

Review Article

Coronavirus Disease 2019 (COVID-19) due to Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV2) Infections – An update

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An outbreak of severe acute respiratory disease due to a novel corona virus was reported from the city of Wuhan, Hubei Province, China in December 2019. Initially named as novel coronavirus 2019 (2019-nCoV), the virus was later officially named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2). The disease caused by it was officially named by the World Health Organization as Corona Virus Disease 2019 (COVID-19). Within a short span of time the epidemic spread to all provinces of China and 88 other countries and caused more than 80,000 confirmed infections and over 3000 (as on 6th March, 2020) deaths. 33 cases were confirmed in India and several suspected cases quarantined. In this review article, the origin of the virus, its genetic make-up, and how the epidemic evolved are discussed. The spectrum of clinical features, important laboratory and imaging findings as per early clinical studies are described in detail. The current treatment principles along with the future prospects of treatment are outlined. Preventive measures taken are narrated. The possible future scenarios of the epidemic are depicted.

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Key words : SARS-CoV2, COVID-19.

The 2019 novel corona virus (2019-nCoV), now known as Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV2) epidemic originated in the Wuhan city, Hubei Province, Peoples Republic of China in December 2019 and as of March, 6th, 2020 there were 98,192 confirmed cases and 3,381 deaths reported from 88 countries including China. At the time of submission of this article, majority of cases and deaths (80,711 confirmed cases and 3,045 deaths) have been in China. Inside China, Hubei province borne the brunt with 67,592 confirmed cases and 2,931 deaths. Outside of China, cases have been confirmed in 88 countries accounting for 17,487 confirmed cases and 335 deaths. In India, there were 33 confirmed cases of which first three were from the state of Kerala¹. Rest of the cases were reported after 16 Italian National tested positive for virus on 4th March, 2020. Bengaluru, New Delhi, Gurugram

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Editor's Comment :

- Coronavirus Disease 2019 (COVID-19) is an infection caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV2), a novel corona virus that emerged in Wuhan, China in December 2019.
- It causes severe acute respiratory distress in some patients, especially in older patients with comorbidities.
- It should be suspected in patients with fever, radiographic evidence of pneumonia, reduced lymphocyte count with no response to 3 days of antimicrobial treatment especially those with history of travel to China or having history of contact with travelers who visited China recently.
- Confirmation of diagnosis is by identification of specific sequences of SARS-CoV2 in the throat secretions of patients using RT-PCR.
- Patients are treated by isolation and by supportive treatment. No specific antiviral treatment or vaccine is available at this point of time.
- Patients should be watched for features of respiratory distress, cardiac arrhythmias and multiorgan dysfunction especially from the second week onwards.
- On serial estimation, progressive elevation of total WBC count, d-dimer, lactate dehydrogenase and creatine kinase associated with decreasing total lymphocyte count indicate worsening of prognosis.

& Ghaziabad had each reported one/two people with travel history of Italy have tested positive on case on 7th March, 2020. On February 11, 2020, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses

officially named the virus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the World Health Organization officially named the clinical disease caused by SARS-CoV-2 as Corona Virus Disease-2019 (COVID-19).

What is Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV2)?

The SARS-CoV2 virus, belonging to the Coronaviridae family, is composed of positive-sense single-stranded RNA viruses. Prior to 2002 this viral family was considered mostly inconsequential as it rarely led to severe illness. In 2002, SARS (Severe Acute Respiratory Syndrome) due a corona virus called SARS-CoV was identified in the Guangdong province of China, that ultimately spread to 29 countries, infected over 8096 individuals, and caused 774 deaths (WHO News 2003; **81(5): 384**).

This was followed by the emergence in 2012, in the Arabian Peninsula, of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Although the clinical manifestations of MERS resembled that of SARS, the case fatality rate (CFR) of MERS was much higher (37.1% versus 9.6%). MERS-CoV lead to 2494 infections and 858 deaths (Zaki AM, 2012). While both SARS-CoV and MERS-CoV caused severe respiratory diseases in humans, four other previously documented human corona viruses (HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1) were responsible for 10-30% of minor upper respiratory tract infections worldwide.

