ISBN: 978-81-946587-9-5

2. A Brief Overview Of SARS-COV2, SARS-Cov And MERS-Cov Coronaviruses Outbreak To Global Health

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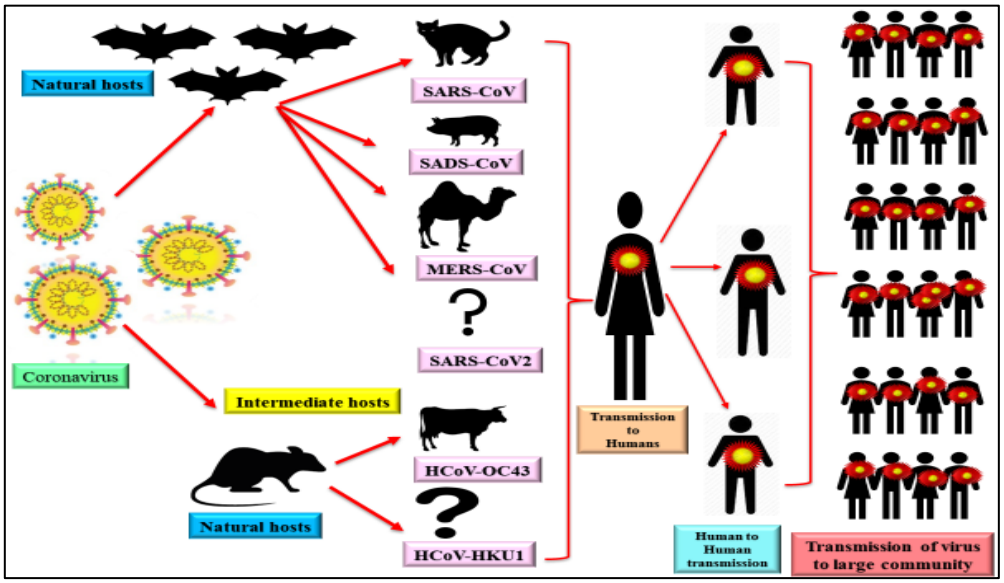
Abstract:

In the previous year's numerous viral infections have observed and affected the human's fraternity and healthcare systems. In all over the world millions of people are at a severe risk due to the several viral infections spread in the environment through various factors. In present investigation we have discussed the comparative forms of various viral infections and their risk factors, infection, methods and prevention Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV) and COVID-19 (severe acute respiratory syndrome (SARS-CoV2) which causes severe damage to the lungs, Kidney and heart and frequently causes normal illness, cold, fever, headache and chills in the human body. All the zoonotic transmissions of CoV that are newly discovered MERS-CoV, SARS-CoV and SARS-CoV2 is associated with the lower respiratory tract infections. We discussed about the recent clinical and pathological information on MERS-CoV, SARS-CoV and SARS-CoV2. The main aim of this review is to discuss about the discoveries related to MERS-CoV, SARS-CoV and SARS-CoV2 pathogeny and develop the methods that will eventually allow the effective control measures of these several severe viral infections. In the present article we have reviewed the literature on the several facets like transmission, precautions and effectiveness of treatments used in patients with MERS-CoV and SARS-CoV and SARs-COV2 infections.

Keywords:

Coronavirus; COVID-19; MARS-CoV; SARS-CoV; SARS-CoV2.

Graphical Abstract:



Introduction:

In recent years, several life-threatening viruses have been emerged in all over the world. They are responsible for causing significant human mortality, in addition to raising serious public health concerns to worldwide [1]. The life style and due to modern life, extensive travel of humans and goods, their outbreak anywhere in the world could potentially be a risk for the living creatures. The coronavirus that causes SARS is called SARS-CoV. In the recent times, two novel viruses were implicated and are said to be responsible for the severe acute illness, i.e. Middle East Respiratory Syndrome-Corona-Virus (MERS-CoV) and severe acute respiratory syndrome-corona-virus (SARS-CoV) [2,3] (Fig. 1). On new virus which is spread in all over the world i.e. SARS-CoV2 is a novel coronavirus identified as the cause of coronavirus disease 2019 (COVID-19) that began in Wuhan, China in late 2019 and spread worldwide [1]. These viruses are causing acute and often fatal illness, headache, fever etc and due to their high fatality rate (20–80%), they have had dual effect: and has great fear among public from contracting one or more of them as well as high burden on the healthcare system, including the treating physician and other health care workers.

The reservoir of the viruses (MERS-CoV, SARS-CoV and SARs-COV2) is said to be usually animal, including: bats, camels, or Cat. And then the transmission of animal to humans occurs and then, human to human transmission has been reported in recent studies, usually from an infected patient and to the member of the health care team and too their patients in

the hospital too. Till now no such specific treatment and vaccine has been recommended for their management and some supportive treatment has shown to improve the outcome in various research [4].

Some articles and research concluded about the process of antiviral vaccines is under process. These novel viruses represent significant challenges to public health in general and to public health services and infection control in specific area [5]. Many educational awareness and multidirectional care can improve the disease outcomes. In the present article we discussed an accurate knowledge of their reservoir, their transmission, presenting symptoms approach to their investigation and best possible management together with preventive steps, is necessary. In the present article we have reviewed the literature on several aspects like transmission, safety and efficacy of the rapies used in patients with MERS-CoV, SARS-CoV and SARS-CoV2 infections [3,6].

