



Review Article

Outbreak investigation steps in the case of 2019 novel coronavirus infection, a review

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Summary

Coronaviruses are a large family of viruses that are common in many different species of animals, including camels, cattle, cats, birds and bats. In January 2020, it causes an outbreak of respiratory illness caused by a novel (new) coronavirus first identified in Wuhan, Hubei Province, China. Additional cases have been identified in a growing number of other international locations, including the United States. Most coronaviruses spread the same way other cold-causing viruses do: through infected people coughing and sneezing, by touching an infected person's hands. The clinical signs displayed from infected patients include runny or stuffy nose, coughing, sore throat, and sometimes a fever. There are no vaccines or antiviral drugs that are approved for prevention or treatment. Scientists were able to isolate a strain of the new coronavirus quickly, with the genetic sequence being made available for laboratories across the world to independently develop PCR tests that can confirm infection in a person. It can be investigated mainly by following outbreak investigation steps, health education, restriction of movement around the outbreak zone and contingency preparedness plans. There are ongoing investigations to learn more. Within short period of time following its outbreak, the 2019-nCoV causes high number of people's death and huge international economic loss associated with health, trade and transportation. The aim of this paper is to understand the cause, identify methods for investigating or controlling it and to prevent any future occurrences.

Introduction to coronaviruses

Coronaviruses are a group of viruses that cause diseases in mammals and birds. In humans, the viruses cause respiratory infections which are typically mild including the common cold but other forms like Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and 2019 novel coronaviruses can be lethal. In cows and pigs they may cause diarrhea, while in chickens they can cause an upper respiratory disease [1,2].

Coronaviruses are viruses in the family *Coronaviridae*, subfamily *Orthocoronavirinae*, in the order *Nidovirales*, in the genera include:- *Alphacoronavirus*, *Betacoronavirus*, *Deltacoronavirus* and *Gammacoronavirus*. Coronaviruses are enveloped viruses with a positive-sense single-stranded RNA genome and with a nucleocapsid of helical symmetry. The genomic size of coronaviruses ranges from approximately 26 to 32 kilobases, the largest for an RNA virus. The name "coronavirus" is derived from the Latin *corona*, meaning *crown* or *halo*, which refers to the characteristic appearance of the virus particles (virions): They have a

fringe reminiscent of a royal crown or of the solar corona. Coronaviruses are also named for the crown-like spikes on their surface [3].

Human coronaviruses were first identified in the mid-1960s. The seven Common human coronaviruses that can infect people are 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), HKU1 (beta coronavirus), MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome or MERS), SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome or SARS), and 2019 Novel Coronavirus (2019-nCoV). People around the world commonly get infected with human coronaviruses 229E, NL63, OC43, and HKU1. Sometimes coronaviruses that infect animals can evolve and make people sick and become a new human coronavirus. Three recent examples of this are 2019-nCoV, SARS-CoV, and MERS-CoV [4].

In domestic animals coronavirus infections include: Infectious Bronchitis Virus (IBV) causes avian infectious bronchitis, Porcine coronavirus (Transmissible Gastroenteritis Coronavirus of pigs, TGEV). Bovine Coronavirus (BCV),

responsible for severe profuse enteritis of young calves, Feline Coronavirus (FCoV) causes mild enteritis in cats as well as severe Feline infectious peritonitis (other variants of the same virus), the two types of canine coronavirus (CCoV) (one causing enteritis, the other found in respiratory diseases), Turkey Coronavirus (TCV) causes enteritis in turkeys, Ferret enteric coronavirus causes epizootic catarrhal enteritis in ferrets, Ferret systemic coronavirus causes FIP-like systemic syndrome in ferrets. Pantropic canine coronavirus, Rabbit enteric coronavirus causes acute gastrointestinal disease and diarrhea in young European rabbits. Mortality rates are high [2,5].