In 2019, the newest member of the corona virus, SARS-CoV2 infection has been identified as the causal virus in the exponentially increasing current epidemic, prompting the World Health Organization to classify the event as a Public Health Emergency of International Concern (PHEIC) on 30-1-2020. Starting in the Wuhan District of Hubei province of China in December 2019, it is estimated that this novel coronavirus has caused over 98,192 confirmed cases and a current death toll of 3,381 as on February 20, 2020. The situation is dynamic and it is clear that the true magnitude of the problem is yet to be determined.

Genetic build-up of SARS-CoV2:

Coronaviruses (order *Nidovirales*, family *Coronaviridae*, subfamily *Coronavirinae*) are enveloped

viruses with single-stranded, positive sense RNA genome having a genome size between 26 to 32 kilobases. The genome codes for four major structural proteins: the spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein. The sequenced genome of SARS-CoV2 (NCBI Reference Sequence NC_045512.2) was 88% identical to two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses called bat-SL-CoVZC45 and bat-SL-CoVZXC21. It was 79% identical to SARS-CoV and 50% identical to MERS-CoV (Roujian Lu, 2020). Phylogenetic analysis showed that it belonged to the subgenus Sarbecovirus of the genus Betacoronavirus. SARS-CoV2 was found to have 96.3% sequence similarity throughout the genome to BatCoV RaTG13 viruses found in bats from Yunnan province of China, but SARS-CoV2 showed discordant clustering with the Bat_SARS-like coronavirus sequences (D Paraskevis, 2020). Though bat coronavirus RaTG13 remains the closest relative of SARS-CoV 2 across the whole genome, a coronavirus found in Malaysian Pangolins (*Manis javanica*), the most common illegally traded endangered mammal in the world, was found to be identical to SARS-CoV 2 at all six key receptor binding domain (RBD) residues (Wong 2020).

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Timeline:

Chronologically, this global health emergency began on December 8, 2019

in Wuhan, China, a city with a population of 11 million, when the first patient was brought into the emergency room with pneumonia of unknown etiology. Thereafter, the emergency department noticed a multitude of similar presentations, and by December 30, 2019, the total number of cases locally rose to 41. The surveillance mechanism for “pneumonia of unknown aetiology”: a system created and implemented to aid in timely identification of novel pathogens causing pneumonia after SARS epidemic, was activated. All subsequent cases were notified to the Chinese National Health Commission (Chaolin Huang, 2020).

On January 7, 2020, the China-CDC identified the causative organism as a novel coronavirus which was phylogenetically in the SARS-CoV clade. Despite measures to counter the illness, the first fatality occurred

COVID 19

(Update 10/03/2020)

- **Global cases** : 113702
- **Global death** : 4012
- **No of countries affected** : 109
- **WHO risk assessment** : Very high (Global)
- **Total no cases in India** : 52
- **Most affected region** : Kerala, Uttar pradesh

on January 11, 2020 in a 61-year-old patient with multiple comorbidities. Around the same time, the full viral genome was sequenced, and shared with the World Health Organization on January 12, 2020. This was subsequently made available on the Global Initiative on Sharing All Influenza Data [GISAI] platform, which currently has 103 SARS-CoV-2 genomes uploaded from worldwide. The availability of the full viral genomic data lead to rapid development of point-of-care real-time PCR diagnostic testing. Ongoing analysis of subsequent genomes received from worldwide will help in early detection of mutations in the SARS-CoV-2 genome.

Origin :

Epidemiological investigations into the first 41 cases found that many of the patients had exposure to a large seafood and live animal market in Wuhan, suggesting an animal-to-person spread. As ongoing investigations occurred, an increasing number of those affected reported no exposure to the market, indicating a person-to-person transmission (Chaolin Huang, 2020). As discussed earlier, current data on the viral genome has suggested bats as a possible reservoir for the virus, propagated by their propensity to inhabit small, enclosed, ill-ventilated spaces in large colonies. Bat-borne viruses generally lack the capability to adhere onto human cell surface receptors, and may need an intermediary host such as dromedary camels in the case of MERS for the cross-species jump enabled by mutations and recombinations. These claims require further scientific investigation before any conclusions could be made. Nevertheless, the SARS-CoV2 has 96.3% sequence similarity throughout the genome to BatCoV RaTG13 viruses (D. Paraskevis, 2020) and share six key receptor binding domain (RBD) residues with a coronavirus isolated from Malaysian pangolins (Wong 2020).