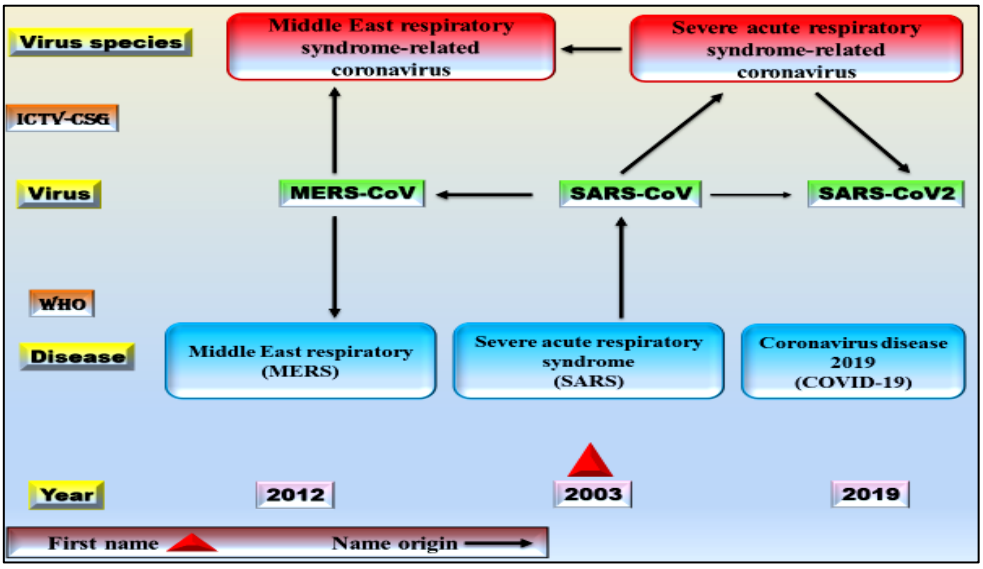


Figure 1: Details of MERS-CoV, SARS-CoV and SARS-COV2.

2. The Order Of Nidovirales:

The name Nidovirales, is derived from the Latin word “nidus” which means for nest, refers to a nested set of viral sub genomic messenger RNAs that is produced during the viral infection[7]. The order of Nidovirales is an order of enveloped, RNA viruses of single-stranded positive genomic. It is been stated that they have the largest known viral RNA genomes and they infect a large range of hosts. The order of Nidovirales includes three virus families: Roniviridae, Arteridae, and Coronaviridae is been summarized in (Fig. 2). The sequence of the coronaviridae family is divided into subfamily subfamily Coronavirinae

which contains the largest number of viruses till now. Several human pathogens are included in subfamily and are grouped in four different subgroups on their genetic properties they are Alphacorona virus, Beta coronavirus, Gamma coronavirus, and Delta coronavirus. On more sub family of coronaviridae is Torovirinae [8-10]. Research indicated that their virions are 60–80 nm in diameter, with club-shaped surface spikes and consist of eight major structural proteins, including a nucleocapsid protein, four differentially glycosylated forms of the membrane protein, and the spike S protein. Another is Roniviridae which contain the genus Okavirus and although still little knowledge has been known about them. (Fig. 2).

