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A Review of the Recent Advance Report of Coronavirus (COVID-19) Outbreak Animal-to-Human-to-Human Transmission, Diagnosis, Treatment and Pathogenesis of COVID-19 from Hospitalized Patients and Post-Mortem Reports of COVID-19 Infected Death Body

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Abstract

Objective: Information on the clinical characteristics and studies of the infected patients have been required from December 2019, When throughout the China and globally spread it rapidly after arose it in Wuhan city first. Day by day this COVID-19 virus is becoming a Global concern of the public health. At present, more than 19,000 people have died globally infected by coronavirus, while more than 400,000 infections have been confirmed in more than fifteen dozens of countries, according to the World Health Organization.

Methods: We methodically searched and reviewed PubMed, Pub Centre, Web of Science, and Scopus with the following terms: "Middle East Respiratory Syndrome", "MERSCoV" and "MERS", Medline, Google scholar, Embase, Science Direct, Clinical Trials.gov, Newspapers, World Health Organization websites, and the Cochrane Central Database of Randomized Controlled Trials and treatment conducted prior to March 20, 2020.

Results: We reviewed published research papers on Coronavirus total 260 up to February 2020. We found that SARS-CoV was transmitted from animal to human. There are several drugs are prescribed for the infected patients of coronavirus such as Interferon Alpha-2B is an antiviral or antineoplastic drugs, Lopinavir plus ritonavir as antiviral therapy and also moxifloxacin to prevent secondary infection. In serious shortness of breathing and hypoxia methylprednisolone, antibody transmission and antiviral drugs are also prescribed for the infected patients. From the biopsy reports of lung in maximum papers showed alveolar damage and hyaline membrane formation.

Conclusion: Overall this review article will help to understand the transmission process, treatment, diagnosis and pathogenesis of the coronavirus.

Keywords: COVID-19 • MERSCoV • MERS • Interferon alpha-2b • Lopinavir plus ritonavir • Zoonotic • Hyaline membrane • Pathogenesis

Introduction

On 13 June 2012 the first cases of coronavirus were identified in Saudi Arabia, specifically Jeddah and spread it throughout the Asia, Africa, Europe and America [1-4]. At the beginning of December 2019, the first cases of pneumonia of unknown origin were identified in Wuhan, the capital city of Hubei Province in China [5,6]. The pathogen was identified as a novel enveloped RNA beta coronavirus [7], currently referred to as coronavirus 2 severe acute respiratory syndromes (SARS-CoV-2) by postmortem biopsy [8-10]. The Patients with coronavirus have been recorded both in hospitals and in family environments phylogenetic similarity to SARS-CoV [11,12]. In general, COVID-19 is an acute resolved disease but it can also be deadly, with a 2% case fatality rate. Severe disease onset might result in death due to massive alveolar damage and progressive respiratory failure. As of Feb 15, about 66580 cases have been confirmed and over 1524 deaths [13]. Coronavirus disease-2019 a public health emergency of international concern has been declared by WHO [14]. In order to help prevent future occurrences of MERS-CoV, public health officials can focus on the mitigation of zoonotic transfers; however, additional research is needed to determine where spillovers could occur between mammals and humans [15,16]. Transmission capacity has important implications for contamination and control methods for any respiratory virus. The recent study indicates the baseline R0 number (replication number) of 2.2, which means that every infected person by coronavirus spreads the infection or disease to an additional two person on average. As noted by the authors, until this number falls below 1.0, it is likely that the outbreak will keep spreading. Latest reports of the upper part or the respiratory system such as oropharynx virus early in the course of the disease raise concerns about increased infectivity during the period of minimum indication [17,18].

