Advances in Bioresearch
Adv. Biores., Vol 11 (3) May 2020: 37-45

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.11.3.3745

Advances in Bioresearch

REVIEW ARTICLE

Symptoms, transmission, prevention and treatment of pandemic corona virus: A review

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ABSTRACT
Corona viruses belong to the largest group of viruses that elicits acute respiratory, enteric and systemic infections in an extensive range of hosts. A few corona viruses from animals can progress into a new human corona virus that can spread from person toperson. On February 12, 2020, WHO officially termed the disease as Corona virus Disease 2019 (COVID-19) and declared as a pandemic on March 11, 2020. COVID-19 is a new emerging viral disease that has an effect on lower respiratory tract and shows as pneumonia. Although laborious worldwide lockdown and quarantine efforts, the occurrence of COVID-19 continues to increase. Presently there is no effective specific vaccine and antiviral drug supported by great-level confirmation. Further research is required to clarify the factors that affect virus pathogenesis and lethal infections.
Keywords: *COVID-19; Corona viruses; diagnostics; vaccines; pandemic*

Received 01.05.2020 Revised 08.05.2020 Accepted 2605.2020

How to cite this article:
T Kebede , D Kumar , P K Sharma. Symptoms, transmission, prevention and treatment of pandemic corona virus: A review. Adv. Biores., Vol 11 (3) May 2020: 37-45

INTRODUCTION

Corona viruses are known to elicit severe infections, in humans (respiratory infection) and animal. The corona virus infections have been known in cats, dogs, cattle, civets, rabbits and various other pet and wild animals [1-2]. For the first time, Human Corona viruses were recognized from respiratory infections in adults other thanin childrenin 1960. Scientific attentiveness in Corona viruses' research grew n 2002-03 after the rise of Severe Acute Respiratory Syndrome Corona virus [3-4]. After SARS-CoV, another virus come in light in 2005 was HKU3-1 to HKU3-3 from Hong Kong [5]. Since then, bats are most favorable natural host for these types of viruses in past and future [6-7]. After SARS-CoV epidemics, are lated virus emerged in the Middle East region and was termed the Middle East Respiratory Syndrome CoV (MERS-CoV [8]. Corona virus is a one of virus belongs to Nidovirales order, consist three families Coronaviridae, Arteriviridae, and Roniviridae and two subfamilies Coronaviridae and Torovirinae [9]. Corona virus has four group alpha, beta, gamma and delta. Viruses are grouped based on serology and phylogenetic cluster [10]. Viruses from Nidovirales order are RNA sense and non-segmented [11,12]. These viruses have 30 kilobase genomes of RNA. Nidovirales order, have many similar characteristics i.e resource of genomes and structural replication of genes, expression of nonstructural gene by ribosomal modification, enzymatic activities as replication and transcription of polyproteins and synthesis of other genomic mRNA [13]. The word Nidovirales comes from the nested 3 mRNA, as the Latin word Nido means nest. Nidovirus order also has many unsimilarities such as size, type and number of structural proteins. Due to these unsimilarities morphology and nucleocapsids of viruses are different [12,14]. Corona viruses had a greater report in the veterinary science field (Table 1).

Table 1. Corona viruses of significant veterinary species [9]

Host	Virus Species	Genus	Dominant pathology
Cattle	Bovine corona virus	*Betacorona virus*	GI tract Respiratory tract
Swine	Transmissible gastroenteritis (TGE) virus	*Alphacorona virus*	GI tract Respiratory tract
	Porcine respiratory corona virus	*Alphacorona virus*	GI tract
	Porcine epidemic diarrhea virus (PEDV)	*Alphacorona virus*	Respiratory tract
	Porcine hemagglutinating encephalomyelitis virus	*Betacorona virus*	GI tract CNS
	Porcine deltacorona virus	*Deltacorona virus*	GI tract
Cat	Feline enteric corona virus	*Alphacorona virus*	GI tract
	Feline infectious peritonitis virus	*Alphacorona virus*	Respiratory tract, Abdominal cavity
Dog	Canine corona virus	*Alphacorona virus*	GI tract
	Canine respiratory corona virus	*Betacorona virus*	Respiratory tract
Horse	Equine corona virus	*Betacorona virus*	GI tract
Camel	Middle East respiratory syndrome (MERS) corona virus	*Betacorona virus*	Respiratory tract
Chicken	Avian infectious bronchitis virus	*Gammacorona virus*	Trachea Kidney Reproductive tract