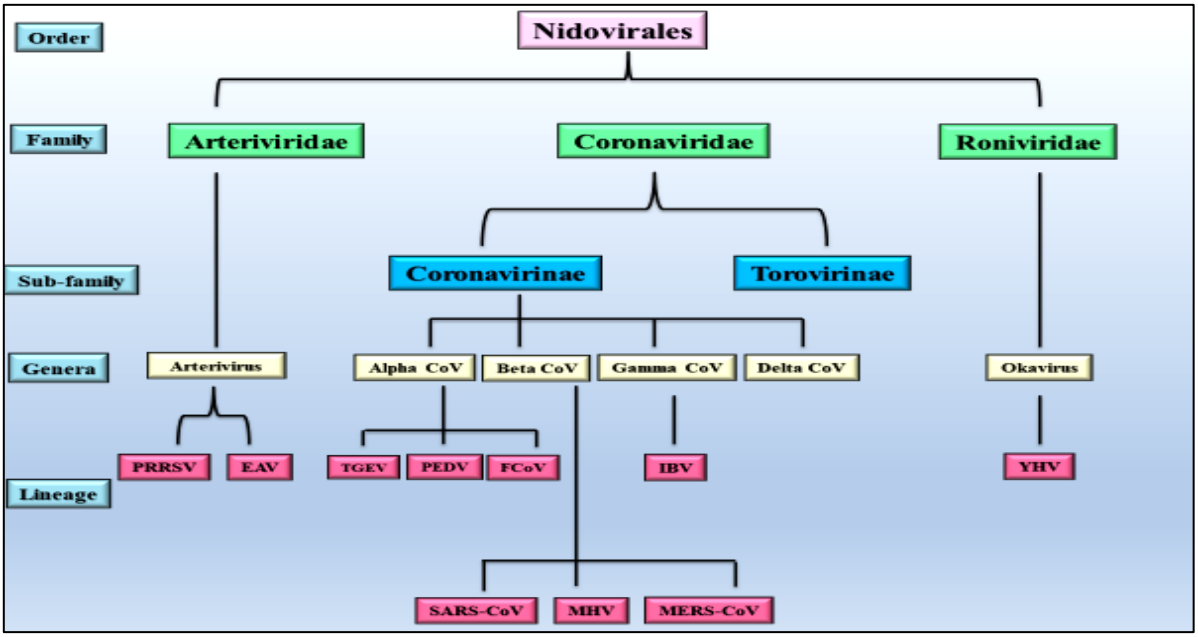


Figure 2: The taxonomy of the order nidovirales.

Abbreviations:

EAV = equine arteritis virus; **FCoV** = feline coronavirus; **IBV** = infectious bronchitis virus; **MERS-CoV** = middle east respiratory syndrome coronavirus; **MHV** = mouse hepatitis virus; **PRRSV** = porcine reproductive and respiratory syndrome virus; **PEDV** = porcine epidemic diarrhea virus; **PToV** = procine torovirus; **TGEV** = transmissible gastroenteritis coronavirus; **SARS-CoV** = severe acute respiratory syndrome coronavirus; **YHV** = yellow head virus.

3. Pathogenesis comparison of SARS-CoV2, SARS-CoV and MERS-CoV:

SARS-CoV and MERS-CoV enter target cells through an endosomal pathway. In all the viruses 5′UTR and 3′UTR are involved in intermolecular and intramolecular interactions and

are functionally important for RNA–RNA interactions and for binding to viral and cellular proteins (Table 1) [1]. At 5 ends, Pb1ab is the first ORF of the whole genome length encoding non-structural proteins with size of 29844bp (7096aa), 29751bp (7073aa) and 30119bp (7078) in COVID-19, SARS-CoV; and MERS-CoV, respectively. In the investigation when even with comparison of the spike protein at 3′ end, among the coronaviruses specifically these three beta coronaviruses, the difference was visualized, 1273aa, 21493aa, and 1270aa in COVID-19, SARS-CoV, and MERS-CoV, respectively. Genetically, COVID-19 was less similar to SARS-CoV (about 79%) and MERS-CoV (about 50%). The arrangement of nucleocapsid protein (N), envelope protein (E), and membrane protein (M) among beta coronaviruses are different as shown in Fig. 3.

Table 1: Pathogenetic Characteristics Of SARS-CoV2, SARS-CoV And MERS-CoV.

S.No.	Characteristic	SARS-CoV2	SARS-CoV	MERS-CoV
1.	First identifies locations	Wuhan, China	Guangdong, China	Jeddah, Saudi Arabia
2.	Period	2019-present	2002-2003	2012
3.	Origin	Clade I, cluster IIa	Clade I, cluster IIb	Cluster II
4.	Animal Source	Bats	Bats	Bats
5.	Intermediate host	Not known	Palm civets	Camels
6.	Receptor	(ACE2) Angiotensin-converting enzyme 2	(ACE2) Angiotensin-converting enzyme 2	(DPP4) Dipeptidyl peptidase 4
7.	Mode of transmission	Respiratory droplets, contact	Respiratory droplets, contact	Respiratory droplets, contact
8.	Fatality rate	3.3%	9.5%	34.4%
9.	R_0	2-3.5	2 -5.9	0.7
10.	Incubation period	Median 5.1 days (95% Cl, 2.2-11.5)	Mean 4.6 days (95% Cl, 3.8-5.8)	Median 5.2 days (95% Cl,1.9-14.7)