Global picture :

As per WHO situation report dated March 6th, 2020, globally there are 98,192 confirmed cases. In China, there are 80,711 confirmed cases (146 new), and 3,045 deaths (30 new). It has spread to all provinces of China including Hongkong, Macau and Taiwan and to 88 countries including India. As diagnostic facilities become available in more countries, the number of countries affected is expected to escalate. In addition to China, human-to-human transmission have been identified in Germany, Vietnam, Japan, USA and France. Italy has been hit hard since the outbreak with more than 4,600 confirmed cases & over 200 deaths.

How is it transmitted ?

The virus probably spreads by airborne transmission via large droplets, aerosols, faecal-oral route or by fomites. A reproduction number or R0 of 1.8 to 3.5 is the current estimation. This means that overall, each patient infected with the virus will spread the infection to 1.8 to 3.5 other people. Preventive measures aimed at reducing the R0 are being implemented, and this will help to curb the epidemic. This can be done with early diagnosis, contact tracing and surveillance, social distancing, personal hygienic measures, appropriate personal protective gear and isolation of known/suspected cases. As a comparison, R0 for various common illnesses are as follows: measles 12-18, mumps 4-7, AIDS 2-5, SARS 2-5, MERS less than 1 and Spanish flu (1918) 2-3. Due to the ongoing nature of SARS-CoV2 epidemic, all estimations are likely to change.

Clinical Features :

From the data on first 425 patients, the mean incubation period was estimated to be 5.2 days (95% confidence interval [CI], 4.1 to 7.0) and the 95th percentile of the distribution was 12.5 days (95% CI, 9.2 to 18). Serial interval between infective cycles is reported to have a mean (\pm SD) of 7.5 \pm 3.4 days (95% CI, 5.3 to 19). Epidemic growth rate was found to be 0.10 per day (95% CI, 0.050 to 0.16). Doubling time for the number of cases reported as 7.4 days (95% CI, 4.2 to 14) (Qun Li, 2020).

According to clinical features of first 41 cases reported in *The Lancet* on January 24th, symptoms during prodromal phase including fever and dry cough were nonspecific and upper respiratory tract symptoms such as running nose and sore throat were notably infrequent (Chaolin Huang, 2020). Similar to SARS-CoV, SARS-CoV2 also binds to hACE-2 receptors (Human Angiotensin converting enzyme-2). hACE-2 receptors are predominantly seen in the lower respiratory tract which may explain the predominance of lower respiratory tract symptoms. Intestinal symptoms in contrast to SARS (Severe Acute Respiratory Syndrome) infections and MERS (Middle East Respiratory Syndrome) were uncommon. 22 patients (55%) developed severe respiratory distress, 13 (32%) needed intensive care and 6 patients (14.6%) died. Blood investigations showed relative reduction of lymphocytes (lymphopenia) and chest x-rays showed bilateral lung field opacities suggestive of viral pneumonia.

A study based on 99 patients with RT-PCR proven SARS-CoV2 infection treated at the Jinyintan Hospital, Wuhan from 2020 January 1st to 20th, published in *The Lancet* on January 29, 2020, the clinical manifestations were

fever (83%), cough (82%), shortness of breath (31%), muscle ache (11%), confusion (9%), headache (8%), sore throat (5%), rhinorrhoea (4%), chest pain (2%), diarrhoea (2%), and nausea and vomiting (1%) (Nanshan Chen, 2020). Average age was 55.5 years and 51% had comorbidities. 17% developed acute respiratory distress syndrome (ARDS) and 11% died of multiple organ failure.

A study CT scans of chest of 21 patients, showed bilateral pulmonary parenchymal ground-glass and peripherally distributed consolidative pulmonary patches with a notable absence of cavitation, pleural effusion, discrete nodules and lymphadenopathy (Michael Chung, 2020).

