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Literature Review

Literature Review on the Recent Pandemic Disease (COVID-19)

Abduleziz Jemal Hamido*

Microbiology Student, Veterinary Science Department, Ethiopia

***Corresponding Author:** Abduleziz Jemal, Microbiology Student, Veterinary Science Department, Ethiopia.

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Abstract

Corona viruses are a group of RNA viruses in the *Coronaviridae* family that are divided in four genera: alpha, beta, gamma and delta that cause disease varying from mild to severe in human and animals. The endemic human corona virus is alpha corona viruses 229E and NL63 and beta corona viruses OC43 and HKU1 that can cause influenza-like illness or pneumonia in humans. But, the two zoonotic corona viruses have emerged causing severe disease in humans: Severe acute respiratory syndrome corona virus (SARS-CoV) in 2002 - 2003 and Middle East respiratory syndrome coronavirus COV-2 is a novel corona virus that was identified in late 2019 as the causative agent of COVID-19. On March 11, 2020, the World Health Organization (WHO) declared the world-wide outbreak of COVID-19 a pandemic. It is spread from person to person via respiratory droplet nuclei. Its incubation time is 3 - 12 days with a median duration of viral shedding of 20 days. This virus is Sensitive to ultraviolet and heat. 75% ethanol, chlorine-containing disinfectant, peracetic acid, and chloroform can effectively inactivate the virus. COVID-19 has spread to the world rapidly (A threat of the word). The disease doesn't have any treatment and vaccine yet. For Prevention and Control of COVID-19. By practicing Respiratory hygiene, especially by ill persons. Respiratory hygiene means to covering the mouth and nose during coughing or sneezing using medical masks, cloth masks, tissues or a flexed elbow, followed by hand hygiene.

Keywords: Novel Corona Virus (COVID-19)

Introduction

Corona viruses are a group of highly diverse RNA viruses in the *Coronaviridae* family that are divided in 4 genera: alpha, beta, gamma and delta that cause disease varying from mild to severe in human and animals. There is endemic human corona virus as alpha corona viruses 229E and NL63 and beta corona viruses OC43 and HKU1 that can cause influenza-like illness or pneumonia in humans. However, two zoonotic corona viruses have emerged causing severe disease in humans: Severe acute respiratory syndrome corona virus (SARS-CoV) in 2002 - 2003 and Middle East respiratory syndrome corona virus (MERS-CoV) [1].

Corona viruses are a group of viruses belonging to the family of *Coronaviridae*, which infect both animals and humans. Human corona viruses can cause mild disease similar to a common cold, while others cause more severe disease (such as MERS - Middle East Respiratory Syndrome and SARS - Severe Acute Respiratory Syndrome). A new corona virus that previously has not been identified in humans emerged in Wuhan, China in December 2019. Signs and symptoms include respiratory symptoms and include fever, cough and shortness of breath. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome and sometimes death. Standard recommendations to prevent the spread of COVID-19 include frequent cleaning of hands using alcohol-based hand rub or soap and water; covering the nose and mouth with a flexed elbow or disposable tissue when coughing and sneezing; and avoiding close contact with anyone that has a fever and cough [2].

Corona viruses (CoVs) are a large family of viruses that cause illness ranging from the common cold to more severe diseases

such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel corona virus (CoV) is a new strain that has not been previously identified in humans. Corona viruses are zoonotic, meaning they are transmitted between animals and people. Detailed investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans. Several known corona viruses are circulating in animals that have not yet infected humans. Corona viruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses. The genome is packed inside a helical capsid formed by the nucleocapsid protein and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: the membrane protein and the envelope protein are involved in virus assembly, whereas the spike protein mediates virus entry into host cells. Among the structural proteins, the spike forms large protrusions from the virus surface, giving corona viruses the appearance of having crowns (hence their name; *corona* in Latin means crown). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses [3].

Corona viruses usually affect mammals and birds, causing a variety of lethal diseases. In general, corona viruses cause widespread respiratory, gastrointestinal and central nervous system diseases in humans and other animals, threatening human health and causing economic loss from mild upper to lower respiratory tract infections. Corona viruses are capable of adapting to new environments through mutation and recombination with relative ease, for this reason, although rarely, certain corona viruses that usually affect only certain animal species can generate new strains that can cross over to human hosts and then be transmitted between humans. Since humans had not been exposed to such viruses before and cannot be protected by existing vaccines or natural immunity, these mutations can rapidly lead to disease outbreaks and, eventually, pandemics. This was the case with the previous outbreaks of SARS and MERS [3].

