

AGENT FACTORS

Because of crown-like spikes on its surfaces the virus got the name 'Coronavirus'. It is an enveloped positive-sense, single-

stranded RNA viruses (+ssRNA), 27-32 kb in size, which is the second largest of all RNA virus genomes. This novel virus shares 79.5% of genetic sequence with SARS-CoV and has 96.2% homology to a bat coronavirus. There are four main subgroups of coronaviruses, known as alpha, beta, gamma and delta. Alpha and beta coronaviruses infects mammals; gamma and delta coronaviruses infects birds [22].

The seven types of CoV that can infect people are: 229E alpha coronavirus, NL63 alpha coronavirus (2004), OC43 beta coronavirus, HKU1 beta coronavirus (2005), MERS-CoV beta coronavirus (2012), SARS-CoV beta coronavirus (2003) and 2019 Novel coronavirus (nCoV). The new novel coronavirus is a new strain of beta coronavirus from group 2B with a 70% genetic similarity to the SARS-CoV. Four unique inserts in the SARS-CoV-2 were found in one of the study which might explain the highly virulent nature of the disease agent.

RESERVOIR OF INFECTION

Bats of the Rhinolophidae and Hipposideridae family are considered to be the natural reservoirs of coronavirus. Bats are known to be hosts for more than 30 coronaviruses with complete genomes sequenced [23-25].

SOURCE OF INFECTION

The virus is transmitted from wildlife to human through contact of infected bats and through intermediate host like civet cats and camels that became infected through contact with bat saliva or faeces. These intermediate hosts play a key role in transmission of coronavirus from bats to humans. In countries like China, slaughtered animals are considered more nutritious, and this belief may enhance viral transmission to humans. Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human. Human-to-human transmission occurs due to close contact mainly by respiratory droplets and thus by coughing and sneezing of infected person. This is the reason behind rapid transmission of infection to health workers and people who are taking care of infected person [26].

The Centres for Disease Control (CDC) defines close contact as being within 6 feet (2 meters) or within a room or care area for a prolonged period without personal protective equipment or having direct contact with secretions of a person with COVID-19 [27].

No evidence of COVID-19 in other body secretions including amniotic fluid, cord blood, breast milk and neonatal nasopharyngeal swab samples have been detected [28].

PERIOD OF INFECTIVITY

The incubation period of COVID-19 is 2-14 days and therefore, it is recommended that infected persons to be isolated for at least 14 days [29,30].

The incubation period has been found to be as long as 24 days [31]. The person remains infectious as long as the virus is present in respiratory secretions. Since we know that the incubation period can extend upto 24 days, the period of quarantine can also be extended from currently following 14 days to 24 days.

HOST FACTOR

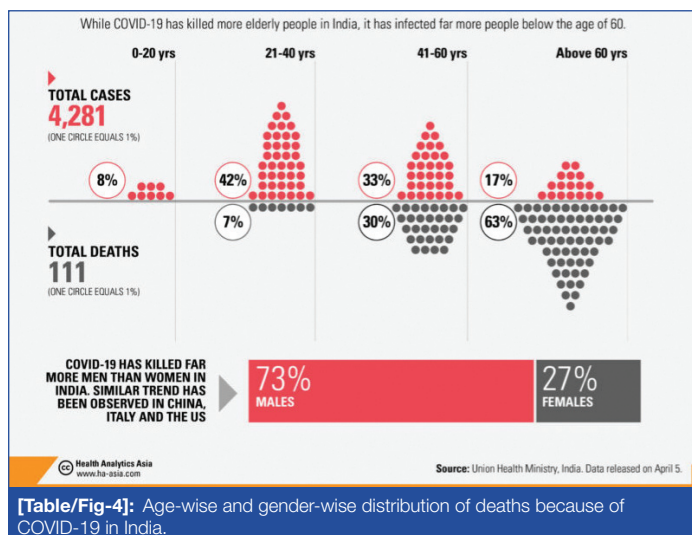
Age and Sex- Found more commonly above 49 years of age 21-46 yeras and male: female ratio for preponderance of disease is 2.7:1 [32].

