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Study Of Studies Related To Epidemiology Of COVID-19 And Public Health Risk Mitigation Strategies: A Review

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Abstract:
The aim of this paper is to study some of widespread infectious epidemic diseases i.e. SARS, MERS and coronavirus which has been impacted global health and economy on vast scale. There are approximately 70,000 coronavirus cases from 2019 (COVID-19) are confirmed, of that over a pair of, 1000 patients are fatal and this disease turned out to be a serious threat to global health. The first approach of this paper is to have in-depth knowledge about the structure of coronavirus, its structural proteins i.e. S protein and their biological activities for the virus have been discussed. The second approach is to focus on different phases of epidemic and response interventions which are mandate to slow down the spread of any disease till its complete elimination this can help to accelerate further work on studies for managing future public health emergencies. Proper and cumulative planning at international/national/community levels and organized strategic preparation for prevention and control of such epidemic diseases is need of the prevailing global risk.

Keywords: epidemic; SARS; MERS; coronavirus; public health emergencies; response interventions.

1. INTRODUCTION:

The 21st century human race has survived major epidemics which are considered responsible for increasing fatality rate while their transmission from different hosts to humans itself. The brutal impact on global public health caused by these epidemics' diseases i.e. SARS, pandemic influenza, MERS, Ebola, Zika virus, SWINE and COVID-19 occurred lately, proved that there is need for a communal and harmonized defense strategies against emerging public health threats by the world's governments and authorities. Whether transmitted by mosquitoes, other rodent, via contact or consumption of animal resources or person-to-person, it is undeniable fact that all such diseases have the potential to spread internationally highlighting the importance of immediate and coordinated response of government authorities towards both physical and mental health of their people.
In 2019, coronavirus has been declared as pandemic disease i.e. COVID-19 and the index cases of pandemic has been reported in china. It is severer than SARS and the fatality rate of COVID-19 is higher than seasonal influenza [1]. Since it was initially appeared in Dec 2019, over 70,000 coronavirus cases from 2019 (COVID-19) are confirmed, of that over a pair of,

1000 patients are fatal [2-5]. So far, the infection continues to unfold and additional cases are confirmed that are exported to alternative provinces of China and alternative countries. Indicate that the sickness may be a serious threat to world health [6-7].

Management of COVID-19 patients consists of a mixture of substantiating measures, antimicrobial medical aid for any associated microorganism or virus infection and rigorous implementation of applicable precautions for infection management [2-5].

The number of corona virus continue to multiply thus need effective antiviral treatment [6-7]. It is supposed that by the entry of antigen into the host body the immunopathological immune response has been detected. For the treatment of the disease to prevent the replication of antigen [8].

The nature of the coronavirus order (non-segmented, fiber ribonucleic acid and positive sense) isn't outstanding, however its size, from twenty-seven to thirty-two KB, is definitely compared to alternative ribonucleic acid viruses. Coronaviruses square measure liable for variety of economically vital diseases. Additionally, to metabolism diseases, which may lead to chickens secondary fatal microorganism infections, some strains additionally cause Bright's disease [9-10].

The viron of the coronavirus may be a wrapped particle that contains the proteins of the height (S), the membrane (M) and therefore the envelope (E). Additionally, some coronavirus strains, however not SCoV, categorical a hemagglutinin (HE) super molecule that's additionally incorporated into the particle. The coronavirus order may be a linear, fiber molecule of ribonucleic acid polarity (mRNA), twenty-eight to thirty-two KB long [11-12-13]. At intervals the particle, the order is encapsulated by multiple copies of the nucleocapsid (N) super molecule and has the conformation of a volute structure of ribonucleic acid / nucleocapsid.

In mice, S protein has been the main goal of studies for pathological method. S protein is the important factor to determine the cell response, species specificity, host choice and sickness [14-15-16].