In a retrospective study submitted to the Lancet based on 52 critically ill patients out of 710 confirmed cases at Wuhan Jinyintan Hospital, the authors found that the average age was 59.7 ± 13.3 years (mean \pm standard deviation), 35 (67.3%) were male, 21 (40.4%) had chronic illness, 51 (98.1%) had fever, 35 (67.3%) developed ARDS and 37 (71.2%) required mechanical ventilation (Xiaobo Yang, 2020). Thirty-three (57.7%) patients deceased, and the duration from hospital admission to death was 7 [3 - 11] days.

In an article under consideration for publication in *The Lancet*, a team of authors reported on 9 patients with known exposure to confirmed or suspected cases, who presented with gastrointestinal symptoms and no fever (Ping An, 2020). Five patients subsequently developed fever and respiratory symptoms, but 4 patients did not develop respiratory symptoms or fever. Multifocal patchy ground-glass pulmonary opacities were found in all 9 patients on CT scan of chest done during the first clinical visit. Hence those with history of exposure to confirmed or suspected cases of SARS-CoV2 infection, presenting with gastrointestinal symptoms should be evaluated for the disease even in the absence of fever and respiratory symptoms.

In a single-centre, retrospective consecutive case series of the 138 hospitalized patients with confirmed SARS-CoV2 pneumonia at Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 28, 2020, authors reported fever (98.6%), fatigue (69.6%), dry cough (59.4%), myalgia (34.8%) and dyspnoea (31.2%) as the most common symptoms (Dawei Wang, 2020). Hospital associated transmission was suspected in 57 (41.3%) of patients, of this 40 were health care workers and 17 were already admitted patients. Of the 40 health care workers infected, 31 worked on general wards, 7 in the emergency department and 2 in the intensive care unit. Median interval

from onset of symptoms to dyspnoea was 5 days, to hospital admission was 7 days and to ARDS was 8 days. Lymphopenia (70.3%), prolonged prothrombin time (59%) and elevated lactate dehydrogenase (39.9%) were observed on lab investigations. Computed tomography showed bilateral opacities or patches in all patients. Transfer to intensive care unit was needed in 36 patients (26.1%) either due to ARDS in 22 patients (61.1%), arrhythmia in 16 patients (44.4%) and shock in 11 patients (30.6%). Patients admitted to ICU were older and were more likely to have comorbidities. At admission, patients who later required ICU care showed statistically significant elevated levels of neutrophil count, D-dimer, procalcitonin, blood urea nitrogen, aspartate aminotransferase, creatine kinase and lactate dehydrogenase. As of February 3, 6 patients died (4.7%), 85 patients (62.6%) remain hospitalised and 47 patients (34.1%) were discharged. Nonsurvivors had higher total WBC counts, elevated neutrophil count, lower lymphocyte count and elevated D-dimer levels on serial investigations after admission to the hospital mainly seen from the second week onwards.

As per the epidemiology report by SARS-CoV2 National Incident Room Surveillance Team of Australia for the week from 26 January to 1 February, there were 12 confirmed cases of SARS-CoV2 infections in Australia and all had history of travel to China. Of the 12 patients, 11 had mild to moderate symptoms, one was admitted in the ICU and there were no deaths. All had fever and 83% had cough (2019-nCoV National Incident Room Surveillance Team, Australia, 2020).

When to suspect Coronavirus Disease 2019 (COVID-19)?

SARS-CoV2 caused pneumonia now officially termed Coronavirus Disease 2019 (COVID-19) should be suspected if it meets all the four criteria below: fever $>38^{\circ}\text{C}$, radiographic evidence of pneumonia; low or normal white-cell count or low leucocyte count; and no reduction in symptoms with antimicrobial treatment of 3 days duration or any of the three criteria with history of contact with an infected person or infectious place with or without recorded fever; radiographic evidence of pneumonia, low or normal white-cell count or low lymphocyte count, and no reduction in symptoms with antimicrobial treatment of 3 days duration.

How to confirm Coronavirus Disease 2019 (COVID-19)?

Throat swabs are collected and sent with virus preservation solution. SARS-CoV2 infection confirmation may be done by next-generation sequencing, real-time RT-PCR, cell culture, or electron microscopy. Isolation of the virus from specimens is not advised for diagnosis.