A coronavirus is a kind of common virus that causes an infection in the nose, sinuses, or upper throat. Most coronaviruses are not dangerous. Some types of coronaviruses are serious, though. About 858 people have died from Middle East Respiratory Syndrome (MERS), which first appeared in 2012 in Saudi Arabia and then in other countries in the Middle East, Africa, Asia, and Europe. In April 2014, the first American was hospitalized for MERS in Indiana and another case was reported in Florida. Both had just returned from Saudi Arabia. In May 2015, there was an outbreak of MERS in Korea, which was the largest outbreak outside of the Arabian Peninsula. In 2003, 774 people died from a Severe acute Respiratory Syndrome (SARS) outbreak. As of 2015, there were no further reports of cases of SARS [6-8].

But in early 2020, following a December 2019 outbreak in China, the World Health Organization identified a new type, 2019 novel coronavirus (2019-nCoV) [9] (Figures 1-4).

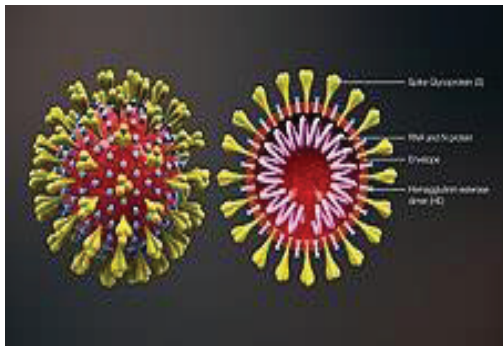


Figure 1: Cross-sectional model of a coronavirus [19].

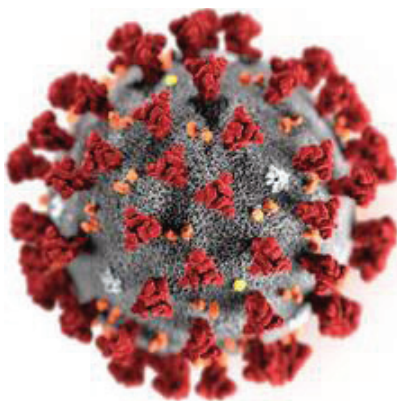


Figure 2: Render of 2019 nCoV virion [19].

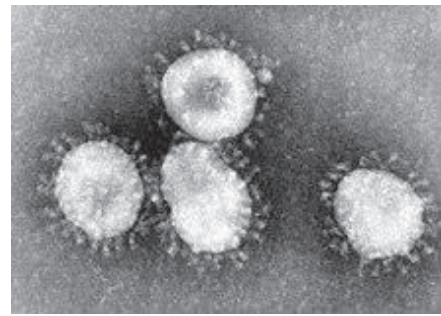


Figure 3: Electron micrograph of Infectious bronchitis virus virions [19].

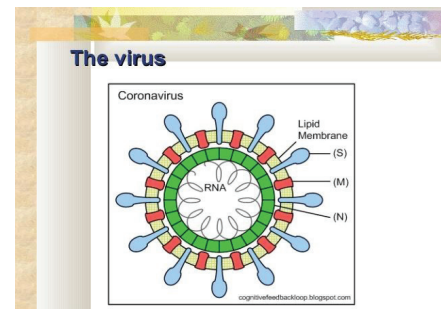


Figure 4: Corona virus [19].

2019 Novel coronavirus infection

In December 31/2019, a pneumonia outbreak was reported in Wuhan, China, the outbreak was traced to a novel strain of coronavirus which was labeled as 2019-nCoV by the World Health Organization [4].

As of 30 January 2020 (16:00 UTC), the number of deaths was 214 and more than 8,230 confirmed cases in this coronavirus pneumonia outbreak. The Wuhan strain has been identified as a new strain of Beta-coronavirus from group 2B with a ~70% genetic similarity to the SARS-CoV. The virus was suspected to have originated in snakes but many leading researchers disagree with this conclusion. Daniel Lucey, an infectious disease specialist at Georgetown University, stated that "Now it seems clear that seafood market is not the only origin of the virus" [4,10].

