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2019 Novel Coronavirus: A mysterious threat from Wuhan, China-A current review

Ramalingam Kothai, Balasubramanian Arul*

Department of Pharmacy Practice, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem – 636008, Tamil Nadu, India

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ABSTRACT

Coronaviruses (CoV) are a huge family of viruses and they cause various diseases from the common cold to very serious illnesses. They also just like the Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). But novel coronavirus (nCoV) is a different strain and newly discovered in humans. Several known coronaviruses circulate in animals not yet infected by humans. It is also a zoonotic virus, which means that they are spread between animals and then to humans. Comprehensive studies showed that SARS-CoV was transmitted to humans by civet cats and MERS-CoV by dromedary camels. Respiratory symptoms, fever, cough, shortness of breath and difficulty in breathing are common signs of infection. It was started from Huanan wholesale seafood market with the admission of 2-3 patients and now crossed 37251 cases with 812 deaths as on 9th February. In some of the days, the number of new admissions was more than 3000 cases continuously. This review summarises the types, morphology, origin, transmission, symptoms, diagnostic methods, Chinese, global and Indian scenario of this novel deadly virus. The world health organization advises for the public about the avoiding of the spread of the virus, general recommendations for individuals and for the risk groups also reviewed.



*Corresponding Author

Name: Balasubramanian Arul
Phone: +91-9944117022
Email: arul1971@yahoo.com

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microscopy, it reveals the presence of Virions (the virus infectious form), which have a wide fringe, reminiscent of either royal crown or a solar corona.

Prior to the 2003 SARS outbreak, only 19 coronaviruses were identified, which includes 2 humans, 4 avian, and 13 mammalian coronaviruses. More than 20 additional novel coronaviruses with full genome sequences have been identified after the SARS epidemic (Lau *et al.*, 2011) and as on date, 7 human coronaviruses were identified including the recent 2019 novel coronavirus.

Among mammals and birds, the coronaviruses cause disease. In humans, the viruses usually cause mild respiratory infections, including common cold; however, rarer types such as SARS, MERS and novel coronavirus can be fatal, causing the current outbreak. They may cause diarrhea in cows and pigs, while they may cause an upper respiratory disease in chickens. No vaccines or antiviral drugs are approved for the prevention or treatment of this

INTRODUCTION

Coronaviruses are a cluster of viruses that belongs to the family Coronaviridae and subfamily Orthocoronavirinae, order Nidovirales (Groot *et al.*, 2011). The name "coronavirus" is derived from the Latin word Corona and the Greek word *korónē*, which means crown. While observing under electron

2019 novel coronavirus.

Human Coronavirus Types

Coronaviruses are classified into four types such as alpha, beta, gamma, and delta coronaviruses. The first human coronavirus was identified in 1960 and to date, there are seven human coronaviruses were identified.

1. 229E (alpha coronavirus)
2. NL63 (alpha coronavirus)
3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)
5. MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
6. SARS-CoV (the beta coronavirus that causes Severe acute respiratory syndrome, or SARS)
7. 2019 Novel Coronavirus (2019-nCoV)

Human coronaviruses 229E, NL63, OC43, and HKU1 were generally infected in people worldwide. Human coronavirus 229E (HCoV-229E) is one of the first reported coronavirus variants. It is related to common symptoms of cold in healthy adults (Vassilara *et al.*, 2018). Younger children and elderly people are considered vulnerable to lower respiratory tract infections (LRTIs). Such viruses account for 4 to 15 % of acute respiratory disease in adults every year and up to 35 % at peak periods. Children's average infection rates touch 8%, with peak rates of up to 20% (Lee *et al.*, 2016).

A new human coronavirus (HCoV-NL63) was isolated from a seven-month-old infant with respiratory symptoms in Holland in 2004. Subsequently, this virus was found in various countries, suggesting a spread worldwide. HCoV-NL63 is primarily infected children and those immunocompromised with either moderate upper respiratory symptoms such as cough, fever, and rhinorrhoea or severe LRTI, such as bronchiolitis and croup, perceived primarily in younger children (Abdul-Rasool and Fielding, 2010). It is estimated that 1-10% of the population is affected annually by cold-like symptoms of HCoV-NL63 (Szelazek *et al.*, 2017).