The Seventies and early Eighties were the time within which the virionic proteins of coronavirus and therefore the inclinations of nested ribonucleic acid pools were known and therefore the discontinuous nature of coronavirus transcription was firstly proved. The primary revealed sequence of a coronavirus appeared in 1983, starting with an era within which all four coronavirus genomes were part cloned and sequenced.

This decade has seen the manipulation of those clones and cDNA (cDNA) of defective RNA (DI) interference to review the structure of coronavirus, structure of processing and transport protein, the assembly of virions, the identification of cellular receptors for the processing of coronavirus.

Table 1: Comparison of coronavirus and SARS and MERS:

	Severe acute respiratory syndrome (SARS)	**Middle East respiratory syndrome (MERS)**	**Coronavirus (CoVID-19)**
Origin	Reported in southern china in 2002	Reported in Saudi Arabia in 2012	Reported in Wuhan, china in December 2019
Transmission	Disease spread from bats, which infected civets.	Often from touching infected camels or consuming their milk or	By touching, eating an infected animal, human to human

	Mainly Spread in human through close contact.	meat. Limited transmission between humans through close contact.	transmission through close contact
Cases	Confirmed cases in 8,098 and 774 deaths occur. So, mortality rate about 10%	Confirmed cases 2,494 and 858 deaths occur till 30-11-2019. So, mortality rate about 34%	Approximately 500 cases confirmed
Dry cough	+	+	+
Fever	+	+	+
Sore throat	+	+	+
Body ache	+	+	+
Shortening in breathing	+	+	+
Common cold	+	+	+

Relative information background:
In 1930, virus was first reported in domesticated chickens. When an acute respiratory infection was caused by infectious bronchitis virus (IBV). MHV (mouse hepatitis virus) and TGEV (transmissible gastroenteritis virus) was reported in 1940 and both are another type of animal corona virus [17].

In 1960s first Human coronaviruses was discovered [18]. The first human coronavirus was studied in human patients. The patient was suffering from the common cold, which was named as human coronavirus 229E and human coronavirus OC43[19]. other strains of human coronavirus have been reported i.e. SARS-CoV (2003), HCoV NL63 (2004), HKU1 (2005), MERS-CoV (2012) and SARS-CoV2 (2019). These are all respiratory tract infection.

There are six species of human coronavirus in which one species is subdivided into different strains. There are seven species of human corona virus. Out of seven strains, four strains show the mild symptoms such as common cold. The four human coronavirus which shows mild symptoms are as: (https://en.wikipedia.org/wiki/Coronavirus)

a) HCoV-OC43 (human coronavirus OC43)
b) β- CoV (human coronavirus HKU1)
c) HCoV-229E (human coronavirus 229E)
d) HCoV-NL63 (human coronavirus NL63)

Other three strains show severe symptoms and they belong to β-CoV strains so these are:

a) SARS-CoV (Severe acute respiratory syndrome coronavirus)
b) MERS-CoV (Middle East respiratory syndrome-related coronavirus)
c) SARS-CoV-2 (novel coronavirus 2019)

A. Structure of coronavirus

Corona virus is spherical in shape and enveloped virus. It contains single stranded Ribonucleic acid associated with nucleocapsid protein and it enclosed inside the capsid protein. The envelop have long spike like glycoproteins projections (S) and these proteins are highly glycosylated type I glycoprotein (Fig. 1).
A subgroup of coronavirus has an extra layer of hemagglutininesterase (HE) protein which is also known as type I glycoprotein [20-21]. The HE is essential protein for causing the viral infectivity.Additionally, to the S and HE proteins, the envelope is related to a smaller type I (M) integral membrane protein, which extends 3 times over the envelope. The envelop protein (E) and smaller membrane protein (sM) are the part of integral membrane of viral envelop. Inside the envelope there's a ribonucleoprotein nucleus (RNP), in which has the RNA and nucleocapsid N protein is present. The length of the RNP os 14 to 16nm long helix [22-23].