In other animals, Coronaviruses have been recognized as causing pathological conditions in different domesticated animals since the early 1970s. Except for avian infectious bronchitis, the major related diseases have mainly an intestinal location. Coronaviruses primarily infect the upper respiratory and gastrointestinal tract of mammals and birds. They also cause a range of diseases in farm animals and domesticated pets, some of which can be serious and are a threat to the farming industry. In chickens, the Infectious Bronchitis Virus (IBV), a coronavirus, targets not only the respiratory tract but also the urogenital tract [11].

Economically significant coronaviruses of farm animals include porcine coronavirus (Transmissible Gastroenteritis Coronavirus, TGE) and bovine coronavirus, which both result in diarrhea in young animals. Feline coronavirus

causes enteric infection and infectious peritonitis. Mouse hepatitis virus (MHV) is a coronavirus that causes an epidemic murine illness with high mortality, especially among colonies of laboratory mice. Sialodacryoadenitis virus (SDAV) is highly infectious coronavirus of laboratory rats, which can be transmitted between individuals by direct contact and indirectly by aerosol. Acute infections have high morbidity and tropism for the salivary, lachrymal and hardarian glands. A HKU2-related bat coronavirus called swine acute diarrhoea syndrome coronavirus (SADS-CoV) causes diarrhoea in pigs [12].

Significant research efforts have been focused on elucidating the viral pathogenesis of these animal coronaviruses, especially by virologists interested in veterinary and zoonotic diseases [13].

Chinese scientists were able to isolate a strain of the new coronavirus quickly, with the genetic sequence being made available for laboratories across the world to independently develop PCR tests that can confirm infection in a person. Of the first 41 people confirmed by real-time PCR and next-generation sequencing to have been infected, two-thirds were found to have a link with the Huanan Seafood Wholesale Market, which also sold live animals. The seventh member of the coronavirus family to infect humans, 2019-nCoV's genome sequence has been reported to be 75- to 80-percent identical to SARS-CoV, and more than 85-percent similar to several bat coronaviruses. Whether this virus is of the same severity or lethality as SARS is unclear [12].

Routes of transmission

Most coronaviruses spread the same way as other cold-causing viruses do: through infected people coughing and sneezing, by touching an infected person's hands or face, or by touching things such as doorknobs that infected people have touched. Human coronaviruses most commonly spread from an infected person to others through: Respiratory droplets released into the air by coughing and sneezing; Close personal contact, such as touching or shaking hands; Touching an object or surface with the virus on it, then touching your mouth, nose, or eyes before washing your hands; and Rarely, fecal contamination [14].

When person-to-person spread has occurred with 2019 Novel coronavirus, MERS and SARS, it is thought to have happened mainly via respiratory droplets produced when an infected person coughs or sneezes, similar to how influenza and other respiratory pathogens spread. Spread of SARS and MERS between people has generally occurred between close contacts [4].

Clinical symptoms

The symptoms of most coronaviruses are similar to any other upper respiratory infection, including runny or stuffy nose, coughing, sore throat, and sometimes a fever. In most cases, people won't know whether they have a coronavirus or a different cold-causing virus, such as rhinovirus. According to different reports, patients present with: fever, elevated body

temperature, dry cough, fatigue or muscle pain, breathing difficulties. Less common symptoms of coronavirus include: coughing up mucus or blood, headaches, diarrhoea but as the disease progresses, patients also come down with pneumonia, which inflames the lungs and causes them to fill with fluid. This can be detected by an X-ray and was present in all 41 cases studied [13,15].

Investigation of novel coronavirus (2019-ncov) outbreak

In epidemiology, an outbreak is a sudden increase in occurrences of a disease in a particular time and place. It may affect a small and localized group or impact upon thousands of animal and/or people across an entire continent. Four linked cases of a rare infectious disease may be sufficient to constitute an outbreak. Outbreaks include epidemics, which term is normally only used for infectious diseases, as well as diseases with an environmental origin, such as a water or foodborne disease. They may affect a region in a country or a group of countries. Pandemics are near-global disease outbreaks. Outbreak legislation is still in its infancy and not many countries have had a direct and complete set of the provisions. However, some countries do manage the outbreaks using relevant acts, such as public health law [16]. Generally the new 2019 novel coronavirus outbreak in many countries especially in China can be investigated by the following steps.

