



CORONAVIRUS RESEARCH: KEYS TO DIAGNOSIS, TREATMENT, PREVENTION AND VACCINATION OF SARS

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ABSTRACT

The novel corona virus disease has been rapidly spreading across the world, which made world health organization to declare it as pandemic. The name indicates because it has been never seen before and corona because it looks like the corona of sun. It's basically a severe acute respiratory syndrome. A zoonotic disease originated in bats initially and then got transmitted to humans through unknown animals for the first time in wuhan, China. It is transmitted by inhalation or contact with infected droplets. The incubation period ranges from 2-14 days. The severity of disease may lead to pneumonia, acute respiratory distress syndrome and multi-organ dysfunction. The symptoms of disease are not very distinctive and include fever, cough, sore throat, breathlessness, fatigue, etc. Thus easy and early diagnosis of disease is difficult. Vulnerability of the disease perhaps seen in mostly elderly, infants and once with acute respiratory disease. Previously different corona viruses have emerged from time to time. The four corona viruses [HcoV-229E, Hco...] mainly associated with mild respiratory illness. Since these are zoonotic disease. They are mainly caused by the host bat. But the intermediate animals for SARS like corona virus are found to be masked palm civet cats and racoon dogs. The disease has become a fatal case in the world because no substantive treatment has yet been found to treat or prevent the disease Scientists all over the world are engaged in finding the solution to this pandemic. All they can do is rely on quarantine, isolation, infection control measures to prevent disease spread and on supportive care for those who become ill. But lack the specific antiviral agents to treat the infected and to optimally decrease viral spreading and subsequent transmission.

Keywords: Corona virus, COVID-19, MERS-CoV, SARS-CoV, Wuhan.

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INTRODUCTION :

The 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as it is now called, is rapidly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world [1]. Till 05/ 03/2020 approximate 96,000 cases of coronavirus disease 2019 (COVID-19) and 3300 deaths have been reported [2]. India has reported 29 cases till date. Fortunately so far, children have been infrequently affected with no deaths. But the future course of this virus is unknown. This article gives a bird's eye view about this new virus. Since knowledge about this virus is rapidly evolving, readers are urged to update themselves regularly.

Evolution of coronavirus :

Corona virus is considered as a fast evolving virus, as the two novel viruses [i.e. SARS and MERS] of same family emerged within a period of 10 years.

An evolutionary prerequisite is the ability to synchronize diversity to allow the fitness selection. Being an RNA virus, coronaviruses rely on RNA-dependent RNA polymerase (RdRp) to replicate the virus genome. An intrinsic error rate of RdRp, in the order of magnitude of 1×10^{-6} mutation per site per replication [3,4], is a continuous source of point mutations for the replicating viral genome. The mutations at critical sites might affect biological properties by accumulation of these points. As for comparison, the well-known stable virus from the family *Herpesviridae*, which depends on DNA polymerase to replicate its viral genome, has an error rate of about 1×10^{-8} [5]. On the other hand, a typical example of high mutation rate is the family *Retroviridae*, which utilizes reverse transcriptase that has an error rate in the range of 1×10^{-4} to 1×10^{-5} [6]. During the process of virus replication, the coronaviruses can be regarded as middle-ranking in terms of the ability to

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generate point mutations in viral genome. The Point mutation alone is not sufficient to create a novel virus such as SARS-CoV, MERS-CoV. Coronavirus can earn a genomic fragment of hundreds or thousands base-pair long from another coronavirus strain when they are co-infecting the same host. This process is said to be recombination, it is more essential than point mutations for viruses to expand or switch ecological niches [7]. Corona viruses are found in distinct species of animal [8]. Recombination between these species is similar but different viruses can create novel strains with the ability to cross species barrier. While coronaviruses can acquire fragments of new genome through the process of recombination, their ability to acquire a big trunk of genome is as worse as influenza viruses that comply segmented genomes, which make the exchange of an entire segment of genome possible. The wide distribution of coronaviruses in distinct avian and mammalian species poses a threat to humans. A novel coronavirus along with the ability to infect humans can be encompassed by recombination among animal or avian virus strains.

History and Origin:

First case of corona virus was notified as cold in 1960. According to the Canadian study 2001, approximately 500 patients were identified as Flu-like system. 17-18 cases of them were confirmed as infected with corona virus strain by polymerase chain reaction. Till 2002, Covid19 treated as simple non fatal virus. In 2003, various reports published with the proofs of spreading the corona to many countries such as United States America, Hong Kong, Singapore, Thailand, Vietnam and in Taiwan. Several case of severe acute respiratory syndrome caused by corona and their mortally more than 1000 patient was reported in 2003. This was the black year for microbiologist. When microbiologist was started focus to understand these problems. After a deep exercise they conclude and understand the pathogenesis of disease and discovered as corona virus. But till total 8096 patient was confirmed as infected with corona virus. So in 2004, World health organization and centers for disease control and prevention declared as "state emergency". Another study report of Hong Kong was confirmed 50 patient of severe acute respiratory syndrome while 30 of them were confirmed as corona virus infected. In 2012, Saudi Arabian reports were presented several infected patient and deaths [9-12]. COVID-19 was first identified and isolated from pneumonia patient belongs to Wuhan, china [13-14].

