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RESEARCH ARTICLE

AN INSIGHT REVIEW ON HISTORY, OUTBREAK, PATHOGENESIS, TRANSMISSION OF SARS-CoV-2 VIRUSAND COVID-19

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a deadly virus which is extended at the end of 2019 globally form seafood market, Wuhan, China and considered as novel coronavirus which has 70% similarity with SARS-CoV and MERS-CoV. SARS-CoV-2 considered as globally pandemic because of high mortality and fatality rate among worldwide by the World Health Organization (WHO). The disease caused by this called Coronavirus Disease 2019 (COVID-19) in which 19 referred to as the year of occurrence of disease. The intermediate sources are humans but it is not known seriously but it is confirmed that the spreading is done by human-to-human transmission rapidly and widely. This review highlights the whole insight and the understanding towards the SARS-CoV-2 and COVID-19 regarding its, spreading history, origin, epidemiology, prevalence rate, sources and modes of transmission, pathogenesis, life cycle entry mechanisms, clinical characteristics, symptoms, complications of comorbidities, diagnosis, treatment, research hindrances, preventive measures, potential pharmacological therapeutics (repurposing of main drugs) research with previous studies of SARS and MERS. The literature review databases were searched from the Scopus, MEDLINE, PUBMED, Elsevier, WHO situation reports. The SARS-CoV-2 infection has a high mortality rate and leads to a high global disaster to human well-being, social as well as economic. Lockdown phases are taken to prevent the spreading of the virus. Solitary confinement procedures followed by the clinical and health care services so, to inhibit the contamination of the areas with suspected patients. The research on the novel coronavirus (n-CoV) is still a concern and in the primary stage in which repurposing of the main pharmacological drugs which act on symptoms of COVID-19 trials are held. As such no clinically tested/approved vaccines/anti-viral drugs are prepared, approaches for preparation in respect to these viral outbreaks and against the COVID-19 and SARS-CoV-2. However, some broad-spectrum antibiotics, anti-viral drugs, angiotensin-converting enzymes 2 inhibitors (ACE 2) are clinically screened for the COVID-19 disease in clinical trials. This review article gives information publically about the COVID-19 and SARS-CoV-2 infection.

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Introduction:-

The coronavirus belongs to those family of viruses which are common in animals globally but not or very minor effect cases were shown in humankind. This can cause an infection in the upper parts of the body such as nose, sinuses, upper throat, respiratory tract and with many more symptoms. As such not all the coronavirus is dangerous to humankind but some strains have potential and dangerous effects which increase the rate of fatality and mortality worldwide. As we know the history and origin of the coronavirus is that the first case occurred in the year 1960 and the researchers identified and noticed it as cold, in 2001 the Canadian study, Flu-like symptoms were identified among humans patients and with the help of detecting tools polymerase chain reaction they found that most of the cases were confirmed and identified in response to coronavirus strain. But in the year 2002, the coronavirus was treated as a normal virus and considered as non-fatal. 2003 is the year which is known as "Black Year for Microbiologist" because various reports and identification of coronavirus suspects from different countries including United States of America, Singapore, Thailand, Vietnam, Taiwan, Hong Kong are suffered from various cases of severe acute respiratory syndrome (SARS) whose mortality rate as much higher with more than 1000 individuals patients. As they are not considered as highly pathogenic for humankind until or unless they have been seen with SARS with severe acute respiratory syndrome coronavirus (SARS-CoV) in the state of Guangdong in China country in the year 2002 and 2003. As per the past outbreaks, the major and most common types of coronavirus are CoVOC43 and CoV229E strains which have mild to moderate infection rate in people who are suffered from the weak immune system [1,2]. And about 10 years later, the new coronavirus occurred in Middle East Countries and cause highly fatality rate in comparison to SARS and endemic known as the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) which causes middle east respiratory syndrome include acute lung injury (ALI), respiratory distress disorders [3] and after the severe deaths and about 8096 patients who are infected with coronavirus the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDCP) in the year 2004 have declared that this situation is the “State Emergency” [4,5]. Then in the year 2012, the country Saudi Arabian presented and reports the severe fatality and mortality rate among infected patients [2,6].Recently at the end of the 2019 year, present time there was the occurrence of a sequential series of many cases of pneumonia-like symptoms and conditions with unknown causative agents in seafood market Wuhan of Hubei, China and experienced an outbreak of novel coronavirus that can kill about the highest number of about 1800 and cause infection over to 17000 persons within 50 days of the epidemic. And this virus is the member of β-group of coronavirus family and the Chinese researchers named it as Wuhan coronavirus or 2019 novel coronavirus (2019-n-CoV) [7]. After few weeks in the year 2020, January the researchers have analyzed the samples taken from the lower respiratory tract of the human body and identified a new strain of coronavirus which is known as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as novel and declared as the causative agent for the observed pneumonia cluster disease [8,9]. The Director-General, Dr. Tedros Adhanom Ghebreyesus of WHO named this disease as “Coronavirus Disease 2019" (COVID-19) in which 19 stands for the year of origination of virus and also give information about causative agent of this disease which is called "SARS-CoV-2", and due to this the WHO declare this as the pandemic situation on 11th March 2020 because numerous countries are under this and stand on the line of high mortality rate with severe infection range among individuals with several 114 countries, 118000 cases and 4000 and more deaths [10]. In this review article, I discuss the whole history, origin, complications, microbiology, transmissions, research scenario of the SARS, MERS, and special attention regarding COVID-19 and n-CoV.

Epidemiology of Coronavirus And COVID-19

The epidemiological study of coronavirus and COVID-19 disease which have their expansion in early 2019 December, from Wuhan city of China which afterwards leads the major causation and exportation of this novel coronavirus and disease to other countries with the increased number of mortality rate. On January 13, 2020, Thailand (Bangkok) is another country other than china which confirmed and reported the first case of coronavirus. Most of the other countries were continuously affected with high range and on 2March 2020 about 67 territories of the world except china reported about 8565 cases of coronavirus disease with 132 deaths and transmission of infections and because of this WHO announces it as pandemic situation among countries. But the world nation was undergoing a very potent crisis with no globally standard usage and because of this, the pandemical chart is not prepared by country properly [11-13]. Based on WHO situation reports132 of 31 May 2020 as shown in Fig. **(1)**, it was estimated that there were several new cases and deaths are reported during 24 hours to include globally 5934936 cases (117551) and 367166 deaths (4461) [14]. The investigations which were performed on patients for Etiology in hospitals due to similar pneumonia-like viral diseases and the history leads to the potential risk of

animals contact with patients which proved to be transmitted from animals to humans and cause infection. On 22 January 2020, it has been declared that novel coronavirus (n-CoV) originated from wild bats and belong to coronavirus family which have SARS-CoV. The genetic level of COVID-19 and SARS-CoV are about 70% identical and the SARS-CoV-2 strain shows variations among the genetic constitution from SARS-CoV and undergo mutation by which its transmission rate is very high [1].

