

A Review of Novel Corona Virus Disease (SARS-CoV-2)

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Abstract

The coronavirus (CoV-19) is exceedingly virulent and disease-causing infection produced by Severe Acute Respiratory Syndrome which is developed in China (Wuhan) and then expended globally. In the evolutionary examination declared that SARS CoV-2 and SARS-CoV are phylogenetically similar to each other while both were belonging to same family, same entry receptor ACE2 and both have common reservoir for viral infection and rapidly spread by the physical contact of suspected person to healthy person. The no. of cases of infected persons increased globally yet not controlled but still there clinically affirmed antiviral medicines have been check out against coronavirus disease. The structural examination of spike proteins and ACE2 receptors further subgroups properly explains the protocol of viral transmission a) alpha, b) beta, c) gamma, d) delta. International committee on taxonomy of viruses (ICTV) named novel virulent infection as SARS-CoV2 as virus and covid-19 as disease. SARS-CoV2 infected patients are of two types asymptomatic and symptomatic, both were capable to transfer the virus from infected individual to healthy individual and disease risk is not same for the all-age groups. We survey the comparison of SARS-CoV and SARS-COV2, Characteristics of coronavirus, molecular characteristics of SARA-CoV2, mechanism of entry, transmission and precautions. We also discussed therapeutic combination and effective drugs used to slow down or overcome with the covid-19 pandemic. At last, 80% infected patients were properly recovered from this viral infection covid-19 without any clinical consideration they recover with their own strong immunity and fight against infection.

Keywords: SARS-CoV-2, SARS-CoV, Virulent Infection, ACE-2 Receptor

1. INTRODUCTION

The novel corona virus belongs to coronaviridae family which is first reported in Wuhan (china), on 3rd DEC 2019. The corona likes spikes present on the surface of corona so, it is called corona virus. Coronavirus were very minute in size about 65-125nm in diameter, 26 to 32 kbs in length and have single stranded RNA. Coronavirus family is further having subgroups are α (alpha), β (beta), γ (gamma) and δ (delta). Severe Acute Respiratory Syndrome & Middle East Respiratory Syndrome which major problems like Acute Respiratory Distress Syndrome (ARDS) & Acute Lung Injury (ALI) which leads to result in pulmonary failure & fatality. Coronavirus caused illness in animals and humans in both and human causes respiratory illness like common to severe disease which include SARS, MERS, HINI influenza etc. The coronavirus disease is extremely transmittable and viral infection or pathogenic due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) and

rapidly spread around all over the world. In Nov 2002, Guangdong (china) first reported pathogenic virus called MERS-COV (middle east respiratory syndrome (Zhong et al., 2003) and give rise to a pandemic in middle eastern countries (wang et al., 2013). Lately 3rd December 2019, in Wuhan (china) emerging a business hub, resulting in that china faced a major outbreak of novel coronavirus in which more than 1800 infected patients of coronavirus were killed and over 70,000 individuals were infected in just two months and these infected individuals from coronavirus was reported, belong to member of beta group of coronaviruses. The researchers of China named novel virulent infection in Wuhan as corona virus and 2019-nCov (2019 novel Corona Virus) and International committee on taxonomy of viruses (ICTV) named novel virulent infection as SARS-COV2 as virus and covid-19 as disease (Cui et al., 2019). In past, SARS-COV 2002, 8098 infected individuals, covering 26 countries in the world with mortality rate 9.6%. On the other hand, till 28 Nov 2020 11:59 PM novel SARS-CoV-2 in 2019 confirmed cases-93,93,039, active cases-4,52,996, recovered cases-88,01,161 and deceased cases-1,36,733 in India. Covid-19 cases globally, confirmed cases-62,634,907 active cases-17,934,039 recovered cases-43,241,540 deaths- 1,459,328 till date of this writing. From the active cases 17,934,039 (currently infected patients) 17,828,774 (99.4%) in wild condition and 105,265 (0.6%) in serious or critical condition. This shows transmission record of SARS CoV is lesser than the SARS-CoV2 and major reason of enhance its transmission ability is recombination of genes on the surface of S protein in the RBD region of CoV2 (Shreen et al., 2020).