Prepare for field work

Team coordinates field investigation of Epidemiologist, Clinician Microbiologist, Environmentalist, Government, Press officer and others involved in the identification and investigation of the disease, The largest known outbreak of 2019 novel corona virus outbreak occurred in 2019 in wuhan province, china. Most of these infections occurred among people exposed to infected seafood's, live animal markets and expected from snakes at agricultural fairs. These infections spread from one person to another through respiratory droplets released into the air by coughing and sneezing, lose personal contact, such as touching or shaking hands can also transmit the virus to healthy one [9].

Confirm outbreak and diagnosis

This can be done by careful correlation of clinical manifestation of the disease with laboratory finding results and epidemiological, host and environmental risk factors, so in our world especially middle east (China) in January 2020, the 2019 novel coronavirus outbreak manifests clinical symptoms of fever, runny or stuffy nose, coughing, sore throat and leading to pneumonia. Depending on Team coordinates field investigation of Epidemiologist, Clinician Microbiologist, Environmentalist, clinical and laboratory findings for all patients whose specimens on initial or subsequent testing by any method had evidence of 2019-nCoV. Residents in Wuhan province in China and other countries in whom 2019-nCoV was potentially indicated by initial nucleic acid or serological and rt-PCR tests expressed a range of symptoms, from mild disease through to lobar pneumonia, which were consistent with the known profile of 2019-nCoV [4,14].

Define/determine the magnitude of the problem

In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. Depending on the epidemiological, clinical, Radiological and laboratory characteristics, the outbreak is of 2019-nCoV pneumonia. Most patients have mild symptoms and good prognosis. So far, a few patients with 2019-nCoV have developed severe pneumonia, pulmonary oedema, Acute Respiratory Disease Syndrome (ARDS), or multiple organ failure and have died [17].

At present, information regarding the epidemiology and clinical features of pneumonia caused by 2019-nCoV; coronavirus disease updated to in China 7700, Singapore 13, Thailand 14, Australia 8, Taiwan 8, Japan 11, Malaysia 8, US 5, South Korea 6, Germany 5, Vietnam 5, France 5, UAE 4, Canada 2, Nepal, India, Finland, Philippines, Cambodia and Srilanka each have 1 cases and around 320 deaths in the world. These and other countries have high number of confirmed (14570 patients) and suspected cases that indicate the current devastating and severe magnitude of the diseases [18]. Samples are collected and transported to well organized and specialized hospitals to be tested for identification and confirmation of the 2019 novel coronavirus infection for sensitivity and specificity from different counties where their population is suffering from the infection.

Descriptive data collection and analysis

The 2019 novel coronavirus outbreak occurred firstly in Wuhan province, China which has a fluctuating agro ecological climatic condition and high population density. The data collection for identification, confirmation and investigation of the 2019 nCoV, is based on temporal and special epidemiological and clinical considerations as follow; any person with travel-history to Wuhan city, China in the 14 days before the onset of illness (or) any person being in close contact with a laboratory-confirmed case of 2019-nCoV in the 14 days before the onset of illness and any person with clinical symptoms compatible with severe acute respiratory infection seeking healthcare or admitted to hospital with clinical or radiological evidence of pneumonia (or) any person with fever or recent history of fever ($>38^{\circ}\text{C}$) and acute respiratory infection (sudden onset of respiratory infection with one or more of the following symptoms: shortness of breath, cough or sore throat) [19].

Hypothesis generation

The 2019 novel coronavirus infection outbreak affects both animals and humans but it severely affects human and the symptoms manifested by infected individual slightly varies between person to person but it becomes more severe in the people with weak immunity, elder or of young age. The disease occurs in the areas where population density is very high in whole selling markets of live animal, seafood and transportation areas. Its incubation period is between 2 to 14 days, but there is evidence that it may still be contagious during this period and possibly for several days after recovery. Symptoms include fever, coughing and breathing difficulties, and it can be fatal [20].