Abbreviations: *R_0 = Basic reproduction number; Cl = Confidence interval*

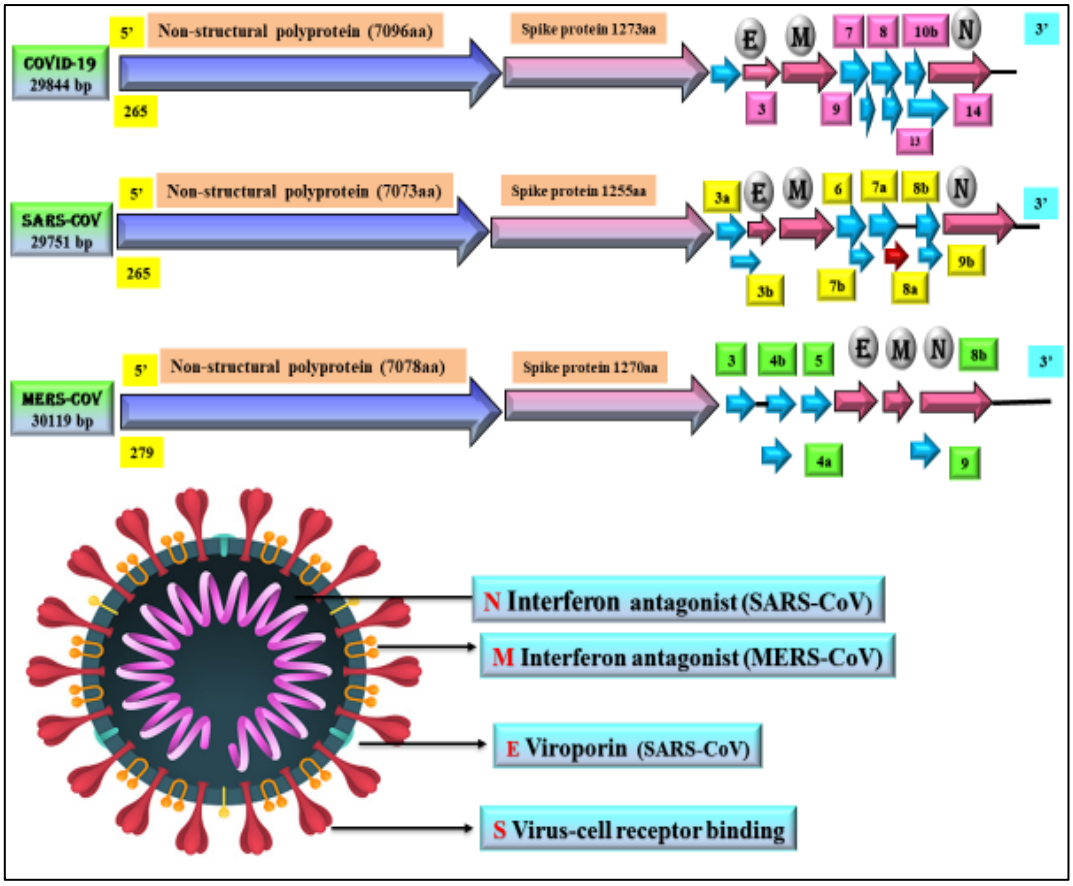


Figure 3: Representation of coding region of COVID-19, SARS-CoV and MERS-CoV in 5' UTR and 3' UTR ends.

4. Pathology Comparison And Life Cycle Of SARS-CoV And MERS-CoV:

In the life cycle of the SARS-CoV2 the S proteins of SARS and MERS bind to cellular receptor angiotensin-converting enzyme 2 (ACE2) and cellular receptor dipeptidyl peptidase 4 (DPP4), respectively. Following entry of the virus into the host cell, the viral RNA is unveiled in the cytoplasm. ORF1a and ORF1ab are translated to produce pp1a and pp1ab polyproteins, which are cleared by the proteases that are encoded by ORF1a to yield 16 non-structural proteins that form the RNA replicase-transcriptase complex [11-15]. This complex drives the production of negative-sense RNAs [(−) RNA] through both replication and transcription. During replication, full-length (−) RNA copies of the genome are produced and used as templates for full-length (+) RNA genomes. During transcription, a subset of 7-9 sub-genomic RNAs, including those encoding all structural proteins, is produced through discontinuous transcription. Although the different sub-genomic mRNAs may contain several open reading frames (ORFs), only the first ORF (that closest to the 5′ end) is translated. Viral nucleocapsids are assembled from genomic RNA and N protein in the cytoplasm, followed

by budding into the lumen of the ERGIC (endoplasmic reticulum (ER)-Golgi intermediate compartment). The Virions are then released from the infected cell through exocytosis. SARS-CoV, severe acute respiratory syndrome coronavirus; MERS-CoV, Middle East respiratory syndrome coronavirus; S, spike; E, envelope; M, membrane; N, nucleocapsid[11-13] (Fig. 4). Genomic analysis on accumulating evidence suggests that SARS-CoV-2 shares with SARS-CoV the same human cell receptor, the angiotensin-converting enzyme 2 (ACE2), while MERS-CoV uses dipeptidyl peptidase 4 (DPP4) to enter host cells according to some review literature [23]. SARS-CoV-2 has no amino acid substitutions were present in the RBD and that directly interacts with human receptor angiotensin-converting enzyme 2 (ACE2) compared with SARS-CoV. The pathogenicity of SARSCoV-2 must be further investigated and detected. Receptor analysis affinity detected that SARS-CoV-2 binds ACE2 more efficiently than the SARS-CoV. Angiotensin-converting enzyme 2 receptor (ACE2) is an ectoenzyme anchored to the plasma membrane of the cells of several tissues, especially those of the lower respiratory tract, heart, kidney and gastrointestinal tract. SARS-CoV highly replicates in the type I and II pneumocytes and in enterocytes, and the SARS-induced downregulation of ACE2 receptors in lung epithelium contributes to the pathogenesis of acute lung injury and subsequent ARDS [24-26].