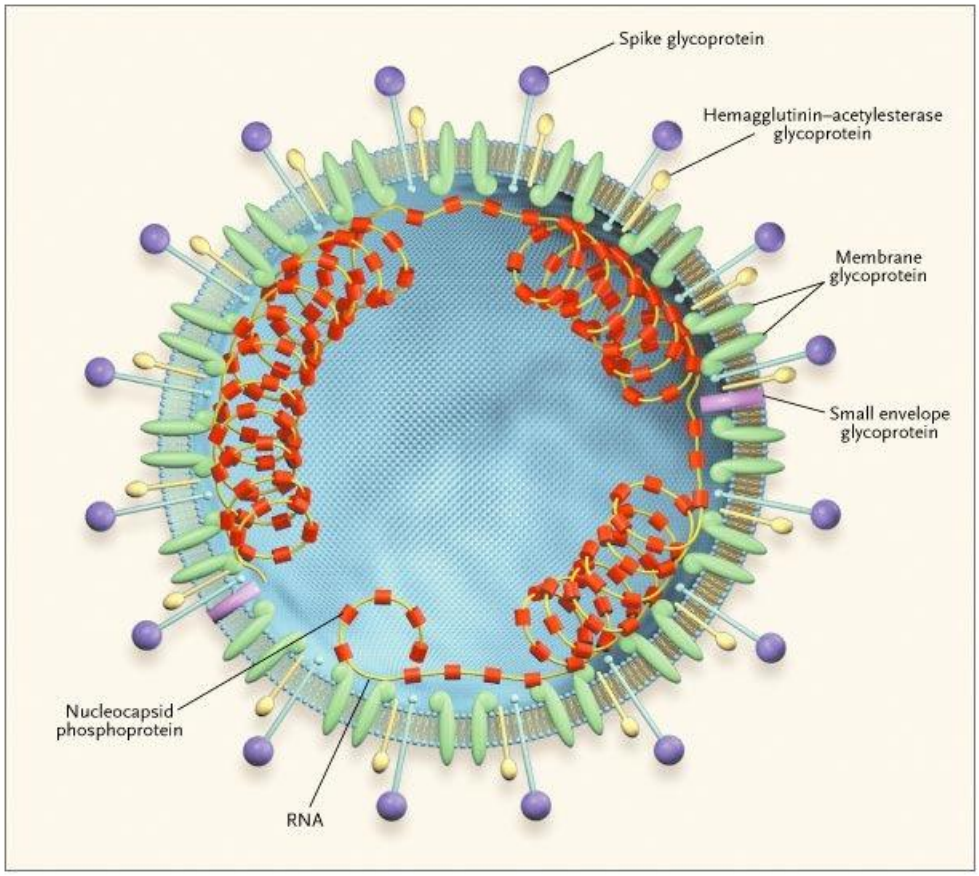


Figure 1: Structure of the coronavirus virion

Source: SARS- Associated Coronavirus, The New England Journal of Medicine, 2003.

B. Structural Proteins

S glycoprotein is the outermost layer of the virion and binding of virus to the host cell occur through S glycoprotein [24-25-26]. It is the first goal of the host's immune responses; Neutralizing antibodies are mainly induced by S [24], and immunization in animals with S can only induce protection against some coronaviruses [27-28].Within a coronavirus species, the sequence variation is usually exhibited more by S than by the other structural protein;

Variation within the protein S sequence probably confers a selective advantage in immune animals. These and other aspects have recently been examined very well [29].
Protein S has two important biological activities for the virus: a) **Membrane fusion induction.** This activity could also be necessary for viral entry into cells or for cytopathic effects. It has been demonstrated that the expression of the recombinant S gene has provided unambiguous evidence [30-31-32-33].
b) **Receptor binding:** monoclonal antibodies (MAb) against the S protein of most coronaviruses can neutralize viral infectivity; therefore, protein S is assumed to mediate the binding of the virus to receptors in target cells. Indeed, protein S or a part of it can bind to viral receptor molecules in vitro. Corona virus causes the cold and lower respiratory tract diseases in humans. In contrast, coronaviruses cause devastating foot and mouth disease of respiratory or enteric diseases in livestock and poultry.
In single host species most, coronavirus cause the diseases. All the Corona viruses which has been identified till now they are found in the three serologically unrelated groups.