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CDC declared Level-3 warning notice to avoid nonessential travel because of widespread community transmission of COVID-19. International Areas with Sustained (Ongoing) Transmission (Last updated February 28, 2020) China (Level 3 Travel Health Notice), Iran (Level 3 Travel Health Notice), Italy (Level 3 Travel Health Notice), Japan (Level 2 Travel Health Notice) & South Korea (Level 3 Travel Health Notice). The virus is thought to spread mainly from person-to-person. Between people who are in close contact with one another (within about 6 feet) and through respiratory droplets produced when an infected person coughs or sneezes. These droplets can land in the mouths or noses 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 sometimes possibly their eyes, but this is not thought to be the main way the virus spreads. Coronaviruses are a large family of viruses that are common in people and many different species of animals, including camels, cattle, cats, and bats. Rarely, animal coronaviruses can infect people and then spread between people such as with MERS-CoV, SARS-CoV, and now with this new virus (named SARS-CoV-2). The SARS-CoV-2 virus is a betacoronavirus, like MERS-CoV and SARS-CoV. All three of these viruses have their origins in bats. The sequences from U.S. patients are similar to the one that China initially posted, suggesting a likely single, recent emergence of this virus from an animal reservoir [19,20]. There is no accurate antiviral treatment recommended for infected patients by coronavirus. Patients with COVID-2019 should receive protective care to relieve from the symptoms. In extreme cases or condition, treatment should include care to assist vital organ functions. People who think they may have been exposed to COVID-19 should contact their healthcare provider immediately as soon as possible and some of the physicians are prescribing some medicines for the coronavirus patients like Interferon Alpha-2B, Lopinavir plus ritonavir as antiviral therapy and also moxifloxacin to prevent secondary infection as serious shortness of breathing and hypoxia methylprednisolone. Sometimes Ibuprofen and some NSAID are also suggested to reduce the fever. This is the overall up to date all guideline for treatment of coronavirus infected patients that have been published in the different international journal [21,22].

Patient infected by the coronavirus the biopsy samples were taken from the patient's lung, liver and heart tissue. Histological analysis of cellular fibromyxoid exudates revealed a bilateral diffuse alveolar damage. The right lung showed clear pneumocyte desquamation and development of hyaline membranes, suggesting acute respiratory distress syndrome (ARDS). The left lung tissue displayed pulmonary edema with formation of hyaline membranes, indicative of early-phase ARDS. In both lungs interstitial mononuclear inflammatory infiltrates were detected, dominated bylymphocytes. In the intra-alveolar spaces were detected multi-nucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cyto-plasma, and prominent nuclei, indicating viral cytopathic changes. No obvious inclusions for intranuclear or intracytoplasmic viruses have been reported [23].

Literature Review

In this severe case of COVID-19 throughout the world, our clinical and pathological finding from the different journal can not only help to identify the causes of death by the coronavirus, but also provide complete package of new knowledge in the pathogenesis of the coronavirus, Animal to Human and human to human transmission and proper diagnosis and treatment guidelines of SARS-CoV-2-related pneumonia, which could help physicians develop a timely therapeutic strategy for specific serious patients and minimize death.

COVID-19 infected patients with pneumonia

Regarding the deaths of pneumonia was unknown disease reported in Wuhan and considering the patients shared history of exposure to the Huanan seafood market, the local health body published a study and analysis of the distribution, patterns and determinants of health and disease conditions affected by coronavirus in defined populations warning on 31 Dec 2019 and on 1 January 2020, the business was closed to the Huanan seafood market. Meanwhile, as of 31 Dec 2019, 59 suspected cases of fever and dry cough have been referred to a designated hospital. After the warning was soon established an expert team of physicists, epidemiologists, virologists, and government officials. As the cause was unclear at the onset of these emerging infections, diagnosis of unknown cause pneumonia in Wuhan was based on clinical characteristics, chest imaging, and ruling out specific pneumonia-causing bacterial and viral pathogens [5].

Transmission scenario of the COVID-19 viruses from Animal-To-Human-To- Human

Human: As much as possible, someone should stay in a specific room and away from other people in their home. Also, He or She should use a separate bathroom, if available.

Animals: In the case of SARS and this coronavirus outbreak, bats were the original hosts and then transmitted to the other animals like pets. Person will avoid contact to pets and other animals; just like you would do with other persons if you're COVID-19 infected. Although there have been no cases of pets or other animals being sick with COVID-19, still it's suggested that people suffering from COVID-19 restrict contact with animals until more data about the virus is available. If you are affected by COVID-19, avoid contact with your pet, including petting, snuggling, being kissed or licked and sharing food with your pets. If you must care for your pet or be around animals while you are sick, wash your hands before and after you interact with pets and wear a facemask [5,24-26].

Biological specimen collection

In compliance with the CDC guidance, clinical specimens for coronavirus diagnostic testing were obtained to identify this virus. By using synthetic fibers swap specimens were collected from nasopharyngeal and oropharyngeal and then transfer it into s separate disinfected tube with 2 to 3 ml of viral transporting medium. In serum separator tube serum was processed and centrifuged it as per CDC rules or guidelines. The biological specimens were collected in sterile containers that are free from any other organism. At 2°C to 8°C the biological specimens were stored for the identification of coronavirus [27,28].