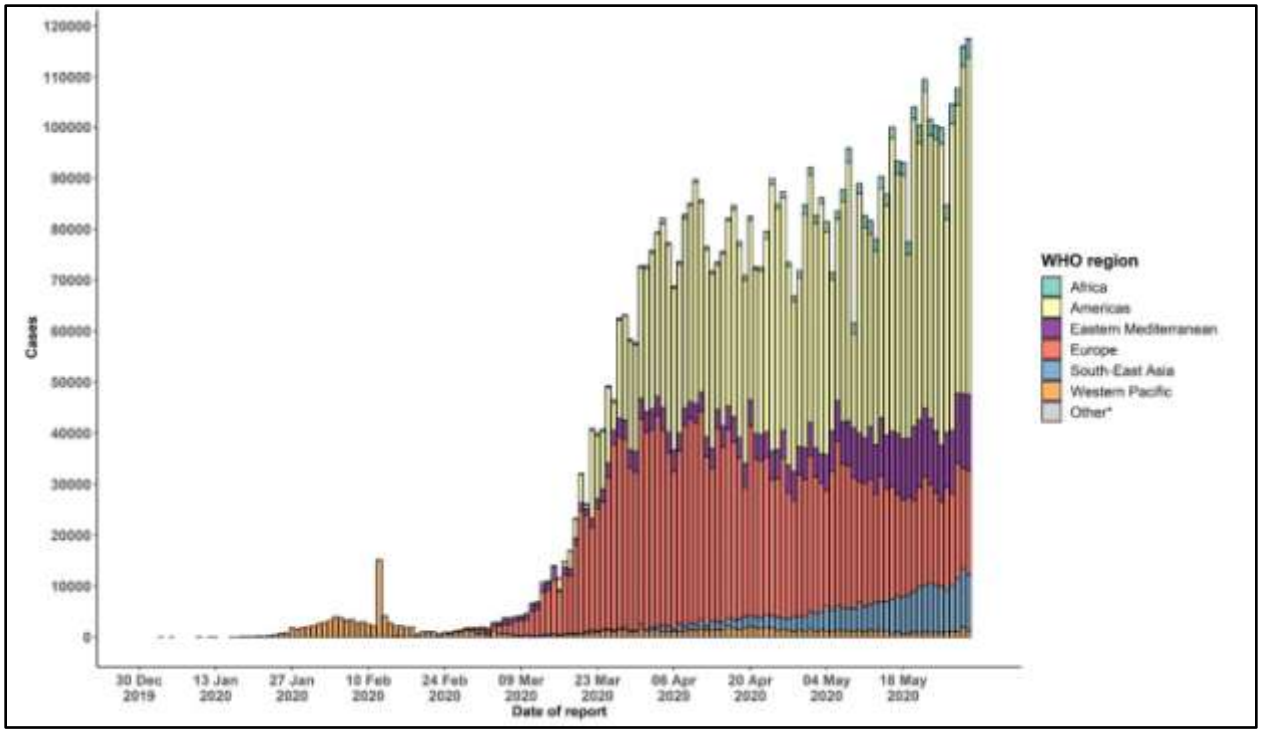

Figure 1: - WHO report of the number of confirmed COVID-19 novel coronavirus cases, from 30 December 2019 through 31 May 2020 [14].

Prevalence Rate of Coronavirus and COVID-19

The prevalence rate is based on the Basic Reproduction Number (R0) which gives the average number of secondary infections by which patients produce in a completely susceptible population without any intervention. This number is varied among different countries by different investigators team [15]. This number is estimated by various models such as SEIR [16] and IDEA model [17]. The R0 value of SARS-CoV is estimated the prevalence rate in between 2.2-3.6 [18] whereas MERS-CoV is in between 2.0-6.7so, because of this reproduction number it was indicated that SARS-CoV-2 has high transmission rate with increase fatality and mortality ratio. In the population the middle age individuals who have 47 median age, 87% cases of 30-79, and 3% about 80 years of ages and older who have suffered from other complications of diseases such as hypertension, diabetes, pulmonary disorder and female either pregnant or non-pregnant about 41.9% are highly susceptible to this virus. In Wuhan, China the overall case fatality rate (CFR) was 2.3%, 8.0% and 14.8% with respective median and older ages. So, it was found that prevalence rate of COVID-19 and the n-CoV is very high and the global population are susceptible to this virus and in 30 days only the Wuhan city of China is rapidly export and spreading the virus in other countries in about just 30 days and leads to the pandemic situation due to the high mortality rate of the population so, the valid measures should be taken to deal with this unfortunate situation among humankind [19].

Microbiology of Coronavirus

The coronavirus is the virus which is an electron microscopic spherical, pleomorphic, and single-stranded RNA virus as shown in Fig. **(2)**, it is covered with enveloped structure with a glycoprotein shaped spike protein (S-proteins) club. The coronavirus has four genera species including α (alpha) coronavirus (alpha CoV), β (beta) coronavirus (beta CoV), γ (gamma) coronavirus (gamma CoV) and δ (delta) coronavirus (delta CoV) as shown in Fig. **(3)**. These all subtypes have different strains which are originated from various wild animals such as wild bats, birds, snakes, rodents, pigs, dogs [20,21].

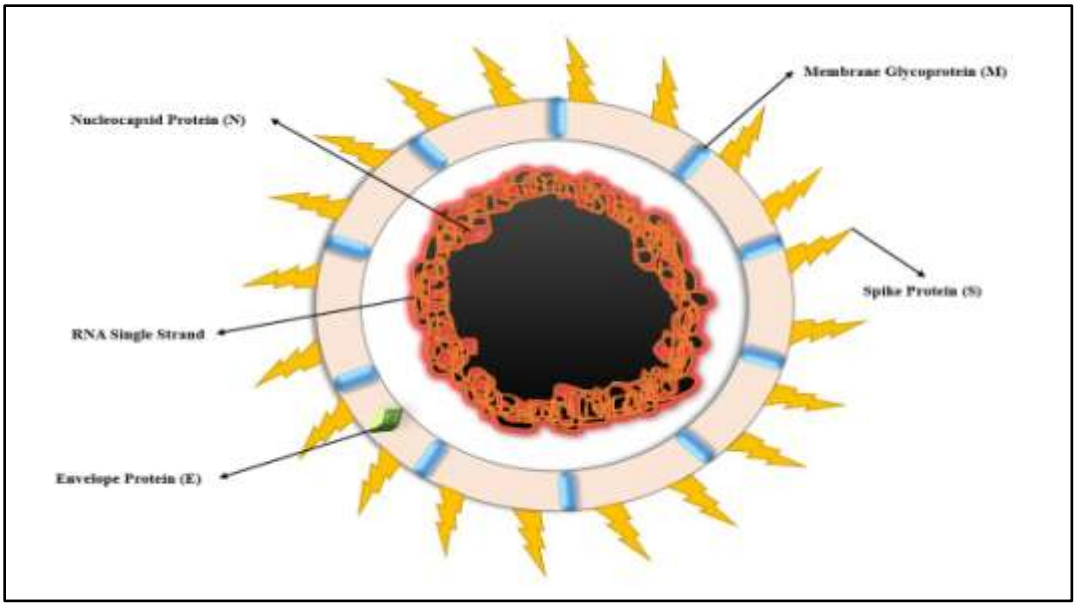

Figure 2: -Structure of SARS-CoV (the strain of beta CoV).

CLASSIFICATION OF CORONAVIRUS						
ORDER	Nidovirales					
FAMILY	Coronaviridae					
SUB-FAMILY	Coronavirinae				Torovirinae	
SUBTYPES	ALPHA (α) Coronavirus	BETA (β) Coronavirus	GAMMA (γ) Coronavirus	DELTA (δ) Coronavirus	TOROVIRUS	BAFINIVIRUS
STRAINS	• HCOV- 229E • HCOV-NL63	• HCOV-HKU1 • SARS-COV • MERS-COV • HCOV-OC43				
NEW STRAINS		• SARS-CoV-2 (NOVEL CORONAVIRUS)				

Figure 3: -Classification of coronavirus which is pathogenic in humans.