Diagnosis is confirmed if RT-PCR (real-time polymerase chain reaction) with SARS-CoV2 specific primers and probes for the targets or the genetic sequence that matches SARS-CoV2 is found in the collected sample. In the laboratory, total RNA is extracted within 2 hours and real-time reverse transcriptase polymerase chain reaction done by amplifying for two target genes of SARS-CoV2: open reading frame 1ab(*ORF1ab*) and nucleocapsid protein(N) (Dawei Wang, 2020). RT-PCR is considered positive if 2 targets (open reading frame 1a or 1b(*ORF1ab*), nucleocapsid protein(N) were positive at a cycle threshold value (Ct-value) less than 37, values more than 40 was considered negative and for values between 37 and 40, retesting should be done. Genetic sequencing done using either Sanger sequencing, Illumina sequencing, or nanopore sequencing (Nanshan Chen, 2020).

Supportive laboratory investigation results are as per *The Lancet* article dated January 29, 2020 about the clinical features of first 99 patients are as follows: decreased haemoglobin in 51%, leucocytosis in 24%, neutrophilia in 38%, lymphopenia in 35%, raised erythrocyte sedimentation rate in 85%, increased C-reactive protein in 86%, raised serum ferritin in 63%, raised interleukin-6 in 51%, D-dimer increase in 36%, hypoalbuminemia in 98%, elevated liver enzymes in 35% and increased lactate dehydrogenase in 76%. On imaging studies, 75% had bilateral pneumonia and 14% had multiple mottling and ground-glass opacity.(Nanshan Chen, 2020)

Treatment at present :

This section is based on the reported treatments in the published articles and online reports of leading journals. The cornerstone of treatment is supportive. Patients should be treated in isolation. Medical history, exposure history, comorbidities, symptoms and physical findings should be recorded. In sick patients, Glasgow Coma Scale, Sequential Organ Failure Assessment (SOFA) Score and Acute Physiology and Chronic Health Evaluation II (APACHE II) Scores should be recorded at ICU admission and serially. Observe the patients for acute respiratory distress syndrome, renal failure and cardiac injury as these are cardinal events that influence the outcome. ARDS is diagnosed as per 2012 Berlin definition (Ranieri VM, 2012). Acute kidney injury diagnosed as per 2012 Acute Kidney Injury Work Group recommendations (KDIGO, 2012). Cardiac injury should be looked for using serum biomarkers such as troponin I and lactate dehydrogenase, serial electrocardiograms and echocardiography. Total WBC count and differential count should be done every 2 days as serially increasing total count, increasing neutrophil

count and decreasing lymphocyte counts suggest poor prognosis. Raised D-dimer, elevated lactic dehydrogenase levels, elevated liver enzymes, elevated creatine kinase, deranged renal function also should be looked for as they indicate worsening. As worsening generally develops in the second week, patients should be more stringently observed during the second week.

Scientifically proven antiviral treatment or specific vaccines are not available at present. Case reports of successful use of antiviral agents along with protease inhibitors have been described. Antiviral agents that have been used include oseltamivir (75 mg every 12 h, orally), ganciclovir (0.25 g every 12 h, intravenously), in combination with protease inhibitors: lopinavir and ritonavir tablets (500 mg twice daily, orally). The duration of antiviral treatment is 14 days. Antibiotics such as cephalosporins, quinolones, carbapenems, tigecycline, linezolid against methicillin-resistant *Staphylococcus aureus* and antifungal drugs are given for secondary bacterial infections. Steroids (methylprednisolone 1–2 mg/kg per day) are recommended for patients with ARDS, for as short a duration of treatment as possible. Non-invasive or invasive mechanical ventilation may be needed if the oxygenation levels are not maintained. Dialysis may be needed if there is associated renal failure.

Future prospects of treatment :

As the event has been classified as a global health emergency, transparency as well as data sharing are essential for a successful outcome. The current trend has shown leading journals publishing articles with real-time peer review, freely available to all. Genomes sequenced so far has been made available to researchers, which allows an international, collaborative effort to evaluate and scrutinize the data. Governmental agencies and private companies are working against time to develop an effective vaccine. Coalition for Epidemic Preparedness Innovations (CEPI), a non-profit formed in 2016 announced on 23 January, 2020 that it will provide 12.5 million dollars to 3 companies (Moderna, Inovio and University of Queensland) to develop and test SARS-CoV2 vaccines faster than any previous effort (Cohen, 2020). Vaccines are expected to be available for phase 1 trials soon. Virologists in Australia have successfully grown the virus in vitro, improving the chances of rapid vaccine and antiviral drug development. Moving forward, it is imperative that the healthcare community and general public work collaboratively to overcome the SARS-CoV2 epidemic rapidly progressing to become a pandemic.

