Review article:

Review of the Corona Viruses Causing Acute Respiratory Syndrome and COVID-2019 (COVID-19) Pandemic

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Abstract:

A new virus, Severe Acute Respiratory Syndrome Corona Virus-2 (SARS CoV-2) emerged in December 2019 and still continuing to pose a great threat all over the Globe claiming to a fatality 980,031 persons. Among the human corona viruses it is the third one causing acute respiratory distress syndrome. The others two are SARS CoV and MERS CoV. The objective of this study is to review the human corona viruses causing severe respiratory distresses which are detected thru analysis of some recently published documents on the deadly SARS CoV-2 as well as information on SARS-CoV and MERS CoV from different world class trust worthy reliable and dependable sources. Genetic analysis reveals that the new human corona virus (SARS CoV-2) has similarities with the severe acute respiratory syndrome like (SARS like) bat virus which thought to be the primary reservoir. SARS-CoV and MERS-CoV also have same bat reservoir but the intermediate host are different for three human corona viruses. Though the clinical picture is more or less similar but efficiency of human to human transmission is not same for these viruses. So, strict control measures are critical to contain this very big pandemic been occurring since December 2019. Everyday new information has been coming causing strategy to change to control this pandemic. Zoonotic origin of corona viruses indicate researchers, public health specialists should keep the continuous surveillance for early detection of new virus alike SARS –CoV-2.

Keywords: Corona virus, SARS-CoV, MERS-CoV, Covid-19, Outbreak, Pandemic,

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Introduction:

In last December 2019, an acute respiratory Corona Virus Disease (COVID-19), caused by the novel corona virus (SARA-CoV-2) was identified first in the Wuhan of China and received immediate worldwide attention. The World Health Organization (WHO) named this corona virus initially as the novel corona virus 2019 (2019-nCoV). Later, the Corona Virus Study Group (CSG) of the International Committee proposed the name of new corona virus as SARS-CoV-2[1] and WHO officially accepted the disease as Corona Virus Disease 2019 (COVID-2019)[2]. The Chinese scientists very fast isolated the new virus SARS-CoV-2 from an infected patient within a very short possible time and done genome sequencing[3]. The WHO officially declared COVID-19 pandemic as a public health emergency of international concerns on 30 January 2020. As of

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25 September 2020, a total of 32,110,656 cases were confirmed as infected by the COVID-19 globally including 980,031 deaths where as in Bangladesh, 356,767 COVID-19 positive cases were detected including 5,093 deaths[4]. The emergence of SARS-CoV-2 considered as the third high pathogenic and large-scale epidemic corona virus into the human beings in twenty-first century, since the outbreak of severe acute respiratory syndrome corona virus (SARS-CoV) in 2002[5] and the Middle East respiratory syndrome corona virus (MERS-CoV) in 2012. The basic reproduction number (noted as the R_0) of SARS-CoV-2 was reported to be around 2.2[6] or even more range from 1.4 to 6.5[7]. Cluster of the pneumonia outbreaks within the families indicates steady human to human transmission of the pandemic COVID-19 worldwide[8].

Corona Virus:

The Corona Viruses (CoVs) belong to the family Coronaviridae, which is the largest family within the order Nidovirales Orthocoronavirinae and Torovirinae are two subfamilies of the Coronaviridae family where Orthocoronavirinae includes four genera: alpha (α)-coronavirus, beta (β)-coronavirus, gamma (γ)-coronavirus, and delta (δ)-coronavirus[9]. Many corona viruses are significant for the animal health threats. The first description of corona virus came from the veterinarian in 1931 which was named as 'Infectious Bronchitis Virus (IBV) of Chickens'[10]. CoVs are then found in mammals, birds, camels, cattle, cats, bats, and other animals. Alpha (α) and Beta (β) corona viruses are found to be circulating in the mammals including bats, whereas γ coronaviruses are found mainly in the avian species including few mammalian species, and δ coronaviruses are detected in the birds and mammals[11]. Evidence shows that the animals CoVs can infect human beings rarely and could attain the ability to spread through the human-to-human transmission[12]. Among different human corona viruses (HCoVs) CoV-229E and CoV-OC43, cause the common cold in the humans[13]. Several other HCoVs were revealed in different period after emergence of those two HCoVs. Severe Acute Respiratory Syndrome-CoV (SARS-CoV) was discovered in 2002, HCoV-NL63 in 2004, HCoV-HKU1 in 2005, and the Middle East Respiratory Syndrome-CoV (MERS-CoV) in 2012[14]. The novel CoV virus2019 (2019-nCoV) which is recently named SARS-CoV-2 is seventh human corona virus detected in China[1].