The production, sell and mortality of chickens are affected by respiratory corona virus every year. Ninety percentages of newborn swine were diseased with different type of corona virus such as transmissible gastroenteritis corona virus, haemagglutinating encephalomyelitis corona virus and porcine epidemic diarrhea corona virus [15-16]. Corona viruses were replicates in respiratory tract, enteric tracks and both depend on strains [10,17]. This period's first corona virus was rise from Wuhan, Hubei province of China, and spread to most parts of the world. Seeing the global hazard of the COVID-19, the World Health Organization (WHO) declared it as a 'Pandemic on March 11, 2020 [19]. As on April 6, 2020, 1,250,000 total number of cases and 69,000 deaths have been reported globally [18]. Additionally, the spread of this novel corona virus, termed COVID-19, has been reported on every continent except Antarctica till date [19]. This review delivers a general idea of the newly emerging corona virus disease 2019 (COVID-19) pandemic with respect to its recent scenario, treatment and prevention.

THE EMERGENCE OF COVID-19 PANDEMIC

An epidemic of an emerging disease (COVID-19) because of a novel corona virus started in Wuhan, China on December 2019 and quickly spread across China and to other countries [20-21]. Corona virus was confirmed in peoples, who have the history of visiting seafood market of Wuhan, China, and peoples have doubt of animal to human transmission [22]. Corona virus infected patients have reported symptoms of pneumonia with some acute respiratory infection characteristics followed by critical condition [23]. The Chinese Center for Disease Control and Prevention (CDC) confirmed that a new corona virus has raised and named COVID-19 on Jan 7th, 2020. Then, WHO declared the epidemic of COVID-19 as a pandemic on March 12th, 2020 [18]. Many Chinese studies reported the fatality rate of corona infected patients i.e 2.3% but in geriatric it was 8.0% (70-79 year age) and 14.8% (more than 80 years age) [24]. There are so much change to human to human transmission or community transmission, and thus the mortality rate may be enhanced [25]. Human to human transmission of corona virus takes place with peoples close contact, airborne droplets due to coughing or sneezing, kissing, smooching, and in contact of same surface [22,26]. So corona virus transmission is more concern than treatment. Some old medicine were used in treatment of corona such as antimalarial, antiviral, antibiotics, because of the safety, side effects and known drug interactions [27-28].

ETIOLOGY

Novel corona virus was first identified in Wuhan, China during its outbreak [65]. Comprehensive viral genome analysis in preliminary report conducted shows that the corona virus has 88% similar sequencing of severe acute respiratory syndrome (SARS [20,29].

Nature contains various virus families such as corona virus family. Corona virus belongs to family Coronaviridae and order Nidovirales and contains single stranded RNA with spikes shape and surfaces with a size 9-12 nm [29-31]. Corona virus contains many structural protein spike protein is most important them because of its role as it binds to angiotensin converting enzyme 2, and responsible for fusion and entry into the new host cell [30,32]. International Committee on Taxonomy of Viruses named

Corona virus Study Group observed and sets its syndrome named it as SARS-CoV-2 based on genes sequence and taxonomy at 11th Feb. 2020 [33]. Previous studies on corona virus transmission indicates that it was initially hosted in bat and pangolin, pangolin and other pet and wild animal transmitted it in to human and now human to human transmission observed daily [34-36]. Still, it is believed that first transmission of corona virus in human was take place in seafood market, Wuhan, China. So that American peoples called it as Chinese virus [31,37].

EPIDEMIOLOGY OF COVID-19

Onset of symptom in confirmed patients initially appeared on December, 2019 [38]. In starting morbidity rate was less but within two weeks it was enhanced, after second week of Jan 2020, morbidity due to corona virus was a new concern in China. In starting of March 2020, corona outbreak was become a serious problem in whole world. As per Guan et al (2020) study, incubation period of corona virus was 3 day (0-24 days) and its transmission was asymptomatic [36,39]. At last week of Jan. 2020, WHO was reported more than ten thousand of corona infected patients in China and at 13 Feb. 2020, WHO has reported 13332 corona infected patient. Total corona case in China was reported on the bases on the number of test of chest CT findings because it was recommended during the treatment of corona virus [22, 26, 43]. It becomes CoVID19 outbreak during a traditional festival known as spring festival in China and about 3 billion gathering in festival was observed [39-40]. During this period nearly 3 billion people travel nationwide These situations caused advantageous circumstances for the transmission of this highly contagious disease rapidly and rigorous difficulties in prevention and control of the epidemic. Wuhan, having 10 million populations, is also an important center in the spring festival transportation network. This large-scale travel traffic has also created favorable conditions for the spread of this challenging disease [41]. Till scientist and WHO was confused in identification and discovering he microbiology, pathogenesis, causes, symptoms and history of corona virus. Many researchers do not believe in reports on its transmission history and origin of corona virus. Scientists are also not clear to know about its relation with influenza virus that it may become seasonal viral or not [42-43].