Transmission is highly quick and pathogenic and the most significant way for transmission of SARS-CoV2 from an infected to healthy person is either through direct or through any of their belongings like droplets, coughing or sneezing is most significant way of transmission and the transmission are of two types asymptomatic and symptomatic both were unable to transfer the disease. The risk of disease is not same for all age groups, more than 50 years of age having high risk and the patients having respiratory diseases, diabetes were also having high risk of the covid-19. Corona Viruses consist of 4 fundamental proteins: NP (Nucleocapsid protein), SP (Spike protein), EP (Envelope protein) & MP (Membrane protein). E & M proteins are required in virus assembly while proteins are required for entry of virus & recognition of host cell (Li et al., 2016). During Viral entry, the sugar receptors of the cell (host) and also the ACE-2 receptors of the cell (host) binds directly with the S1 sub-unit while the S2 sub-unit go symmetrical changes & come by post fusion state (Millet et al., 2015). The antibodies testing platforms plays an important role to slow down or overcome the pandemic. In this novel covid-19 three different diagnosis experiment were performed 1) CT SCAN (chest computed tomography) 2) RT-PCR (RNA detection using reverse transcription-polymerase chain reaction and 3) lateral flow assay, ELISA (Enzyme linked immunosorbent assay, full aromatic chemiluminescence method used for detection of antibodies (Chu et al., 2020). But there were many shortcomings for this experiment like time consuming (it takes 4h to complete only 1 test), high cost and only present in urban areas. Precautions used to slow down the pandemic, it is very simple to stop the spreading of virus happening in the first place rather than to cure or treat disease after it has happened and globally spread like novel coronavirus.

Table 1: comparison of two viral infections CoV-1 & CoV2 that belongs to coronaviridae family

| CoV-1 | CoV-2 |
|-------|-------|
|-------|-------|

| | |
|--|--|
| <ul style="list-style-type: none"> • The emergence date of CoV-1 is Nov 2002 Guangdong in china (Huang et al., 2004). | <ul style="list-style-type: none"> • The emergence date of SARS CoV2 is December 2019, in Wuhan (china) (yet not controlled) |
| <ul style="list-style-type: none"> • In case of SARS-CoV, the primary host was found to be dogs, bats, palm civets (bolles et al., 2011) • 26 countries infected from CoV-1 and entry receptors ACE-2 in human causes virulent infection (sui et al., 2003). • Total infected patients are 8098, recovered-7322, died-776 (mortality rate-9.6%) (shareen et al., 2019). | <ul style="list-style-type: none"> • In SARS-CoV2 only bats could be the key reservoir (lu et al., 2020) • SARS-COV2 spread all over the world and yet not controlled and having same entry receptor ACE2 for viral infection (perlman et al., 2020). • Total infected patients are 62,634,907, recovered cases-43,241,540 death-1,459,328 (mortality rate is 2.32%) (Till date of this writing). |
| <ul style="list-style-type: none"> • Major sign and symptoms of SARS-CoV; cough, fever, shivering, headache, myalgia, diarrhea, malaise and shortness of breath (shi et al., 2003). | <ul style="list-style-type: none"> • Major sign and symptoms of SARS-CoV2: shortness of breath, dry cough, fever, chest pain and pressure and loss of taste or smell (Rhiu et al., 2020) |

Characteristics of Corona Virus Virion

Corona viruses are enveloped and have +ssRNA genome. Coronavirus family having subgroups are α (alpha), β (beta), γ (gamma) and δ (delta). In negative- stained electron microscopy corona virus has shown a fringe on their surface like spikes (Artika et al., 2020). The approx. size of corona virus is 80-120 nm and they are roughly spherical in shaped. The genome of corona virus codes for four different types of spherical proteins i.e. Corona Viruses consist of 4 fundamental proteins: NP (Nucleocapsid protein), SP (Spike protein), EP (Envelope protein) & MP (Membrane protein) (Artika et al., 2020). The envelope of corona virus contains basically Spike and Membrane protein, a third type of protein i.e., E protein is also present but not on all corona virus. The E proteins are present in less quantity but are very crucial structure constituent of the virus (de haan et al., 1999).