The novel coronavirus is mutated from the SARS and MERS which are highly identical, pathogenic to humans and the strains are known as the SARS-CoV-2 from bat derived SARS coronavirus in which the genome variations of bat-SL-CoVZC45 and bat-SL-CoVZXC21 leads to high mortality rate because they are genetically different from SARS-CoV and MERS-CoV [22].

Sources of Coronavirus

The source of coronavirus is important to determine because this can lead to help in taken preventive strategies to prevent pathogenic infections to the humankind. The novel coronavirus is the virus which affects the upper respiratory tract and because this it is also known as respiratory tract virus and it is identified in the individuals collected samples by the researchers in 1962 [23]. The coronavirus is the large family viruses which are found in different animal species such as camels, cats, pigs, bats. But rarely, these animal sources can infect the humans but after some time the sources become fatal and spread the virus infection in humans during epidemics such as MERS, SARS and COVID-19 as shown in Fig. **(4)** [24,25]. Due to the onset of major outbreaks which was caused by a coronavirus, cats were proposed to natural primary reservoir of human coronavirus for SARS and dromedary camels

are the primary source or zoonotic source of MERS. After many pieces of research, virologists and genetic studies it was found that bats are the primary sources and considered as hosts for the strains of viruses such as SARS-CoV and MERS-CoV before spreading to humans, but in actual it can use the intermediate hosts such as camels, cats, pigs for infecting the humans as they were used commercially by humans in means of food. Studies proved that the genomic sequences of alpha-CoV and beta-CoVs subtypes of coronavirus are originated from the bat and most of the birds are the carrier and gene source of gamma-CoV and delta-CoVs. The novel coronavirus spreadingwassupportingthe Wuhan Seafood Market [1].

Table1:- Difference between the biological features of SARS-CoV and Novel SARS-CoV-2.

Biological features	SARS-CoV	SARS-CoV-2	References
Origination Date	November 2002	December 2019	[26]
Area of Origin	Guangdong, China	Seafood Market Wuhan, China	
Controlled Date	July 2003	The situation becomes worst and not yet controlled	
Hosts	Bats, palm civets (cats), racoon dogs	Bats	[27]
Family	Beta (β) CoV	Beta (β) CoV	
Intermediate Hosts	Camels, pigs	Not confirmed	
Binding Receptors	ACE2 receptor found in the lungs	ACE2 receptor found in the lungs	[28]
Clinical Signs and Symptoms	Fever, headache, shivering, malaise, myalgia, shortness of breath	Cough, fever, sneezing, shortness of breath	
Diseases Occurred	SARS, lungs diseases	SARS, COVID-19	
Countries Affected	26	109 (this led to pandemic)	[29]
Total Infected Patients	8098	123882	
Total Recovered Patients	7322	67051	
Total Died Patients	776	4473	
Mortality Rate	9.6%	3.61%	

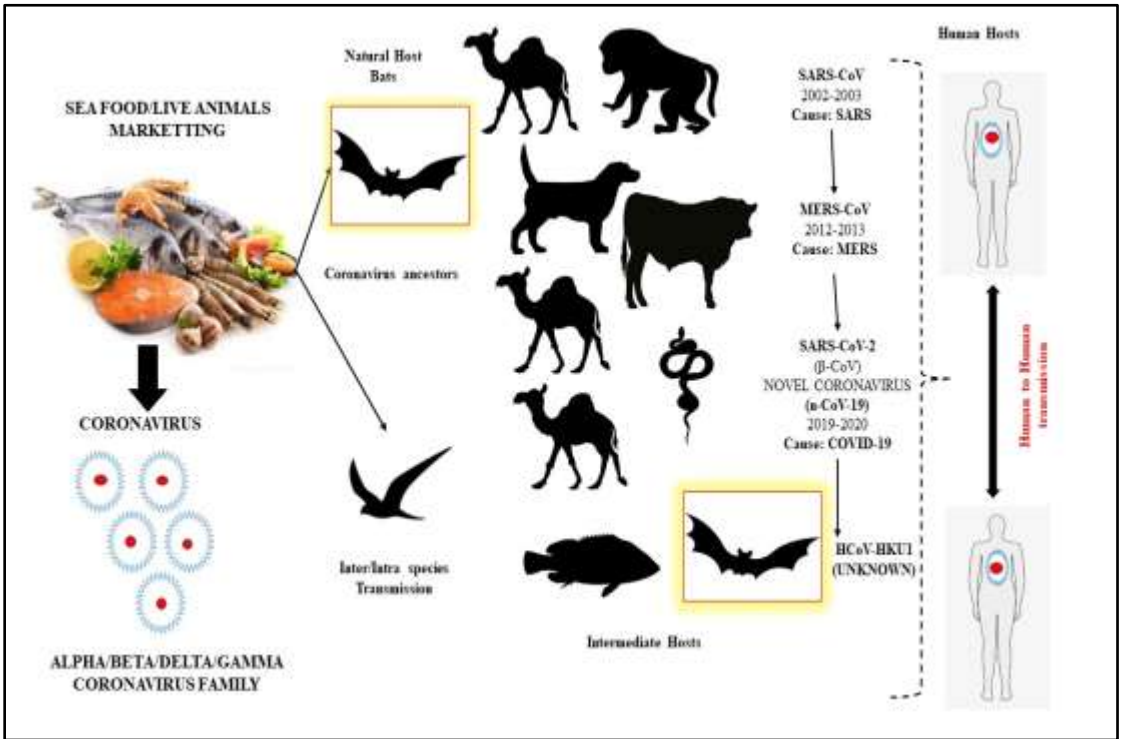

Figure 4:- Zoonotic primary sources of the coronavirus (SARS-CoV-2) infection and transmission to humans.

Clinical Characteristically Features of SARS-CoV-2

The characteristically/biological features of the novel SARS-CoV-2 as shown in Table **1** is determined based on a report which was published on 24 January 2020, in which it was stated that virus-infected patients have common symptoms include fever, cough, myalgia and fatigue while the other symptoms such as diarrhoea and dyspnoea were found to be uncommon symptoms and abnormalities in an individual patient. This virus was isolated from bronchoalveolar lavage fluid in China, 2020. The virus is detected in blood samples but till now there is no evidence of detection of the virus in the urine sample and the faeces of patients [26,30,31]. COVID-19 produces an acute viral infection in about 3 days after exposure in humans, and this is similar to SARS whose exposure days range from 2-10 days [32]. The biopsy of coronavirus manifestation is done by using various organ and tissues of the human body such as the stomach, duodenum, and rectal mucosa which confirmed the occurrence and positive confirmation of SARS-CoV-2 RNA as shown in Fig. **(5)**[33]. Examined patients by X-rays/thorax CT scan images, show bilateral and unilateral involvements which are identical and compatible with viral pneumonia and the in the intensive care units (ICU) of the hospitals in which the patients are hospitalized have found multiple bilateral lobular and subsegmental areas [26].

