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COVID-19: Current Status and Management

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Abstract: ***The 2019 novel corona virus disease (COVID-19; previously known as 2019-nCoV) outbreak that originated from Wuhan, Hubei province, China, at the end of 2019 was declared a public health emergency of international concern on Jan 30, 2020, by WHO. With more than millions of confirmed cases around the world and claiming thousands of lives, COVID -19 has emerged as a pandemic that had affected more than 200 countries and territories around the world (till 07/04/2020). Even with the prevention plans in place, new cases continue to be reported everyday and death toll continue to rise. The disease is caused by a supposedly mutated strain of the corona virus family.***

Keywords: COVID-19, 2019-nCoV, Wuhan, China

1. Introduction

As a newly appearing infectious disease, COVID-19 garnered not only great research interest but evoked fear in the mind of people akin to plague outbreak.

On December 31, 2019 China reported an epidemic of diseases of respiratory origin from Wuhan in Hubei province. The cause was not known with surety; hence initially it was called as 'Pneumonia of unknown etiology", but it was thought to have originated from a wet market in Wuhan. Although it is speculated by many sources that the cases were reported way before the Chinese authorities brought them to light.

Intense epidemiological investigations were carried out by the China Centre for Disease Control and Prevention and other authorities and subsequently the cause was discovered to be a corona virus, more commonly known as novel corona virus or Covid-19.

In the past twenty years, two additional corona virus epidemics have occurred. SARS-CoV provoked a large-scale epidemic beginning in China and involving two dozen countries with approximately 8000 cases and 800 deaths, and the MERS-CoV that began in Saudi Arabia and has approximately 2,500 cases and 800 deaths and still occurring as sporadic cases. And hence the Corona Viruses have become major pathogens which cause respiratory illnesses

Corona viruses cause respiratory and intestinal infections in animals and humans[1]. They were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS) in 2002 and 2003 in Guangdong province, China[2–5], as the corona viruses that circulated before that time in humans mostly caused mild infections in immunocompetent people. Today it had caused havoc across the globe, the new cases being identified everyday globally are in millions, deaths tolls are in thousands.

Corona Viruses: General Characteristics

Corona viruses are positive-stranded RNA viruses with a crown-like appearance under an electron microscope (*coronam* is the Latin term for crown) due to the presence of numerous spike glycoproteins on the envelope. The subfamily *Orthocoronavirinae* of the *Coronaviridae* family (order *Nidovirales*) classifies into four genera of Corona viruses: *Alpha corona virus*, *Beta corona virus*, *Gamma corona virus*, and *Delta corona virus*. The former two genera primarily infect mammals, whereas the latter two predominantly infect birds. The Corona viruses have become the major pathogens of emerging respiratory disease outbreaks. These viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases such as MERS and SARS. Interestingly, these latter viruses have probably originated from bats and then moving into other mammalian hosts, the Himalayan palm civet for SARS-Corona viruses, and the dromedary camel for MERS- Corona viruses, before jumping to humans. The dynamics of SARS- Corona viruses-2 are currently unknown, but there is speculation that it also has an animal origin. The recent reports point out that chances are that the intermediate host in the Covid-19 outbreak are pangolins, bats etc.

In this corona viruses, the genomic structure is organized in a +ssRNA of approximately 30 kb in length and known to be the largest known RNA viruses. It belongs to the beta Corona viruses' category. It has round or elliptic and often pleomorphic form, and a diameter of approximately 60–140 nm. Like other Corona viruses, it is sensitive to ultraviolet rays and heat. Furthermore, these viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine.

In genetic terms, it have been proven that the genome of the new Corona viruse, isolated from a cluster-patient with atypical pneumonia after visiting Wuhan, had 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV. For this reason, the new virus was called SARS-CoV-2[6]. In a report by WHO, it was said that alignment of full length genome sequence of the COVID-19 virus with other available genomes of Beta coronaviruses showed the closest relationship was with the bat SARS-like corona virus strain RaTG13, identity 96%[3].