Envelope Protein (E)

Molecular weight of E (Envelope) protein is approx. 8.4-12 KDa. A variety of functions are performed by E protein in corona virus replication cycle; assembly, envelope formation, budding and pathogenesis. These E proteins were spotted after a long time as compared with rest three structural proteins because of their small size and limited quantity. The E protein has N-terminal (7-12 amino acids) which is hydrophobic in nature, TM Domain (25 amino acids) and a carboxy end which is hydrophilic in nature (Schoeman et al., 2019). Valine and Leucine are the two non-polar amino acids which makes TMD strongly hydrophobic in nature. A bunch of positively charged residues are present on the C-terminal which also provide hydrophobicity but the level is not strong enough compared with TMD, the CoV Envelope protein has a remarkable capacity to shape homotypic cooperation prompting

development of Viroporins (Schoeman and fielding; 2019). These viroporins are fundamental aquaphobic proteins that can make stoma on the cell membrane, can influence the arrangement of vesicles as well as glycoprotein dealing and increase cell membrane porousness (Liao et al., 2006).

Spike Protein (S)

These spike proteins are glycosylated transmembrane proteins having 1162-1452 amino acids residues. These Spike glycoprotein helps the virus to attach to the receptors of the host cell and mediate fusion between viral and cell membrane. These S (spike) protein is divided into two different sub-units i.e., S1 sub-unit and S2 sub-unit. S1 sub-unit helps in the receptor recognition and S2 sub-unit is helpful in membrane fusion (Tortorici et al., 2019). There are three domains of corona virus (fig:1). The domain outside the space of virus is termed as ectodomain, the domain middle domain is termed as transmembrane domain while the interior or intracellular tail (IC) is termed as end domain (Li et al., 2016).

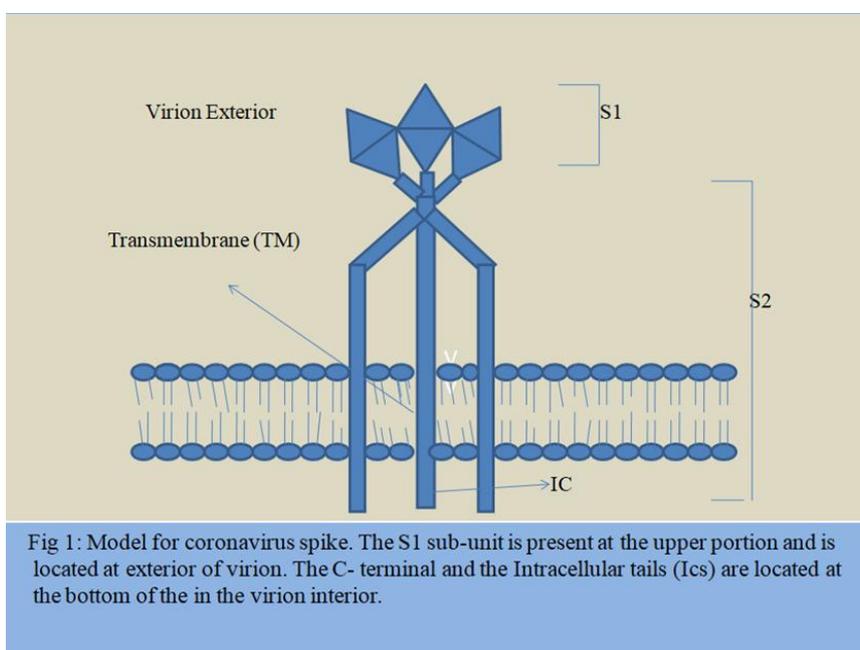
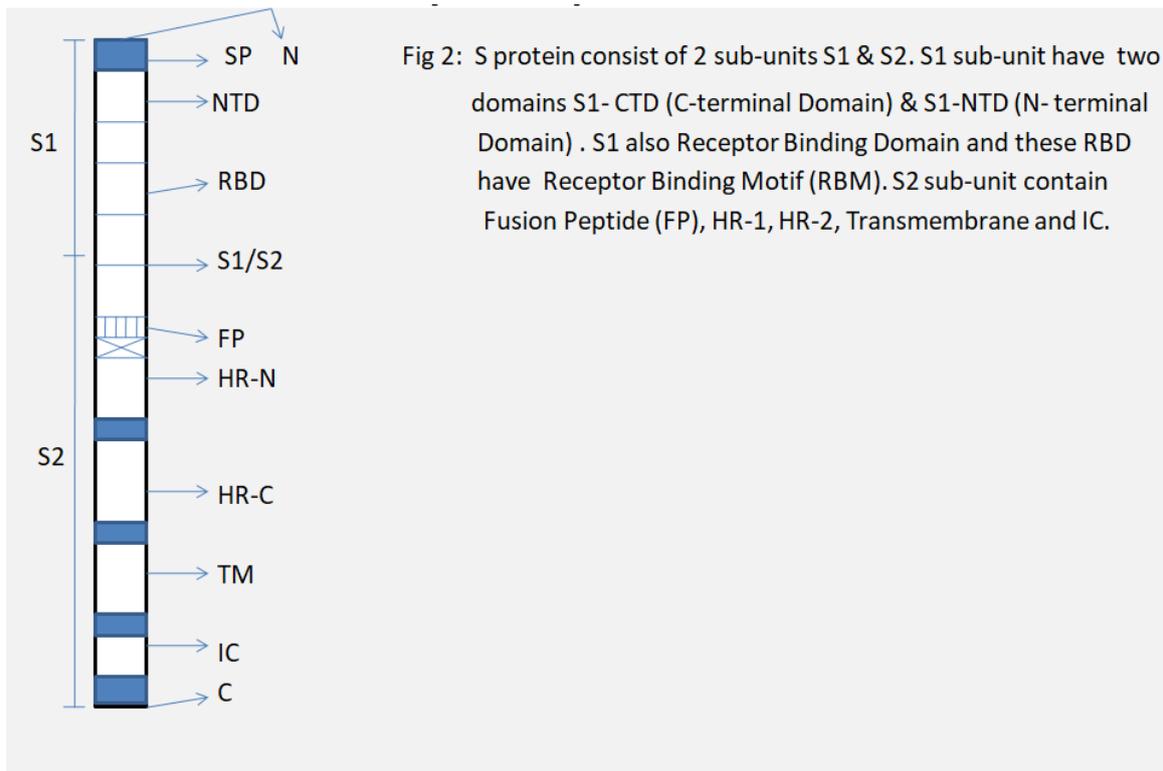