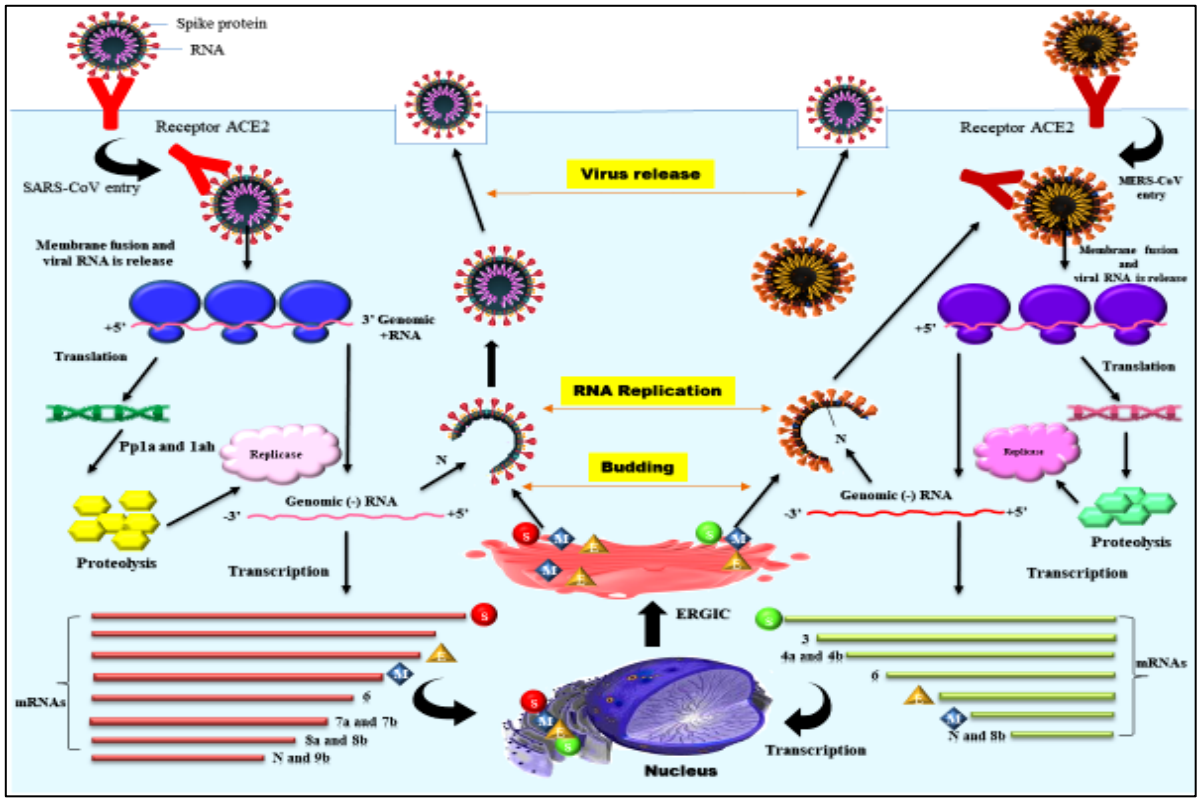


Figure 4: Representation of life cycle of SARS-CoV2 and MERS-CoV in host cells.

4. SARS-CoV-2 Virus:

4.1. Origin:

All types of coronaviruses that have caused diseases to humans have had animal origins-generally either in bats or camels as per the review literature [16]. Previously research review convoluted that the outbreaks of beta coronaviruses in humans was involved directly due to the animals except bats, but in case of SARS-CoV and MERS-CoV, they were transmitted directly to humans' transmissions from civet cats and dromedary camels and in case of SARS-CoV2, it is still unknown. The spike proteins that contain a variable receptor-binding domain (RBD) can be covered by SARS related coronaviruses. The receptor-binding domain binds with angiotensin-converting enzyme-2 receptor that are found in the heart, kidney, lungs and gastrointestinal tract and entered to the target cells [17]. The RBD of the SARS-CoV2 appears to be a version of various other related virus and RaTG13 in Rhinolophus affinis bats. Therefore, it is estimated that the SARS-CoV-2 can be also originated from bats. The pangolin is believed to be the intermediate host of SARS-CoV-2 according to some research [18-20].

4.2. Transmission Of SARS-CoV2:

The transmission of the early COVID-19 cases was linked from the Wuhan market, china and it is estimated that the virus was initially transmitted from animals to humans from Wuhan market. Human to human transmission spread through human contact with infected secretions with large respiratory droplets. Researchers are still learning how readily this virus spreads from human to human or how sustainable infection will be in a population, although it appears more transmissible than SARS-CoV and spread is probably more similar to that of influenza. Isolation and Quarantine measures are being applied to limit the local, regional, and global spread of this SARS-CoV outbreak [21,22].

4.3. Symptoms And Signs:

SARS-CoV2 people may have few to no symptoms, although some become severely ill and die. Some symptoms can include Fever, Cough, Shortness of breath or difficulty breathing, Chills, Muscle pain, Headache, Sore throat and new loss of smell or taste according to the investigation of the COVID-19 patients (Fig. 5). The incubation time ranges from 2 to 14

days after exposure to the virus. The risk of serious disease and death in COVID-19 cases increases with age and in people with other serious medical disorders, such as heart or lung disease or diabetes [1].