While it was thought that human coronavirus OC43 (HCoV-OC43) accounts for 5 to 30 % of human respiratory tract infections (Lau *et al.*, 2011). Both HCoV-229E and HCoV-OC43 cause LRTI and otitis media. Even though the virus-infected patient's stool containing particles like coronavirus, no evidence was observed that both the viruses may cause enteric disease in humans (Burrell *et al.*, 2017).

The first group A human β -CoV HKU1 virus, was discovered in 2004 at Hong Kong and was later found worldwide in humans. Just like other human coronaviruses, this new coronavirus HCoV-HKU1 is also causing 0.9% of LRTI and URTI. (Woo *et al.*, 2009). HCoV-HKU1-related respiratory tract infections are identical to other respiratory viruses. Mostly the URTI patients reported with fever, running nose and cough; while LRTI patients come with fever, productive cough, and dyspnea like symptoms.

Usually, children under the age of 6 are estimated for exposure to HKU1 (Zhou *et al.*, 2013). Generally, HKU1 infections cause mild URTI and some cases it cause severe respiratory infections, including pneumonia in paediatric, geriatric, and patients with immunocompromise (Gralinski and Baric, 2015).

Coronaviruses are usually infecting animals and sometimes it can develop as a new human coronavirus and make people sick. The 2019-nCoV, SARS-CoV, and MERS-CoV are three recent examples of that.

SARS-CoV

Severe acute respiratory syndrome coronavirus (SARS-CoV) was first identified in November 2002. SARS-CoV is believed to be an animal virus which often transmitted to other species (civet cats) and first affected individuals in southern China's Guangdong province in 2002 from an unknown source of animals, possibly bats. In 2002-2003 it triggered a worldwide epidemic of 8,098 suspected cases and 774 deaths. No confirmed incidents of SARS-CoV infection have been recorded in any part of the world since 2004.

SARS-CoV is primarily transmitted from one human to another. This seems to have happened mostly during the second week of sickness, which correlates to the peak in respiratory secretions of virus excretion. Many cases of transmission from human-human happened in the health care environment, in the absence of sufficient measures to prevent infection. Implementation of appropriate practices to control infection brought an end to the global outbreak.

Symptoms of SARS CoV include mainly fever but severe cases often grow quickly, leading to respiratory failure and requiring intensive treatment.

MERS-CoV

The first case of the Middle East respiratory syndrome Coronavirus (MERS-CoV) case was identified at Saudi Arabia in 2012. A total of 2499 laboratory-confirmed cases of MERS-CoV were reported globally at the end of December 2019, including 861 related deaths (case -fatality rate: 34.4%). Most

of the cases have been reported from Saudi Arabia (783 deaths in 2106 cases, with a 37.2 % fatality rate).

2019 Novel Coronavirus (2019-nCoV)

The World Health Organization declared on January 9, 2020, that Chinese authorities have identified a novel coronavirus. The virus is related to a pneumonia outbreak in Wuhan City, Hubei Province, China. 2019-nCoV is the 7th member of the coronavirus family and like MERS-CoV and SARS-CoV, it also infects humans.

First Case

Three adult patients had serious pneumonia and were admitted to a Wuhan hospital. The first patient (M, 61Yrs) was reported with fever and cough on December 20, 2019. He related to a wholesale seafood market as a regular visitor. His condition became worsened and mechanical ventilation was given. The second patient (F, 49 Yrs) was admitted on 23 December 2019 for fever with the temp of 37-38°C, cough and chest discomfort. She owns a retail shop in the seafood wholesale market. Her fever was reduced after four days but the cough and chest discomfort became worsened. Pneumonia was diagnosed based on CT scan. The third patient (M, 32) admitted on 27 December, but his clinical data was not available. The first patient died on 9th January and biopsy specimen was obtained (Zhu *et al.*, 2019). The remaining two patients were discharged from hospital on 16th January 2020.

