

Historical Analysis and Scientific Overview of Coronaviruses

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Abstract: Corona viruses (CoVs), enveloped to be a strand RNA virus, which are described by the name due to its crown-like spike protein substances with bulbous surface projection. CoVs cause an assortment of illnesses in birds, animals like bats, pigs, snake, chickens, and extend to human. It is a type of respiratory tract diseases. The family Coronaviridae envelops an expansive range of animal and human infections, all portrayed by a particular morphology. Coronaviruses are probably circular in shape with outer membranes. Every molecule is encompassed by a halo or "crown" which refers to the bulbous distal parts of the membrane embedded glycoproteins. Before 2003 individuals from this family were accepted to cause just gentle respiratory sickness in people. But after 2003 the virus got derived themselves in different characteristic forms creating extreme intense respiratory infection (SARS-CoV). The later raise of MERS-CoV and now recent nCoV creating COVID-19 disease are creating more challenges to humans. This paper gives the overall knowledge about various coronaviruses from historical background to till date.

Keywords: Coronavirus, COVID-19, Epidemiology, MERS-CoV, SARS-CoV.

Introduction

CoVs are normal families of viruses that can affect human beings and other living creatures. In which there are various human infecting CoVs [1] which create mild to moderate respiratory tract diseases with the basic common cold symptoms.

In such series of viruses from the family includes the MERS (Middle East Respiratory Syndrome) [2], particularly found in Saudi Arabia and nearest regions. Then SARS (Severe Acute Respiratory Syndrome), seen primarily in China leads to highest risk of serious complications in human. Among various viruses, CoVs are an important cause of creating severe critical respiratory tract infections with 50% mortality rates in elderly people and immunity challenged patients.

People living with or caregiver for someone with a coronavirus infection are most at high risk of developing the infection themselves. Coronavirus transmission is mainly due to droplets transmission of saliva while coughing and

sneezing. Cases have been exported to Asian destination such as Thailand, Japan, and South Korea external icon. Patients have experienced fever, cough, shortness of breath and pneumonia. CoVs has crown like spikes [3] that protrude from their integral membrane proteins, like the sun's corona. Such viruses cause mild to severe illnesses of the respiratory tract, normally starts from the common cold to major diseases such as SARS [4].

Common symptoms of infection include throat pain, fever, cough, head ache, and breathing difficulties like shortness of breath. Serious cases can lead to pneumonia, kidney, lungs and vital organ failure or even death. At present in 2019 a novel coronavirus came in to picture creating more harassing infection to all types of people like SARS creating more death rate. As of April 2020, this epidemic had further spread to 25 other countries with 10 lakhs confirmed CoVs cases that includes more than 50,000 deaths.

History of CoVs

A few known CoVs are circulating in creatures that have not yet infected people. CoVs are enormous, encompassed, positive-stranded RNA viruses. They have the biggest genome among all RNA infections. CoVs are kinds of infections that ordinarily affect the respiratory tract of humans. The first coronavirus was discovered and diagnosed in 1937 from an infected [5] bird which has the potential to truly demolish the whole poultry stocks. These infections are responsible for somewhere in the range of 18 and 32 percent of basic cold symptoms. Throughout the most recent 70 years, researchers have discovered that CoVs can taint mice [6], rodents, hounds, cats, turkeys, ponies, pigs, and cows.

In an evaluation completed in Canada in 2001, among 500 patients gave influenza like symptoms. Biological analyses [1] indicated that 3.6% of these cases were exposed to HCoV-NL63 strain by polymerase chain response (PCR). Until 2002, CoVs infection was viewed as a generally basic, nonfatal infection. But in 2002-2003 an epidemic disease in Guangdong region from China, which brought about spread to numerous different nations, including Thailand,

Vietnam, Taiwan, Hong Kong Singapore, and the United States of America, caused extreme intense respiratory disorder SARS-CoV and high death rates in more than 1000 patients.