Bats as an ancestor of emerging virus:

The SARS-CoV might have originated from bats did not come as a surprise. Before SARS, there was at least once in a decade a virus linked to bats had emerged to infect humans which includes Marburg virus causing haemorrhagic fever in 1967, In 1976, Ebola virus causing haemorrhagic fever, In 1994, Hendra virus causing severe pneumonia, and Nipah virus causing neurological and respiratory diseases in 1998. Bats carry numerous special features making them an ancestor or source of emerging viruses [15]. It was originated about 50-52 million year ago with wee-wee

changes till recent time. It has more than 1,000 species and no, of species can exist in huge colony sharing the same habit. fts together large colony size of more than 200,000 and the long fly range of hundreds to thousands kilometers allow frequent recombination between virus strains. As they are asymptomatic in nature, they often harbor multiple viruses for a long period. ftese together with their long life span (3.5× longer that mammals of similar size) allow persistence and spreading of newly emerged virus strains.

Bats and SARS CoV:

The novel Covid 19 has been detected from a number of bat species. The SARS-CoV which is the closest virus to the corona viruses was found in horseshoe bats [16]. By using BT-PCR technique, a high seroprevalence was found and anal swabs were positive among horseshoe bats. It is compliancated to isolate the virus. Ftese bat ie SARS-Like CoV distributes 87-92% overall sequence homology with human and civet SARS-CoV, i.e., refusing a 29-nt site considered to be a civet's signature and early human cases. fe key difference between bat SARS-Like CoV and human SARS-CoV lies in the spike. The spike protein posseses two domains designed as S1 and S2. Among them S1 is responsible for attachment to the host cell surface receptor ACE2. S2 is responsible for fusing with the host cell membrane. The S2 of bat SARS-Like CoV is about 96% identical to that of SARS-CoV recommending both viruses share a similar mechanism of membrane fusion. In contrast, the sequence conformity between S1 proteins of bat SARS-Like CoV and SARS-CoV is low. While bat SARS like CoV is likely to be the ancestor of SARS-CoV, there is still an important genetic gap at S1 which needs to be filled up, probably, by recombination. There is no SARS-CoV has been identified in bats and bats do not have the appropriate receptor (ACE2) for SARS-CoV at longer extent [17]. At present study, It is little but known about where, when and in which animal species had this recombination occurred.

Microbiology:

Corona virus is spherical or pleomorphic, single stranded, enveloped RNA and covered with club shaped glycoprotein. Corona viruses are four sub types such as alpha, beta, gamma and delta corona virus. Each of sub type corona viruses has many serotypes. Some of them were affect human of other affected animals such as pigs, birds, cats, mice and dogs [18-22].

Epidemiology and Pathogenesis:

All ages are susceptible. Infection is transmitted through large droplets generated during coughing and sneezing by symptomatic patients but can also occurs from asymptomatic people and before onset of symptoms [23]. Studies have shown higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people [24] can be infectious for as long as the symptoms last and even on clinical recovery. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected 11 other people while staying in a resort in the disinfectants like sodium hypochlorite, hydrogen peroxide etc. [25]. Infection is acquired either by inhalation of

these droplets or touching surfaces contaminated by them or then touching the nose, mouth and eyes. Contaminated by them and then touching the nose, mouth and eyes. The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/feco-oral route is also hypothesized. These infected droplets can expand 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed in less than a minute by common disinfectants like sodium hypochlorite, hydrogen peroxide etc. The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/ feco-oral route is also hypothesized.

Mode of Spreading:

Peoples can get the infection through close contact with a person who has symptoms from the virus includes cough and sneezing. Generally corona virus was spread via airborne zoonotic droplets. Virus was replicated in ciliated epithelium that caused cellular damage and infection at infection site. According to a study published in 2019, Angiotensin converting enzyme 2 (ACE.2), a membrane exo-peptidase in the receptor used by corona virus in entry to human cells. Virus transmission routes were represented in fig. 1 and 2.