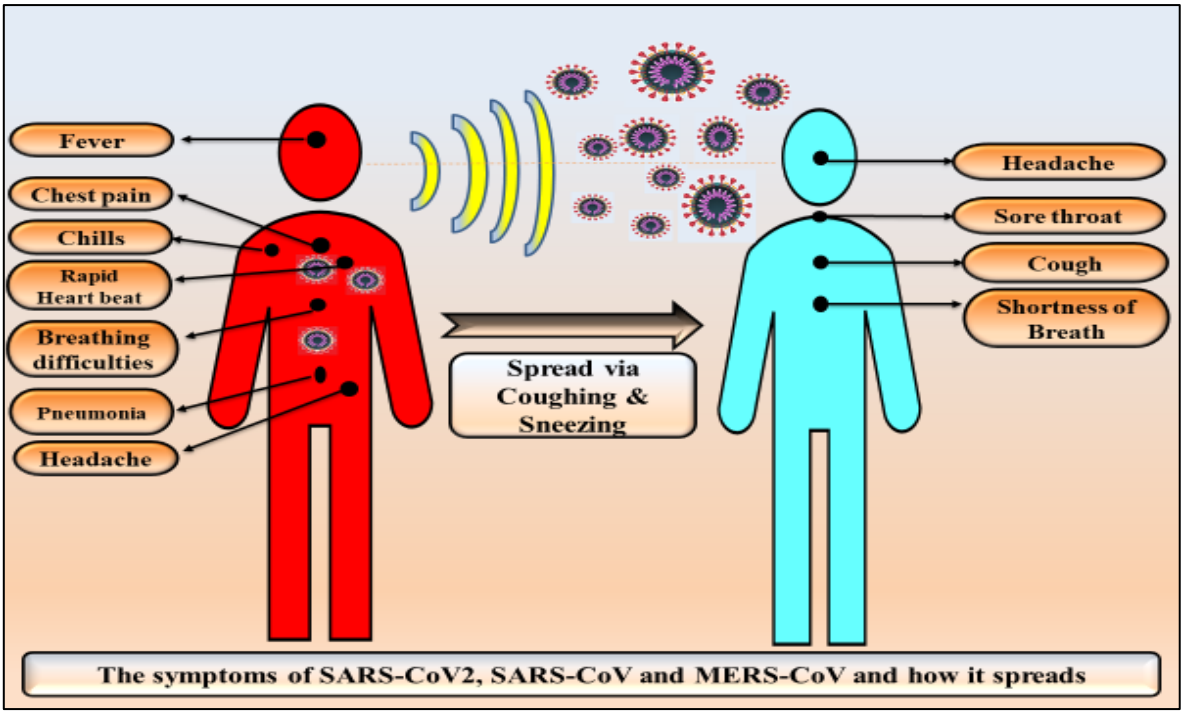


Figure 5: Representation of the symptoms of SARS-CoV2, SARS-CoV and MERS-CoV and how it spread.

4.4. Diagnosis of SARS-CoV2:

In the diagnosis of SARS-CoV2 reverse transcriptase-polymerase chain reaction (RT-PCR) testing is increasing through hospital-based laboratory for upper and lower respiratory secretions diagnostic testing. Initial diagnostic testing for COVID-19, the CDC recommends collecting and testing a single upper respiratory nasopharyngeal swab. According to WHO the collection of nasal turbinate and/or oropharyngeal swabs is acceptable if nasopharyngeal swab is not identified or available. COVID-19 patient a lower respiratory tract aspirate or bronchoalveolar lavage sample should be collected and tested as a lower respiratory tract specimen and invasive mechanical ventilation should be provided. Nasopharyngeal swab should be used for the collection of oropharyngeal swabs and combined.

4.5. SARS-CoV2 Treatment:

No vaccine, antiviral drug, or other specific treatment is available till now and all over 175 treatment and vaccine clinical trials are currently registered, but still the data on effective therapy remains sparse. Current therapeutic strategies in practice for severe disease include antiviral agents (notably redelivers, in clinical trial), chloroquine derivatives, and immunomodulatory agents, namely Il-6 inhibitors such as tocilizumab. Therapeutic agent are benefits and weighed against possible risks for each patient suffering from the virus and to help prevent spread from suspected cases, health care1. Airborne precautions are particularly relevant for patients undergoing aerosol-generating procedures. Respiratory symptoms Patients should be identified and masked immediately upon entry to any healthcare facility.

5. SARS-CoV Virus:

5.1. Origin:

It was first identified in 2002 in China. WHO has defined SARS as a global threat caused by SARS-CoV coronavirus Severe acute respiratory syndrome (SARS) was considered among newly emerged infectious diseases, with a significant morbidity and mortality, Due to a high case fatality rate, accurate knowledge of the SARS-CoV remains a Mistry? According to the Centers for Disease Control and Prevention, Challenges presented by MERS corona and SARS corona viruses reports as many as 8273 cases were confirmed from 37 countries around the world with 775 deaths, a case-fatality of about 10%.

5.2. Transmission Of SARS-CoV:

It is believed that SARS transmitted and penetrates through respiratory aerosols, which were released while a SARS patient coughs or sneezes. Viral infection will spread from the droplets of cough or sneeze of an infected patient are propelled in surroundings via air and will infect the nearby people who are nearby through several ways like mouth, nose or eyes. The virus also can spread by touching infected surfaces, and then touching the mouth, nose, or eye etc. [27].