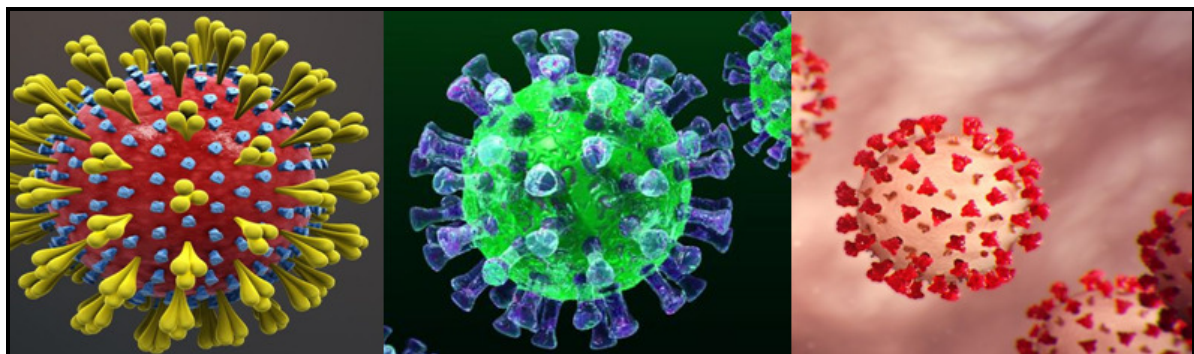
After this flare up, microbiologists and infectious ailment specialists concentrated on the comprehension of the pathogenesis [7] of the ailment and found that this disease was brought about by another type of CoVs. A sum of 8096 people was tainted with this infection, bringing about 774 fatalities; therefore, in 2004, the CDC (Centre for Disease Control and Prevention) and WHO declared a critical public health welfare emergency situation [8].

In reality, one more outbreak in Saudi Arabia in 2012 brought about numerous fatalities, spread to different nations in the Middle East, and then around the world referred to be MERS-CoV which is time lined in table 1.

In figure 1 the structural model of the various coronaviruses such as SARS, MERS, COVID-19 have been illustrated below;

Table-1: General comparison of different Coronaviruses						
Coronavirus	Place of origin	Year of Origin	Incubation period	Receptor Cell	Countries spreading	Mortality Rate
SARS	China	2002	2-7 days	ACE2	29	10.8%
MERS	Saudi Arabia	2012	2-14 days	DP4	27	34.4%
COVID-19	China	2019	2-14 days	ACE2	~130	~6%

Fig-1: SARS, MERS, COVID-19 Coronavirus Model



Structure & Functions

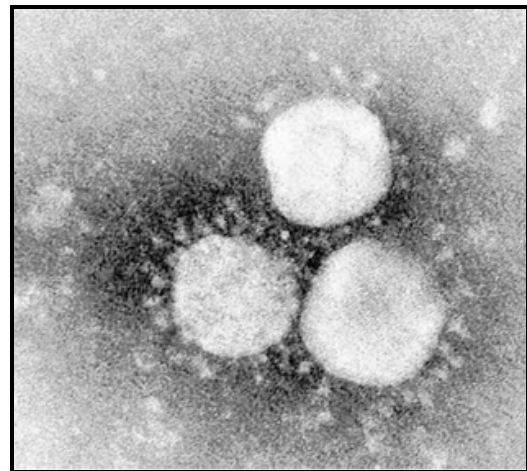
Coronavirus viruses are circular to pleomorphic encompassed particles as appeared in figure 2. The envelope is studded with anticipating glycoproteins [9], and encompasses a centre comprising of matrix protein encased inside which is a solitary strand of positive sense RNA (6×10^6) related with nucleoprotein. The genome is pressed inside a helical capsid framed by the nuclei capsid protein and further encompassed by an envelope. The viral envelope has three auxiliary proteins. The first being the membrane protein [10], the envelope protein engaging in virus assembly, the spike protein intervening infection section into host cells. Among the structural proteins, the spike frames enormous distensions from the infection surface, giving CoVs the presence of having crowns. In addition to mediating virus entry, the viral spike is a basic determinant of viral host range and tissue culture tropism and a significant inducer of host insusceptible responses.

CoVs are equipped for adjusting to new conditions through change and recombination without any difficulty. All things considered, they can influence new hosts and tissues. Thus, certain CoVs that typically influence certain animal species can produce new strains can traverse to human hosts and afterward be transmitted between people. Since people had not been presented to such infections previously and can't be secured by either existing immunizations or common invulnerability, these transformations can quickly prompt sickness outbreaks and, in the long run, pandemics.