Sources and Modes of Transmission

Corona virus may be transmitted via various modes as shown in figure 1.

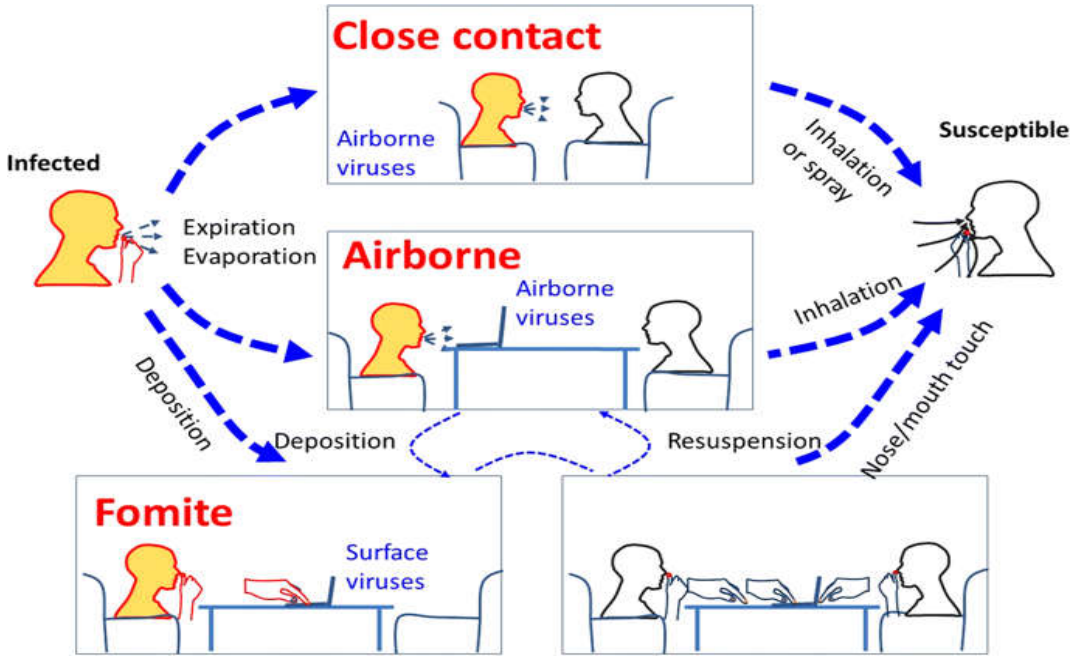

Figure:1. Mode of transmission of corona virus

Advanced virological and genetic studies have revealed that bats are reservoir hosts of both SARS-CoV and MERS-CoV and before these viruses spread to humans, they use the other responsible animals as intermediate hosts. Studies have stated that most of the bat corona viruses are the gene source of alpha-CoV and beta-CoVs, while most of the birds CoVs are the gene source of gamma-CoVs and delta-CoVs [44]. In current studies, it has been detected that the novel virus causing epidemics coincides with the CoV isolated in bats. Existence of wild animal trade in Huanan Seafoods Market where the first cases

appeared, aids this outcome [45]. The possible mode of transmission of this infection is thought to be animal to human transmission. There have been numerous evidences, reporting the animal to human and inter-human transmission of the virus [46]. As in SARS and MERS epidemics in the past, human tohuman transmission has speeded the spread of the outbreak and case reports have also started from other states of China. Frequently, the human to human transmission happens with close contact. The transmission principally happens when an infected person sneezes and through the respiratory droplets. These droplets can settle in the mouth or nasal mucosa and lungs of people with inhaled air. A person can be infected by COVID-19 by touching an infected surface or object and then touching their mouth, nose, or possibly eyes [47-48].