Origin

How 2019-nCoV came to Wuhan is currently unknown, but 66% of the initially infected patients (27/41) were directly exposed to the Huanan seafood market (Huang *et al.*, 2020).

Morphology

This morphology is formed by peplomers with a viral spike (S), proteins that populate the virus surface and determine host tropism. The spike (S), envelope (E), membrane (M), and nucleocapsid (N) are proteins that contribute to the overall structure of all coronaviruses. The defined receptor binding (RBD) structure suggests ways to create truncated, disulfide-stabilized variants of RBD for use in coronavirus vaccine design (Li, 2005). Some β -coronaviruses also have a shorter spike-like protein (Groot *et al.*, 2011).

Electron micrographs of the negative-stained 2019-nCoV particles were spherical in shape with a diameter of 60 to 140 nm and quite distinctive spikes of 9-12 nm, also present which gave the solar corona appearance to the virions. This observed morphol-

ogy is consistent with the family Coronaviridae (Zhu *et al.*, 2019).

Transmission

2019-nCoV also a zoonotic coronavirus, meaning it is transmitted from animals to humans. Bats may be the likely source for 2019-nCoV, based on samples collected from early admitted patients with pneumonia, an identity of 85 % with SARS-like coronavirus bat genome (bat-SL-CoVZC45, MG772933.1) (Ji, 2020). The 2019-nCoV clade lies within the subgenus Sarbecovirus, subfamily Orthocoronavirinae (Zhu *et al.*, 2019). The infection of Shenzhen-based family, after visiting infected family members in Wuhan, confirmed human-to-human transmission of 2019-nCoV (Chan *et al.*, 2020).

Dr. Li Wenliang, the health care professional who warned first about the new virus also died on 6th February due to the infection. He is an ophthalmologist and he was infected with this virus while treating a glaucoma patient without knowing that she was infected with 2019-nCoV. His family also infected with this virus and admitted to the hospital.

The new coronavirus is a respiratory virus that spreads primarily through contact with an infected person through respiratory droplets when the affected individual coughs or sneezes, or through saliva droplets or nose discharge. Everyone should practice good respiratory hygiene like sneeze or cough into a flexed elbow or use a tissue and immediately discharge it into a closed bin. It is also very important for people to regularly wash their hands with either alcohol-based hand rub or soap and water.

Symptoms

The common 2019-nCoV symptoms include acute respiratory disease syndrome, including shortness of breath, fever, cough, weakness, and diarrhea. For some people, it may be more severe and may lead to pneumonia or difficulty in breathing. More rarely, the disease can be fatal. Older people and people with pre-existing medical conditions (such as diabetes and heart disease) seem more vulnerable to the virus and became seriously ill.

Diagnostic methods

A real-time reverse transcription PCR (RT-PCR) assay was used to detect viral RNA by targeting a consensus RdRp region of pan β -CoV. Virus isolation from the clinical specimens was performed with human airway epithelial cells and Vero E6 and Huh-7 cell lines.