Integral membrane protein:
For production of coronavirus-like particles the M protein is essential structural protein. All the coronaviruses M protein, amino-terminal 20 or so residues are hydrophilic and have small glycosylation sites. Therefore, the envelope and the internal core of the virion both roles may be played by the protein.
For the virus particle assembly M protein required: (1) In vitro, the purified Nucleocapsid binds to the M protein [34]. (2) Near the location where virus particles bud it was localized in the Golgi complex When the M protein was expressed alone [35-36]. It has been shown that for viral particle budding the location of M protein in the Golgi was slightly different [37] signifying that the virus particle assembly additional factors are involved.

Hemagglutinin-Esterase Glycoprotein (HE)
Hemagglutination occur more efficiently in the coronavirus which contain HE in their virions. hemagglutination and hemadsorption can be mediated by HE alone as compared to S protein [38-39-40-41-42-43] though as compared to S protein HE protein show weak activity [43].
The esterase activity also shown by the HE protein because it is a neuraminate-O-acetylesterase. So, on erythrocytes it hydrolyzes the 9-0- acetylated sialic acid, thus the HE or S protein induced by reversing hemagglutination; therefore Hemagglutinin-Esterase Glycoprotein is considered a receptor destroying enzyme [44-45-46-47]
The importance of HE protein for coronavirus is not known. For infectivity only BCV requires HE among all the coronavirus; Though the pathogenicity of some coronaviruses may be affected by the presence of HE, as demonstrated that passive administration of HE-specific MAb in mice altered pathogenicity that HE has different neuropathogenicity with MHVs [48-49].
Small Membrane Protein (E)
It was assumed that coronavirus have three (S, N, M) or four (including HE) structural proteins. But now one more additional virion protein is also present i.e. E protein. This E protein play role in the virion assembly. It is also informed that the E and M proteins both are required for virion assembly [50-51].
A distinctive crown with an oversized peak on the envelope makes it possible to spot the coronavirus by microscopy. Spikes, oligomers of the pointed glycoprotein (S), bind to the receptors on the host cells and merge the viral envelope with the membranes of the host cell.

Hemagglutinin-acetyl esterase (HE) glycoprotein that binds to sugar residues in cell membranes of group 2 Coronaviruses.

Interestingly, the gene for **Hemagglutinin-Esterase Glycoprotein** was introduced into an ancestral coronavirus genome by recombination. The exclusive RNA-dependent coronavirus RNA polymerase often changes model chains during replication, causing recombination of RNA when a cell is infected with multiple coronaviruses. Point mutation generated through error prone polymerase. In viral genome huge deletion or insertion of foreign RNA is observed.

SARS-CoV and MERS-CoV:

Both SARS associated corona virus and MERS associated corona virus come under corona virus genus. Both are the positive sense RNA and the size of the SARS associated corona virus genomes is 27.9 kb and size of MERS associated corona virus 30.1 kb (Fig. 2 a). Both SARS associated corona virus and MERS associated corona virus have exclusive method of encoding. 66% of the Ribonucleic acid of virus translate into two large polyproteins and 34% Ribonucleic acid of viral genome is transcribed into Sub genomics sets of mRNA.