The SARS-CoV-2 is a novel strain of corona virus that was first detected in Wuhan, china, in the province of Hubei, in the People's Republic of China. The outbreak started as pneumonia of unknown causal agent at the end of December 2019. Phylogenetics analyses undertaken with available full genome sequences suggest that bats appear to be the reservoir of COVID-19 virus, but the intermediate host(s) has not yet been identified. WHO on 30 January 2020, declared the outbreak a Public Health Emergency of International Concern. The WHO recommended that the interim name of the disease causing the current outbreak should be CoV-19 acute respiratory disease. In the 2019-nCoV acronym, "2019" is the year the virus was first detected, "n" means "new", and "CoV" corresponds to the corona virus family. On 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) decided to name the virus as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), and the WHO finally decided to name the disease caused by this virus as COVID-19 [2].

Taxonomy

The name "corona virus," was observed in 1968, is derived from the "corona "which means -like or crown-like morphology when the observer detects under electron microscope. In 1975, the *Coronaviridae* family was established by the International Committee on the Taxonomy of Viruses. In June 2005, it was proposed that the *Coronaviridae* family be divided into two subfamilies, that is the corona viruses and the toroviruses, the toroviruses cause enteric diseases in both cattle and humans. The *Coronaviridae* family, along with the *Arteviridae* and *Roniviridae* families, forms the *Nidovirales* order. The *Arteviridae* family includes swine and equine pathogens, and the *Roniviridae* family is composed of invertebrate viruses [4].

Coronaviruses are divided into three genera (I to III), usually referred to as groups and based on serological cross-reactivity [5]. Group I coronaviruses include animal pathogens, such as TGEV of the pig, porcine epidemic diarrhea virus (PEDV), and feline infectious peritonitis virus (FIPV), as well as the human corona viruses HCoV- 229E and HKU1, which cause respiratory infections (see below). Group II also includes pathogens of veterinary relevance, such as BCoV, porcine hemagglutinating encephalomyelitis virus, and equine coronavirus, as well as human coronaviruses viruses OC43 and NL63, which, like HCoV-229E, also cause respiratory infections. Group II also includes viruses that infect both mice and rats. MHV is often studied as a prototype coronavirus; MHV is a group of highly related strains causing a variety of diseases, such as enteric disease, hepatitis, and respiratory disease, as well as encephalitis and chronic demyelination. Rat sialodacryoadenitis coronavirus also belongs to group II [6]. Group III thus far includes only avian coronaviruses, such as IBV, turkey coronavirus, and pheasant coronavirus (38). Recently, using reverse transcription- PCR (RT-PCR), coronavirus sequences were detected in the graylag goose (*Anser anser*), feral pigeon (*Columbia livia*) and mallard (*Anas platyrhyn-*

chos) [7]; phylogenetic analyses of the replicase and nucleocapsid (N) sequences suggest that these viruses are members of group III, but as yet they have not been isolated or characterized.

Antigenic properties

Strong humoral immune responses are elicited by the structural proteins S, M, N, and, when present, HE. The S and HE proteins are the predominant antigens involved in virus neutralization. Reduction of infectivity with anti-M antibodies also has been shown, but generally in the presence of complement. Protection against coronavirus infections (IBV, MHV, TGEV) is provided by S protein that has been affinity-purified or expressed by recombinant adenovirus. N- and M-specific antibodies also give some protection *in vivo*. The most efficient induction of virus neutralizing antibodies has been achieved with a combination of S and N proteins. The globular portion of the S protein contains many dominant antigenic sites targeted by the humoral immune response and also by cytotoxic T lymphocytes. Other important antibody epitopes are also found in the stem portion, at least for MHV. Both the amino- and carboxy-termini of the M protein elicit strong immune responses. While neutralizing antibodies can prevent disease if present prior to infection, cytotoxic T cell responses are important in virus clearance. Hypervariable domains in the S1 portion of the S protein facilitate the selection of virus escape mutants that evade both humoral and cellular immune responses. N protein also elicits a protective cellular immune response. The immune system is known to play a major role in the pathogenesis of some coronavirus-induced diseases, such as the experimental induction of demyelination by MHV, and the antibody-dependent enhancement of disease (feline infectious peritonitis) caused by FCoV [8].