What is being done now to control the disease?

The Chinese government has taken significant steps to contain the disease. A public health emergency has been declared, entire Hubei Province has been declared as *cordon sanitaire* (a quarantined area preventing anyone from leaving) and vehicular transport have been banned. The effectiveness and its impact on human rights of *cordon sanitaire* is controversial. As a reported number of 5 million people have already left the area prior to the enforcement of quarantine of the entire region, the effectiveness of this method remains to be determined (Shih G, 2020). In addition, as animal reservoir of the virus is not yet known, further spill over to human beings cannot be ruled out. The SARS-CoV2 epidemic has been declared as Public Health Emergency of International Concern (PHEIC) by the WHO on 30-1-2020 due to sustained disease transmission in China and human-to-human transmission has been reported in Germany, Japan, Vietnam and USA. Flights to China are being stopped and the borders with neighbouring countries are being closed. But how long these measures may have to be continued and how long it can be maintained is not yet known. Different countries including India have repatriated their nationals from the epidemic zone including Wuhan. Once repatriated, these individuals are being quarantined for 14 days. Entry of the virus into low income countries which may not have the resources for preventive measures is a global concern.

In India, the Ministry of Health and Family Welfare has issued guidance statements for the surveillance of cases and is developing laboratory testing capability in case of spread of the disease. The government of Kerala had declared emergency status which was subsequently revoked following no new cases.

In Indian response : The Government of India has made 52 more labs functional across India in wake of 33 confirm cases of Coronavirus in India.

Practical Considerations :

Physicians encountering patients with new onset acute respiratory or flu like syndromes must get a detailed travel history that includes a personal travel history and exposure to individuals who might have returned from China. All high risk cases, at this time, should be quarantined and admitted to designated hospitals (usually medical college hospitals, large government or private hospitals) and appropriate infection prevention and treatment protocols must be initiated. (Guidelines on Clinical management of severe acute respiratory illness (SARI) in, 2020). In busy out-patient departments, signage for infection control and triage must be instituted in order to prevent person to

person transmission. Physicians, and other healthcare workers, including nurses, ambulance workers and staff must follow universal infection control and hand hygiene precautions. (WHO)

Future projections :

The emergence of SARS-CoV2 has raised concerns and fears that it is the beginning of a global pandemic due to a highly contagious novel virus with a significant mortality and morbidity. The exponential rise in the number of new cases, suspected cases and deaths has led the WHO to declare the epidemic as a public health emergency of international concern (PHEIC) as of January 30, 2020. Inherently RNA viruses have a higher mutation rate, though coronavirus has a lower than normal mutation rate than other RNA viruses due to the presence of a genome-coded error-detection capable exonuclease. Nevertheless, the exponential increase in new cases, deaths, reported transmissions while asymptomatic, and widening geographic spread are elements which should elevate the level of significance.

Along with this, it is important to understand the cultural context and significance to timing. The entire event is unfolding amid the largest annual human migration event on Earth, the Chinese New Year also known as Chunyun. Over the 40 days long Chunyun period, roughly 400 million Chinese workers and students travel home to have reunion dinner with their families on the new year eve and then back resulting in 3 billion passenger-travels. The Chinese authorities have taken unprecedented measures to contain the spread of the virus by restricting travel to affected areas, by extending the new year vacations and by closing down public spaces and work spaces.

In a manuscript submitted to *The Lancet*, a team of investigators used a SEIR (Susceptible, Exposed, Infected and Resistant) model with an assumed R0 of 0.5, 0.25 and 0.125 predicted that the estimated numbers of cumulative cases would reach the peak on 3rd, 4th and 5th of February, 2020, which were 11,116, 11,373, 11,966, respectively, in Chinese Mainland. (Huwang Wang). Another team of researchers have estimated the reproduction number (R0) based on number of confirmed cases on January 23, 2020 as 2.90 (95%CI: 2.32-3.63) using exponential growth model and 2.92 (95%CI: 2.28-3.67) using maximum likelihood model for future projections. (Tao Liu, 2020). As per the WHO situation report dated February 8, 2020 the cumulated figures were 34,886 confirmed cases, 6101 severe cases and 723 deaths in the Mainland China. The majority of the cases have been restricted to China.