Table 2: a comparative study between S1 and S1 sub-unit of spike proteins

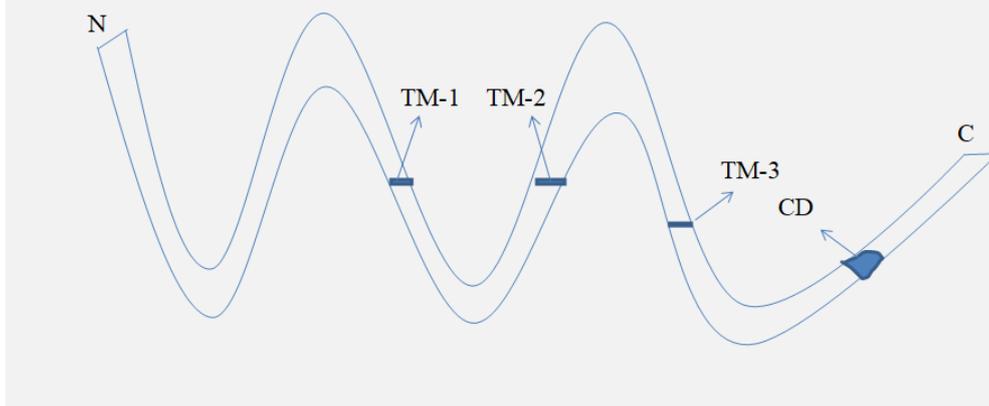
| S1 sub-unit | S2 sub-unit |
|---|---|
| It includes 2 domains; S1-N Terminal Domain (S1-NTD) and the S1-C Terminal Domain (S1-CTD). These both domains have the ability to bind with receptors and function as a Receptor Binding Domain (RBD). The S1 sub-unit of Beta coronavirus S protein is divided into four different Beta domains; D,C,B,A. B & A Receptor Binding Domain while C & D is suggested that they form Beta sheet structures nearby S2 sub-unit (Artika et al., 2020). | S2 sub-unit have different segments and these segments help to facilitate virus-cell fusion. 2 Heptad Regions; the Heptad Region-1 (HR-1 or HR-N) and the Heptad Region (HR-2 or HR-C), Fusion Peptide & a Transmembrane Domain are segments of S2 sub-unit(Artika et al., 2020). |