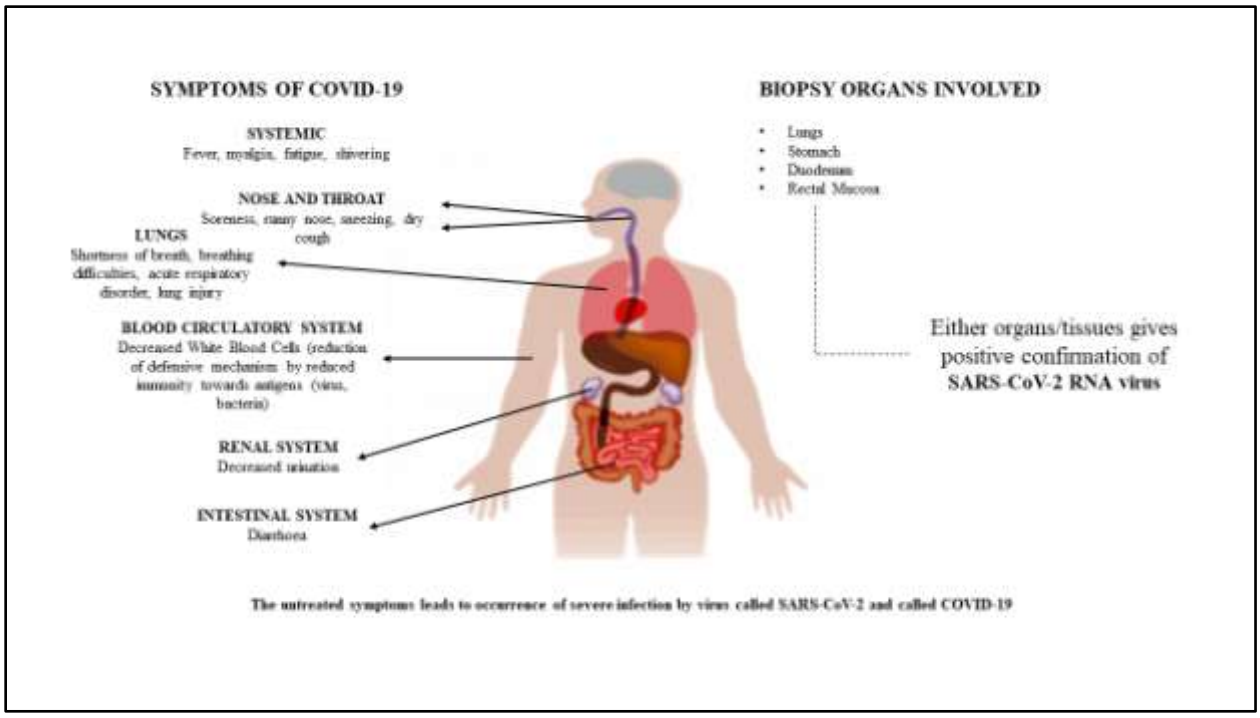

Figure 5:- Symptoms and the biopsy organs involved in SARS-CoV-2 infection.

Mode of Transmission of SARS-CoV-2

The peoples get affected by the infection of coronavirus through close contact with the human to the human who has various symptoms such as coughs, sneezing. In general, the virus can be transmitted or spread through airborne zoonotic droplets and these droplets can infect the human and leads to disease COVID-19, SARS. The virus replication held in the ciliated epithelium and leads to cause cellular physiological changes, damage and infection at the site of infection. The various families subtypes of coronavirus it was found that only α and β coronavirus can infect the humans due to consumption of these infected animals such as snakes, bats, pigs, birds, as these acted as the source of food which is the major cause of the transmission of the virus which infects the healthy person. initially, as per the researcher's investigation, it was proposed that snakes are the possible reservoir host for infecting the humans with the virus but after several findings in the genomic sequences similarity and variations of the novel coronavirus with SARS-like bat viruses proved the investigation that snakes are not the key reservoirs but only the bats have potential to transmits this virus and act as key reservoirs. Homologous recombination technique analysis revealed that angiotensin-converting enzyme (ACE) 2 receptor binding with the enveloped spike glycoprotein od the novel coronavirus is developed from SARS-CoV (CoVZXC21 or CoVZC45) but the beta coronavirus activity is yet to be unknown. And for this numerous works is used to perform regarding the aspects of the identification of the

intermediated hosts and sources which caused the transmission of the virus to humans by consuming the animals as shown in Table **2** [34].

Table 2:- Different modes of transmission of SARS-CoV-2 and its associated descriptions.

CONDITIONS OF TRANSMISSION OF SARS-CoV-2 IN HUMANS		
Modes	**Description**	**References**
Source of infection	Bats act as natural hosts of the virus, and pangolins and snakes act as intermediate hosts. In a study, it has similarity that SARS-CoV-2 isolated from pangolins and the virus strains infecting the humans currently about 99% by using various sequencing techniques. But in the present situation, the main infectious source of SARS-CoV-2 is COVID-19 patients in the worldwide population, the patients which were kept under incubation period is still a dispute to prove that transmissions held by these or not.	[35]
Route of transmission	Transmission by aerosol or airborne droplets is the main for the virus transmission to human to human. The gastrointestinal tract, stools, urine samples were taken and proved to have SARS-CoV-2. Tears, conjunctival secretions, and gastrointestinal tissues of COVID-19 patients have the presence of SARS-CoV-2 RNA which infect the healthy humans.	[33,36]
Viral susceptibility	Susceptibility to the SARS-CoV-2 is most dangerous to old age persons. Maximum latency is about 24 days for the virus transmission but it was found that 20 days is for older age because of complications and leads to higher disease progression as compared to young.	[37]

Risk and Causative Factors of Sars-Cov-2 And Complications by Other Major Disorders in COVID-19

In between the age of 34-59 years of male adult patients who are infected with SARS-CoV-2 virus are the risk potential for infection-prone because the physiological systems if undergo any disturbance they were susceptible to the disease COVID-19. Most of the severe cases occur in adults who are ≥ 60 years of age and with certain kind of underlying diseased condition, such as cardiovascular diseases (CVDs), diabetes, cerebrovascular diseases, any kind of bacterial and fungal diseases which are caused superinfections or coinfections along with the SARS-CoV-2 virus strain of beta coronavirus and leads to chronic comorbidities as shown in Fig. **(6)** [38].

These all complications are thought to be for COVID-19 because of cytokine storm which was triggered by the host (human) immune response against the virus. The virally triggered inflammation causes venous thromboembolism (VTE) and acute respiratory distress problems and its relationships which manifests COVID-19 and this is still under research and investigation process. As such the pulmonary embolism (PE) suffered patients increases in hospitals morbidity and mortality, the primary or the acute infection triggered the VTE [39]. The respiratory tract infections are the higher impact on the VTE and PE than the non-respiratory infections. Coagulatory inflammation which was triggered by viral infection is widely observed in COVID-19 [40].