Will these preventative measures succeed? Will the virus become an endemic that spreads at lower rates of transmission much like Chikungunya, Dengue, and others? Or will the event evolve into a global pandemic similar swine flu which occurred in 2009, going on to kill more than 200,000? We will be cautiously optimistic, while working collaboratively to prevent transmission and treat those infected.

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Conflict of Interest : None

REFERENCES

- 1 WHO News — *Bull World Health Organ* 2003; **81(5)**: 384.
- 2 Zaki AM, Boheemen SV, Bestebroer TM, Osterhaus AD, Fouchier RA — Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia. *New England Journal of Medicine* 2012; **367(19)**: 1814-20.
- 3 Lu R, Zhao X, Li J, Niu P, Yang B, Wu H — Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet* 2020; [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8).
- 4 Paraskevis D, Kostaki E, Magiorkinis G, Panayiotakopoulos G, Sourvinos G, Tsiodras S — Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the

FAQs :

(1) Does Vaccination against Pneumonia and Influenzae protect against Coronavirus infection?

No.

(2) Is it safe to receive a package /article made in China ?

Yes absolutely safe .Virus survive only for 3 hr in vitro.

(3) Does antibiotics effective in coronavirus infection?

No. it is viral infection, antibiotics not effective

(4) Who are more Susceptible ?

All age group may be affected , but in older , children and in persons with comorbid conditions morbidity and mortality higher .

(5) Can Pets at Home can spread Corona infection ?

At present no such evidence . But it is good practice to wash hands properly after handling pets.

(6) Can Coronavirus can spread by faeces ?

Yes like other coronavirus it can be present in Faeces. So after using toilet, after changing diaper hands should be properly cleaned.

(7) Does corona Virus infection transmitted by mosquito ?

No such evidence till now.

(8) Any thing that should not Do

Smoking, taking multiple antibiotics , wearing multiple masks

PREVENTIVE MEASURES

- Keeping a distance of at least one metre from persons showing symptoms remain particularly important for all travellers.
- Perform hand hygiene frequently, particularly after contact with respiratory secretions. Hand hygiene includes either cleaning hands with soap and water or with an alcohol-based hand rub.
- Cover your nose and mouth with a flexed elbow or paper tissue when coughing or sneezing and disposing immediately of the tissue and performing hand hygiene;
- Refrain from touching mouth and nose;
- A medical mask is not required if exhibiting no symptoms, as there is no evidence that wearing a mask – of any type – protects non-sick persons.

hypothesis of emergence as a result of a recent recombination event. *Infection, Genetics and Evolution* 2020; **79**: 104212.

- 5 Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y — Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020;<https://doi.org/10.1016/>

RESPONSE FROM INTERNATIONAL COMMUNITY

- The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020.
- Since WHO declaration of a public health emergency of international concern in relation to COVID-19, and as of 6th march 2020, 88 countries have been affected as per WHO report. WHO declared it an Pandemic on 12th March, 2020.
- UN, Humanitarian Chief Mark Lowcock released US\$15 million from the Central Emergency Response Fund (CERF) to help global efforts to contain the COVID-19 virus on March, 2020.
- WHO has shipped nearly half a million sets of personal protective equipment to 47 countries, but the global supply is rapidly depleting. To meet rising global demand, WHO estimates that industry must increase manufacturing by 40 per cent.
- The international community has asked for US\$675 million to help protect states with weaker health systems as part of its Strategic Preparedness and Response Plan.
- All Journal articles on COVID 19 to be made open access.
- Entire Cities and Regions in lockdown. International travel ban for affected regions.
- Many factories closed; conferences & sports events cancelled.