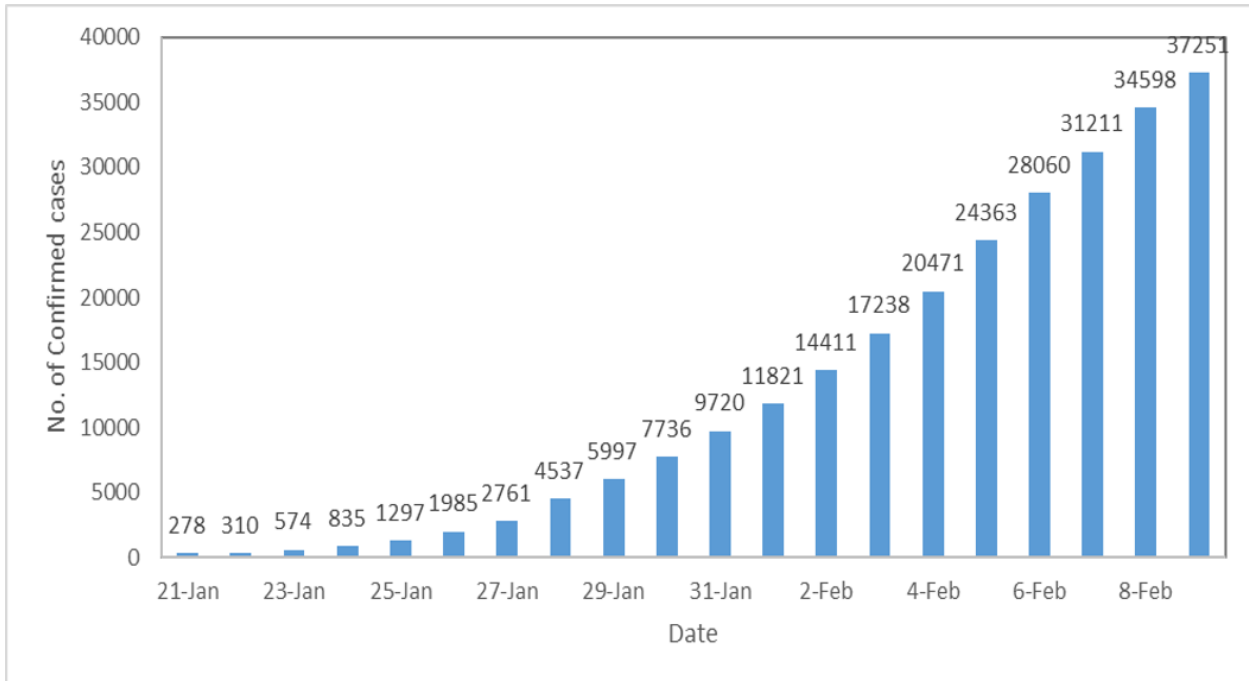


Figure 1: No of confirmed cases of 2019-nCoV infections in China* (*Information reported to WHO Geneva by 10 AM CET on every day)