This was the situation with the past outbreaks of SARS and MERS. The envelope glycoproteins [11] are answerable for connection to the parasitic host cell and furthermore convey the primary antigenic epitopes [12], especially the epitopes [13] perceived by killing antibodies. This is encased inside a lipid bilayer layer envelope in relationship with a trans-membrane protein (M), which is the most inexhaustible infection basic protein. The S protein is the significant inducer of killing neutralizer, next the Hemagglutinin esterase protein is additionally an objective for killing antibody. Monoclonal antibodies raised against M protein can kill infectivity within the sight of supplement. Antigenic variety is a

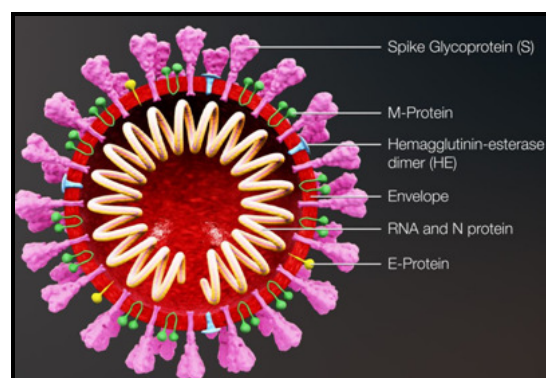
component of the protein, though the N protein is moderately conserved.

Fig-2: Electron micrograph showing coronavirus



CoVs internal structure consists of five proteins in their genomes as shown in Figure 3. They are 1. Spike (S), 2. Membrane (M), 3. Envelope (E) glycoproteins, 4. Hemagglutinin Esterase (HE) and 5. Nucleocapsid (N) protein. Generally envelope proteins as well as N protein is present in all type of viruses but HE is specifically present only in some sort of beta CoVs [14].

Fig-3: Internal structural parts of Coronavirus model



Symptoms, Incubation Period & Severity

Discussing on the symptoms of recent COVID-19 to past series of coronavirus family are vague, the disease presentation can range from no indications (asymptomatic) to serious pneumonia and fatality. Common human CoVs, typically cause upper respiratory tract illnesses with different range of vitality. The vast majority get contaminated

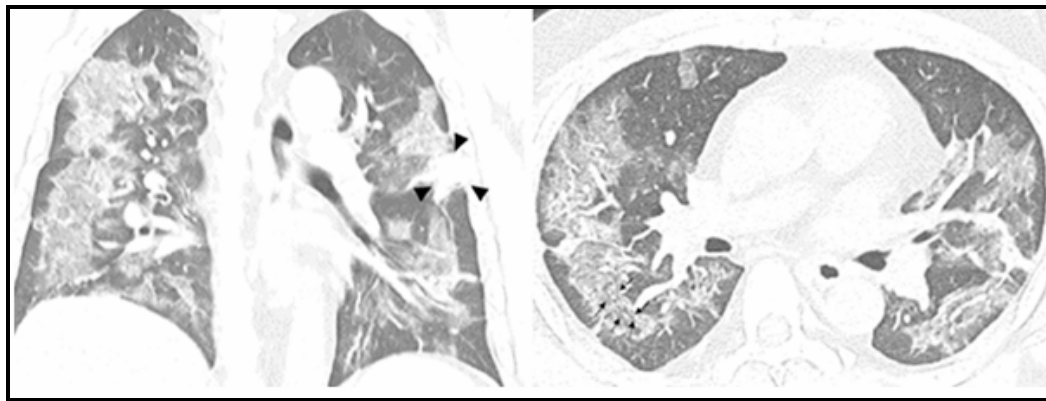
with these infections at a few point in their lives. These sicknesses normally just keep going for a short measure of time. Symptoms may include Runny nose, Headache, Cough, Sore throat, Fever. A variety of abnormalities may be expected on chest radiographs, but bilateral lung infiltrates appear to be common (similar to what is seen with other types of viral pneumonia).

a) *Physical examination:* Patients with mild indications may not show positive signs. But patients in critical condition shows the symptoms and effect of shortness of breath,

sodden riles in lungs, debilitated breath sounds, bluntness in percussion, and expanded or diminished speech tremor.

b) *CT imaging examination:* The computed tomographic imaging of lungs which was infected due to diseases is given below. It is expressed to picture the Lesions occurred in the peripheral bilateral lungs along bronchi vascular bundles. It vary with the patient's age, immunity status, stage of disease during the hour of examining, basic illnesses, and medication.