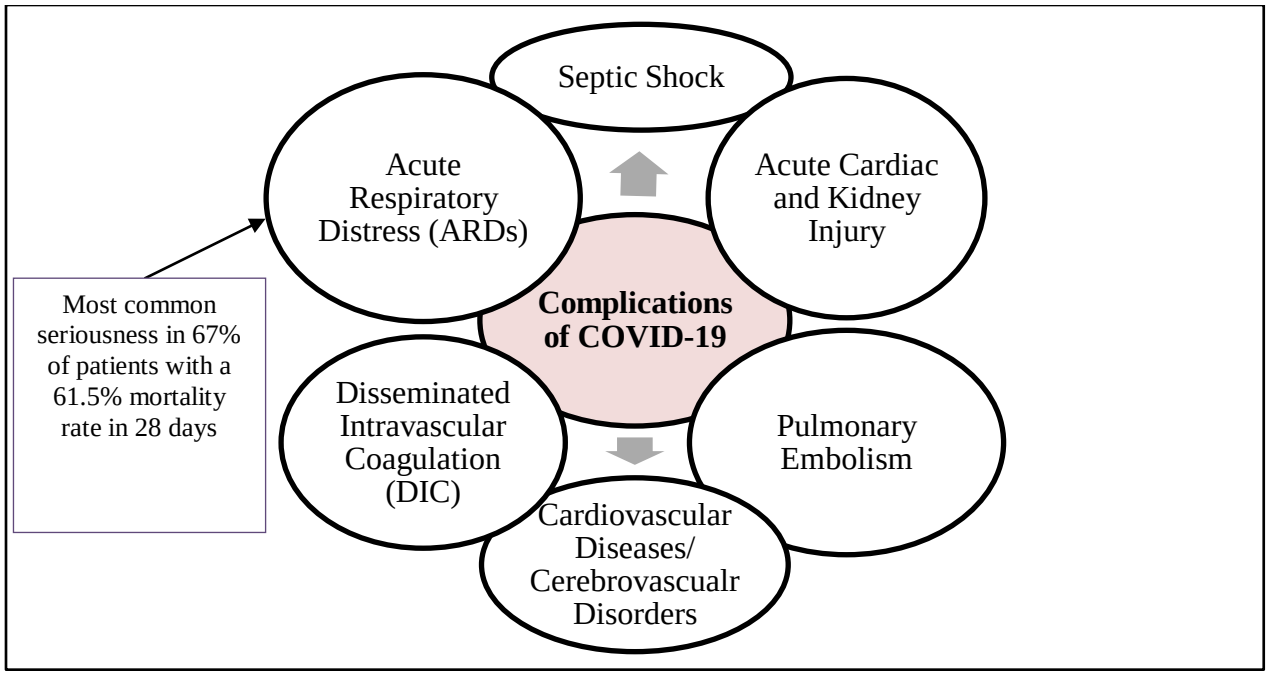

Figure 6:- Shows complications in humans can trigger the chronic fatality of COVID-19.

Life Cycle and Pathogenesis of SARS-CoV-2

The coronaviruses are the viruses whose genetic structure are best known among all RNA viruses. Most of the RNA viruses encode for viral polymerase enzyme, RNA synthesis, and having two non-structural polyproteins such as open reading frames genes (ORF1a-ORF1b) which are not involved in host response modulation. Along with this the genome of virus encodes for structural proteins spike (S) which responsible for the attachment with the cellular surface of the cell and helps in the entry of virus to host cell, envelope (E), membrane (M), nucleocapsid layer (N) and various other helper proteins which regulate and maintain the viral structure [41,42]. The virus can infect multiple hosts by its receptor-binding domain (RBD) which is loosely attached to the virus. The entry mechanism/transmission as shown in Fig. **(7)** and Fig. **(8)** which shows the life cycle of coronavirus is mostly recognizes aminopeptidases or sugar act as receptor molecule which helps in entering into human cells while SARS-CoV and MERS-CoV can determine the exopeptidases. The mechanism of coronavirus entering in host cell depend upon features such as cellular proteases includes human airway trypsin-like proteases (HAT), cathepsins and transmembrane protease serine 2 (TMPRSS2) responsible for penetration changes for viral structure. The two receptors are mainly responsible for entering such as for MERS-CoV have dipeptidyl peptidase 4 (DPP4) and HCoV-NL63 and SARS bind with the ACE2 receptor which was found in lungs, kidneys, stomach [43-45].

In respect to SARS-CoV-2 life cycle these all proteins are present but the spike protein contains 3D structure in the RBD to maintain the van der Waals forces. It is recognized by the critical lysine 31 residue on the human host cell receptor ACE2 [46].

The pathogenesis of SARS-CoV-2occurred in patients of SARS and COVID-19 which have similar patterns of inflammatory damage or the fluid storm of antibodies occurrence in the patients. In the biosamples taken from the patient's serum diagnosed with SARS,high range of proinflammatory cytokines are present in infected patients such as interleukin (IL)-1, IL-6, IL-12 interferons gamma (INFγ), macrophages, monocytes, high levels of T-lymphocytes which can have severe damage to the lungs and causes pulmonary inflammation, embolism conditions as compared to healthy ones. Due to severe complications such as ARDs, CVDs, bacterial and fungal superinfections it was found that it makes the COVID-19 worst [26].

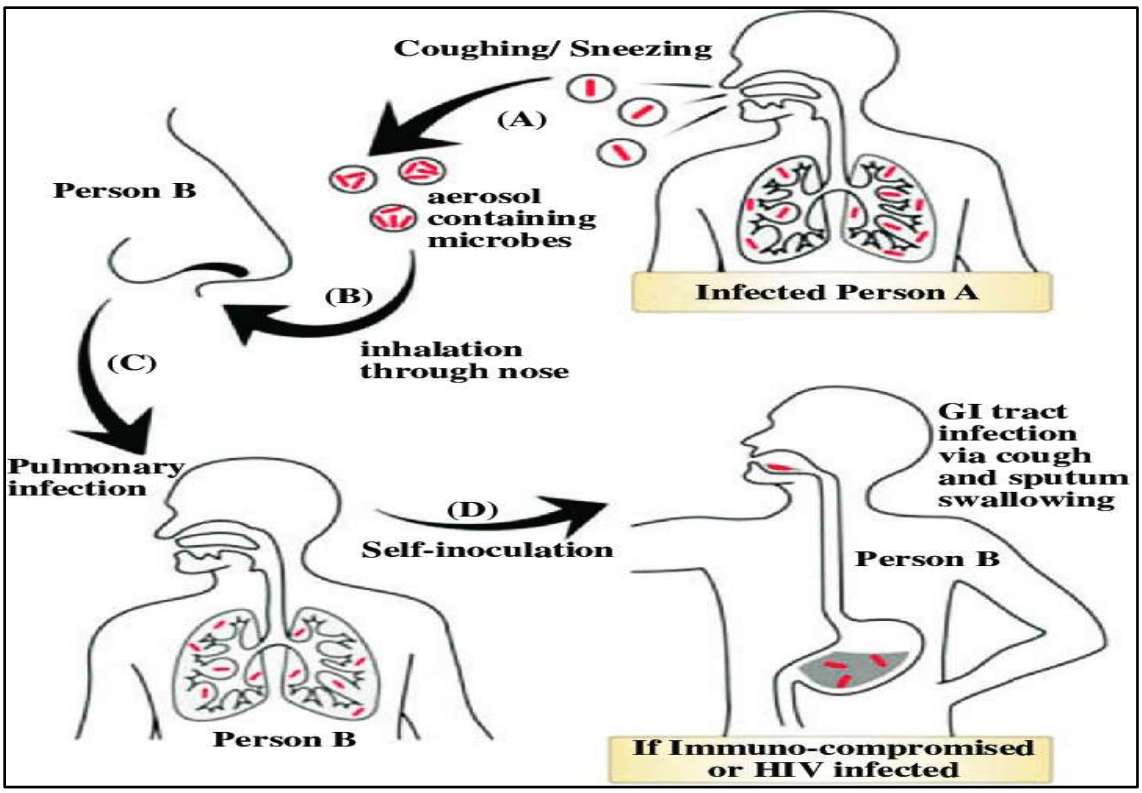

Figure 7:- Transmission of SARS-CoV-2 from human to human infection.