Biological properties

SARS-CoV-2 (COVID-19) is single-stranded RNA, enveloped virus that likely spread to humans from a zoonotic source, possibly bats or pangolins [9].

Corona viruses infect birds and many mammals, including humans. The respiratory tract, gastrointestinal tract and neurological tissues are the most frequent targets of coronaviruses, but other organs including liver, kidney, heart and eye can also be affected. Epithelial cells are the main target of coronaviruses, plus, with some coronavirus species, widely distributed cells such as macrophages. Coronaviruses have a wider host range *in vivo* than would be expected from *in vitro* studies. In experimental infections BCoV caused enteric disease in turkeys. FCoV and CCoV replicated in experimentally infected pigs, clinical disease being caused by virulent FCoV. Turkey coronavirus has been demonstrated to replicate in chickens asymptomatically. Type II FCoV has arisen by natural recombination of type I FCoV with CCoV. The cause of severe acute respiratory syndrome (SARS) in man is a corona virus that is believed to have jumped from another animal species. BCoV and some isolates of HCoV-OC43 have > 99% aa identity in their S and HE proteins, raising the possibility of a shared host range *in vivo*. Leader-switching between a defective RNA of BCoV and HCoV-OC43 virus has been demonstrated, and the BCoV defective RNA could be replicated by the replicative machinery of HCoV-OC43 and other members of coronavirus Group 2, suggesting a potential for recombination between members of Group 2. Biological vectors are not known. Respiratory, fecal-oral and mechanical transmission are common. Although coronaviruses may bind cells through ubiquitous acetylated forms of glycoproteins and lipids, a more specific binding between the virus and a cellular receptor is required for the establishment of viral infection. Coronaviruses are divided into three groups called 1, 2 and 3 (see below). MHV in Group 2, uses as receptors CEACAM1 glycoproteins in the immunoglobulin superfamily. SARS-CoV uses angiotensin converting enzyme 2 (ACE2) as a receptor. Members of the group 1 coronaviruses (including TGEV, FCoV and HCoV-229E) use aminopeptidase N (APN or CD13) as a receptor for cell entry. Sialic acid (N-acetyl-9-O-acetylneuraminic acid)- containing glycoproteins are probably a component of the cell surface molecules required for BCoV and HCoV-OC43 infectivity, and 2,3-linked sialic acid in the case of the Group 3 coronavirus IBV. Nevertheless, binding to CEACAM1 and APN receptors does not explain the differences in coronavirus tropism. In addition to the binding to the aforementioned receptors, a second factor mapping in the S protein (possibly, a second receptor binding site) has been implicated in coronavirus tropism. Infections of man and animals by coronaviruses seem to be ubiquitous, as evidence of infection has been obtained in every country where serological or virological studies have been done [8].

Transmission

Respiratory secretions formed as droplets and produced when an infected person coughs, sneezes or talks, contain the virus and are the main means of transmission.

There are two main routes by which people can spread COVID-19:

- Infection can be spread to people who are nearby (within 1 metre) by breathing in droplets coughed out or exhaled by a person with the COVID-19 virus.

- People may become infected by touching contaminated surfaces or objects (fomites) and then touching their eyes, nose or mouth (e.g. a person may touch a door knock or shake hands and then touch their own face). This is why environmental disinfection is so important.

According to current evidence, transmission may start just before symptoms become visible. However, many people infected with COVID-19 experience only mild symptoms. This is particularly true at the early stages of the disease. It is therefore possible to catch COVID-19 from someone who has, for example, just a mild cough and does not feel ill. WHO is assessing ongoing research on the period of transmission of COVID-19 and will continue to share updated findings [10]. In general the transmission of SARS-CoV-2 occurs by the following mechanisms:

- Most often, spread from person to person among close contacts (about 6 feet or 1.8 meters).
- 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, noses or eyes of people who are nearby or possibly be inhaled into the lungs.
- It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose or possibly their eyes, but this is not thought to be the main way the virus spreads [11-16].
- There is evidence that corona viruses can remain infectious on inanimate surfaces for several hours or even days [17].
- There have been reports of spread from an asymptomatic infected patient to a close contact [11-16]
- Also, patients may remain contagious up to two weeks after the remission of symptoms. According to some authors, whereas symptoms mostly occurred by the end of the first week, viral RNA remained detectable in throat swabs at the second week. Stool and sputum samples remained RNA-positive over even longer periods, in spite of full resolution of symptoms [18].
- Minimal information is available regarding COVID-19 during pregnancy. Intrauterine or perinatal transmission has not been identified. In two reports including a total of 18 pregnant women with suspected or confirmed COVID-19 pneumonia, there was no laboratory evidence of transmission of the virus to the neonate. However, two neonatal cases of infection have been documented. In one case, the diagnosis was made at day 17 of life after close contact with the infant's mother and a maternity matron who were both infected with the virus. The other case was diagnosed 36 hours after birth; the source and time of transmission in that case were unclear [19].
- There are rare exceptions when breastfeeding or feeding expressed breast milk is not recommended. The CDC has no specific guidance for breastfeeding during infection with similar viruses like SARS-CoV or Middle Eastern Respiratory Syndrome (MERS-CoV) also both corona viruses. In a similar situation to COVID-19, the CDC recommends that a mother with flu continue breastfeeding or feeding expressed breast milk to her infant while taking precautions to avoid spreading the virus to her infant. Given low rates of transmission of respiratory viruses through breast milk, the World Health Organization presently states that mothers with COVID-19 can breastfeed [20].

Incubation period

The SARS-CoV-2 has an incubation period of 2 to 14 days before the onset of symptoms. A study led by researchers of the Bloomberg School of Public Health yielded an estimate of 5.1 days for the median disease incubation period. This median time from exposure to onset of symptoms suggests that the 14-day quarantine period recommended by the WHO and other organizations is reasonable. The analysis suggests that about 97.5% of people who develop symptoms of SARS-CoV-2 infection will do so within 11.5 days of exposure. The researchers estimated that for every 10,000 individuals quarantined for 14 days [21].

Survival of the disease in the environment

Human corona viruses can survive on inanimate objects and can remain up to 5 days at temperatures of 25°C and relative humidity of 40 - 50% (which is typical of air-conditioned indoor environments). Survival on environmental surfaces is dependents' on the surface type. An experimental study using a SARS-CoV-2 strain reported viability on plastic for up to 72 hours, for 48 hours on stainless steel and up to 8 hours on copper. Viability was quantified by end-point titration on Vero E6 cells. Extensive environmental contamination may occur due to an aerosol generating procedure (AGP). The rate of clearance of aerosols in an enclosed space is dependent on the extent of mechanical and natural ventilation. The time required for clearance of aerosols, and that can be entered

without a filtering face piece respirator, can be determined by the number of air changes per hour (ACH) as outlined in WHO guidance. Environmental decontamination should be performed when it is considered appropriate to enter the room without an FFP3 respirator. A single air change is estimated to remove 63% of airborne contaminants, after 5 air changes less than 1% of airborne contamination is thought to remain. A minimum of 20 minutes i.e. 2 air changes, in hospital settings where the majority of these procedures occur is considered pragmatic (Guidance for infection prevention and control in healthcare settings. Version 2020).

Pathogen characteristics

Coronaviruses are a large family of viruses found in both animals and humans. Some infect people and are known to cause illnesses ranging from the common cold to more severe diseases, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). A novel corona virus is a new strain of corona virus that has not previously been identified in humans. The latest novel corona virus, now called COVID-19 virus, had not been detected before the outbreak reported in Wuhan, China, in December 2019. So far, the main clinical signs and symptoms reported in people during this outbreak include fever, coughing, difficulty in breathing, and chest radiographs showing bilateral lung infiltrates. Although the current outbreak of COVID-19 is still evolving, infection may present with mild, moderate or severe illness and can be passed from human to human, primarily by droplet spread. While about 80% of cases manifest as a mild illness (i.e. non-pneumonia or mild pneumonia), approximately 20% progresses to a more severe illness, with 6% requiring specialist medical care, including mechanical ventilation. The Most estimates of the incubation period of COVID-19 range from 1 to 14 days, with a median of 5 - 6 days [2].

The pathological features of COVID-19 in lungs greatly resemble those seen in SARS and MERS infection with showing morphological features bilateral diffuse alveolar damage with cellular fibromyxoid exudates.