M Protein

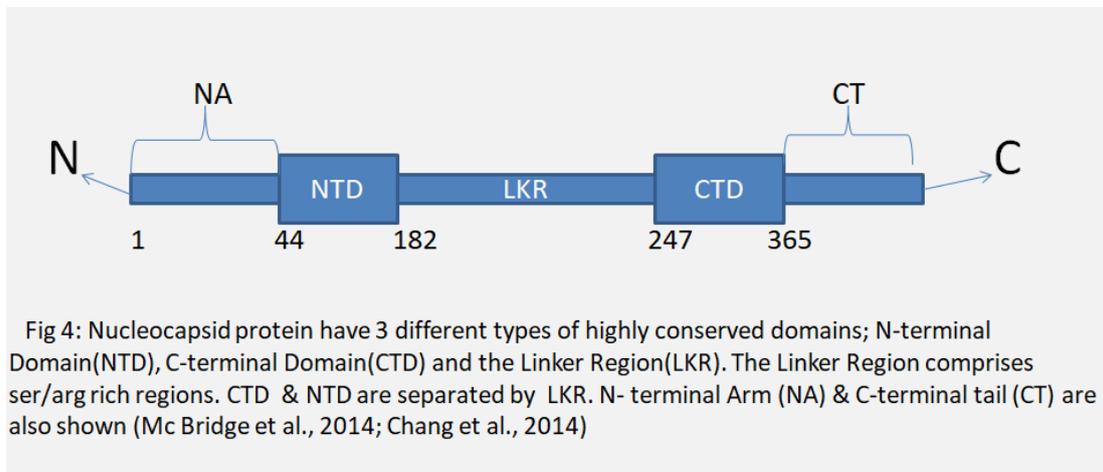
Membrane (M) protein is referred as extreme significant envelope protein and these proteins are helpful in the assembly of Virion by Membrane-Membrane, Membrane-Spike, Membrane-Nucleocapsid interaction (Arndt et al., 2010). Membrane proteins are unit proteins with amino group localised in the exo-domain and a extended carboxy group located in the end domain of the virus (Perrier et al., 2019). This Membrane(M) protein has 3 transmembrane groups (domains) bounded in between amino and the carboxy group (domain). An Amphipathic domain is also present after third TM Domain. A 12 amino acid group (domain) with SMWSFNPETNIL sequence is present at the amino terminal of the Amphipathic domain. This Conserved Domain (CD) is very much important for the membrane proteins to participate in assembly of virus (Artika et al., 2020).

Fig 3: The M protein of corona virus has three TM domains & these domains are bounded by amino terminal & carboxy terminal domain. The carboxy endodomain terminal have a conserved domain after the three transmembrane domain (Perrier et al., 2019).



Nucleocapsid Protein (N)

The Nucleocapsid proteins have a molecular weight of 43-46 KDa. The fundamental characteristics of Nucleocapsid(N) protein is that it interconnect with the VMP (viral membrane protein) & improves the efficiency of virus transcription and assembly. Nucleocapsid protein have 3 different types of highly conserved domains: C,N-terminal Domain and the Linker Region (LKR). The Linker Region comprises ser/arg rich regions that contain various phosphorylation sites. This sites plays a critical character in attachment of heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1), M-protein & RNA with the N(Nucleocapsid) protein (Chang et al., 2014) & CTD spans from 248-365 amino acid residues. Homo-oligomers formation is facilitated by CTD mechanism of domain-swapping. Stable confirmation of N protein is achieved by oligomerization.



Bio-molecular features of Covid-19

Genomic analysis of several patients were done, which showed that the length of genome has twenty nine thousand eight hundred ninety one (29,891) bases, that are 79-80 % similar to CoV-1, with respect to another corona virus. Genome of CoV-2 has 6 ORFs. When amino acids sequences of conserved 7 replicase domain in ORF1-ab were compared, the sequence identity between CoV-1 & CoV-2 were 94.4%. It was then concluded both SARS-CoV & SARS-CoV-2 are of the same species (Zhou et al., 2020). When more studies were done on CoV-2, it revealed that it has similarity with bat coronavirus(genomic similarity), BatCoV RaTG13, found in *Rhinophilus affine* and have 96.2% of sequence identity. Evolutionary analysis was then executed that revealed that RaTG13 is the nearest relative of CoV-2. This relationship also suggested that CoV-2 may have derived in bats (Zhou et al., 2020) and also are the reservoir of CoV-2 (Lu et al., 2020).