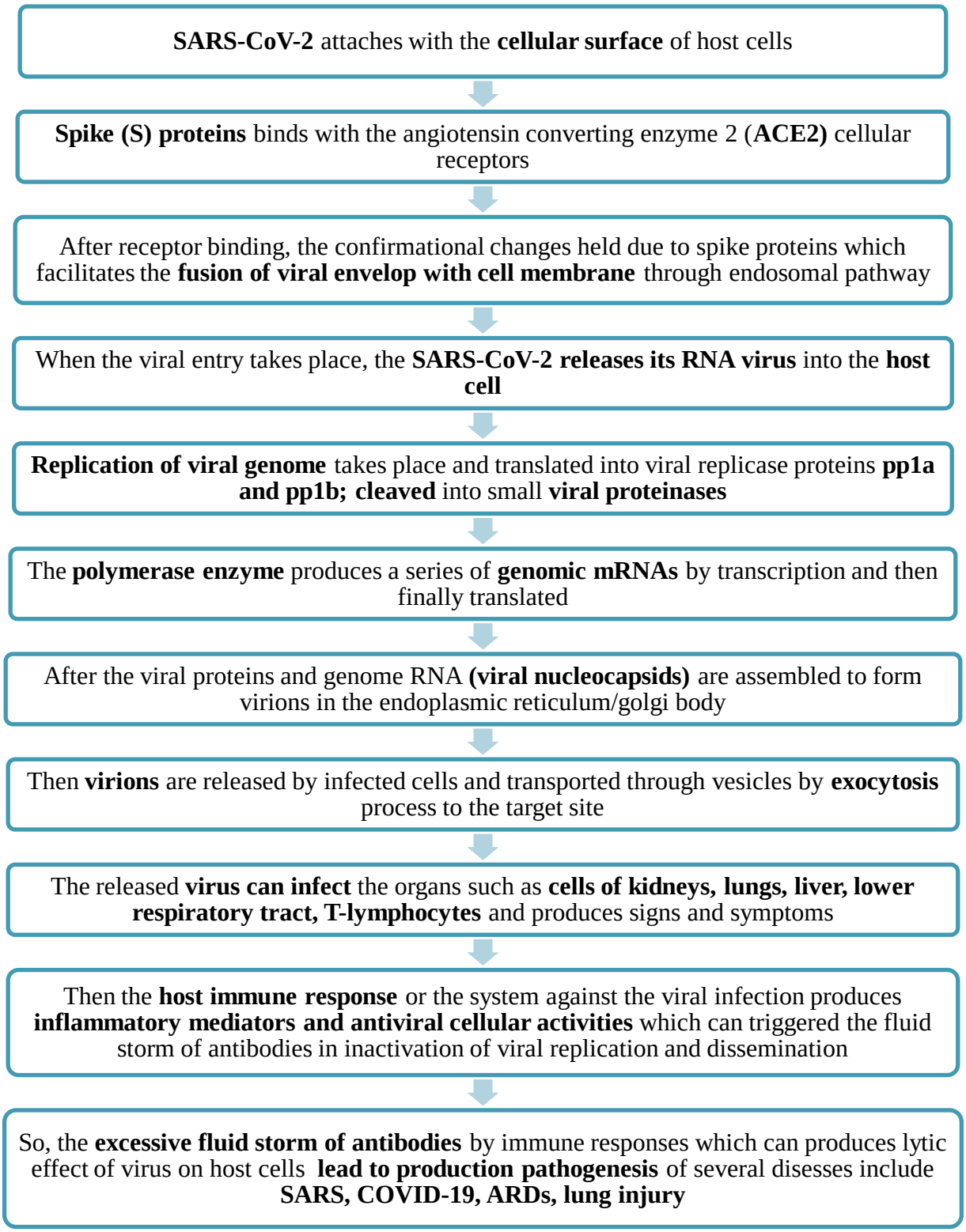

Figure 8:- Flow charts for the life cycle and pathogenesis process of SARS-CoV-2 virus.

Diagnosis of COVID-19 and SARS-CoV-2

The diagnosis of the n-CoV 2019 infection which is suspected in the patients is done based on historical levels of detailed contacts, travel and by using precise laboratory testing (either by serology and viral culture medium) and

radiology testing (molecular levels) as done in SARS and MERS infection testing. Many diagnostic tools were used nowadays for diagnosis of COVID-19 patients suffered from SARS-CoV-2 infection as follows:

Radiological Testing

For diagnosis of COVID-19 patient's diagnostic tools were used and one is most commonly used known as reverse transcription or real-time fluorescence polymerase chain reaction (RT-PCR), it works on the molecular levels. It is used to detect the positive nucleic acid present in the viral genome of the SARS-CoV-2 virus in the sputum, swabs of throat, secretions and mucus of the respiratory tract. They were using RNA from the respiratory tract either upper or lower and both samples include oropharyngeal swabs, sputum, nasopharyngeal aspirate, bronchoalveolar lavage. But in comparison to higher respiratory tract samples, it was found that lower area of the respiratory tract of samples has high viral load and genome sequences. As per these techniques are much effective for diagnosis process because it can give better result with highly accurate and can also identify the better viral genome structure in a patient [29,47].

Laboratory Testing

laboratory testing which worked on the screening of the abnormalities present in the blood or the serum of the infected COVID-19 patients in which there was found about the elevated and abnormalities in lymphopenia, prolonged prothrombin time, reduced lactate dehydrogenase enzymes, creatinine levels, aspartate aminotransferase. The blood of COVID-19 patients has high levels of concentration of various IL1β, IFN-γ, MCP1, MCP1A, TNF-α, granulocyte colony-stimulating factor (GCSF) [48,49].

Treatment of COVID-19 and SARS-CoV-2

The treatment possibility is very low for SARS-CoV-2 infection and COVID-19 because there is no specific antiviral drug is contemporary, so, there is no strong evidence of specific treatment option for this virus there is only a supportive care treatment which deals with drugs, lifestyle as shown in Table **(3)**. The isolation of the patients and supportive care such as oxygen therapy, fluid management, antibiotics treatment for superinfection or secondary bacterial infections is determined. COVID-19 patients are more prone towards the initial management with proper effort because they were more triggered to have ARDS, septic shock, lung injury and various multiple organ failure. So, they were strictly addressed to more care and proper treatment by immediate isolation and infection control measures. Despite this several interferons-α nebulization, broad-spectrum antibiotics, and the anti-viral drugs combination were used in the treatment option to reduce the infected patient symptoms and the viral loads of the viral genome sequences [44,50]. The drugs were screened and evaluated based on past investigational researches towards the SARS-CoV/SARS and MERS-CoV/MERS and gives the potential therapeutic efforts towards infection. As it was also found that there is no applicable vaccine against COVID-19, while previous drugs and vaccines are used for the development of vaccines against SARS-CoV-2 virus. The recombinant protein Urbani (AY278741) strain of SARS-CoV as shown in Fig. **(9)** was administered in animal rodent models which in turn show positive result towards protection against SARS-CoV infection. The fragment of DNA leads to inactivation of the whole virus or a live vectored strain (AY278741) of SARS-CoV, reduced the viral infection in animals [51-54].