Transmission

As with other respiratory pathogens, including flu and rhinovirus, the transmission is believed to occur through respiratory droplets from coughing and sneezing. Aero-

sol transmission is also possible in case of protracted exposure to elevated aerosol concentrations in closed spaces. Analysis of data related to the spread of SARS-CoV-2 in China seems to indicate that close contact between individuals is necessary. The spread, in fact, is primarily limited to family members, healthcare professionals, and other close contacts. It can also occur via fomites during close contact with the infected fomite. Airborne transmission has not been reported so far and faecal oral route does not play an important role.

Other features

Based on data from the first cases in Wuhan and investigations conducted by the China CDC and local CDCs, the incubation time was thought to be within 3 to 7 days and up to 2 weeks as the longest time from infection to symptoms was 12.5 days (95% CI, 9.2 to 18). This data also showed that this novel epidemic doubled about every seven days, whereas the basic reproduction number (R0 - R naught) is 2.2. In other words, on average, each patient transmits the infection to an additional 2.2 individuals. Of note, estimations of the R0 of the SARS-CoV epidemic in 2002-2003 were approximately 3. According to WHO, the Case fatality rate of Covid-19 till now is around 4.8% while that of SARS was 14-15%.

Pathophysiology and virulence mechanisms of CoVs, and therefore also of SARS-CoV-2 have links to the function of the norspermidine sensor precursor (nsp) and structural proteins[6]. For instance, research underlined that nsp is able to block the host innate immune response. Among functions of structural proteins, the envelope has a crucial role in virus pathogenicity as it promotes viral assembly and release. According to a recent research, a spike mutation, which probably occurred in late November 2019, triggered jumping to humans[1]. In particular, comparing the Sars-Cov-2 gene sequence with that of Sars-CoV[7] it was observed that the transmembrane helical segments in the ORF1ab encoded 2 (nsp2) and nsp3 and found that position 723 presents a serine instead of a glycine residue, while the position 1010 is occupied by proline instead of isoleucine, key for explaining potential virulence.

How is Covid-19 different?

It was found that the SARS-CoV-2 S glycoprotein harbors a furin cleavage site at the boundary between the S_1/S_2 subunits, which is processed during biogenesis and sets this virus apart from SARS-CoV and SARS-related CoVs. Both SARS-CoV and SARS-CoV-2 are closely related and originated in bats, who most likely serve as reservoir host for these two viruses. It was identified the presence of an unexpected furin cleavage site at the S_1/S_2 boundary of SARS-CoV-2 S, which is cleaved during biosynthesis—a novel feature setting this virus apart from SARS-CoV and SARSr-CoVs. The 8a protein is present in SARS-CoV and absent in 2019-nCoV; the 8b protein is 84 amino acids in SARS-CoV, but longer in 2019-nCoV, with 121 amino acids; the 3b protein is 154 amino acids in SARS-CoV, but shorter in 2019-nCoV, with only 22 amino acids. This probably is cause of more infectious but less fatal than SARS AND MERS[6].