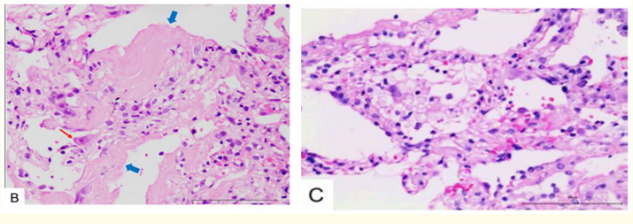

Figure 1: Hyaline membrane formation blue arrow. Intersectional mononuclear inflammatory infiltrates (Xiaohong Yao., *et al. Chinese Journal of Pathology*. 2020) [21].

Epidemiology

On December 29, 2019, the first cases of an acute respiratory syndrome of unknown etiology were reported in Wuhan City, Hubei Province, China among people linked to a local seafood market ("wet market"). It appears that most of the early cases had some sort of contact history with the original seafood market. Soon, a secondary source of infection was found to be human-to-human transmission via close contact. There was an increase of infected people with no history of exposure to wildlife or visiting Wuhan, and multiple cases of infection were detected among medical professionals [23]. It became clear that the COVID-19 infection occurs through exposure to the virus, and both the immunosuppressed and normal population appear susceptible. Some studies have reported an age distribution of adult patients between 25 and 89 years old. Most adult patients were between 35 and 55 years old and there were fewer identified cases among children and infants [24]. A study on early transmission dynamics of the virus reported the median age of patients to be 59 years, ranging from 15 to 89 years, with the majority (59%) being male. It was suggested that the population most at risk may be people with poor immune function such as older people and those with renal and hepatic dysfunction [23].

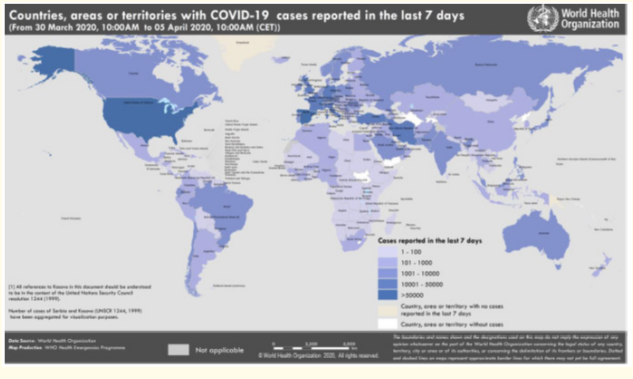

Figure 2: Countries, territories or areas with reported confirmed cases of COVID-19, 5 April 2020 (WHO).

Clinical manifestation

Illnesses associated with the new corona virus, named COVID-19, are similar to several respiratory illnesses and include fever, dry cough, sore throat and headache. Less frequent symptoms included coughing sputum or blood, headache and diarrhea.

Most cases are considered mild to moderate with a subset experiencing more severe illness with shortness of breath and difficulty breathing For confirmed COVID-19 cases, reported illnesses have ranged from people with little to no symptoms to people be-

ing severely ill and dying. Symptoms can include (on admission to hospital) [25]:

- Fever (> 80% of the patients)
- Cough (> 80%)
- Shortness of breath (31%)
- Muscle ache (11%).

The disease may also occur with mild symptoms only, including: low-grade fever, cough, malaise, sore throat without any warning signs, such as shortness of breath or difficulty in breathing, increased respiratory secretions (i.e. sputum or haemoptysis), gastrointestinal symptoms such as nausea, vomiting, and diarrhea and without changes in mental status like, confusion and lethargy (World Health Organization, 2020).

Preliminary data report 11% lethality among hospitalized patients. From these patients, Complications occurred in 33% of the patients, and acute respiratory distress syndrome (ARDS) (17%), acute renal injury, acute respiratory injury, septic shock and ventilator-associated pneumonia [25].

Disease in children appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported among individuals aged less than 19 years. A very small proportion of those aged under 19 years have developed severe (2.5%) or critical disease (0.2%) (World Health Organization, 2020).

Diagnosis

For patients those suspected by infection(COVID-19), diagnosis performed by real-time fluorescence (RT-PCR) to detect the positive nucleic acid of SARS-CoV-2 in sputum, throat swabs, and secretions of the lower respiratory tract samples [26].