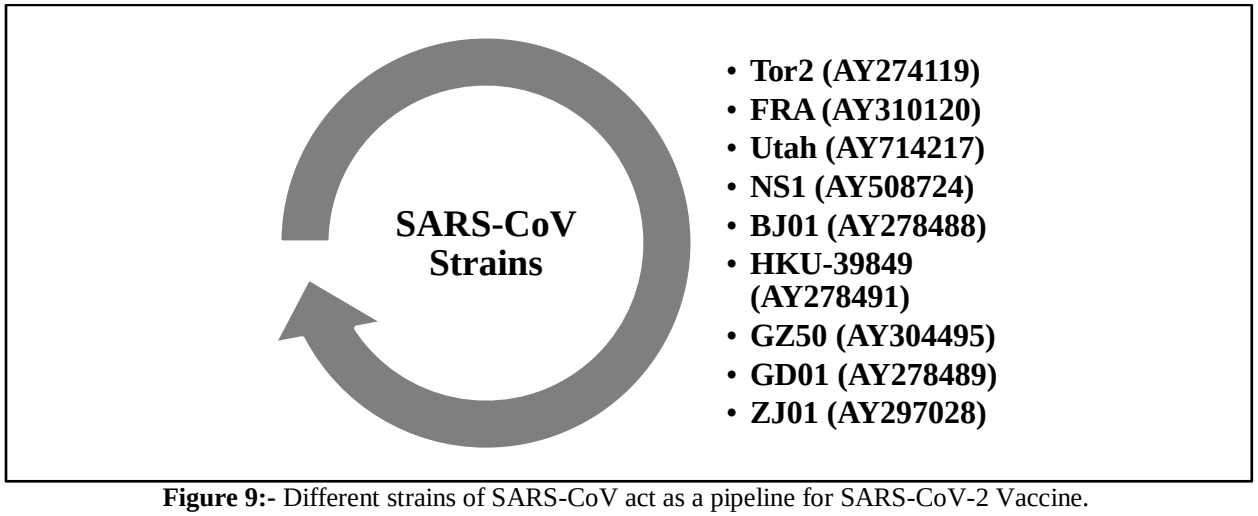

Figure 9:- Different strains of SARS-CoV act as a pipeline for SARS-CoV-2 Vaccine.

The other strains of SARS-CoV are now used to decreases the viral load by producing either inactivated or live vectored vaccines for the patients. Different centers and pharmaceutical companies undergo clinical trials for the formation of potent vaccines against SARS-CoV-2 are as follows:

1. ***United States National Institute of Allergy and Infectious Diseases:*** prepared mRNA-based vaccine which is now under phase 1 clinical trial [55].
2. ***Chinese Centre for Disease Control and Prevention (CDC):*** involved in the development of an inactivated vaccine against the virus [56].
3. ***Geo Vax-Bravo Vax:*** developed Modified Vaccina Ankara (MVA) (working) [57].
4. ***Clover Biopharmaceuticals Company:*** developing a recombinant n-CoV 2019 depend upon the S protein structure-based vaccine [58].

Table 3:- Different treatment categories for SARS-CoV-2 viral infection/COVID-19 disease.

SYMPTOMATIC TREATMENT OF SARS-COV-2/COVID-19		
Treatment Options	**Description**	**References**
Antiviral treatment	**Drugs** • Remdesivir (anti-viral drug) • Hydroxychloroquine (antimalarial drug) • Lopinavir/ritonavir (combined anti-viral drug)	[59]
Chinese treatment	**Traditional Chinese Medicine Prescriptions** • *Shuanghuanglian oral liquid (baicalin, chlorogenic acid and forsythin):* reduce inflammatory response by a virus. • *Lianhuaqingwen capsule:* having a wide-spectrum effect; regulate immunity, and reduce inflammatory responses in early stages of infection.	[60,61]
Immunoenhancement therapy	• *Synthetic recombinant interferon-α:* effective inhibitor of replication of MERS-CoV so, used in COVID-19. • *Immunomodulator:* IV immunoglobulin block production of proinflammatory responses/mediators. • *Thymosin alpha-1 (Ta1):* immune enhancer for SARS patients.	[62]
Convalescent plasma therapy	• Monoclonal antibodies against SARS-CoV-2 infection by limiting the virus because of plasma globulin in the serum.	[63]
Auxiliary blood purification treatment	• remove inflammatory mediators and control patient's capacity load effectively.	[64]

Recently in Shanghai, China clinicians/doctors/physicians isolated the blood plasma from the patients who are recovered clinically from COVID-19 and then inject this samples of blood into the infected patients who showed the positive symptoms of COVID-19 and cause to show the better result with rapid recovery rate [65]. In another recent study, it was determined or identified that the recombinant monoclonal antibody such as CR3022 binds with the spike protein of receptor-binding domain regions of the SARS-CoV-2 and the epitope regions of the antibody are diverged to ACE2 receptor binding motif present in the lungs, kidney, stomach. This antibody is likely to have better therapeutic efficacy towards the particular patients of the COVID-19 alone or in combined with other neutralizing antibodies to prevent and treat the SARS-CoV-2 infection [66].

Respiratory illness as such occurred with SARS, MERS, COVID-19, but it is found that COVID-19 patients increases if the persons have various following conditions:

1. travelling in the area of prone community transmission of SARS-CoV-2 within the prior of 14 days of infection.
2. When a person has close contact with each other and the confirmed suspected case of COVID-19 in 14 days. As such the close contact includes the range within six feet (about 2 meters distance in between the two persons) of the patients for those who are not wearing PPE (personal protective equipment) kit, or with direct contamination (infectious secretions) [67].

The basic period of onset of SARS-CoV-2 infection in COVID-19 from symptoms to death is lie in between 6-41 days and with a median range of 14 days to total exposure. As the period is dependent on the immune system of the one's individual because the immunity provides the basic needs towards the deterioration of the antigens either it is in the form of bacteria, virus, pathogens.

World Health Organization facility and their report showed that the incubation period for COVID-19 is in between 2-10 days. But some researchers suggest that incubation period as much as long and more than about 2 weeks and sometimes showed the double reflection of exposure of infection. Investigational studies suggested for medical observation period when the person is exposed to the pathogen. There is as such no valid explanations are held that the severity of illness in more than 70 years aged patients who are suffered from hypertension, diabetes, obesity and many other chronic comorbidities diseases are a critical condition and cause exacerbation of COVID-19 symptoms [68].

Prevention of SARS-CoV-2 and COVID-19

COVID-19 is now a day a very clear and potentially serious disease of international level concern who considered as pandemic due to high mortality rate ratio. As such SARS-CoV-2 infection is having more reproduction cycle number as a comparison to SARS-CoV [69]. The terminating od chain transmission is the main criteria to stop the spreading of virus and disease [70]. There were numerous strategies applied concerning health care facilities at the local as well as worldwide regions [71]. According to WHO and European Centre of Disease Control formed the guidelines which provide the proper and complete guidance for prevention of SARS-CoV-2 virus and Inspite of this there is no any potential possibility which is used for prevention of the COVID-19 disease as shown in Table **(4)**. Unfortunately, so far, the vaccine production against the SARS-CoV-2 virus is expected to be prepared in about 18 months because there is no specific antiviral treatments present said by Dr. Tedros, director-general of WHO. The clinicians provide only the support and modifying care until now in worldwide. Due to high mortality case, it is extremely important to develop a safe and stable vaccine against COVID-19. As SARS-CoV-2 is an RNA virus family so, RNA virus related vaccines such as measles, influenza, polio, encephalitis virus could be used to prepared promising alternative vaccines. The interpersonal transmission mode is inhibited and prevented by immunizing health care workers and the non-infected community [72]. As due to these reasons, the management of the COVID-19 is in support in favoring the disease severity range which has been introduced by WHO.