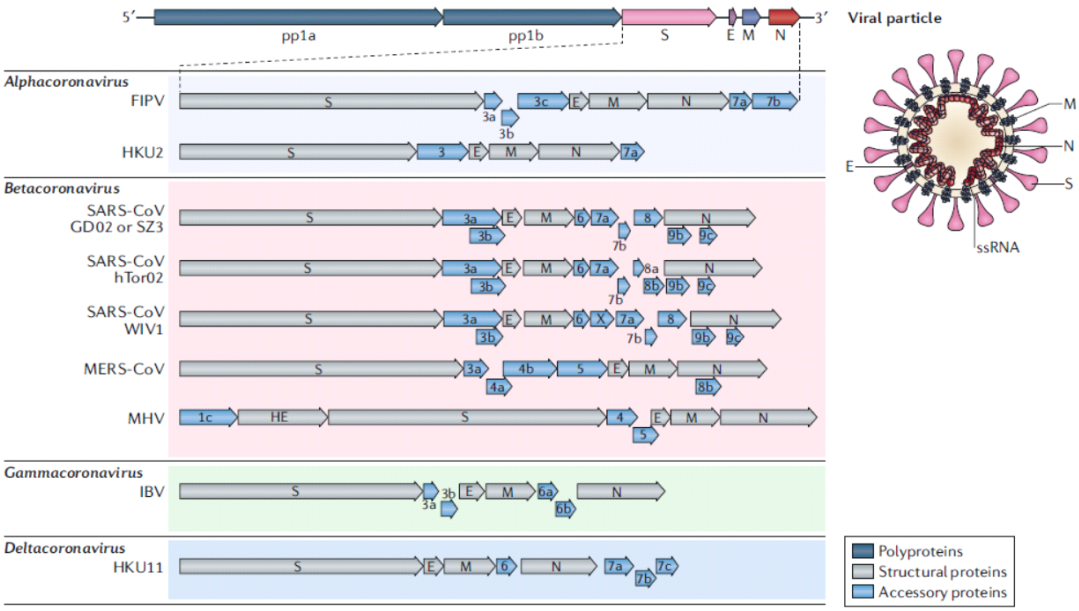

Figure: Comparison of Different Corona Viruses (From internet)

The genomes, genes and proteins of different corona viruses (Above figure)

Corona viruses form enveloped and spherical particles of 100–160 nm in diameter. They contain a positive- sense, single- stranded RNA (ssRNA) genome of 27–32 kb in size. The 5'-terminal two- thirds of the genome encodes a polyprotein, pp1ab, which is further cleaved into 16 nonstructural proteins that are involved in genome transcription and replication. The 3' terminus encodes structural proteins, including envelope glycoproteins spike (S), envelope (E), membrane (M) and nucleocapsid (N). In addition to the genes encoding structural proteins, there are accessory genes that are species-specific and dispensable for virus replication. Here, we compare prototypical and representative strains of four corona virus genera: feline infectious peritonitis virus (FIPV), *Rhinolophus* bat corona virus HKU2, severe acute respiratory syndrome corona virus (SARS- CoV) strains GD02 and SZ3 from humans infected during the early phase of the SARS

epidemic and from civets, respectively, SARS- CoV strain hTor02 from humans infected during the middle and late phases of the SARS epidemic, bat SARS- related corona virus (SARSr- CoV) strain WIV1, Middle East respiratory syndrome corona virus (MERS- CoV), mouse hepatitis virus (MHV), infectious bronchitis virus (IBV) and bulbul corona virus HKU11.

Characteristics of Covid-19

- The statics say that one person is enough to transmit the disease to thousands of individuals. Since the mode of transmission is aerosols, the virus is easily and quickly transmitted between people in close contact like family members, neighbors and staff taking care of the patients.
- The common clinical signs include dry cough, sneezing and fever but during the transition of weathers which is occurring in many parts of the world during flu and common cold are common so, it becomes difficult to differentiate.
- New COVID-19 is thought to be a mutant of SARS causing virus and so its mechanism of action, host invasion, pathogenicity etc is still to be elucidated which will take time.
- This virus can survive on fomites for a variable amount of time depending on the nature of the surface. If any person comes in contact of the surface during the time virus is viable, the chances are high that the person will get infected.
- The basic reproduction rate as estimated by some early works on the virus say that it is around 2.2 i.e one person infects 2.2 people. Chances are that there have been an increment in the rate but it is not cited in any of the works.
- There are high chances that this virus also possess the ability to have drift and maybe shift mutations.
- As it will take time to develop adequately good vaccine or drugs which works against it and it will continue to affect people around the world till then.
- The average incubation period determined by WHO is 2-14 days, which is short enough so that transmission can take place without the person noticing that one is sick.