The median age of cases detected outside of China is 45 years, ranging from 2 to 74 years. Seventy one percentages of cases were male.

People of all ages can be infected by new coronavirus (COVID-19). Older people and people with pre-existing medical conditions are vulnerable population for COVID-19 [33].

According to a study done by Dong Y et al., Children are less

likely to be infected and also less likely to be hospitalised than adults. Illness is less likely to be severe in children than in adults [Table/Fig-4] [34,35].



[Table/Fig-4]: Age-wise and gender-wise distribution of deaths because of COVID-19 in India.

ENVIRONMENT

Climate-COVID-19 outbreaks in Wuhan, China suggest that the onset of these outbreaks was associated with high-relative humidity and low temperature. At 4°C, COVID-19 virus persists for approx. one month, inactivation occurs more rapidly when the humidity level increases more than 20°C [36].

MODE OF TRANSMISSION

Initially, the suspected cases were found in Wuhan seafood market and identified as fever, with respiratory symptoms. A travel history or contact with people from Wuhan within two weeks and travel history of exposure to wildlife. Mainly human-to-human transmission identified [37,38].

The spread occurs mainly through respiratory droplets (when a sick person coughs), close contact and from fomites. The virus remains stable for several hours to days in aerosols and on surfaces, according to a new study from National Institutes of Health, CDC. They had found that virus was detectable in aerosols for few hours on copper, cardboard and few days on plastic and stainless steel [39].

The Chinese authorities reported that the possible aerosol transmission occurs in a closed environment with long-term exposures to high concentration of aerosols found mainly in ICUs and CCUs [40].

CLINICAL FEATURES

According to CDC, people with confirmed COVID-19 presents with fever, cough and shortness of breath. The clinical features of illness are varies from no symptoms or mild respiratory symptoms to severe along with acute respiratory distress syndrome (ARDS), rapidly progressive pneumonia, multi-organ failure resulting in death or septic shock [41].

DIAGNOSIS

1. By medical history
2. By physical examination
3. By lab tests of blood, sputum, a sample from a throat swab, or other respiratory specimens
4. Imaging examination

Medical History

According to the US CDC and WHO, people meeting the following criteria's should be tested for COVID-19 [42].

1. People who had a history of recent international travel (within 14 days with respiratory symptoms.

2. Have a history of close contact (social contact, household contact and close-setting contacts).
3. Healthcare workers involved in treatment of lab confirmed cases of COVID-19.

Physical Examination

Patients with mild symptoms may not show positive signs and patients in severe condition may present with weakened breath sounds or shortness of breath, moist rales in lungs, increased or decreased tactile speech tremor and dullness in percussion.

Laboratory Test

According to CDC, two viral tests are available nucleic acid or antigen tests. Viral testing for SARS-CoV-2 is considered to be diagnostic when performed in symptomatic patients [43].

Sample Collection [44]:

1. Upper Respiratory Tract Specimen

- a. Nasopharyngeal swabs
- b. Oropharyngeal swabs

2. Lower Respiratory Tract Specimen

- c. Sputum
- d. Bronchoalveolar lavage
- e. Tracheal aspirate

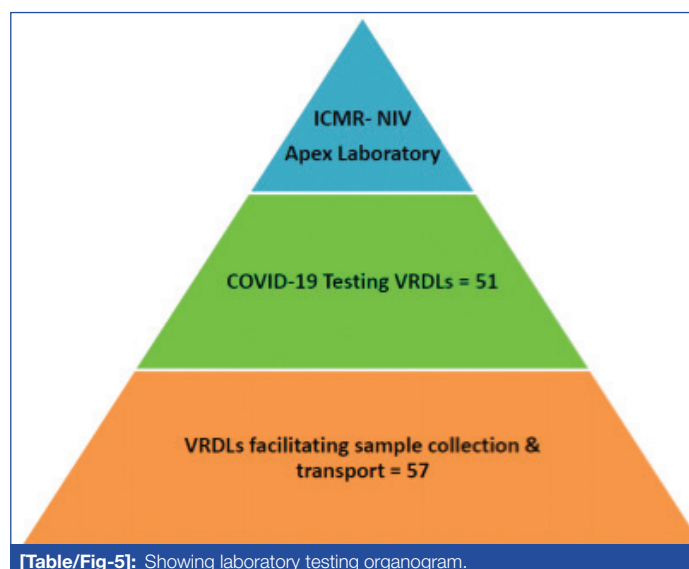
Lower respiratory tract specimens are preferred over upper respiratory tract specimen for detecting SARS-CoV-2.

Patient should be re-sampled, if the initial test for COVID-19 comes negative and additional specimen may be collected such as blood, urine, and stool for COVID-19 testing [45,46].

Also, saliva for serial saliva viral load can be used [47].

Role of ICMR in Establishing Diagnosis of COVID-19 [3]

The ICMR-National Institute of Virology (NIV), Pune functions as the resource centre for the VRDL network and is responsible for providing technical training [Table/Fig-5].



[Table/Fig-5]: Showing laboratory testing organogram.

India made test kit approved by (Mylab, Pune) PCR test 100 per kit. Currently, Pool testing of the samples has been done to identify the cases rapidly.

Storage and Transport of Samples

For transport of samples for viral detection, use Viral Transport Medium (VTM) containing antifungal and antibiotic supplements. Samples should be transported under cold chain (≤ 4 degrees) and with proper labeling on each specimen container.

Handling and processing specimens should be preferred in accordance with national biological safety guidelines [48].

Imaging Examination/Imaging Features of CT

Ground glass density shadows in both lungs [49].

CASE DEFINITIONS OF COVID-19

According to WHO, the case definitions of COVID-19 are:[50]

Suspected Case

A. Patient with severe acute respiratory infection (fever, cough, and requiring admission to hospital), and with no other aetiology 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 and contact with a confirmed or probable case of COVID-19 infection within 14 days prior to symptom onset.

Probable Case

A suspect case for whom testing for SARS-CoV-2 is unresolved.

Confirmed Case

A person with laboratory confirmation of COVID -19 infections. Apart from presence or absence of COVID-19 signs and symptoms.

PREVENTION

A 14-day health observation period or quarantine period should be advised to those persons who had close contact and suspicious exposure. The period starts from the last day of contact with the suspicious environmental exposure or from the contact with COVID-19 infected patients [51].

TREATMENT

Supportive Treatment [52]

Maintain Airway, Breathing and Circulation.

Ventilation, if required (If $PO_2 < 55\%$)

Isolation to prevent spread

Correction of electrolyte imbalance

Correction of temperature

Drugs

Few drugs are found to be effective in the treatment of COVID-19 namely, Lopinavir-Ritonavir [53], Favilavir [54], Remdesivir [55], Hydroxychloroquine [56], and newly identified Ivermectin.

Vaccines

MERS-CoV Vaccine [57]

Three potential MERS-CoV vaccine candidates have progressed to phase one clinical trials.

A DNA vaccine (GLS-5300)

Two viral vector-based vaccine (MVA-MERS-S and MERS001)

mRNA-1273 [58]

This is a phase I, open-label, and dose-ranging clinical trial among adults, 18 to 55 years of age.

CONCLUSION(S)

Newly identified disease agent SARS-CoV-2 has infected one million roughly around the world. With international lockdown and individual countries efforts the spread of the disease has been slowed down but in spite of the best global efforts we are still not able to contain

the disease. While several drug trials are ongoing, there is currently no proof that any drug can cure or prevent from COVID-19.

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