Fig-4: Disease infected Lungs having Lesions



Epidemiology - Reservoirs and Transmission

As of saying about novel coronavirus occurred at present above 10 lakhs have been diagnosed in 199 countries with over 60000 fatalities. The WHO says about the coronavirus in their dashboard with individual country information.

Saying about viral entry it is mediated by fusion of the viral envelope with the host cell membrane. The combination of the viral and cell membranes (either at the cell surface or inside the endocytic vesicle) is interceded by the S2 segment of the infection spike protein [11] which works as a class 1 combination protein. Then the RNA of virus is discharged into the host cell cytoplasm, a RNA-dependent RNA polymerase interpreted from the stranded genomic sRNA makes a negative strand format from which that point incorporates a progression of three co-terminal nested viral genomic mRNAs [15]. The infections duplicate in the cellular cytoplasm with a development pattern of 10–12 framing virus bud into the unpleasant endoplasmic reticulum (where the M protein limits) and amass into intra

cytoplasmic [16] vesicles which is shown in Figure 5. These recently shaped virus are transported through the Golgi [17] apparatus to the intermediate plasma film where they are discharged by exocytosis. Viral infection may bring about cell lysis or a combination of neighbouring cells that may prompt the development of syncytia.

Fig-5: TEM infected cell images due to coronavirus

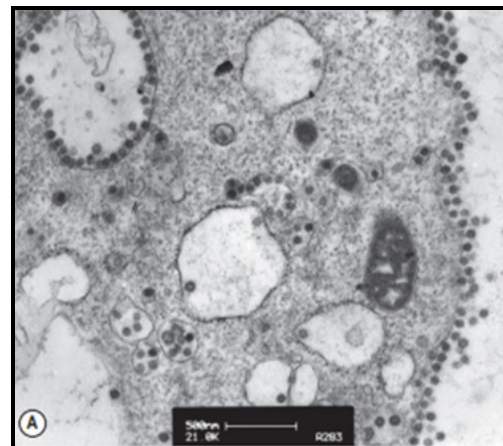
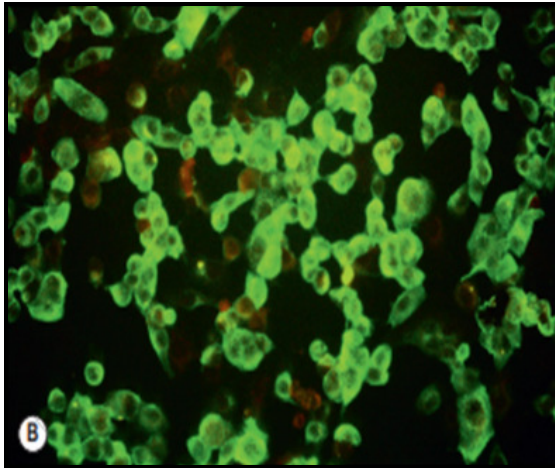


Fig-6: Immuno Fluorescence of a CoV infected cell serum.



Generally CoVs is transmitted through coughing and sneezing, close to general contact, shaking hands, using an object or material surface with the infection on it, then make contact of the mouth, nose, or eyes without washing the hands, Domestic or International travel getting contact with infected people [18]. More recent evidence from studies with SARS-CoV-2, however, concluded that the virus remains stable and viable on different materials for up to 72 hours, as per the table below:

Table-2: Viability of SARS-CoV-2 on different surfaces		
Type of surface	Viability	Half-life
Aerosols	Up to 3 hours	1.1-1.2 hours
Stainless steel	Up to 48-72 hours	5.6 hours
Cardboard/paper	Up to 24 hours	3.46 hours
Plastic	Up to 72 hours	6.8 hours
Copper	Up to 4 hours	0.7 hours

The recent 2019 nCoV SARS CoV2 is found to be highly epidemic and pandemic. It is being more infectious than SARS CoV and MERS CoV. Besides, being infected within a very short exposure time to the development of symptoms is possible in the absence of face masks. SARS CoV 2 binds to ACE2 (Angiotensin Converting Enzyme 2) receptors with a higher affinity than SARS CoV. Here due to COVID -19 virus the diverse stages of the spread of the infection are illustrated below.