Normally, like most respiratory viruses, COVID-19 is considered to be the most contagious when people are most symptomatic. However, cases, which were infected from an asymptomatic person in the prodrome period of COVID-19, were also reported. Adequate data are not presented on infectiousness of the disease and research is continuing [22,49].

CLINICAL SYMPTOM SPECTRUM

Clinical picture differs from simple respiratory infection findings to septic shock. Similar to SARS CoV and MERS CoV that caused epidemics in the previous years, the first symptoms are regularly seen as fever, cough, and shortness of breath [29]. Intestinal symptoms not often stated in patients with COVID-19. On X-rays or thorax CT imaging of the observed patients, unilateral or bilateral involvement compatible with viral pneumonia was found, and bilateral multiple lobular and subsegmental consolidation areas were observed in patients hospitalized in the intensive care unit [29,39]. Few patients of CoVID19 were reported headache or hemoptysis and other patient have no symptoms [20]. Geriatric patient have more symptoms as respiratory failure due to alveolar damage [45]. Most of people have start with slow symptoms progress and turned to organ dysfunction and even to death. Many patient showed low white blood cell count, thrombocytopenia and lymphopenia with increased in C-reactive protein levels. Peoples have elevated body temperature with upper respiratory tract symptoms have most chance of corona infection and must be checked for corona virus [20].

PHYLOGENETIC ANALYSIS AND SEQUENCE IDENTITY

Scientist from all over the world working on corona virus to revealed its genomic nature and 15 genomic sequence of this virus were revealed till. Scientist has doubt about its natural host i.e snake or bat. According to a report snake (based on codon analysis) was the natural host but later studies reported bat (based on phylogenetic analysis) as its natural source [9,29].

DIFFERENCES IN SYMPTOMS OF CORONA VIRUS AND OTHER RELATED VIRAL INFECTIONS

Novel Corona virus is similar to various virus infections but its symptoms are quite different then other viral infection as listed in table 2.

Table 2: difference in symptoms of corona virus and other related viral infection

Diseases	Respiratory symptoms	Constitutional symptoms	CT imaging findings
Common cold	Stuffy nose, runny noses, sneeze	No obvious discomfort	Usually normal
Influenza	Stuffy nose, runny noses, sore throat and dry cough	High fever, muscle ache, malaise	Small patch GGO and consolidation with subpleural or peribronchial distribution
SARS	Cough, dyspnea	Fever, chill, malaise, headache, diarrhea	Subpleural GGO and consolidation prominent lower lobe involved, interlobular septal and intralobular septal thickening
MERS	Sore throat, dry cough, dyspnea	Fever, chill, rigor	Bilateral, basilar and subpleural airspace, extensive GGO and occasional septal thickening and pleural effusions
Mild COVID-19	Cough or not, sore throat	Fever	Multifocal patchy GGOs with subpleural distribution
Severe COVID-19	Breathless, respiratory failure	Fever, muscle ache, confusion, headache	Diffuse heterogeneous consolidation with GGO

Abbreviations: GGO: Ground-Glass Opacity SARS: Severe acute respiratory syndrome
MERS: Middle East respiratory syndrome

DIAGNOSIS OF COVID-19 INFECTION

Corona virus is diagnosed on the basis of traveling history, contact, symptoms, and laboratory testing. Corona virus diagnosed can be done using various methods such as serology, viral culture and molecular methods. The most common diagnostic techniques are molecular methods as reverse transcription or real-time PCR, which are made using RNA obtained from various sources of samples such as oropharyngeal swabs, sputum, nasopharyngeal aspirate, deep tracheal aspirate, or bronchoalveolar lavage. Specifically, lower respiratory tract samples can gives significantly higher viral load and genome fraction than upper respiratory tract samples. These techniques are advantageous in terms of assessing the outcomes quickly, showing the genome structure and viral load [29]. Viral culture is a more time wasting technique compared to the other methods. Culture is much more valuable in the first stage of outbreaks before other diagnostic approaches become clinically available. In addition, viral cultures can be used in the in vitro and in-vivo antiviral treatment and vaccine evaluation trial [44]. The question of how long the novel COVID-19 outbreak will last is a question that everyone is curious about.