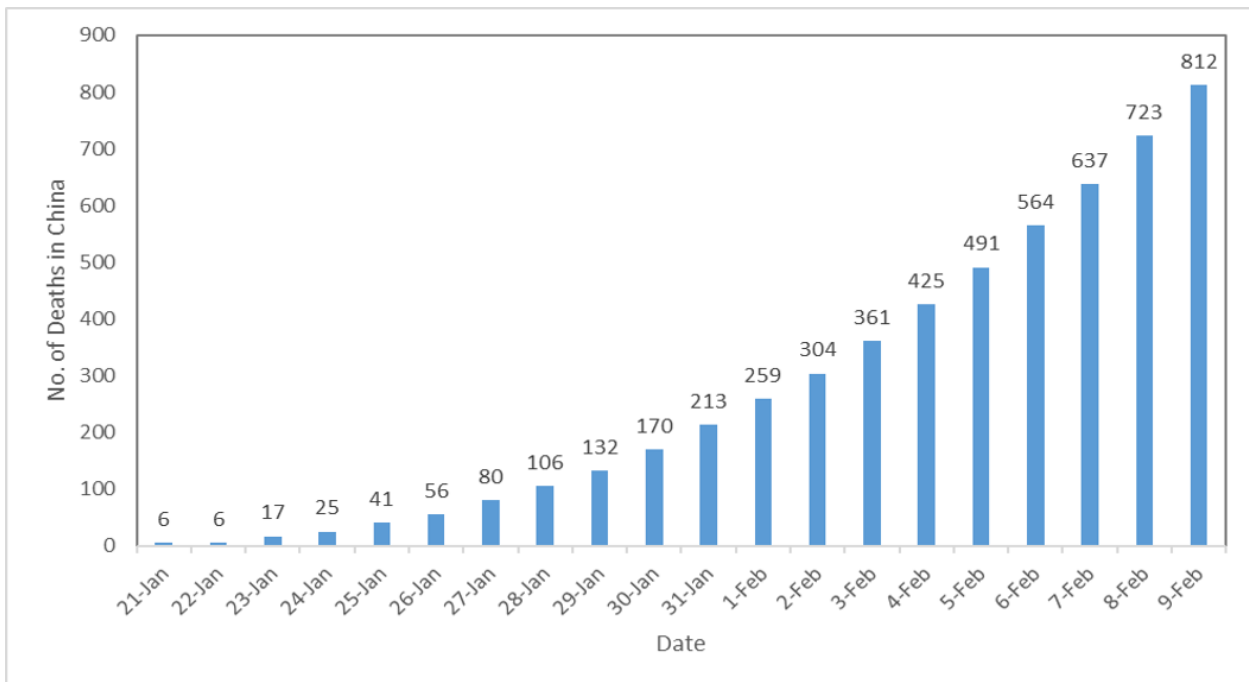


Figure 2: No of deaths due to 2019-nCoV infections in China* (*Information reported to WHO Geneva by 10 AM CET on every day)