5.3. Signs And Symptoms:

Signs and symptoms of SARS-CoV include: discomfort in respiration, high fever, migraine, and body pains, slight respiratory problem, diarrhea (10–20%), and cough (after 2–7 days). Incubation period of the SARS-CoV ranges from 2 to 10 days.

5.4. Diagnosis Of SARS-CoV:

In PCR testing SARs is a new viral disease that is caused by the human to human transmission and anti-SARS-CoV antibodies are not found in populations that have not been exposed to the virus. Antibody testing using immune fluorescent antibody (IFA) tests is being developed by various research laboratories. Meanwhile, additional antiviral therapy, RNA silencing methods, anti-monoclonal antibody, anti-viral peptides, and vaccines are under development process.

5.5. Prevention:

Scientist and Scholars are working on various types of vaccines for the treatment of SARS, but still these vaccines need to be approved to test in humans.

6. MERS-CoV Virus:

6.1. Origin:

Middle East respiratory syndrome (MERS) is a severe, acute respiratory illness caused by the MERS coronavirus (MERS-CoV). MERS-CoV infection was first reported in September 2012 in Saudi Arabia, but the resources concluded that an outbreak in April 2012 in Jordan was confirmed retrospectively. Till 2019 in whole world wide affrox 2500 cases were reported due to MERS-CoV infection (with at least 850 related deaths) have been reported from 27 countries; all cases of MERS have been linked through travel to or residence in countries in and near the Arabian Peninsula, with > 80% involving Saudi Arabia. In the report it state that the largest known outbreak of MERS is been detected in the Arabian Peninsula occurred in the Republic of Korea in 2015. The main reason of the outbreak is associated with the travelling from the Arabic Peninsular region. According to WHO report in January, 2016 said that 1638 human cases, including 587 deaths due to Middle East Respiratory Syndrome (MERS-CoV) [4,28]. Recommendation of the WHO, MERS is a

deadly disease caused by coronavirus, ‘‘is a threat to entire world” [29-32]. MERS-CoV is considered a deadly virus with a single strand RNA [33]. The MERS-CoV has been identified in various countries in the gulf region, Korea and European region with an obviously high death rate and dangerous conditions. According to the nosocomial transmission it is been compared to the SARS-CoV which is involved in various respiratory diseases and infections in the various parts of the body [34]. The person travelling from Saudi Arabia to USA was the first case found and identified on 2nd May 2014 due to MERS-CoV. The second instance of MERS-CoV was reported on 11th May, 2014, and was confirmed in a traveler who is also from the Kingdom of Saudi Arabia. Another instance was from Republic of Korea’s first, or ‘‘index”, case was confirmed on 20 May 2015 and notified from WHO. MERS virus from nasal swabs of camels and demonstrated that the whole genome sequence of human and camel obtained virus is in distinguishable [30]. Although person-to-person transmission is low, in these cases and it does occur from patients to health care workers and close contacts with them.

6.2. Sources Of Virus:

Studies indicated that the main source and reservoirs of the MARS-CoV was “Camels”. The people affected by the infection were found to be closed contact with the animal in the form of drinking camel milk etc. 100% of Oman camels and 16% of Spanish camels had antibodies against MERS-CoV according to the Lancet Infections Diseases reports on 2013 August.

6.3. MERS-CoV Transmission:

In humans Camels are considered the source of infection. Subsequently, human to human transmission of MERS-CoV occurs from patients to health care workers through drop let infection, or through touching contaminated surfaces according to the reports [35] (Fig. 6).