Cov-2 were 91-92% genomically similar with MP (Malayan Pangolins) & MP are also 90.55% similar to BatCovRaTG13 (Zhang et al., 2020(b)). This sequence similarity revealed that Pangolins CoV may be the 2nd nearest relative of CoV-2. One important difference between SARS-CoV-1 & SARS-CoV-2 is that SARS-CoV-2 has 3 small infusions in the N-terminal and change was seen in 4 out of 5 residues in the RBM (Receptor-Binding-Motifs). Shang and Co-workers (2020) made us clearer about the structure of CoV-2 RBD involved with ACE-2. Change in the four residue motifs 482-485: Gly;Val;Glu;Gly of RBM of SARS-CoV-2 lead stronger connection b/w CoV-2 Receptor Binding Motifs & ACE-2(human) & one important characteristic of CoV-2 is the existence of polybasic separation sites at the center point of S1-S2 due to insertion of (PRRA) amino acids residues at CoV-2 S position six hundred eighty one to six hundred eighty four (Anderson et al.,2020). Along with this, a

proline is also inserted in the poly basic cleavage sites of the S position of CoV-2 & CoV-2 is also triggered (proteolytically) via Cathepsin L (Ou et al., 2020). SARS-CoV-2 has a much high AU content which may be a key feature for finer adjustment to host (human).

Mechanism of Entry

Corona Viruses consist of 4 fundamental proteins: NP (Nucleocapsid protein), SP (Spike protein), EP (Envelope protein) & MP (Membrane protein). E & M proteins are required in virus assembly while proteins are required for entry of virus & recognition of host cell (Li et al., 2016). The corona likes spikes present on the surface of corona so, it is called corona virus and Coronavirus were very minute in size about 65-125nm in diameter, 26 to 32 kbs in length and have single stranded RNA. When infection occurs, the S1 sub-unit attaches with the cell(host) receptors while the S2 sub-unit fuses the host and viral membrane and this fusion leads to the viral genomic transmission to the cell(host). During Viral entry, the sugar receptors of the cell(host) and also ACE-2 receptors of the cell(host) binds directly with the S1 sub-unit while the S2 sub-unit undergoes symmetrical changes and obtains Post-fusion-state (Millet et al., 2015). At this stage 3 pair of heptad regions forms a 6-helix-bundle-structure (Hofmann et al., 2004). The buried aquaphobic merging peptides become turned out & inserted into the cell membrane of host. Throughout this course, a huge quantity of entry is liberated, that speed up the membrane fusion. The membrane fusion can also trigger by low pH & receptor binding (Li et al., 2016). As, spike proteins has great cross-linking affinity for sugar receptors, they use this mechanism to enter the cell. The SARS-CoV-2 possess affinity for ACE-2. So, the Spike(S) protein CoV-2 ties with the peptidase domain of Human ACE-2 with approx. 15 nm Kd (Wrapp et al., 2020). Transmembrane protein series 2(TMPRSS2) is also very crucial for entry of CoV-2(Gralinski et al., 2020). Endocytosis is the process by which SARS-CoV enters the cell, where their S proteins are treated by Cathepsin B & Cathepsin L lysosomal protease. Endocytic pathway & non-endosomal pathway are only the two pathways by which virus can enter the cells (Zumla et al., 2016). Catherin depending endocytosis is largely considered for virulent entry of MERS-CoV and SARS-CoV. As the Covid-19 also utilize similar receptor as virulent infection of SARS-CoV. So, this can be described the same viral entry mechanism is also utilized by CoV-2.

Transmission

Before the symptoms occur, CoV-2 can be detected in blood, urine, sputum and saliva. The most significant way for transmission of SARS-CoV-2 from an infected to a healthy person is either through direct contact or through any of their belongings. Examination of data from china linked to transmission of CoV-2 indicated that physical touch between the two individuals is essential. The droplets debar during wheezing and hacking is the major significant way of transference. When healthy person is directly contact with a suspected person within 6 feet for 15 min are said to be at high risk of exposure and this can result in contamination or transference of virulent virus CoV-2 (Chu et al., 2020). Virus adheres at higher level on impenetrable surface than that of penetrable. Impenetrable surface such as non-reactive metal or plastics and penetrable surface; posterboard(Van et al., 2020). Studies was done and it was found that the duration of contamination on stainless steel (two-three days), on plastic (two-three days), cardboard (one day) and for copper (four hrs). Transmission via fomites (contaminated objects like door knob, clothes, and cutlery) and a tiny drop disperse or physical touch are regarded as the secondary method of transference. Furthermore, in hospital virulent infection is greater in ICU than that of normal wards(Guo et al., 2020). Covid-19 infected individuals are both asymptomatic and symptomatic; both were capable to transfer the virus from infected to healthy individual whereas symptomatic refers to those that infected individuals shows symptoms like dry cough, fever, shortness of

breathing and on the other hand asymptomatic refers to those which does not shows any symptom (engl et al., 2020).