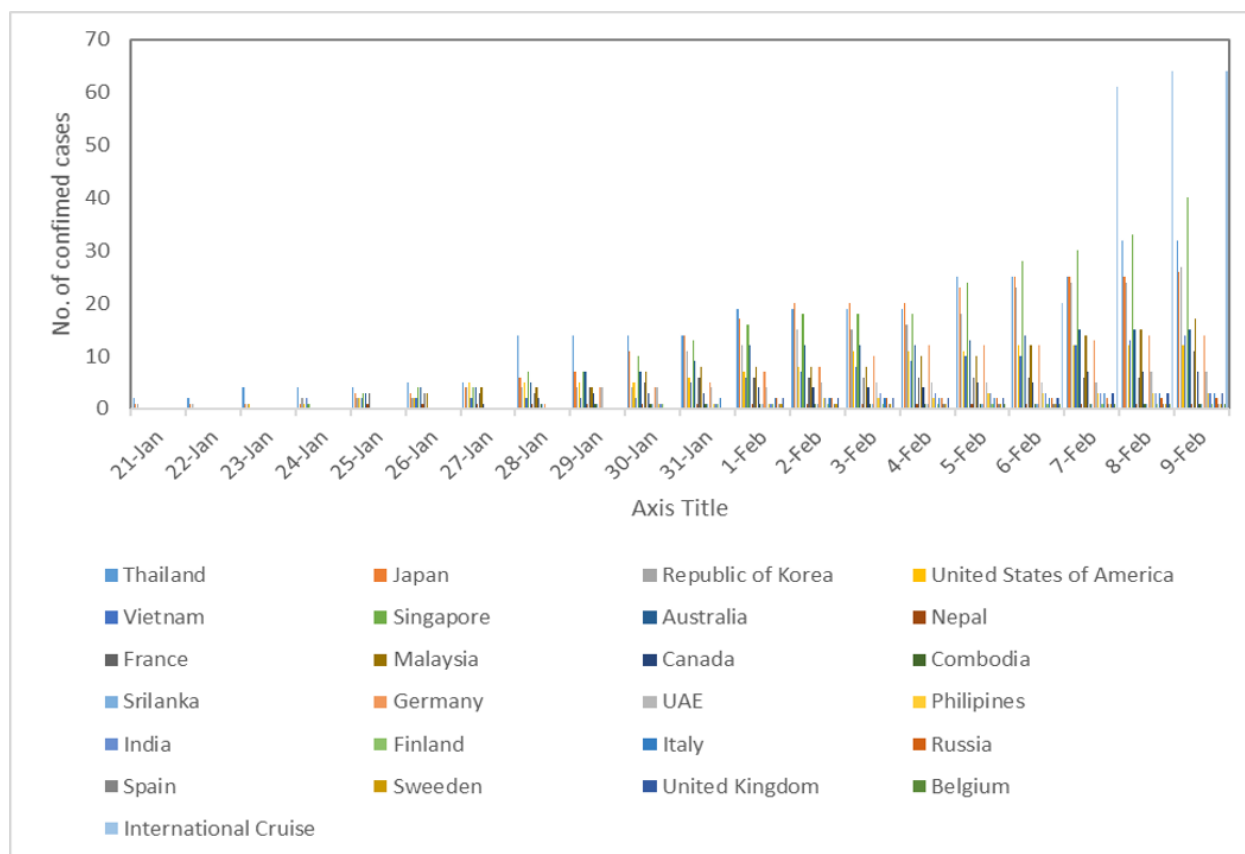


Figure 3: No of confirmed cases of 2019-nCoV infections in outside of China* (*Information reported to WHO Geneva by 10 AM CET on every day)

Currently, WHO authorized 15 laboratories to provide reference testing support for 2019-nCoV. These laboratories include,

1. Armed Forces Research Institute of Medical Sciences, Thailand
2. Erasmus Medical Center, The Netherlands
3. Hong Kong University, Hong Kong SAR, China
4. Institute of Tropical Medicine, Nagasaki University, Japan
5. Institute of Virology, Charité, Robert Koch Institute, Germany
6. National Institute for Communicable Diseases, South Africa
7. National Institute of Health, Thailand
8. National Institute of Virology, India
9. National Public Health Laboratory, Singapore
10. Institut Pasteur Dakar, Senegal
11. Institut Pasteur, Paris
12. Public Health England, UK

13. State Research Center for Virology and Biotechnology, Vector Institute, Russia
14. United States Center for Disease Control and Prevention, USA
15. Victorian Infectious Diseases Reference Laboratory, Australia

Laboratory and Radiographic Findings

Among hospitalized patients with pneumonia on admission, the most common laboratory abnormalities included leukopenia (9–25%), leukocytosis (24–30%), lymphopenia (63%), and elevated levels of alanine aminotransferase, and aspartate aminotransferase (37%). On admission, most patients had normal serum procalcitonin levels and chest CT images showed a bilateral presence. Typical findings identified to date are the various areas of consolidation and ground-glass opacities.

2019-nCoV RNA was found in upper and lower respiratory tract specimens and was isolated from bronchoalveolar lavage fluid. The shedding duration of 2019-nCoV RNA in the upper and lower respiratory tracts is not yet known but may be several weeks or longer, as was observed in MERS-CoV or SARS-CoV infections.

Clinical Management and Treatment

Currently, there are no specific treatments available for the 2019-nCoV infection. Clinical management requires the timely implementation of prescribed interventions for infection, prevention and control, and supportive management for the complications including advanced organ support if indicated.

Care for Patient

Health care personnel should take care of the patients and they should be kept in an Airborne Infection Isolation Room (AIIM). When caring for the patient, standard precautions, contact precautions, and airborne precautions and eye protection should be used.

Chinese Scenario

Three adult patients with worsened pneumonia were admitted to a Wuhan hospital, China, on 27th Dec 2019. In this, two of them came earlier on 20th and 23rd Dec for cough and fever. Then on Dec 30th cluster of pneumonia patients in Wuhan City, Hubei Province of China, was reported and it alerts WHO on 31st Dec. The causes of pneumonia were unknown and most of them related to the Huanan seafood wholesale market. The Govt closed the market on New year and one week later, on 7 January 2020, Chinese authorities confirmed that they had identified a novel (new) coronavirus as the cause of pneumonia. On January 20th, the No. of cases reported with 2019-nCoV was 278 with 6 deaths and health care workers who are taking care of this 2019-nCoV patients also affected with this virus and the first case was reported. Day by day the no of cases was increased drastically. Within the next five days, the No. of cases was increased to 1297 and 41 deaths. On January month-end, the no. of confirmed cases was increased in 9720, with 213 deaths. 1st February, it crossed 11820 and on the 4th of February, it crossed 20470. Then from the 1st February, onwards the No. of newly admitted cases were increased to approximately 3000 per day. As of 5th February, the total No. of cases crossed 24500 and 8th February. It crossed 34500. Within that just four days 10044 new cases were reported to the hospital. It seems the severity of the spreading of the virus. On 9th February, the total no. of cases reported in China was 37251 with 812 deaths. Most of the patients from Hubei Province (27100 confirmed cases 2019-nCoV) followed by Guangdong (1120), Zhejiang (1075) and Henan (1033). The drastic growth rate of 2019-nCoV confirmed cases and death was graphically shown in Figure 1 and Figure 2. (WHO.(a), 2020).