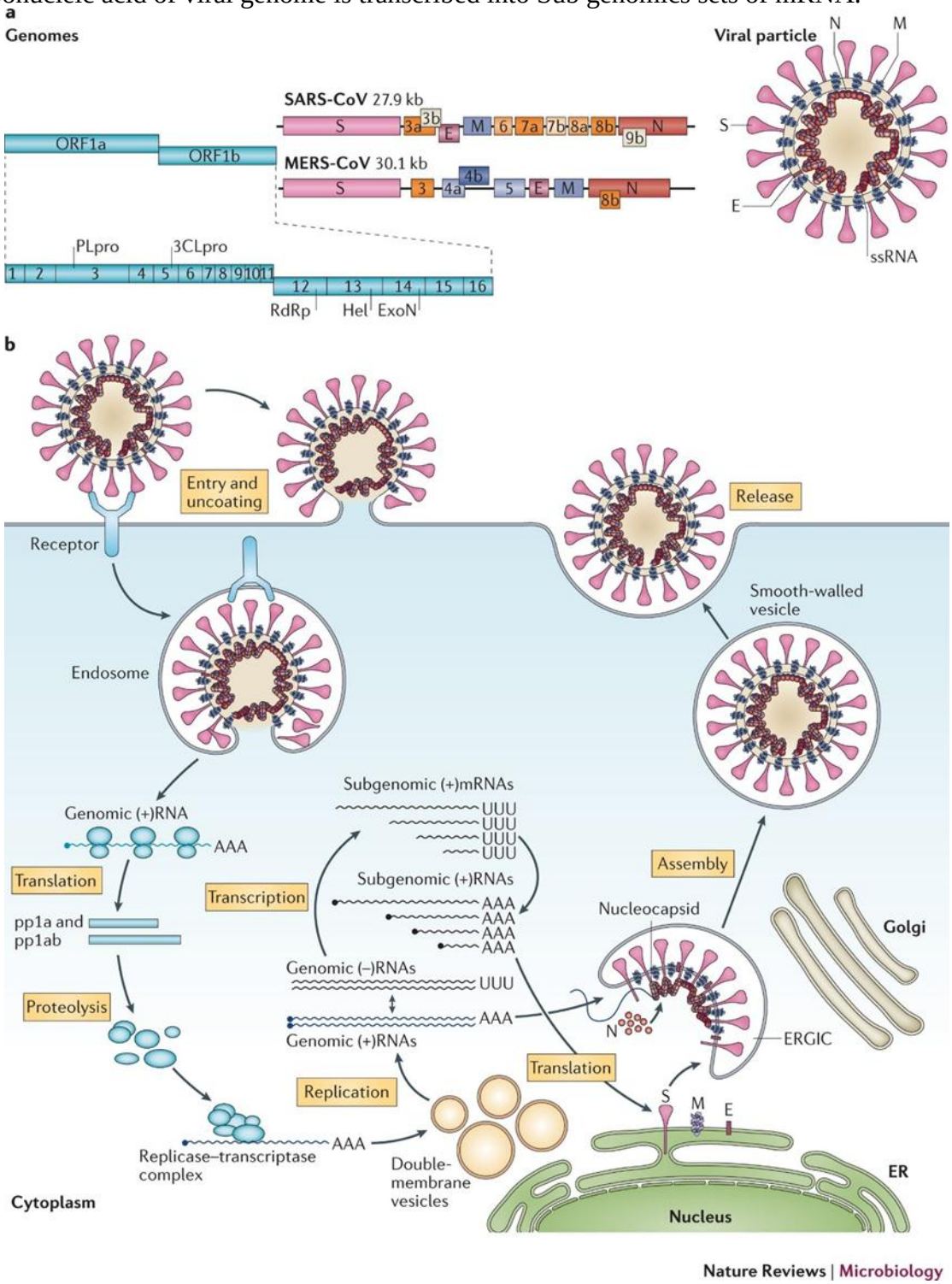


Figure 2: SARS-CoV and MERS-CoV structure and replication
Source: Nature Reviews Microbiology, SARS and MERS: recent insights into emerging coronaviruses, 2016

a) Both SARS-CoV and MERS-CoV code for pp1a and pp1ab polyproteins which are divided proteolytically into 16 non- structural proteins along with papain-like protease (PLpro), 3C-like protease (3CLpro), RNA-dependent RNA polymerase (RdRp), helicase (Hel) and exonuclease (ExoN). ORFs are coded by series of sub genomic RNAs between 9-12 ORFs. SARS-CoV and MERS-CoV made up of four structural proteins i.e S, M, E and N. S is glycoprotein that project outward from envelop layer. Inner side of E and M layer positive sense single stranded RNA is present.