Stage 1: Imported Cases

Stage 1 are cases who have gone to virus affected foreign countries and returned back to home town. The initial stage, as per the report, is when cases of infection are brought into a nation which was not the source of the disease. Right now, the nation's outside of China which started reporting cases of coronavirus, reached Stage 1 of the outbreak as soon as they reported their first case. Following large outbreaks of the disease in multiple countries, with thousands of deaths around the world, the WHO declared to be a pandemic.

Stage 2: Local Transmission

In stage 2 infection is due to the persons getting contact with the patients who is returning back from other countries with infection. This implies that the individual from whom the disease spread to another person is from the country itself. In this stage, the trajectory of the virus can be identified from the source to all the infected individuals.

Stage 3: Community Transmission

Huge areas get infected when community transmission happens. Right now, to the report, it turns out to be difficult to track the chain of transmission of the infection in countless cases. This implies that the virus has started circling inside the network and can also affect those person who have neither travelled to a country affected by the outbreak nor have come into the contact of an individual tainted by the virus.

Stage 4: Epidemic

This is considered to be final stage and worst stage in which the disease start spreading epidemically to a broad geographical area around the infected patients.

Prevention

Prevention of infection involves avoiding exposure to infect and taking care of not taking any raw food without boiling, particularly for those with diabetes, chronic lung disease, renal impairment, the immune compromised, or the elderly. Confirmed cases should be isolated to avoid nosocomial spread.

Controlling infection sources: Patients tainted with 2019-nCoV are the primary contamination sources. So patients tainted by novel coronavirus ought to be isolated at home or admitted to emergency clinics under the guidance of healthcare services relying upon the seriousness of their ailments. Try to give single rooms to isolated and decrease the opportunity of contact with the co-occupants. There are tremendous demands for room ventilation, cleaning, and purification work regarding the articles utilized. Disposable masks are the crucial one and it should be properly removed after use when sick.

Blocking transmission routes: General mode of spreading at epidemic situation is when someone touches the infected objects. So hygienic of the hand is essential for preventing the spreading of virus using either soap or hand sanitizer. The WHO recommends that hand rub formulations where it should have an alcohol content of 80% ethanol or 75% isopropyl alcohol.

1. After coming from any public places, clean your hands thoroughly. One should not touch mouth, nose, or eyes before cleaning hands thoroughly. One should cover their mouth while coughing or sneezing; regularly clean the children’s toys using disinfectants with 75% alcohol or chlorine containing disinfectants [19], and ultraviolet rays or by heating at 60 °C to 75 °C for 30 min. Table 2 shows the list of disinfectants for commonly contaminated objects to use.
2. Reduce exposure to infection: Try to be at home and avoid public transport at epidemic areas, and wear face masks when going outside; avoid touching or eating animals, and going to wildlife animals market.
3. Babies delivered by infected moms must finish a pathogen test [7] and be separated in a solitary ward or at home according to their ailments.

Boosting immunity: Balanced eating routine, oral wellbeing, satisfactory exercise, regular rest, and boosting resistance are powerful measures to prevent CoVs. Vaccination is an effective way to prevent virus infection. The research and development of anti-virus vaccines has been carried out in China at present.

Table-3: Infected Surfaces and suitable disinfectants	
Surface for disinfection	Type of disinfectant
Environmental object surface	Chlorine-containing disinfectant (1000mg/L), chlorine dioxide (500mg/L), Both should have 75% alcohol
Hands	Alcohol hand disinfectant chlorinebased disinfectant hydrogen peroxide
Skin	0.5% iodine-based disinfectant hydrogen peroxide
Mucosa	0.05% iodine-based disinfectant
Indoor air	Per-acetic acid chlorine dioxide hydrogen peroxide
Pollutant	Chlorine-containing disinfectant (5000-20000 mg/L) disinfectant powder bleach powder
Textiles such as clothes, bed	Chlorine-containing disinfectant (500 mg/L) Ethylene oxide