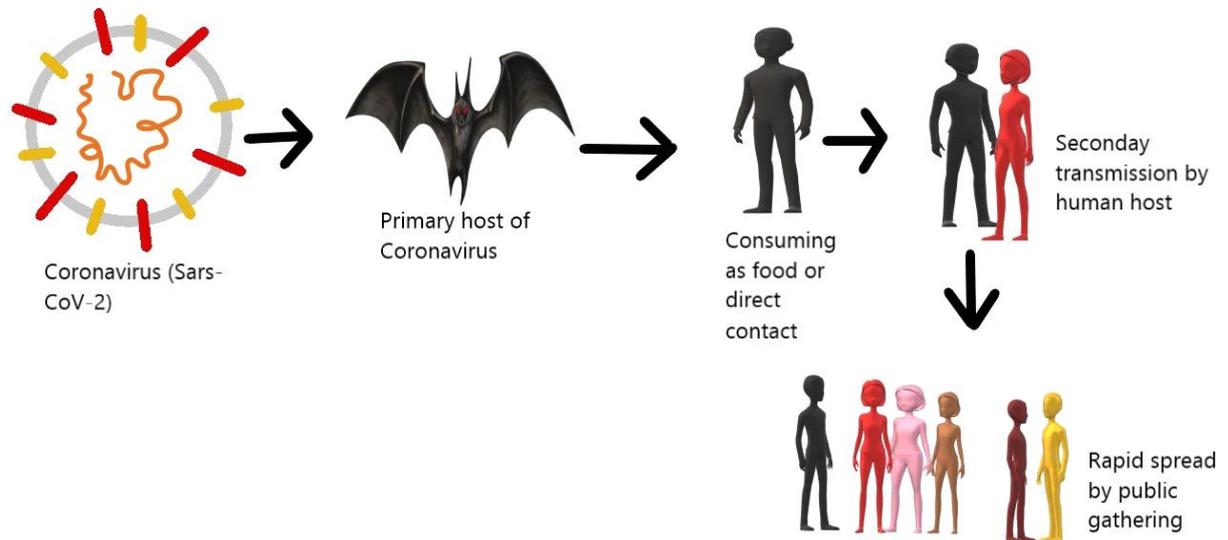


Figure 5: Transmission cycle: primary host (bat), consuming as food, direct contact infected individual with healthy person, and at last rapid spread by public gatherings without using any precautions like mask, social distancing.

Disease risk is not same for all age groups: 80% infected patients were properly recovered from the covid-19 without any clinical consideration, they recover with their own strong immunity fight against the virus (wang et al., 2019). The individuals more than 50 years have medical problems like high BP, heart disease, live disease or cancer, diabetes was having high risk of effect of disease (shereen et al., 2020).

Diagnosis

As recommended by WHO, specimens can be collected from both Lower (expectorated septum, endotracheal aspirate or broncho alveolar lavage) and Upper Respiratory tract. The sample collected are stored at 4 degree Celsius. The testing approach for COVID-19 detection fall under 2 groups: Serological & Nucleic Acid. Nucleic-acid analysis is done for the detection of RNA of viruses taken out from a nasal passage or patient's throat, whereas serological tests is done for the diagnosis of antibodies present in the serum of the patient. Nucleic Acid test is the very sensitive technique for the identification of CoV-2. The Reverse Transcription or real time PCR test introduced by CDC have been considered the 'Au (gold) standard' for the identification but it is very time consuming & required specialized equipment's, training and reagents (Centre for Disease Control & Prevention). Other method alternative to this involving nucleic acid test is isothermal amplification and CRISPER-based detection. More techniques like sequencing, digital PCR & DNA nano switches are other tools that can be used for COVID-19 detection.