b) when the virus enters the host cell uncoating of RNA occur in the cytoplasm. pp1a and pp1ab protein produce by the translation of ORF1a and ORF1ab. ORF1a is code for protease and these proteases will cleave pp1a and pp1ab into 16 nsps and these nsps form the replicase-transcriptase RNA complex.

This complex derived from the perinuclear region of rough endoplasmic reticulum and found in modified intracellular epithelium. It guides the assembly of negative sense RNA. Positive sense RNA act as template for the synthesis of negative sense RNA genome during the replication. Through discontinuous transcription 7-9 sub genomic subset RNA, s produced along with all structural proteins. (+) mRNA produced through transcription of (-) RNAs.

Sub genomic mRNA have many ORFs but only ORFs which is present near to 5' end is translated. In intermediate ER-golgi compartment (ERGIC), All structural proteins assembled into the nucleocapsid within viral envelop.

MERS belong to c lineage instead of b lineage. MERS is a beta coronavirus. MERS causes the renal failure and pneumonia with high death rate. Initial cases of disease were reported from Jordan, Qatar, Asian nation and also the United Arab Emirates and the cases having travel history were diagnosed in France, Germany, Italy, Tunisia and also the UK. (http://www.who.int/csr/don/2013_09_07/en/index.html).

Susceptance and exposure of disease is more pronounced in the people belonging to higher age groups and along with age factor they were having history of other underlying disease. In France this disease doesn't appear to healthy workers instead it appears in immunocompromised patients [52].

High rate of Transmission occur in patients and family members as well as a hew HCWs in a health institute of Al-Ahsa in the Eastern Province of Saudi Arabia [53]. In Europe and Africa, closely related MERS-CoV viruses are detect in Pipistrellus bats [54]. In Oman and Egypt, high neutralizing antibody titers of MERS-CoV found in dromedary camels as it signifying that they will intermediate of virus [55-56].

The receptors of MERS-CoV found in human respiratory tract and in many animal species such as bats, these receptors are known as dipeptidyl peptidase IV (DPP4) [57].

The biological understanding obtained of the interactions between the viral receptor and also the host within the restriction of transmission between SARS-CoV species are going to be relevant for MERS-CoV.

Recently published studies related to structure information of MERS CoV gave information about confirmed presence of two crystalline structure between the binding domain of the spike protein receptor and DPP4 [58-59] which is also confirmed by structural information of Solo RBD [60].

A crystalline structure has also been reported for the most MERS-CoV protease [61] and a piece of writing on the macro-domains of the viruses of Lei et al. it's in preparation. All of

those structures are going to be included within the reviews of this series that describe the individual SARS-CoV and MERS-CoV proteins.

In human respiratory tissues, MERS-CoV replicate and affect the epithelial cell and endothelial cells of blood vessels within the lung [62]. As seen in SARS-CoV, It spread beyond the respiratory tract (see Cheng et al., during this series). SARS-CoV inhibit the response of interferon [62-63-64].

Distinctive response studies conducted on SARS-CoV, it has been observed that the response of host interferon is restricted by virus itself up to large extent bit it also remain responsive towards the action of host interferon [62-63-64]. The virulence of the corona virus is depending upon host factor and viral factors and the disease more prevalent in infants. The symptoms of immunocompetent animals are different as compared to immunosuppressed animals. the virus can be killed for long periods of time and accumulate and spread mutant viruses in immunosuppressed animals.