Most often, spread from person-to-person happens among close contacts (about 6 feet). Person-to-person spread is thought to occur mainly via respiratory droplets produced when an infected person coughs or sneezes, similar to how influenza and other respiratory pathogens spread. These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. It's currently unclear if a person can get 2019-nCoV by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes [21].

Analytical and environmental studies to test hypotheses

As the patients with suspicion, probable and confirmed cases are studied retrospectively in the areas where disease causing vehicles are found, the attacking rate of the disease progresses in accelerating rates. The disease epidemic distributes too many countries (28 countries) causing the world suffering from becoming a pandemic outbreak. Locations with Confirmed 2019-nCoV Cases; China, Hong Kong, Macau, Taiwan, Australia, Cambodia, Canada, Finland, France, Germany, India, Italy, Japan, Spain, Malaysia, Nepal, Philippines, Russia, Sri Lanka, Singapore, Spain, Sweden, Thailand, The Republic of Korea, United Arab Emirates, United Kingdom, United States, Vietnam [22] (Figure 5).

Control measures and recommendations

Public Health Measures: Once the outbreak was reported, routine coronavirus-control measures were instituted. After findings suggesting possible involvement of SARS-CoV were reported, these measures were enhanced, and flu and SARS-type respiratory and contact precautions were exercised around symptomatic cases [13].

The best way to prevent infection is to take precautions to avoid exposure to this virus, which are similar to the precautions you take to avoid the flu. Center for communicable disease control always recommends these everyday actions to help prevent the spread of respiratory viruses, including: Wash your hands often with soap and water for at least 20 seconds, if soap and water are not available, use an alcohol-based hand sanitizer, avoid touching your eyes, nose, and mouth with unwashed hands, avoid close contact with people who are sick, stay home when you are sick, Cover your cough or sneeze with a tissue, then throw the tissue in the trash, clean and disinfect frequently touched objects and surfaces [20].

Use Personal Protective Equipment/PPE: For appropriate use of personal protective equipment, employers should select appropriate PPE and provide it to HCP in accordance with personal protective equipment standards (29 CFR 1910 Subpart I) external icon. Any reusable PPE must be properly cleaned, decontaminated, and maintained after and between uses. Facilities should have policies and procedures describing a recommended sequence for safely donning and doffing PPE. The most important PPE that are used to prevent from 2019 novel coronavirus infection and others are included as follow; gloves, gowns, respiratory, eye Protection, use caution when performing aerosol-generating procedures [20].