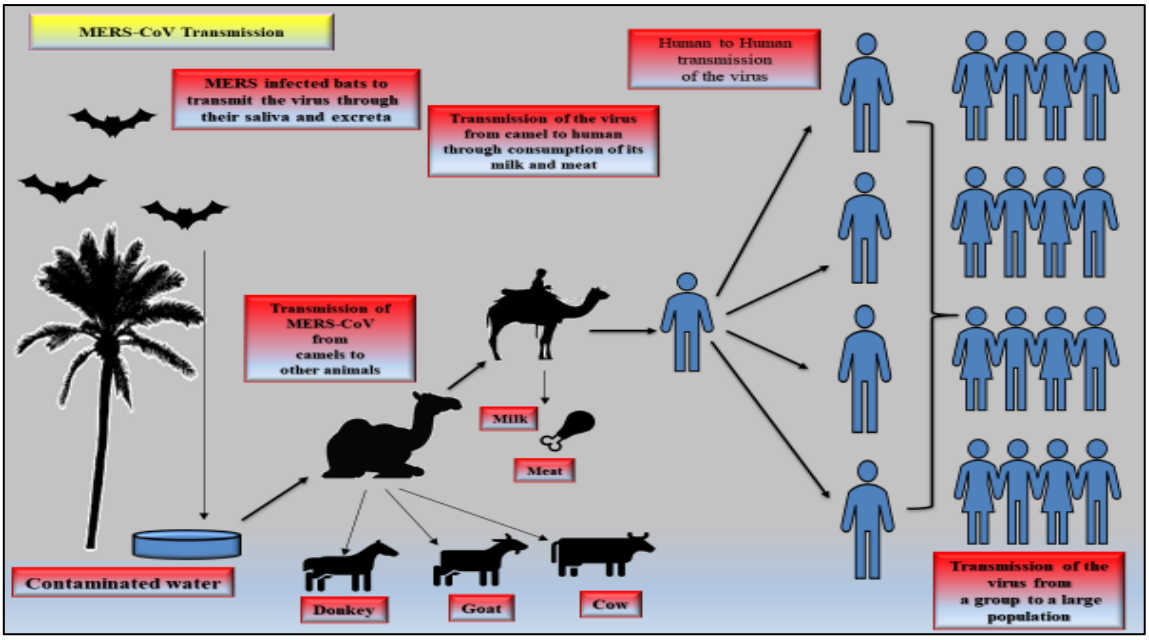


Figure 6: Representation of MERS-CoV transmission.

6.4. MERS-CoV Incubation:

MERS-CoV infection was incubated during the period of ranges from 2 to14 days [29].

6.5. MERS-CoV Epidemiology:

In the summers 2012 in Saudi Arabian city in Jeddah a CoV coronavirus was detected and identified from the saliva of a patient suffering from acute pneumonia and renal failure. Till September 2012 a similar type of virus was transmitted in human was named as human coronavirus was isolated by a patient suffering from severe respiratory infection who traveled from the Middle Eastto London, United Kingdom [4,29,36,37]. In Oman they confirmed that it was second MERS-CoV case of 2014 and its overall fourth apparently a contact of the most recent MERS patient, who has died, according to media reports.

After confirming eight MERS-CoV cases, Saudi Arabia reported 833 confirmed cases, including 358 deaths, for a case-fatality rate of 43% in the first 9 days of 2015.

6.7. Signs And Symptoms:

Signs and symptoms comprise for MERS-CoV: rigor, feeling cold, shivering, migraine, cough, sore throat, difficulty in breathing, muscular rheumatism, chest pain, kidney failure,

pneumonia, giddiness, nausea and vomiting, dysentery, and stomach pain. In the various reports and reviews it has been reported that the symptoms are same as development of pneumonia. It must be noted that by MERS-CoV immune-compromised people are thought to be a thigh risk to get infected.

6.8. Diagnosis Of MERS-CoV:

Identify and diagnose several infectious diseases through PCR testing diagnosis method is used used to confirm MERS-CoV positive cases by collecting sputum or any other sample from the patient. A blood test can decide whether a person has earlier been infected, by anti-MERS-CoV [38]. MERS-CoV in USA remains serious, with the evolution of a new wave of cases during early 2015, with still a high fatality rate ranging from 30% to 40%. Drinking unsterilized camels' milk must be avoided till convincing proof is obtained, so that chances of infection were reduced.

6.9. Infection Control:

Viral disease control is the key to ensure protection for healthcare employees and patients. Convalescent plasma, lopinavir and interferon (IFN) are prescribed for better management of MERS-CoV infected persons. The effect of steroids on viral infection control in MERS is not well known, even though systemic corticosteroid usage delayed clearance of the related coronavirus, SARS-CoV. MERS-CoV has been compared with delayed replication of other respiratory infections. According to Various medical research stated that Cyclosporin A (CsA), cycloheximide, mycophenolate, IFN-b, omacetaxine mepesuccinate, anisomycin, and emetine dihydrochloride hydrate were identified to show the best result in protective effect from MERS-CoV [39].

7. Safety Guidelines Recommended By WHO (Fig. 7):

Fig. 7. Representation of infections control and prevention measures.

8. Conclusions And Future Aspects:

The most important lessons we have learned from the past from the SARS-CoV and MERS-CoV coronavirus epidemic are the most specific weapons we have to face in the new global era. There is still much more to know about the emergence of recent coronavirus outbreak in all worldwide COVID-19 caused by SARS-CoV-2, and has proved that these viruses has the capacity to mutate and recombined to become pathogenic and has the intensity to cross the barriers can cause virus transmission in animals and human and much more to understand its capacity and mortality to spread and keep on emerging all over the world. As, it can spread through aerosol droplets, indirect and direct contact, person to person transmission as well as in the laboratory setting. Also, it can be transmitted from bats to humans, which confirms its zoonotic importance. It is very important and essential to develop the effective vaccines and antiviral therapeutics. With the comparative analysis of the recent SARS-CoV2 coronavirus outbreak with the previous corona-virus outbreaks (i.e SARS-CoV and MERS-CoV) as these disease has no treatment and proper measures should be taken to control the virus and can help and provide to used and leads for developing therapeutics and vaccines for this virus. To control SARS-CoV2, prevention and recommendation for future that each country

of the worldwide should give proper attention to the quarantine and diagnosis facilities, in which the suspected person is kept in the isolation. As many pharmaceutical organization, medical workers, Scientists, Researchers are working hard to prepare the vaccine or drug and control the virus. Most important are the prevention measures that are implemented all over the world and are fighting against the viral disease. This work will be very helpful for the discovery of COVID-19 vaccine.

Conflicts Of Interest:

The authors declare no conflict of interest.

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