DEVELOPMENT OF COVID-19 DIAGNOSTICS

A fast, precise, dependable, and cheap process for restricting the transmission of corona virus is surveillance and rapid test for infected or suspected patients. Scientist are working to found the cellular level factors that affect the tissue with high concentration during presymptomatic stage corona infection. Reports were revealed that corona virus mainly appear and located in respiratory system that is a main challenge to collection [50]. After the emergence of Novel Corona virus 2019 (COVID-19) pandemic, real time RT-PCR remains the principal technique for diagnosing of novel corona virus [41]. Researchers claimed that respiratory specimens and serum were positive and negative respectively for virus in early stages. It has also recommended that virus appears high level with less symptoms in early stage of virus of initial days. Additionally, there are potential rapid diagnostic kits available on the market for COVID-19. Mostly are used in research labs. Still, a kit from Beijing Genome Institute, China is approved and used for rapid diagnosis in clinical purposes. RT-PCR is used in most of available kits. Currently, two kits are available for testing and identification based on pathogens sequencing and microarray technology from BGI (China) and Veredus (Singapore) [41]. On March 31, 2020, the U.S. FDA approved corona virus test for use in emergencies. The test designed by Bodysphere Inc., can return a diagnosis in just 2-10 minutes [18].

DEVELOPMENT AND ADVANCEMENT IN VACCINES AND THERAPEUTICS

Potential Vaccine

Scientists across the world are working to fight the current ongoing corona virus disease 2019 (COVID-19) outbreaks, ascertaining the promising origin of this novel virus, and to design and develop effective vaccines and therapeutics [51-52]. With the emergence of Novel Corona virus Disease 2019 (COVID-19), various formulations with different target sites are developing against corona virus. Different techniques are used to investigate the first anti-corona agents such as RNA, DNA based formulation, nanoparticles, modification of proteins etc. Many clinical studies are submitted or started. Maximum od clinical studies will complete after Dec. 2021. Some of them were initially improved for their study design on emergency based [53-54]. It is a distant thing to believe medicine or vaccine. Authorities focused to reduce transmission, enhanced prevention [55]. Most of scientists are working to develop vaccine targets spike glycoprotein because it is the main inducer of neutralizing antibodies [57].

Potential Therapeutics

Up on searching of different articles from different data bases regarding to ongoing therapeutics options, we recorded twenty three (23) clinical trials. From the recorded clinical trials, few of them (9) were officially registered in registration website of clinical trials for COVID-19 therapeutics[58]. From registered clinical trials, majority of them (5 trials) focuses or targets on some specific drugs which is previously approved for another diseases. These drugs include: hydroxychloroquine, lopinavir/ritonavir, glucocorticoid therapy, arbidol, traditional Chinese medicine and mesenchymal stem cells. These drugs are under recruitment stage and predicted to give a good clinical outcome. The other four studies concentrate on drugs such as: darunavir, interferon beta, cobicistat, arbidol and remdesivir [59-60]. These mentioned drugs also previously approved for another diseases. Effectiveness of chloroquine and hydroxychloroquine on coronavirus diseases 2019 (abbreviated as COVID-19) have been on showing good clinical outcomes on some peoples infected by COVID-19 [61]. The others anti-viral therapies which are predicted to have efficacy on COVID-19 infected patients but not started randomized trials either in animal or humans include: RBD–ACE2 blockers, protease inhibitors, S cleavage inhibitors, neutralizing antibodies and S protein inhibitors[50]. These mentioned drugs were suggested to undergo clinical trials

by different researchers. The other anti-viral drug, Remdesivir, has inhibitory action on previously occurred outbreaks (SARS and MERS) and also showing good efficacy against patients infected by COVID-19 [62-63]. Generally, different clinical trials by different scientists were ongoing but still there was no any drug which is approved for COVID-19 treatments supported by good clinical evidence.

PREVENTION AND CONTROL MEASURES

Prevention plays an important role in minimizing the risk of infection in COVID-19 diseases. As a result people should give attention to prevention methods forwarded by Health Organizations and different health professionals [55]. Recommendations forwarded by World Health Organization (WHO) includes: Since coronavirus is zoonotic disease, contact with animal and using animal products should be completely avoided [26]. CDC reminds basic measures such as hand washing, using disinfectant solutions, maintaining 6-feet social distancing, wearing cloth masks and avoiding contact with patients in order to prevent the spread of viruses by droplets during coughing, sneezing and kissing [65]. Preventive measures comprising the delivery of medicines supply chains, personal protective equipment, and hospital supplies time for the protection of the global health.This devastating disease can be controlled by designing different strategic methods including proper awareness creation within communities by educating prevention means of the disease and control strategies if infection occurred, discovering rapid test kits, working efficiently on producing effective vaccines and therapeutic options.[51, 63]. Generally, Using face masks, social distancing, regular hand washing with soap for at least 30 seconds, using hand sanitizers containing more than 60% alcohol, and Quarantine of peoples either which have contact with infected person or travel history are some of recommended common practices forwarded by World Health Organization[53,63].