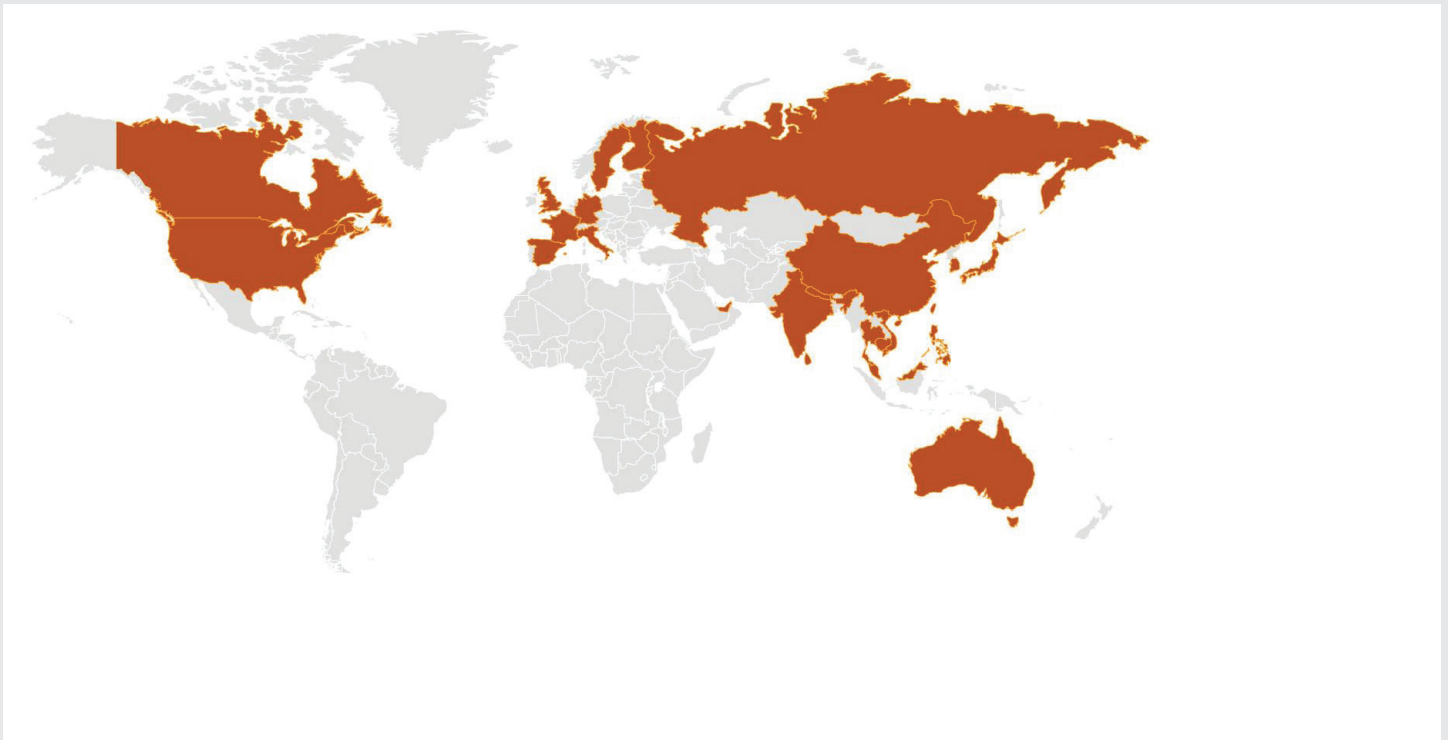


Figure 4: Corona virus [19].

Immediate Provision of Information: Appropriate, recent and valid information must be given to different population groups who are necessarily going to be exposed and infected by the disease associated with 2019 novel coronavirus. Information about the route of transmission, clinical symptoms, severity and control and prevention methods of the disease for the public, travelers, healthcare professionals, laboratories, public health, news media and others related with animal origin transmission. Currently the CDC has issued a Warning Level 3, Avoid Nonessential Travel to Wuhan, China [11].

Quarantine Measures: On January 2020 following this outbreak, a quarantine on travel in and out of Wuhan was imposed in an effort to stop the spread of the virus out of Wuhan. Flights and trains in and out of Wuhan, public buses, the metro system and long-distances coaches were suspended until further notice. Large-scale gatherings and group tours were also suspended. By 24 January 2020, a total of 15 cities in the Hubei province, including Wuhan, were placed under similar quarantine measures. Thus, the entire Hubei province came under quarantine, save for Xiangyang and the Shennongjia Forestry District [6].

Due to quarantine measures, Wuhan residents rushed to stockpile essential goods, food, and fuel. The prices of goods rose significantly. Medical staff faced difficulties in commuting to their hospitals, as they were now limited to walking and private cars. Taxis and private-hire vehicles shunned them upon learning of the destination. 5,000,000 people left Wuhan, with 9,000,000 left in the city [23].

2019-nCoV does not have any effective medications or vaccines, though development efforts are underway. It is however possible to attempt to relieve the symptoms of the coronavirus,

which include taking regular (over-the-counter) flu medications, drinking fluids and resting. Oxygen therapy, intravenous fluids, and breathing support may be required. Some countries require people to report flu-like symptoms to their doctor, especially if they have visited Mainland China [20].