SARS-CoV can be spread through faecal contamination and respiratory droplets. The detection of SARS-associated coronavirus in patient's stool, serum samples and in respiratory samples. Some species or strains of virus which is going to infect the other species may cause the death of the host, so Host genes influence the viral receptor, viral production and immune responses. For example: in cheetahs, domestic cat coronaviruses always the cause death. SARS associated corona virus is worsen with other viruses, parasites or bacteria in animal. Host factors that aggravate the Deaths of SARS patients. Even though there is no appropriate drug available against the virus, there are potential targets for the development of new drugs.

The processing of RNA polymerase or cleavage of viral S glycoprotein could be prevented by protease inhibitors. Coronavirus acetyl erase activity inhibitors and neuraminidase inhibitors can inhibit the viral replication and replication of influenza A and B viruses. Viral entry and several drug against the human immunodeficiency virus can be inhibited by membrane fusion inhibitors. Virus entry can be blocked by antibodies or viral S glycoprotein or the unidentified coronavirus receptor associated with SARS. For some animal corona viruses' vaccines are available.

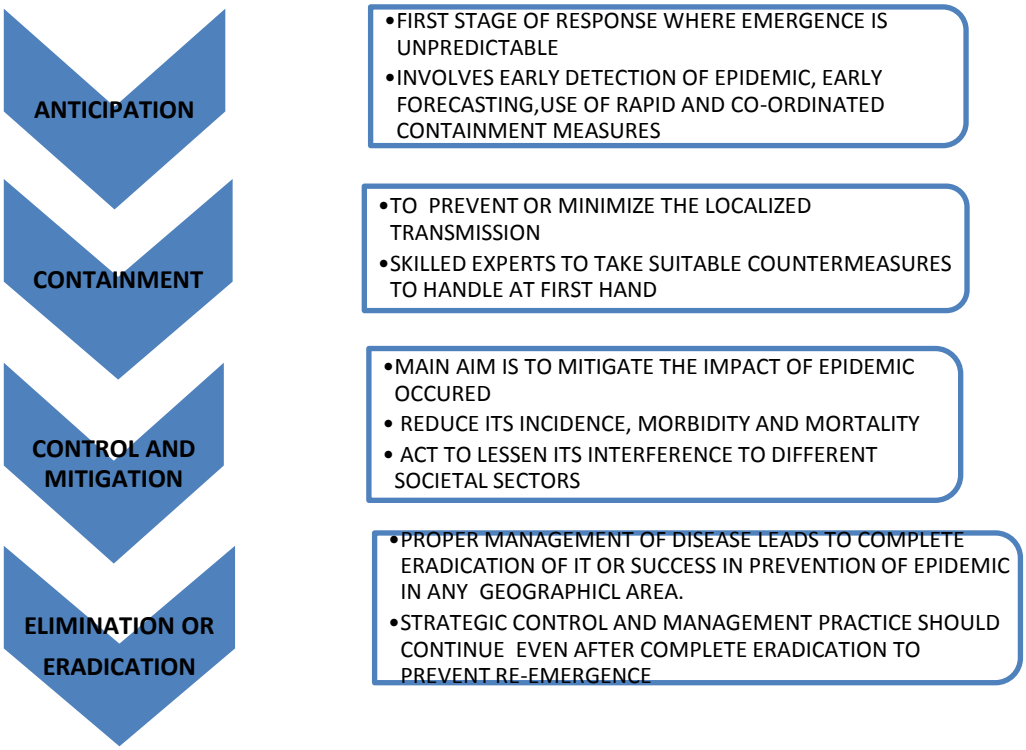
Against the swine diarrhea virus and the bird's bronchitis virus vaccination of live attenuated viruses generated from recombination of genomes of vaccines strains is considerably effective. Though there are potential risk associated are prominent when strains are incorporated with wild type corona virus and the symptoms are exhibited up to large extent.