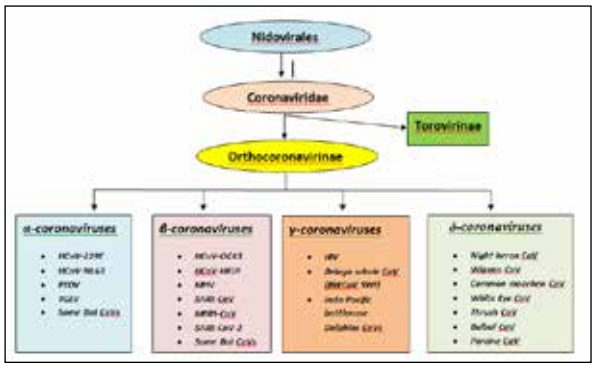

Fig-1: Classification of Corona Viruses

Corona virus structure and entry in the host cell:

Corona viruses are the spherical enveloped virus with a positive-sense single-stranded RNA genome where the spike proteins on envelope showed appearance of crown under microscope led to the name "corona virus", a Latin word means 'The Crown'[15]. The viral structures found primarily of structural proteins such as spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, and hemagglutinin-esterase (HE) protein in the some β-corona viruses. The S, M, and E proteins are all embedded in viral envelope. However, N protein is located in the core of the viral particle[16].

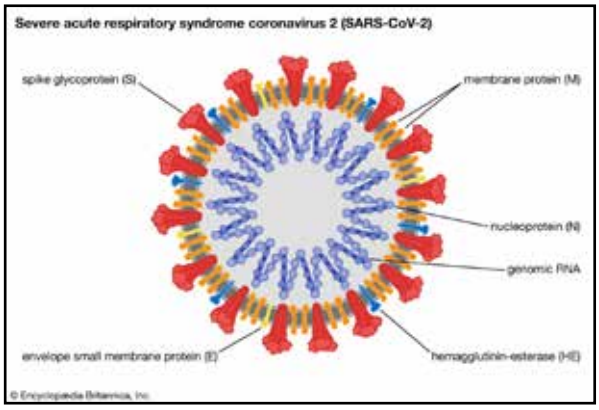

Fig-2: Corona virus structure

Spike (S) of protein of the virus is sole responsible for entry of CoVs into the host cells[17]. Within S-1 domain, the receptor-binding domain (RBD) binds with receptor of the host cell and S-2 domain causes the fusion between the host cell membrane and the viral envelope, required for viral entry into the host cells[18,19]. Several cellular receptors were found for different CoVs. For an example, amino-peptidase N (APN) receptor was identified for several α-corona viruses,[20] angiotensin-converting the enzyme 2 (ACE2) receptor for SARS-CoV,[21] HCoV- NL63,[22] and newly discovered SARS-CoV-2,[23] and dipeptidyl-peptidase 4 (DPP4) receptor for MERS-CoV[24].

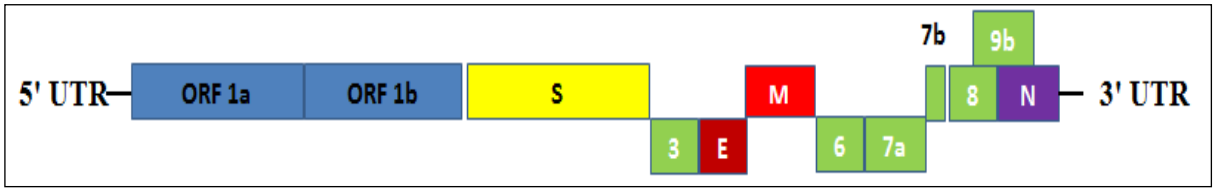

Fig-3: Genome of SARS CoV-2

Genomic Organization:

The genome of CoVs including recently evolved SARS CoV-2 is the largest among all human beings RNA viruses which range from 26 to 32 kilobases (kb) in size[25]. The genome codes for the nonstructural and structural proteins[26]. The genome for CoVs comprises of the 5'-untranslated region (5'-UTR), the open reading frame (ORF), non-structural proteins (NSP) for replication, structural proteins including the spike (S), envelop (E), membrane (M), and nucleocapsid proteins (N), accessory proteins such as ORF 3, 6, 7a, 7b, 8 and 9b in the CoVs genome, and the 3'-untranslated region (3'-UTR)[27]. The ORF 1 translates two poly-proteins, pp1a and pp1ab, and encodes 16 non-structural proteins (NSP) which comprise about two-thirds of the whole genome, while the remaining ORFs encode accessory and structural proteins. The rest one-third of the genome encodes four essential structural proteins, which includes the spike(S) glycoprotein, small envelope (E) protein, membrane protein (M) and the nucleocapsid (N) protein[28].

Origin and evolution of SARS CoVs

There is a long history of the cross-species transmission of CoVs[29]. SARS-CoV has been thought to be originated from the Chinese wet market where it crosses the species barrier from Chinese horseshoe bats through an intermediate species palm civet and the raccoon dogs to the human beings[30]. A lot of studies have proved that the bats and other small animals harbor SARS-related CoVs (SARSr-CoVs) that might be ancestral to the SARS-CoV in humans[31]. It was found that SARS-CoV has been circulating for a long time in bats before the genetic modification and jumping to humans. This genetic modification leads to adaptation SARS-CoV to the bind human ACE2 as a receptor and efficiently infect human cells[32].

MERS-CoV is highly related particular to two bat corona viruses, HKU4 and HKU5, identified previously[33]. Detection of the MERS-related CoVs (MERSr-CoVs) in bats indicates a potential bat origin[34,35] but likely had an intermediate host. Studies have identified that the camel MERS-CoV strains are almost identical to human MERS-CoV strains[36] which could be the intermediate host. RBD of MERSr-CoVs' share only 60% – 70% sequence identity with that of the human and camel MERS-CoVs[37]. For adaptation in the human host, MERSr-CoVs had to undergo several amino acid changes in the RBD of S-protein to become capable of infecting the camels and humans[38]. This amino acid changes might lead to the emergence of MERS-CoV strains that enable to bind to the human DPP4 with high affinity and infecting the humans.

The early cases of SARS-CoV-2 pneumonia indicate that many cases have been exposed to the Huanan Seafood Market in Wuhan, Hubei province of China[39]. The Genetic Analyses of the viral samples from the patients with SARS-CoV-2 infections revealed that the SARS-CoV-2 shares 79.5% nucleotide (nt) identity with SARS CoV, only 50% identity to MERS-CoV and 96% identity with the bat-CoV-RaTG13[40,41]. It indicates that SARS-CoV-2 is new virus that is distinct from SARS-CoV and MERS-CoV but might have a bat origin, similar to SARS-CoV and MERS-CoV[41]. The Huanan Seafood Market was trading variety of live animals such as the snakes, marmots, badger, hedgehog, and birds, probably pangolin but not the bats[42,43] suggests that bats have less chance to direct contact with the human and direct transmission of the virus from bat to human is less likely[44]. Therefore, like SARS CoV and MERS CoV there may be an intermediate host in the market transmitting the virus to a human. Recently SARS CoV-2 has been isolated from pangolins, genetic sequences of which showed 99% identity with that SARS CoV-2 in humans. Now, it has been thought that transmission and evolution path of SARS CoV-2 was from bat-CoV to pangolins (intermediate host), from where it transmits to human[45].