Global Scenario (Excluding China)

The first case of 2019-nCoV was reported outside China was from Thailand on 13th January 2020, followed by Japan on 16th January and South Korea on 19th January 2020. All these three cases were exported from Wuhan city, China. Up to January 20, 2020, only four cases were found outside of China, ie. Thailand (2), Japan (1) and the Republic of Korea (1) and they were exported from Wuhan City, China. The next day one more case was found in the United States of America. On 24th January 2020, Eleven cases were confirmed in six countries outside of China, which includes Singapore and Vietnam, and out of eleven cases, 10 had a history of travel to Wuhan city. The remaining case is not traveled to China but he was the family member of another confirmed case, who had visited the Wuhan. It confirmed the human-human transmission of the virus. On 25th January 2020, another twelve new cases were reported from the existing six countries along with another 3 new countries Australia, Nepal, and France. In a total of 23 confirmed cases, 21 cases had a history of travel to Wuhan city. On the next day, the confirmed cases increased to 29 with the inclusion of Malaysia. 27th January one case from Canada and 28th January it increased to 2 and each one case from Cambodia, Sri Lanka, and Germany were reported. On 29.01.2020 the United Arab Emirates announced four cases were confirmed with 2019-nCoV, and all are traveling from Wuhan City. The next day Finland, India, and the Philippines were announced each one confirmed case and all 3 cases are having travel history of Wuhan. 31st January 2020, 2 new cases were reported by Italy and both the cases were traveled to Wuhan. Now the total no. of confirmed cases was increased to 106 from 19 countries. At that time China had 9720 confirmed cases with 213 deaths.

February 1st, 6 cases were reported from four more countries, Russian Federation (2), Sweden (1), Spain (1), and the United Kingdom (2). But for the first time outside China, the healthcare worker was infected with this virus and fall on ill in France. He treated the two patients in earlier stages and later, they become probable cases. The third-generation transmission of human-human also observed the first time outside China. A new case was identified in Germany who is exposed to a confirmed case. Then a patient identified in South Korea confirmed the export of the case from a country other than China. He had exposure to a case in Japan and then he traveled to South Korea and become confirmed case there. In Japan, also a similar type of another country human to human transmissions were reported for a tourist guide, who guided the tourists of Wuhan and all these confirmed the virus make human to human transmission in other countries. A taxi driver

from Thailand also reported on that day but he was never traveled to any part of China.

In the next 3 days, there were no newer countries with confirmed cases, but the first death of confirmed cases outside China was reported on 2nd February 2020 in the Philippines, who had close contact with the first confirmed patient of the Philippines. On 5th February 2020, Belgium confirmed the first case of 2019-nCoV. The next four days no more countries were added to the list but 106 new cases were reported in the existing 24 countries and Cruise Ship Diamond Princes. That cruise ship was now harboured at the Yokohama port of Japan. It was found that the crew and passengers of Diamond princes ship also infected with 2019-nCoV on 6th February (20 Passengers). The next day it was increased to 61 and then 64 passengers. All the infected passengers were admitted to the hospitals of the Yokohama area and the remaining crew and passengers are advised for a quarantine period of 14 days in their cabins. So as on 9th February, there are 307 confirmed cases with one death in all 24 affected countries and one cruise ship WHO.(a) (2020). No of total infected patients in all the 24 Countries were shown in Figure 3.