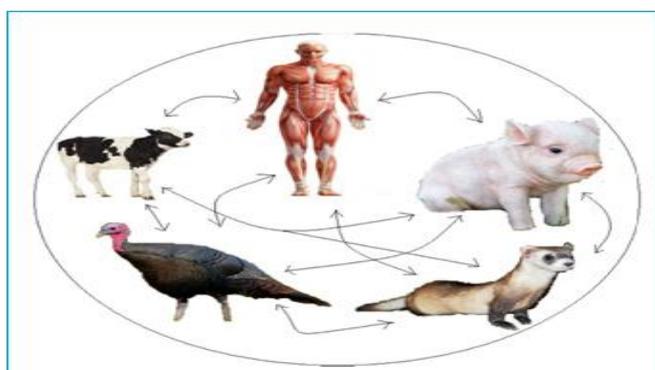


Figure 1: Transmission of corona virus via airborne droplets.

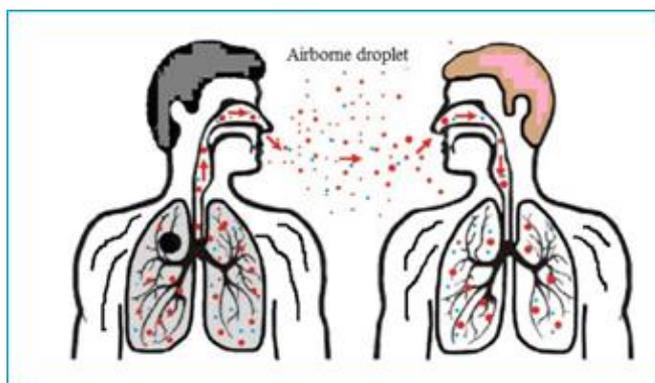


Figure 2: Corona virus targets.

Clinical Features:

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common

clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset of patients, by the end of the first week the disease can progress to pneumonia, respiratory failure and death. This progression is associated with extreme rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF α [26]. The median time from onset of symptoms to dyspnea was 5 d, hospitalization 7 d and acute respiratory distress syndrome (ARDS) 8. The need for intensive care admission was in 25–30% of affected patients in published series. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2nd or 3rd wk. The median duration of hospital stay in those who recovered was 10 d. Adverse outcomes and death are more common in the elderly and those with underlying co-morbidities (50–75% of fatal cases). Fatality rate in hospitalized adult patients ranged from 4 to 11%. The overall case fatality rate is estimated to range between 2 and 3% [27].

Diagnosis :

Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/sputum/ endotracheal aspirates and bronchoalveolar cleavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. Commercial tests are also not available at present. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India or the National Institute of Virology in Pune. As the epidemic progresses, commercial tests will become available. The chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease.

Treatment:

Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extra corporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if co-infections are suspected or proven. The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS [28,29]. Detailed guidelines for critical care management for COVID-19 have been published by the WHO [30]. There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin,

lopinavir-ritonavir have been used based on the experience with SARS and MERS. In a historical control study in patients with SARS, patients treated with lopinavir-ritonavir with ribavirin had better outcomes as compared to those given ribavirin alone.

Prevention :

The healthcare workers have the greatest risk in COVID-19 due to transmission. In the SARS outbreak of 2002, 21% of those affected were healthcare workers [31]. Till date, almost 1500 healthcare workers in China have been infected with 6 deaths. The doctor who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. While COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control measures recommended are those for category the agents (cholera, plague). Patients should be placed in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination.

Management and Vaccination:

There is no special vaccine for this yet. Only supportive therapy is the treatment strategy followed by health professionals. Supportive therapy includes administration of antipyretic and analgesic, maintenance of hydration, mechanical ventilation as respiratory support and uses of antibiotic in bacterial infections. Some research studies claimed that ribavirin and interferon alpha have offered synergetic effect in early stage. While other studies reported mycophenolic acid as monotherapy. Still health professionals were not fully satisfied with any therapy so further clinical research needed.

CONCLUSION:

Corona virus was spreading human to human to transmission by close contact via airborne droplets generating by coughing, sneezing, kissing and smooching. So avoid these activities with infected partners and family members. Corona virus may transmit through pet animals such as dog, cat, pig, cow, turkeys. So avoid contact and separate them if observed any infection activities like diarrhea, cold, fever. As per WHO and ECDC guideline avoid the contact with sick person and also avoid the market or public place as per possible. The anti corona vaccines are not available to prevent or treatment but some sufficing therapy work. Future re- search needed to fight with corona virus. Till only 'Distance is rescue'.

REFERENCE:

1] Wang C, Horby PW, Hayden FG and Gao GF. A novel coronavirus outbreak of global health concern. *Lancet*. 2020. [https://doi.org/10.1016/S0140-6736\(20\)30185-9](https://doi.org/10.1016/S0140-6736(20)30185-9).
 2] DD, Whitley RJ, Hayden FG. *Clinical Virology*, 4th ed. Washington: ASM Press; 2016. Coronavirus Outbreak. Available at: <https://www.worldometers.info/coronavirus/>. Accessed 23 Feb 2020.]

3] Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003;8:S9-14.
 4] Middle East Respiratory Syndrome Coronavirus. Available at: <https://www.who.int/emergencies/mers-cov/en/>. Accessed 16 Feb 2020.
 5] World Health Organization. Situation reports. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 22 Feb 2020.
 6] H, Zhao Y, Zhang J, *et al*. Date of origin of the SARS coronavirus strains. *BMC Infect Dis* 2004;4:3.
 7] Vega VB, Ruan Y, Liu J, *et al*. In 2003, the mutational dynamics of the SARS coronavirus in cell culture as well as human populations have been isolated. *BMC Infect Dis* 2004; 4:32.
 8] Centers for Disease Control and Prevention (CDC). Update: Outbreak of severe acute respiratory syndrome-worldwide, 2003. *MMWR Morb Mortal Wkly Rep*. 2003;52(12):241-6.
 9] World Health Organization. Coronavirus never before seen in humans is the cause of SARS- update 31. Geneva: The Organization; 2003.
 10] World Health Organization. Situation reports. Available at: http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed 14 feb 2020.
 11] Peiris JS, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, *et al*. *Lancet*. 2003;361:1319-25.
 12] World Health Organization. WHO Statement Regarding Cluster of Pneumonia Cases in Wuhan, China Geneva 2020 [updated 9 January 2020 and 14 January 2020]. Available from: <https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumoniacases-in-wuhan-china>.
 13] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, *et al*. A Novel Covid19 from Patients with Pneumonia in China, 2019. 24 January 2020. *New England Journal of Medicine*.
 14] Mith I, Wang LF. Bats and their virome: an important source of originating viruses capable of infecting human beings. *Curr Opin Virol* 2013;3:84-91.
 15] Balboni A, Battilani M, Prosperi S. fte SARS-like coronaviruses: the role of bats and evolutionary relationships with SARS coronavirus. *New Microbiol* 2012;35:1-16.
 16] Ren W, Qu X, Li W, *et al*. Coolness in receptor usage between severe acute respiratory syndrome (SARS) coronavirus and SARS-like coronavirus of bat origin. *J Virol* 2008;82:1899-907.
 17] Mailles A, Blanckaert K, Chaud P, van der Werf S, Lina B, Caro V, *et al*. First cases of Middle East respiratory syndrome Coronavirus (MERS-CoV) infections in France, investigations and implications for the prevention of human-to-human transmission, *Euro Surveill*. 2013;18:20502.
 18] Buchholz U, Müller MA, Nitsche A, Sanewski A, Wevering N, Bauer-Balci T, *et al*. Contact investigation of human's case novel coronavirus infection treated in a German hospital, October-November 2012. *Euro Surveill*. 2013;18:20406.
 19] Saif LJ. Animal coronaviruses: *Rev Sci Tech*. 2004;23:643-60.

- 20] Gwaltney JM Jr. Virology and immunology of the common cold. *Rhinology*. 1985;23:265.
- 21] Tyrrell DAJ, Myint SH. Chapter 60: Coronaviruses. In Barson 1 S, editor. *Medical microbiology*. 4th edition. Galveston: University of Texas Medical Branch at Galveston; 1996.
- 22] World Health Organization. Situation reports. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 22 Feb 2020.
- 23] Rothe C, Schunk M, Sothmann P, *et al*. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001468>.
- 24] Zou L, Ruan F, Huang M, *et al*. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001737>.
- 25] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. *J Hosp Infect*. 2020 Feb 6. pii: S0195-6701(20)30046-3.
- 26] De Souza Luna LK of Heisser V, Regamey N, Panning M, Drexler JF, Mulangu S, *et al*. *J Clin Microbiol*. 2007;45:1049-52.
- 27] Woo .PC, Lau SK, Huang Y, Yuen KY. Coronavirus diversity, phylogeny and interspecies jumping. *Exp Biol Med (Maywood)*. 2009;234:1117-27.
- 28] Letko M, Munster V. Functional valuation of cell entry and receptor usage for lineage B β -coronaviruses, including 2019.
- 29] Coronavirus Outbreak. Available at: <https://www.worldometers.info/coronavirus/>. Accessed 23 Feb 2020.
- 30] Chen N, Zhou M, Dong X, *et al*. Epidemiological and clinical features of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507-13.
- 31] WHO. Clinical management of SARS infection when novel coronavirus [nCoV] infection is suspected. Available at: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novelcoronavirus-\[ncov\]-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novelcoronavirus-[ncov]-infection-is-suspected). Accessed 9 Feb 2020.