Comparison between SARS-CoV, MERS-CoV, and the Newly Discovered SARS-CoV-2:

The pandemic potential human corona viruses started to cause the Severe Acute Respiratory Syndrome (SARS) in humans in 2002-2003. That outbreak initiated in the Guandong area in China,

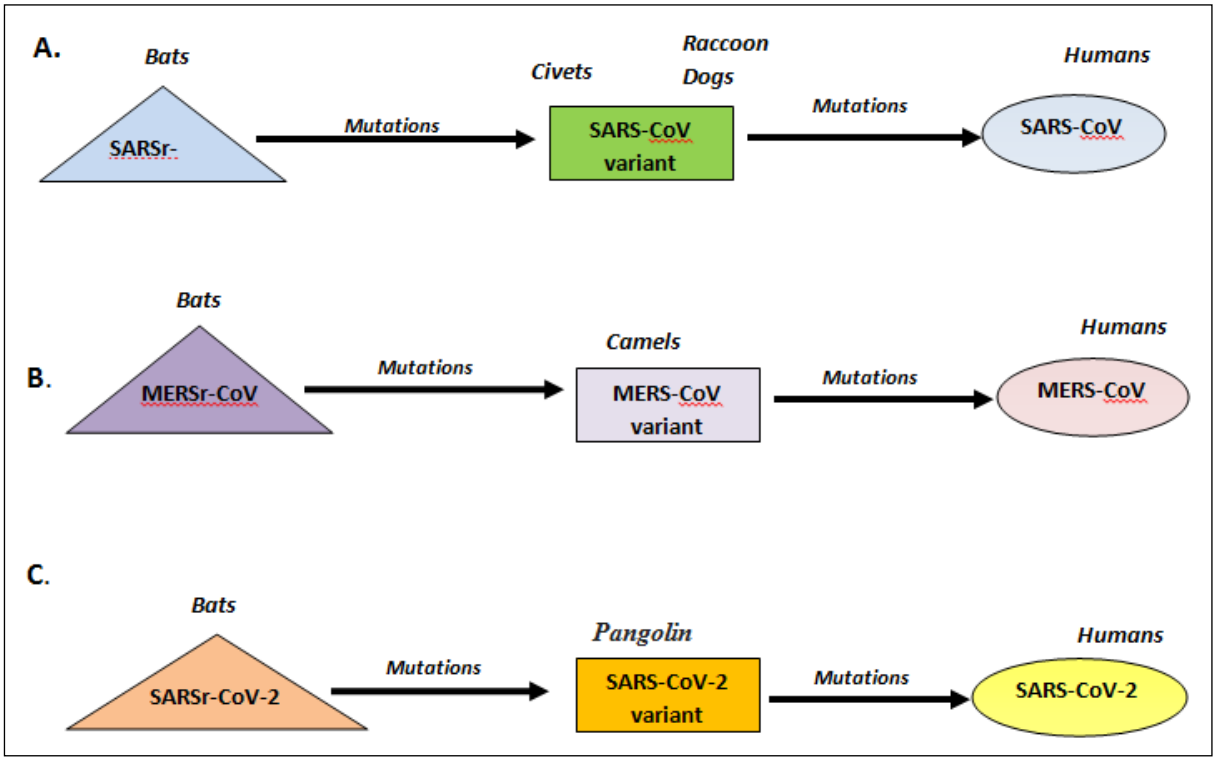

Fig-3: Diagram of origin of corona viruses

and resulted in 774 deaths out of a number of 8,098 cases over the nine months period with about 10% fatality[46]. The un-ciliated bronchial epithelial cells and the type II pneumocytes were infected and resulted in fever, cough, shortness of breathing, and severe complications such as pneumonia and kidney failure ailments[21,46]. The Incubation Period for the SARS-CoV was observed for 2 to 14 days[47]. In 2012, another new CoV detected in Saudi Arabia that causes a severe respiratory disease named MERS-CoV[48]. MERS-CoV caused a similar type of clinical features as that of SARS-CoV. The incubation period of MERS-CoV is quite similar to SARS-CoV and ranging from 2 to 14 days[49]. Since 2012, 862 patients died out of a total 2,506 infected cases in 27 countries with a case fatality about 35%, which is more than three times than that of the SARS-CoV infections[50].

The third identified human Corona virus is SARS-CoV which causes the respiratory symptoms with the severe disease. It was isolated and sequenced from the patients that showed symptoms of respiratory illness and pneumonia in Wuhan in China during December 2019[51]. Incubation period is the same as SARS-CoV and MERS-CoV infections[39,52]. Similar to SARS-CoV and unlike MERS-CoV, human-to-human transmission was confirmed[41]. The Respiratory Symptoms include fever, dry cough, respiratory distress, and in severe case pneumonia. The mortality seems to be caused by Acute Respiratory Distress Syndrome (ARDS)[53] usually associated with comorbidities and followed by multiple organ failures leading to death.