Contingency plan and preparedness

Management and vaccination

The main treatment strategy for typical coronavirus infection is supportive therapy, including administration of antipyretics and analgesics, maintenance of hydration, respiratory support by either mechanical ventilation or extracorporeal Membrane Oxygenation (ECMO), and treatment with antibiotics in the case of bacterial super infections. However, such treatments may not be sufficient for 2019-nCoV and MERS-CoV infections, which may be more severe. Ribavirin and interferon alpha have been shown to have synergistic effects and are more beneficial when started early. Additionally, mycophenolic acid has been shown to be efficacious and can be used as a mono therapy; however, initial clinical trials included few patients, and further studies are necessary. There is currently no vaccine to prevent 2019-nCoV infection. In January 2020, several organizations and institutions began work on creating vaccines for 2019 n-CoV based on the published genome. Although several companies are attempting to develop 2019-nCoV SARS-CoV and MERS-CoV vaccines, none are available yet. Improving our understanding of viral antibodies will facilitate the design of appropriate and efficacious vaccines [11].

Protection and surveillance zones

The geographical delimitation of those two zones must take into account; the administrative borders and natural barriers,



where will be taken the surveillance and control measures that can stop animal disease virus spreading. Protection zone will have a radius of a minimum 3 kilometers, having the center into outbreak, and the surveillance zone will have a radius of a minimum 10 kilometers, having the same center. These two zones will be at least of 3 and 10. kilometers, but they might be enlarged, not necessary as a circle, but as any other geometrical form, varying with natural barriers and the administrative border [9,24].

Developed interim guidance for laboratory diagnosis, clinical management, infection prevention and control in health care settings, home care for patients with suspected novel corona virus, risk communication and community engagement. Prepared disease commodity package for supplies necessary in identification and management of confirmed patients; Provided recommendations to reduce risk of transmission from animals to humans; Providing guidance on early investigations, The first protocol that is available is; a household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection [4,25].

Coronavirus in Ethiopia

January 28/2020 in the wake of the coronavirus outbreak currently enduring in Wuhan China, Ethiopia isolated four suspected cases in isolation that arrived at the Bole Airport from China. Samples were taken from these four suspected cases in isolation and medical samples were sent to South Africa for further test. Coronavirus has been detected in Ethiopia yet. However, all the samples were tested and the preliminary results showed negative with no positive case of the virus so far. Ethiopia still has no coronavirus positive case, she noted adding that the country will step up its surveillance and testing facilities to ensure that it can manage to provide immediate health care response [20,21]

Ethiopia has heightened preparedness to prevent the entry and spread of the coronavirus to the country. The State Minister underscored that adequate preparations are in place, particularly at the Bole International Airport for thermal screening, preliminary surveillance, and testing of arrivals from China and its neighboring countries. The Ethiopian Public Health Institute (EPHI) leads and coordinates national preparedness activities through a national Technical Working Group (TWG). The TWG, which meets several times a week to devise plans, monitor progress, develop guidelines and standard operating procedures, oversee logistics and strengthen surveillance at the Addis Ababa Bole International Airport [9,16].

Conclusion and recommendations

The outbreak of coronavirus that began in China and spread across the world, leaving more than around five hundred (493 deaths) people dead and 24623 confirmed cases until February 5/ 2020, has raised alarm about the ability of countries to handle an epidemic or pandemic. The recent Global Health Security Index gives insights into which of 195 nations including Ethiopia are ready to fight a major health emergency that could wreak havoc on the global economy. For that great

social, public health and economic impact of the current 2019 novel corona virus outbreak prevention, the following recommendations are forwarded;

- Advice for entry screening in countries/ areas without transmission of the novel coronavirus 2019-nCoV;
- Limit human to human transmission including, reducing secondary infections among close contacts and health care workers, preventing transmission amplification events, and preventing further international spread from China;
- Identify and reduce transmission from the animal source by proper provision of health education;
- Address crucial unknowns and about clinical severity, extent of transmission and infection, treatment options, and accelerate the development of diagnostics, therapeutics and vaccines;
- Communicate critical risk and event information to all communities and counter misinformation;
- Minimize social and economic impact through multi sectorial partnerships;
- Prevention of the emergence or release of pathogens;
- Early detection and reporting for epidemics of potential international concern;
- Rapid response to and mitigation of the spread of an epidemic;
- Sufficient and robust health system to treat the sick and protect health workers;
- Proper collection, submission and laboratory analysis of probable and suspected cases by using current and updated serological and molecular investigation techniques.

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