Molecular detection of COVID-19 virus using well-designed protocols is usually very specific; thus, a positive result confirms the detection of the virus. On the contrary, a negative result might not always mean the absence of COVID-19 virus infection (WHO Laboratory testing guideline, 2020). Several reasons might explain a negative result in a person infected with COVID-19 virus, mainly:

- Poor sample quality, handling, transportation and/or storage (to control for this, the qualitative detection of a human housekeeping gene.
- Poor/failed sample extraction, presence of PCR inhibitors in the extracted RNA (to control for this, an extraction control can be used.
- The sample was collected at a time where the patient was not shedding sufficient amounts of virus, for instance very early or very late during infection.
- As with any molecular detection assay, virus mutations in the regions that are targeted by the assays might affect the sensitivity of the detection.

Serological methods

Assays based on the detection of IgM/IgG antibodies can support outbreak investigation and seroprevalence studies. Several assays (both ELISA and rapid diagnostic tests) are available for the detection of IgM/IgG antibodies and are marketed for the detection of COVID-19 virus infections. However, to date, these tests are not recommended for use. These tests may be limited due to cross-reactivity with other corona viruses that are normally present in the community and that make the interpretation of results difficult [27]. However, the dynamics of antibody response and production during the different stages of infection are not yet fully established at present. Some studies have shown that during the first 6-7 days from the onset of symptoms, less than 40% of patients have detectable antibodies [28]. Thus, serological tests should not be used to rule out a case during the first days of illness. But, the detection of antibodies after day 7 only indicates previous contact with the virus but does not confirm the presence and shedding of the virus. So many commercial products are marketed for the detection of antibodies (IgM and/or IgG) induced by COVID-19 virus infection, including rapid diagnostic tests (RDTs). Any such test should be validated and its performance in terms of specificity and sensitivity assessed. However, the use of rapid tests is not recommended since, these types of tests might have low sensitivity. For these reasons, antibody detection is not considered (as yet) an appropriate test for confirmation or diagnosis of COVID-19 cases.

Antigen detection

During the first days after symptom onset (approximately 1 to 5), viral proteins are generated that can be detected by different tests (like ELISA, immunofluorescence). In general, this type of assays has acceptable specificity (depending on the assay).

Rapid diagnostic tests (RDTs)

So far there are no rapid diagnostic tests (immunochromatography or colloidal gold detection) that have been authorized by competent regulatory authorities and/or have been formally validated. In general, these types of tests have low sensitivity. Therefore, their positive predictive value is good (they can be used to rule in cases), but their negative predictive value is low (they should not be used

to rule out cases). Also, the limitations described above for serological tests and antigenic detection apply to RDTs.

Treatment

Currently, there is no effective and or specific medicine or vaccine for COVID-19 and no medicines or vaccines have been fully tested yet.

Isolation and support treatment of COVID-19

- All confirmed patients should be isolation.
- Suspected case should be treated in isolation in a single room.
- Hospital and ICU admission decision was according to disease severity.
- Strengthening support treatment (most patients complicated with hypoproteinemia):
    - Sufficient caloric.
    - Water and electrolyte balance.
- Oxygen therapy.
- Closely monitoring vital sign and laboratory.
- WBC; Lymphocyte.
- Biochemical indicators (liver enzyme, myocardial enzyme, renal function…..).
- Marker of inflammation (serum ferri4n, IL-6, cytokine).
- Chest imaging.

Antiviral for COVID-19: other potential choices

- Alpha-interferon: 5 MU, atomization inhalation twice daily.
- Ribavirin: used together with interferon or lopinavir, 500 mg twice or three times of intravenous injection daily, no longer than 10 days.
- Chloroquine phosphate: 500 mg bid for 7 days for adults aged 18 - 65 with body weight over 50 kg; 500 mg bid for Days 1&2 and 500 mg daily for Days 3 - 7 for adults with body weight below 50 kg.
- Arbidol: 200 mg three times daily for adults, no longer than 10 days.

Use of corticosteroid is still controversial

- Only for patients with rapid progressive deterioration oxygenation, radiology imaging and excessive inflammation.
- Contraindications: Allergy; un-controlled diabetes; uncontrolled hypertension; glaucoma; GI bleeding; immunodepression; lymphocyte less than 300/ul; severe bacterial and/or fungal infections Short term, 3 - 5 days and Low-moderate dosage [29].

Convalescent plasma therapy

For COVID-19 patients with rapid disease progression, severe and critical illness, and convalescent plasma therapy can be tried by National Health Commission of the People's Republic of China, 2020. Convalescent plasma therapy can utilizes a certain titer of virus-specific antibodies in the plasma of the convalescent individual to enable the patient receiving the infusion to obtain passive immunity and remove pathogens from the blood circulation. These methods have been successfully used in the treatment of SARS and H1N1 influenza and are an effective treatment [30].