Testing and Diagnosis

There are currently different types of tests are available for diagnosing COVID-19 (SARSCOV-2) infection based on complex PCR or reverse transcription RT-PCR technique by USA, China, Korea and other countries. It target to analyse different parts of the viral genome. After nasopharyngeal sampling (either nose, throat swabs, and/or nasopharyngeal aspirate) performed by qualified nursing or medical staff, and once received by clinical laboratories, available tests generally take less than six hours to deliver a result. Tests are generally not equal in terms of diagnostic sensitivity due to the viral genomic sequence or the targeted viral gene(s). It was found to have 100% concordance among genuine positive and genuine negative samples.

Treatment

There is no particular medicine to cure people with coronavirus (antibiotics help fight bacterial infections, not viral). Maintaining a

healthy and strong immune system is recommended. Currently antiviral treatment [19] is mostly utilized, just as symptomatic and supportive treatment dependent on the clinical state of the patient. Supportive treatment incorporate oxygen therapy, hydration, fever/pain control, and antibiotic agents within the sight of bacterial co-infection.

For SARS treatment, a few medications were attempted clinically with no clear benefit, and from that point various medications incorporating protease inhibitors utilized in HIV have been researched for efficacy in vitro. For mild cases in the community, patients are advised to stay home in isolation, except for patients at higher risk of developing severe forms of the disease, including older adults (>65 years old in some countries, >70 in others), people with underlying conditions (such as cardiovascular diseases, diabetes, respiratory diseases) and patients with compromised immunity.

General treatment: The general treatment procedures incorporate bed rest and supportive treatment; ensuring adequate calorie and water consumption; keeping up water electrolyte balance and homeostasis; observing fundamental signs and oxygen saturation; keeping respiratory tract unhindered and breathing in oxygen when essential; estimating blood schedule, urine routine, reactive protein, and other blood biochemical indexes including liver and kidney work, myocardial enzyme spectrum and coagulation work as per patients' conditions. Blood gas investigation and convenient reconsideration of chest imaging ought to be performed when essential.

Symptomatic treatment: The patients with high fever ought to be effectively controlled. In the event that patients' internal heat level surpasses 38.5°C with obvious inconvenience, physical cooling (warm water shower, utilization of antipyretic fix, and so on.) or antipyretic medication treatment ought to be performed. Regular medications include ibuprofen orally, 5–10 mg/kg without fail; acetaminophen orally, 10–15mg/kg unflinchingly. Keep children calm and administrate sedatives promptly when seizures happen.

Oxygen therapy: At the point when hypoxia shows up, effective oxygen treatment ought to be given quickly including a nasal catheter, mask oxygen. Nasal high-flow oxygen treatment, and non-invasive or invasive mechanical ventilation ought to be embraced when necessary. Lopinavir / ritonavir [20] has been attempted to apply to the treatment of grown-up patients with 2019-nCoV pneumonia.

Conclusion

The outbreak of COVID-19 generated across China quickly spread to 199 countries/ regions/ zones outside of China made us to recall the series of coronavirus and its impact to the society. Here overview of all types of coronavirus from its family in different perspectives. Here similarity and differences among the novel COVID-19 and the rest of the corona viruses such as flu, MERS-CoV, SARS-CoV had been illustrated in detailed with its characteristics and behaviours. Also broad visualization of the treatments and immunizations against the infection.

This bridged the present information on SARS-CoV-2 as follows:

Firstly, the rising pneumonia, COVID-19, brought about by SARS-CoV-2, exhibits strong infectivity yet less destructiveness, contrasted with SARS and MERS, as far as morbidity and mortality.

Secondly, the vulnerable population includes the older and individuals with certain basic ailments, which requires more consideration and care.

Thirdly, until this point, the supporting medicines, combined with powerful antiviral medications, for example, remdesivir, chloroquine (CQ), or lopinavir / ritonavir, have been led with distinct impact on treat COVID-19 patients, while strong information from progressively clinical preliminaries are required. In any case, questions stay obscure and more examinations are dire to investigate the transmission and pathogenicity system of the rising CoVs.

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