Indian Scenario

Approximately fifty thousand Indians are living in China and most of them are students studying medicine there. Once the problem aroused Govt of India planned to evacuate the Indians stuck on the Wuhan. On January 30th, the first case of 2019-nCoV was reported from Kerala, India, who is the student at Wuhan and returned to India. He was admitted to Thrissur General Hospital. Two Air India flights were arranged to China to evacuate the Indians and they brought around 650 people from there on 31st January and 1st February 2020. All the passengers were screened and kept as quarantine. The second case was reported on 2nd February, who is a student of the University of Wuhan, admitted at Alappuzha Medical College hospital. The third case was reported on the next day who is also a medical student and now admitted Kanjangad District Hospital in Kasaragod, Kerala. So far, a total of 3 positive cases were reported and all from Kerala state.

Advice for the public

The standard recommendations of the WHO for the general public are as follows,

1. Clean the hands frequently with alcohol-based hand rub or soap and water.
2. Cover the mouth and nose while coughing or sneezing, with flexed elbow or tissue-

immediately discard the tissue and wash your hands immediately;

3. If anyone had a fever and a cough, don't have close contact;
4. If you are suffering from fever, cough, and difficulty in breathing means immediately report to the Govt. hospital and share your travel history with the physician;
5. If you are visiting any live animals markets, especially in counties with nCoV, don't have direct contact with live animals and animal-contact surfaces;
6. Don't consume raw or uncooked animal products. Raw meat, milk or animal organs should be handled with care.

General recommendations

The WHO makes the following general recommendations based on the available evidence and past experience (WHO.(b), 2020).

Anyone visiting live animal or animal products markets or wet markets must follow general hygiene like frequent hand wash with soap and water after touching animals and animal products, avoiding rubbing of the eyes, touching nose or mouth with hands and avoiding contact with sick animals or contaminated animal products. Avoid any possible contact with other market-living animals (e.g., stray cats and dogs, rodents, birds, bats). Also, care should be taken to avoid contact with potentially contaminated animal waste or fluids in the soil or shop/market Structure facilities. Don't consume raw or uncooked animal products. Raw meat, milk or animal organs should be handled with care

Recommendations for at-risk groups

Before understanding completely about the 2019-nCoV, people with underlying medical conditions are considered at a higher risk of severe disease. Individuals with these underlying medical conditions should, therefore, avoid contact with the live animal markets, stray animals and wild animals should not eat raw meat from animals. Such recommendations should also be disseminated to underlying medical conditions for travelers and tourists. Slaughterhouse workers, animal, and food inspection veterinarians on the markets, market workers and those who handle live animals and animal products should exercise good personal hygiene, including frequent hand washing after touching animals and animal products. They should consider wearing protective gowns, gloves, masks while the animals

and fresh animal products are handled professionally. Equipment and workstations should be routinely disinfected, at least once a day. After work, protective clothing should be removed and washed every day. Workers should avoid exposure to soiled work clothes, shoes or other items to the members of the family. Therefore, it is recommended that protective clothes and articles remain for daily washing at the workplace. Based on the information available, it is not clear whether the 2019-nCoV has any effects on animal health, and no unusual occurrence has been recorded in any species. Sick animals should never be eaten for food, as a general recommendation; dead animals should be buried safely and contact with their body fluids should be avoided without protective clothing. Veterinarians should maintain a high degree of vigilance and report to veterinary authorities any unusual occurrence observed in any animal species found on the markets.

CONCLUSIONS

2019-nCoV is also making a human to human transmission, just like of earlier viruses SARS and MERS. More than 3000 people were reporting each and every day for this virus infection. Healthcare professionals were infected while treating this infection and their family members also got infected. It indicates the speed and severity of the spreading of this virus. WHO risk assessment says China is at very high and regional and global levels are at high. Personal hygiene and avoiding such types of foods may reduce the further spreading of this deadly virus. Reduced % of new admissions during the last 3 days of the study also hope for the early sign out of this virus. Above all, the service rendered by the health care professionals at their life risk situation is must highly appreciable and as per the social media quote, "A safer public health environment... requires tens of millions of Li Wenliang".

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