The lower respiratory tract diseases could be prevented by dead vaccines or subunits containing spiked glycoprotein, perhaps with other viral proteins. But sometimes when the vaccinated animals were exposed to wild type virus then disease will actually increase. an increase in antibodies to the disease poses a potential risk for human SARS vaccines. At present to control the spread of virus through quarantine and best method for controlling the disease is to develop the safe and effective drug against the virus. For the prevention and treatment of other animal and human coronavirus diseases through the development of SARS drugs and vaccines will also provide new strategies

For public health sustenance it is mandatory to understand the spread of infectious diseases and designing optimal control strategies for a community structure that ultimately affects disease dynamics [65]. Isolating symptomatic individuals followed by contact tracing and quarantining their contacts are the major public health measures in controlling infectious disease outbreaks [66].

PHASES OF EPIDEMIC AND RESPONSE INTERVENTIONS

In many different regions of the world we witnessed epidemics of infectious diseases with more recurrence rate and high potentiality to spread. Prevailing pandemic i.e. COVID-19 has already impacted a huge number of people and approximately more than 1.3 million people lost their battle of life till date. It cannot be denied that, these diseases completely hit the economy of every affected country and different sectors like travel, trade, big budgeted industries and livelihoods are majorly affected and suffering major losses. These epidemic diseases are both social and medical problems and cannot be treated by following traditional biomedical treatments. Planning and preparation for prevention and control of such epidemic diseases is need of the present era.



2. CONCLUSION:

This infectious disease has become pandemic which reached and flourished well in different countries of the world, although the disease has been known to be originated from China. The symptoms observed in COVID-19 patients are fever, sore throat, dry cough, body ache, fatigue, pneumonia, common cold, shortening in breathing, gastric disturbances and death. The disease is mostly affecting the infants (1-10 yrs.) and old age people (above 60-year-old) more severely and they face the respiratory distress. In order to alter the pace of spreading epidemic, social distancing from the susceptible individuals can disconnect the chain of pathogen to spread further to any non-infected individual [67]. Very limited medicinal approaches are workable only to treat the symptoms and their adverse impacts on human health so lone option left with humankind for survival is to plan and work upon cooperative measures to fight with such public health threats.

Recommendations

To accelerate studies for future public health emergencies, we consider that this comes out to be a big functional responsibility at international, national and community levels.

A) INTERNATIONAL LEVEL: Synchronized and cumulative work in action by all the international governments for maintaining:

1. Co-ordination between local and international researchers for and from research initiation,
2. Work on template agreements for data exchange and indiscriminate/ethical use of samples for prevailing studies on bio-banks,
3. For commencing work of diverse independent Scientific Advisory and Data Safety Review Committees in collaboration for all studies linked to alike intervention or group of interventions,
4. Framework of Ethics in form of review committees or making representatives from different institutions around the world to establish ethical and true component of reviews through different perspectives in unbiased and non-liable manner.
5. Proper channel to exchange confined information between different authoritative and advisory chairs for safety review and projected implementations,
6. Inclusion of pregnant women and children in socio-scientific-experimental studies as they are major risk bearers and prone to be under irreversible fatal consequences.

B) National Level:

1. First requisite is, to comprehend viewpoint and related ideology and substantive thoughts of both sides for establishing a midway between government authorities, regional respondents and communities.
2. Incorporating persons of trusted backgrounds to reach out for cooperative solutions to reduce transmission it is essential to build trust through their mutual understanding.
3. Even execution of necessary measures to curb the disease by empowering communities through easy and quick access to them with necessary medical and other supplies, and gradually conveying related information for persistent and secure mediations within the community.

C) Societal level:

1. Accepting themselves as frontline respondents in their own community.
2. Providing sufficient information to support groups to detect any upsurge of new or previously infected people.
3. Minimizing any kind of harmful practices like public gatherings/functions which favors the instance of widespread infection exposure at both individual as well as community levels.
4. Adoption of defensive practices for both medical and nonmedical consequences also enabling authorities to organize efficient system for providing health care as advised.
5. Acceptance and merging of recovered members again in community and to minimize taint related to their any present or past medical history.
6. Identifying and managing misinformation and rumors prevailing around them.

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