In RT-PCR, CDC approved RT-PCR test involves 3 main steps: Collection of the sample & transport, lysis, purification of RNA and amplification. Nasopharyngeal Swab are collected & transferred into a vial having few ml of VTM (Viral Transport Medium), which is then transferred to the lab for analysis. Now, to lyse or inactivate viral particles; chemical lysis buffer is used or heating is performed & then after performing all the above described steps the test considered as + (positive) if intensification or amplification is examined for viral

targets (more than two), whereas it is supposed as - (negative) if intensification or amplification is seen only in the positive control RNA but none for virulent targets (CDC 2020). In Isothermal Amplification, another technique for the recognition of SARS-CoV-2 is isothermal amplification and the benefit of this strategy is that it doesn't need thermocycling step. For quick and delicate analysis two isothermal strategies are utilized; RAP(Recombinase-Polymerase-Amplification) & LAMP (Loop-Mediated-Isothermal-Amplification)(Piepenburg et al. 2006). In CRISPER Cas, researchers recently have found that a group of Cas nuclease (including Cas 12 & 13) that have the ability to cleave RNA OR DNA (Gootenberg et al., 2017), which is then can be used for nucleic acid detection. A recently emerged technique combining CRISPER & isothermal amplification can be used as rapid detection for COVID-19 Viral RNA.

Treatment

Since SARS-CoV-2 is a recently arisen infection and no possible treatment is accessible till now, yet a few methodologies has been proposed to fight against the virulent infection caused by CoV-2, such as; Ritonavir or Lopinavir; a protease inhibitor(Bimonte et al., 2020) helpful in preventing disease, Chloroquine or Hydrochloroquine can be utilized for SARS-CoV-2 antiviral activity yet the information on the side of this is inadequate(Yazdany et al., 2020), Azithromycin is essentially used to treat bacterial respiratory infections and may help in treating or forestalling co-infection with SARS-CoV-2 (Oldenburg et al., 2020), Camostat mesylate; a serine protease inhibitor that is dynamic against TMPRSS2 can repress the virulent infection of Covid-19 in pulmonary cells (human)(Wang et al., 2020). Other medication like augmentin (an anti-biotic having amoxicillin and clavulanic acid) can deal with diseases of the lungs like pneumonia, Montair LC (a mix of levocetirizine and montelukast) can provide relief from sneezing and runny nose. However, there is no information supporting that these are successful against SARS-CoV-2. As research is currently going everyday on SARS -CoV-2 new and compelling approaches to treat SARS-CoV-2 disease are coming day by day.

Precautions:

Precautions used to slow down the pandemic, it is very simple to stop the spreading of virus happening in the first place rather than to cure or treat disease after it has happened and globally spread like novel coronavirus. These are some precautions: clean hands regularly with the help of cleansers like soaps and liquor based, keep a proper protection in good ways from any individuals who is having hacking or wheezing, maintain the physical distance, avoid crowded places, properly cover face with mask when physical separating is not possible, if any individuals feel unwell like fever, hack and trouble in breathing then remain at home and properly cover the face with tissue or twisted elbow and immediately look for clinical consideration.



Figure 6: precautions used to slow down the pandemic: use mask and keep your social distancing, use sanitizer to kill the germs, avoid crowded places.

2. CONCLUSION

The coronavirus (CoV-19) is exceedingly virulent and disease-causing infection produced by Severe Acute Respiratory Syndrome which is developed in the seafood market of China (Wuhan) where palm civets, racoon dogs, , bats, snakes many other animals are supplied and widely expanded all over the world. The somatic cause of SARA-COV-2 is yet not proved and in the genomic examination declared that SARS CoV and SARS-CoV-2 is phylogenetically similar to each other while both were belonging to same family, same entry receptor ACE2 and both have common reservoir for viral infection and rapidly spread by the touch of suspected person to healthy person. The no. of cases of infected persons increased globally yet not controlled but still there clinically affirmed antiviral medicines have been check out against coronavirus disease. At last, 80% infected patients were properly recovered from this viral infection covid-19 without any clinical consideration they recover with their own strong immunity and fight against infection.

Future Prospects

Coronavirus targeting vaccines should be designed against pandemic and slow the spreading of virus. Around worldwide firms working to slow down the virulent infection of SARS-COV2 virus, such as vir biotechnology, Curevea, inovio pharmaceuticals and moderns therapeutics. But there is requirement of rapid treatment to control the pandemic as this vaccine still need time around 5-10 months for the proper commercialization and there should be properly prohibition on consuming birds & animals as a food consumption. Therefore, there is accurate and quick detection required to isolate the suspected patients like biosensors were present in Smartphone to immediately detect the virus and to control viral infection of novel covid-19.

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