THE IMPACT OF COVID-19 PANDEMIC

After occurrence of COVID-19 outbreak, different measures were undertaken by different countries for preventing and minimizing the risk of the diseases. As a result most countries declared nationwide lockdown measures and also closed their boundaries. For this reason export and important of materials was extremely reduced. This causes challenge towards the economy of countries [50]. Due to this disease, many factories and organizations reduced their workers, manufacturing was significantly reduced, trade among countries, cities was stopped, schools were closed, different flights were cancelled and different activities were stopped. This pandemic is leading to major economic, social and political crisis within countries. Therefore, appropriate prevention and control methods must be employed properly [64]. Immediate discovery of effective vaccine and therapeutic options should be found to reduce rapid spread of the disease and minimize the risks on economy, political and social crisis on different countries [51].

FUTURE PREDICTIONS

Since COVID-19 pandemic is comparable to previously occurred SARS-CoV epidemic, some vital characteristics of SARS epidemic are directing the projections on current pandemic. According to the logistical modeling studies conducted by combining daily numbers from COVID-19 cases with data obtained in SARS epidemics; timely diagnosis is elemental for quarantine and incorporated interventions to control the outbreak [9].As a result of the actions taken by Chinese government, including ratifying laws for effective infection management supports quickening the diagnosis and treatment such as distribution of more than 30,000 PCR fluorescent probe kits to determined diagnosis centers in Wuhan, and closing Wuhan and nearby Huang Guang provinces, which prevented physical contact, as result the number of infected peoples greatly decreased. Since there are many characteristics of the diseases that we haven't understand yet, it is difficult to predict about the disease properly. Quick diagnosis strategies, discovery of effective vaccine and drugs, proper implementation of prevention measures and quarantine of either infected or which have travel history will have a great effect on future trends of the outbreak. As imposition of globalization, corona viruses will cause spreads and outbreaks with different-mutant strains similarly in the coming years [50].

LESSONS FROM COVID-19 FOR NEXT OUTBREAKS

Learning from COVID-19 outbreaks, different public health policy creators should formulate strategies for quickly replying for any kinds of outbreaks. This can be achieved by working cooperatively with different stakeholders. World Health Organization is responsible to lead and facilitate countries to work together in formulating and implementing international health regulations and also work cooperatively in discovery of vaccines and drugs for the diseases[10]. Generally, an appropriate system which guides all

countries should be formulated and prepared to respond rapidly for any emerging diseases and to restrict spread of the disease through facilitating networking between countries [65].

CONCLUSION

After outbreak of SARS and MERS, third coronavirus outbreak is occurred, COVID-19, which is caused by novel coronavirus, is spreading very rapidly across a world. This disease can transmit from person to person easily unless prevention methods implemented properly and effectively. Corona virus disease 2019 (abbreviated as COVID-19) spreads mostly through close contact with infected person. That means when infected person coughs, sneezes or kisses, the respiratory droplets produced have an access to enter to the healthy persons or when a person touches his eye, nose or mouths after touching objects (clothes, plastics or metals) that has the virus on it. According to guidelines forwarded from World Health Organizations (WHO), various measures help to prevent the COVID-19. Measures include: avoiding contact with sick person, using facemasks in the public, regularly washing our hands with soup at least for 30 seconds, social distancing, cleaning our hands with sanitizers containing more than 60% alcohol and avoiding the market place. Discovery of quick diagnostic kits, vaccines and therapeutics are important to prevent and control this disease to minimize the spread, risk and death of peoples. However, at the time of writing this review, there was no any kind of vaccine and treatment which is approved by great level of clinical outcome as evidence. Further research about the disease must be performed in order to discover effective prophylaxis and drugs for controlling the pandemic.

CONFLICT OF INTEREST STATEMENT

No potential conflict of interest was reported by the author(s)

ACKNOWLEDGEMENT

Authors thanks to College of Veterinary Medicine, Haramaya University, Haramaya, Ethiopia and Galgotias University, Noida, India to provide facilities to do the work in health environment.

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