Table 4: - Main sources of preventive measures of COVID-19/SARS-CoV-2 infection.

PREVENTIVE MEASURES	**REFERENCES**
• Cover face with proper masks to prevent airborne droplets contact. • Wash hands regularly for about 20 sec either with alcohol-based (60%) sanitizer, disinfection with hand sanitizer or soap water. • Avoid contact with an infected person, the room will be decontaminated after the patient discharged, follow lockdown phases. • Maintain proper distance about 1 m (3 feet) in between any person either infected or non-infected. • Keep social distancing, avoid visiting markets of dead and live animals dealing, avoid contact with pets. • Avoid touching of eyes, nose, mouth. • If symptoms arise, firstly contact and follow the healthcare provider advice. • Recommend to use particulate respirators: aerosol-generating procedure; FF2for caring of suspected or confirmed cases. • HEPA filters are used to filter exhausted air. • Medical staff/personnel should wear PPE kit such as gloves, masks, gown, eye protection. • Isolating and quarantine of suspected persons/close contact.	[73]
MEDICATION MEASURES	
Astragalus, liquorice, fangfeng, baizhu, honeysuckle (Chinese Traditional Herbal medicines)-decoction is used. Vitamin C, D, E (supplements)-enhance resistance against SARS-CoV-2	[74]
Personal hygiene, lifestyle, nutritional intake-to maintain personal immunity	

HEPA= High-Efficiency Particulate Air; FF2= Filtering Face Piece; PPE= Personal Protective Kit

Research Hindrances and Repurposed Pharmacological medicationsagainst Sars-Cov-2 And COVID-19

The numerous researches were held nowadays and the animals played a vital and important role to uncover the various characteristically features, mechanisms of entry, the pathogenesis of the occurrence of viral disease, modes of transmission and the designing basic therapeutics approaches and strategies [75-77]. In the past years, when SARS-CoV occurred it was examined that the replication process is held rapidly and various animal models are used for screening of the virus and viral symptoms which was occurred due to severe infection. As the genetic regions of the SARS-CoV-2 are about 80% similar to the previous human SARS-CoV like bat virus and the screening models which was previously used for their evaluation, at present, it was used to screen the advent mechanism of perceptive about the pathogenesis of the SARS-CoV-2 which is responsible for the occurrence of COVID-19. ACE2 receptor which was found either in lungs, kidneys, the stomach is identified by both virus either it is SARS-CoV or n-CoV.

Table 5:- List of pharmacological experimented drugs used as repurposing medication for SARS-CoV-2/COVID19 nowadays.

Glucocorticoids: steroidal drugs
Remdesivir: anti-viral effect, by blocking viral replication
Angiotensin-Converting Enzyme 2 (ACE2): block the ACE2 receptor in lungs, kidney
Non-Steroidal Anti-inflammatory Drugs (NSAIDs): treat symptoms of Covid-19 such as sough, sneezes, fever, soreness in the throat
Tocilizumab: anti-viral effect
Lopinavir-Ritonavir/interferon α 2b (combination): anti-viral effect
Chloroquine/Hydroxychloroquine: immunomodulating effect (Anti-malarial)
Azithromycin (mainly used in combination): prevent superinfection (Antibiotic)

The researchers have used rodents and modified genetically transgenic hamsters or small species of animals for the screening models of viral identification. The potentially suitable investigation purpose option for the determination of pathogenesis mechanism entry of SARS-CoV-2 is that to develop a spike glycoprotein whose main targeting therapeutics against the newer virus. Recently it is found that COVID-19 induced disease model is used in mice models to develop a therapeutic pharmacological strategy against SARS-CoV-2. There were many randomized clinical trials held. But besides this, it is now very important to the research scientists of the world to contribute and collaborate the design the screening model which is most suitable for the screening of SARS-CoV-2/COVID-19 by investigating the new in-vivo mechanism of action approach associated with the pathogenesis of SARS-CoV-2 [50,78-80].

As critically used the repurposing of therapeutics drugs which are pharmacologically active against symptoms and can be used for screening of evaluation of viral diseases as shown in Table **(5)**.

Various therapies are introduced such as studies reported about the mycophenolic acid which is considered as monotherapy. But despite these hindrances the health professionals, physicians, scientist, researchers are not fully satisfied by any of the tested investigation or any therapy because it was not showing any potential therapeutic effect on the human life/well-being as the situation becomes worst till now so, it is very necessary to take further clinical research needed until or unless the potential pharmacologically active drug or vaccine is not prepared [81,82].

Conclusion and Future Perspective: -

This insight review concludes the current situation and present art of the current state of the SARS-CoV-2 infection (n-CoV-19) and Covid-19 in respect to its impact on human well-being, pathogenesis, epidemiology, clinical characteristics, management, prevention, situation reports, preparative preventive measures, pharmacologically repurposed drugs. Due to pandemic situation nowadays, which is considered as global disaster leads to a great impact on social, financial, economic status worst and after its ends then we can assess the individual health condition. As such the virus is originated from the seafood market of Wuhan, China, in which the whole animals live and dead were marketed. But the zoonotic sources of SARS-CoV-2 RNA virus is not known till now, however, the genetic constitution of the SARS and MERS manifest the high percentage of similarity so, it is assumed that the virus is originated from the bats and it acts as primary key sources for spreading of transmission with intermediate hosts and then to human hosts. It was found that rapid replication and infection rate is high because they have spike glycoprotein envelope which has better receptor domain and leads to rapid binding with the receptor and causes infection. It can also conclude that the transmission to human's capability is high due to the recombination of

homologous genes of the spike proteins. As such until now, there are no promising shreds of evidence of anti-viral drugs, vaccines or any other therapies which are used to treat the COVID-19. As such follow the guidelines of the WHO which states to take preventive measures either for suspected, infected, or normal persons by maintaining the lockdown, quarantine phases, social distancing, PPE kit to medical staffs. As there were many pharmaceutical companies, research scientists involved in the preparation of vaccines for the present as well as future epidemics occurrence which uses broad-spectrum anti-viral drugs/antibiotics such as Remdesivir, lopinavir, hydroxychloroquine, azithromycin etc. different treatment medications and therapies like convalescent plasma therapy (most effective) approaches followed. Repurposing clinical trials for drug targeting approach is used as about 5-10 months is required for the vaccine production and its manufacturing commercialization in regions. For future perspective, it is needed to increase the research, scientific coordination which used the approaches, drugs, for fighting or inhibit the SARS-CoV-2 infection and also known about the genetic structure of the virus in the future, introduced the rapid diagnostic kit as PCR fluorescent probe kits techniques are costly and time-consuming and cannot be granted for every human being. Till now the "the distance is everything" for the prevention of infection of SARS-CoV-2.

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