Maintenance under current geo climatic conditions

It is an enveloped virus and like other enveloped viruses, is susceptible to disinfectants and heat and UV light. According to the data collected from Climate-Data.org about the climatic conditions of Wuhan (China), Milan (Italy), Île-de-France (France), Asgabat (Turkmenistan), Maleru (Lesotha) etc, it can be said that the virus requires both low temperature and high humidity for survival in the environment[8]. Lack of any one of the two could be detrimental to its survival.

Place	Avg. High Temp. (°C)	Avg. Low Temp. (°C)	Avg. Mean Temp. (°C)	Humidity (%)	Wind Speed (km/h)
Wuhan, China (December)	8	1	4	75	6
Mila, Italy (February)	10	1	5	79	5
Ile-de-France, France (March)	12	4	8	72	15
New York, U.S.A (March)	10	2	6	57	12
Madrid, Spain (March)	16	5	10	54	11
Tehran, Iran (February)	11	3	7	52	9
Lilanywe, Malawi (March)	25	18	21	-	-
Dushanbe, Tajikistan (March)	16	5	11	62	6
Freetown, Sierra Leone (March)	31	26	28	72	16
Asgabat, Turmenistan (March)	19	6	13	58	8
Maleru, Lesotha (March)	26	13	19	60	8
Moroni, Comoros (March)	32	29	28	82	10
Honiara, Solomon Islands (March)	31	23	27	85	6
Port Vila, Vanuatu (March)	31	25	28	82	11
Apia, Samoa (March)	31	24	28	84	10

It can be seen from the above table that the countries where there is recorded vast spread of Covid-19, there is a combination of high humidity and low temperature. The average time that these cities receive the sunlight during the mentioned months can also be a determining factor in the survival of the virus. While the countries where there have been no reports of the virus (several of them are landlocked) the combination does not exist. In most of the cases if there is a high humidity, the corresponding temperature is also high.

Is the lockdown help mitigate the situation?

It would seem like lockdowns across the globe may help in decreasing the number of cases but more often than not, there had been a simple but important observation that decreasing the transmission rate (achieved, for example, by more rapid quarantining of all exposed cases) does, as might be expected, reduce the size of an outbreak but may increase rather than decrease the duration of the outbreak. When some of the major consequences of an epidemic are indirect—such as closure of schools, restrictions on travel or trade or loss of tourism revenue—and reflect only the presence of disease rather than the absolute numbers of cases, then the increased duration represents a serious problem[9].

It is often unclear whether the latent period (time from exposure to becoming infectious) is longer or shorter than the incubation period (time to showing clinical symptoms or signs), yet this basic information is crucial when control efforts depend on detecting infection on the basis of clinical observation, as is the case for many epidemic diseases including influenza, severe acute respiratory syndrome (SARS) and FMD and maybe COVID-19.

2. Treatment

Till now there has been no confirmed treatment for the disease. The only way to treat the severe cases is ventilators and frequent blood transfusion so, the countries where the health care and infrastructure is not strong will find themselves in trouble.

There have been speculations that anti-malarial drug Hydroxychloroquine, anti-parasitic drug ivermectne and anti-viral drugs like Ritonavir and Lopinavir may prove effective in the treatment of COVID -19 but no health authority in the world has yet confirmed[10].

The only possible as well as agreed upon way of treatment seems to be the blood/plasma of the recovered patients. Reports say that the Chinese doctors used the plasma of recovered patients to treat the cases and American doctors are seeking permission from their health authorities to do the same. If this method turns out to be successful then, then a lot of lives around the globe can be saved.

3. Will this re-emerge?

COVID-19 is an emerging disease but is there a possibility that there will a re-emergence cycle? There have been no reports of latency in the coronaviridae family. The last outbreak that drew attention of the health authorities was MERS in the year 2012 and since then there have been no large scale outbreaks of respiratory diseases caused by corona viruses until now[11]. So it is very difficult to say whether COVID-19 will make another appearance in the near future.

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