Education from outbreak of SARS-CoV, MERS-CoV, and SARS-CoV-2:

Alpha (α)-corona virus (HCoV-229E, & HCoV-NL63) and β-coronavirus (HCoV-OC43 and HCoV-HKU1) have been known to cause mild, self-limiting respiratory infections with symptoms of the common cold in a human before the outbreak of SARS-CoV. The severe form of the acute respiratory syndrome was found to be caused by SARS-CoV, MERS-CoV, and very recently SARS-CoV-2, all are β-corona virus[55]. The diversity of corona-viruses reflects the fact that this family of viruses has an RNA dependent RNA polymerase with the poor fidelity[56], and high frequency of RNA mutation[57], and also easy transmission from one species to another[12,58]; all these factors may contribute to severe respiratory outbreaks in the human. Corona viruses that cause severe respiratory diseases have come from ancestral CoVs harbored by the bats (Fig-3) whereas animals function as intermediate hosts (civets, raccoon dogs, camel, pangolin etc.), and the humans served as terminal hosts.

In China, the live animals are sold mainly for food items or medicine at most of the wet markets. The wildlife and/or parts from the rare animals

(such as the pangolin scales and paws from a tiger) used for medicine or the magical purpose in China[59]. But it is to be noted that most of these folk remedies are not prescribed by the Traditional Chinese Medicine (TCM) hospitals. The Wuhan market also involved with selling of several exotic animals and their parts[41]. Thus, SARS-CoV-2 disease can be considered a zoonotic disease that initially spread from animals to the humans then human-to-human transmission also confirmed[60]. It is found that new CoVs causing outbreaks repeatedly, evolved in China. The cause for this repeated occurrence of these outbreaks is not at all well understood. Although, it can be assumed that those viruses may be predominantly circulating in the animals in China rather than animals of the world. One of the reasons could be the close interactions with live and the wild animals in the wholesale food market in China[54] and the practice of eating raw meat.

Such a pandemic outbreak like the COVID-19 is a concern for public health specialists to understand the magnitude of the pandemic where basic reproduction number which is known as the R_0 is an important indicator[61]. This number measures the potentiality of the disease which represents average number of healthy people infected from an infected person in a population. The mean estimate of R_0 was found in a study between 2.24 and 3.58[62] and in another study with the high average value of R_0 was found to be 2.5[63] which is consistent with a report from the other groups ranged from 2 to 3[64-66]. The R_0 estimates for the SARS-CoV-2 are consistent with the SARS- and MERS-CoVs ranging from 2 to 5[67,68]. The R_0 above 1(one) should always be taken seriously. The target should be to reduce the R_0 below 1. An important point here is R_0 estimates can vary from the "true" R_0 values if the infected people remain asymptomatic or do not report their symptoms to the authority[57].

Conclusion:

In any sorts of natural disaster, the people come together to get rid of that disaster whereas outbreaks of highly contagious infectious diseases divide the people to prevent the spreading of viruses. But viruses cross from country to country irrespective of borders and move from birds to an animal to the human. So, controlling such a pandemic outbreak requires an active and prompt international efforts and cooperation. The climate change, changes in ecology, continuous invasion of natural habitats of the animals by human for food and shelter, advanced practices in agriculture lead the wildlife to come to the human habitat which causes spillover of viruses from natural host to human. Even in this huge advancement of science, invisible viruses have been found to have devastating effects on human beings. Thus SARS-CoV, MERS-CoV, H5N1, H7N9, Ebola, and very recent COVID-19 outbreaks give an alarm to the world for the future pandemic threats by any other novel virus. Researchers should have continuous efforts and the surveillance to reduce the probability of occurrence of new infections through the sustainable investigation of animal etiology, keep strict bio-security of the high-risk pathogens, control of the wildlife trading, and decreasing direct contact with wildlife and thus control the transmission of naïve virus to human.

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Authors Contribution:

Data gathering and idea owner : AN Alam
Writing and editing final draft: All authors.

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