The use of convalescent plasma therapy treatment can follow two major principles according to the National Health Commission of the People's Republic of China, these principles are, the first one is, the course of disease does not exceed three weeks. However, the patient should have a positive viral nucleic acid test or viraemia that certified by clinical experts. The second principle is the Patients with severe disease with rapid disease progression or critically ill at early stage patients, or patients comprehensively evaluated by clinical experts as requiring plasma therapy. The infusion dose is determined according to the clinical situation and the weight of the patient, usually the infusion dose is 200 - 500 ml (4 - 5 ml/k).

Prevention and control

Infection prevention and control

Routine practices

For all patients, at all times, in all healthcare settings including when performing a point-of-care risk assessment, and adherence to respiratory hygiene and hand hygiene.

Contact and droplet precautions (should be implemented empirically)

- Wear gloves and a long-sleeved gown upon entering the patient's room, cubicle or designated bed-space.
- Wear facial protection (surgical or procedure mask and eye protection, or face shield, or mask with visor attachment) when within two metres of a patient suspected or confirmed to have COVID-19 infection.

Airborne precautions

When performing aerosol-generating medical procedures (AGMPs). A respirator and face/eye protection.

Whenever possible, AGMPs should be performed in an airborne infection isolation room.

The WHO's standard recommendations for the general public to reduce exposure to and transmission of this and other respiratory illnesses are as follows, which include hand and respiratory hygiene and safe food practices:

- Frequently clean hands by using alcohol-based hand rub or soap and water;
- When coughing and sneezing cover the mouth and nose with a flexed elbow or tissue - throw the tissue away immediately and wash hands;
- Avoid close contact with anyone who has fever and cough;
- If you have fever, cough and difficulty breathing seek medical care early and share previous travel history with your healthcare provider;
- When visiting live markets in areas currently experiencing cases of novel corona virus, avoid direct unprotected contact with live animals and surfaces in contact with animals;
- Avoided consumption of raw or undercooked animal products. Raw meat, milk or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices (World Health Organization, 2020).

Self-isolation by persons with symptoms and/or persons who may have been in contact with infected persons; this means avoiding situations where you could infect other people. This means all situations where you may come in contact with others, such as social gatherings, workplaces, schools, child care/pre-school centres, universities, faith-based gatherings, aged care and health care facilities, prisons, sports gatherings, supermarkets, restaurants, shopping malls and all public gatherings [31-33]:

- By practicing Respiratory hygiene, especially by ill persons. Respiratory hygiene means to covering the mouth and nose during coughing or sneezing using medical masks, cloth masks, tissues or a flexed elbow, followed by hand hygiene.
- Discard materials used to cover the mouth or nose or clean them appropriately after use (e.g. wash handkerchiefs using regular soap or detergent and water).
- Avoid direct contact with bodily fluids, particularly oral or respiratory secretions, and stool. Use disposable gloves and eye protection to provide oral or respiratory care and when handling stool, urine and waste. Gloves, tissues, masks and other waste generated by ill persons or in the care of ill persons should be placed in a lined container in the ill person's room before disposal with other household waste.
- Avoid other types of possible exposure to ill persons or contaminated items in their immediate environment (e.g. avoid sharing toothbrushes, cigarettes, eating utensils, dishes, drinks, towels, washcloths or bed linen). Eating utensils and dishes should be cleaned with either soap or detergent and water after use and may be reused instead of being discarded.
- Clean and disinfect bathroom and toilet surfaces at least once daily with regular household disinfectant containing a diluted bleach solution.
- Do not shake soiled laundry. Countries may consider measures to ensure that waste is disposed of at a sanitary landfill, and not at an unmonitored open dump, wherever possible. Additional measures may be needed to prevent unhygienic reuse of gloves and masks, and to avoid direct contact of the skin and clothes with the contaminated materials (Centre for Health Protection Hong Kong, 2020).

Conclusion/Recommendation

- The basic principles of infection prevention and control and standard precautions should be applied in all health care facilities, including outpatient care and primary care.
- Emphasis on hand hygiene, respiratory hygiene and medical masks to be used by patients with respiratory symptoms.
- Appropriate use of contact and droplet precautions for all suspected cases.
- Prioritization of care of symptomatic patients.
- When symptomatic patients are required to wait, ensure they have a separate waiting area.

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