- S0140-6736(20)30183-5.
- 6 Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y — Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *New England Journal of Medicine* 2020;DOI: 10.1056/NEJMoa2001316.
 - 7 Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y — Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet* 2020;https://doi.org/10.1016/S0140-6736(20)30211-7.
 - 8 Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X — CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology* 2020; 200230.
 - 9 Xiaobo Yang, Yuan Yu, Jiqian Xu, Huaqing, Shu Jia'an, Xia Yongran, *et al* — Clinical Course and Outcomes of Critically Ill Patients of 2019 Novel Coronavirus pneumonia. *The Lancet* Manuscript number THELANCET-D-20-00897.
 - 10 Ping An, Hongbin Chen, Xiaoda Jiang, Juan Su, Yong Xiao, Yijuan Ding, *et al* — Clinical features of 2019 novel coronavirus pneumonia presented gastrointestinal symptoms but without fever onset. The Lancet manuscript number. *The Lancet-D-20-00863*. Under consideration.
 - 11 Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al* — Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *Jama*. 2020Jul; *JAMA*. doi:10.1001/jama.2020.1585 Published online February 7, 2020.
 - 12 Walker LJ. 2019-nCoV acute respiratory disease, Australia - Epidemiology Report 1 (Reporting week 26 January – 1 February 2020). *Communicable Diseases Intelligence* 2020Jun;44.
 - 13 Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, *et al* — Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012; **307(23)**: 2526-33. doi: 10.1001/jama.2012.5669.
 - 14 Kellum JA, Lameire N — Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Critical Care* 2013; **17(1)**: 204.
 - 15 Cohen J — Scientists are moving at record speed to create new coronavirus vaccines—but they may come too late.https://www.sciencemag.org/news/2020/01/scientists-are-moving-record-speed-create-new-coronavirus-vaccines-they-may-come-too. accessed on 08-02-2020.
 - 16 Huwen Wang, Zezhou Wang, Yinqiao Dong, Ruijie Chang, Chen Xu, Xiaoyue Yu, *et al* — Estimating the number of 2019 novel Coronavirus cases in Chinese Mainland. Manuscript under consideration Manuscript Number *The Lancet-D-20-00694*.
 - 17 Tao Liu, Jianxiong Hu, Min Kang, Lifeng Lin, Haojie Zhong, Jianpeng Xiao, *et al* — Transmission dynamics of 2019 novel coronavirus (2019-nCoV). Manuscript under consideration. *The Lancet-D-20-00553*.
 - 18 Wong MC, JavornikCregeen SJ, Ajami NJ, Petrosino JF — Evidence of recombination in coronaviruses implicating pangolin origins of nCoV-2019. bioRxiv 2020.02.07.939207 (2020) doi:10.1101/2020.02.07.939207.

USE OF MASKS

INDICATIONS

- (a) **Healthy workers or caretakers who are coming in contact with proven or suspected patients.**
- (b) **Any persons who are suffering from Cough and Cold**
- (c) **Otherwise healthy persons should not use Masks**
- (d) **Use of Mask is effective if only associated with proper handwashing with alcohol based handrub or soap with water.**

HOW to USE

- (a) **Wash hand properly before putting masks**
- (b) **Cover mouth and nose with mash in a fashion that there should be no gap between mask and skin.**
- (c) **Avoid touching mask while using particularly front side.**
- (d) **Identify proper side of masks- front , back , top – buttomans sides. Observe any holes in Mask.**
- (e) **During removing mask remove from back , immediately discard in bin , clean hands with alcohol based rub or soap water.**
- (f) **Do not reuse masks.**

FUTURE RESEARCH

- **Gilead's remdesivir, an intravenous treatment, has already been used to treat one infected patient in the U.S. and will soon be deployed in a pair of large, late-stage studies in Asia. (Stage 3)**
- **mRNA-1273, a vaccine candidate identified just 42 days after the novel coronavirus was sequenced. (still in phase 1)**
- **An intranasal Covid-19 vaccine is being developed by US-based clinical-stage biopharmaceutical company, Altimmune**
- **The National Medical Products Administration of China has approved the use of Favilavir, an anti-viral drug, as a treatment for coronavirus.**
- **Indian Council of Medical Research (ICMR) got approval from the Drug Controller General of India (DCGI) to use Lopinavir & Ritonavir in Corona virus infection if it turn into a Public Health Emergency in India.**