Diagnosis of COVID-19

Clinical analysis of COVID-19 is particularly based totally on epidemiological records, scientific manifestations and a few auxiliary examinations, such as nucleic acid detection, CT scan, immune identity era Point-of-care Testing (POCT) of IgM/IgG enzyme-linked immunosorbent assay (ELISA) and blood culture. However, the clinical signs and symptoms of sufferers inflamed with SARS-CoV-2 are extraordinarily abnormal, together with respiration signs, cough, fever, dyspnea, and viral pneumonia. Therefore, auxiliary examinations are necessary for the prognosis of COVID-19, just as the epidemiological records [29].

Materials required for RT-PCR

- QI Aamp Viral RNA Mini Kit
- Taq Man Fast Virus Master mix
- Ethanol (96–100%)
- Micro Amp Fast Optical 96-well reaction plate (TheromFisher, Cat# 4346907)
- Micro Amp optical adhesive film (Therom Fisher, Cat# 4311971)
- Micro centrifuge (adjustable, up to 13 000 rpm)
- Adjustable pipettes (10 µl, 20 µl, 100 µl, 200 µl)
- Sterile, RNase-free pipette tips with aerosol barrier
- Vortex
- Micro centrifuge tubes (0.5ml and 1.5 ml)
- Thermo cycler (Therom Fisher, ViiA™ 7 Real-Time PCR)
- Positive control
- Primer sets [30-33].

Genetic sequence detection of 2019 novel coronavirus (2019-nCoV) in suspected human cases by RT-PCR

The emergence of 2019-nCoV in respiratory specimens was detected by sequencing of the next generation, or RT-PCR methods in real time. Extract viral RNA from clinical specimens by using QIAamp viral RNA mini kit according to manufacturer's instructions. Preparation of master mixture for one-step monoplex RT-PCR is mentioned in Table 1 and the temperature of the RT-PCR mentioned in Table 2 [34-37].

Genetic sequences of COVID-19

The primers and probe target are used to envelope gene of coronavirus and the sequences were as follows: forward primer 5′-ACTTCTTTTTCTT-GCTTTCGTGGT-3′; reverse primer 5′-GCAGCAGTACGCACACAATC-3′; and 5′CY5-CTAGTTACACTAGCCATCCTTACTGC-3′BHQ1 (probe target). Conditions for the amplifications were 50°C for 15 min, 95°C for 3 min, followed by 45 cycles of 95°C for 15 min and 60°C for 30 min at RT-PCR and another primers and probe target sequence are given below and that is published by the LKS Faculty of Medicine School of Public Health:

Assay 1 (Target: ORF1b-nsp14) Forward primer (HKU-ORF1b-nsp14F): 5′-TGGGGYTTTACRGGTAACCT-3′ Reverse primer (HKU-ORF1b-nsp14R): 5′-AACRCGCTTAACAAAGCACTC-3′ Probe (HKU-ORF1b-nsp141P): 5′-FAM-TAGTTGTGATGCWATCATGACTAG-TAMRA-3′

Assay 2 (Target: N) Forward primer (HKU-NF): 5′TAATCAGA-CAAGGAACTGATTA-3′ Reverse primer (HKU-NR): 5′-CGAAGGTGT-GACTTCCATG-3′ Probe (HKU-NP): 5′-FAM-GCAAATTGTGCAATTTGCGG-TAMRA-3′ [38,39].

Pathogenesis of Coronavirus in the human body

Highly serious symptoms of COVID-19 are associated with increasing numbers and death rates, especially in China's epidemic area. The China National Health Commission announced details of the first 17 deaths on January 22, 2020 and on January 25, 2020 the death cases increased to 56. Higher numbers of leukocytes, irregular respiratory findings and increased levels of plasma pro-inflammatory cytokines were recorded in patients infected with COVID-19. One of the COVID-19 case reports reported an apatient with a cough, harsh breathings of both lungs and a body temperature of 39.0°C at 5 days of fever. Laboratory studies revealed leukocyte leukopenia with counts of 2.91×10^{-9} cells/L, 70.0% of which were neutrophils. However, a blood C-reactive protein value of 16.16 mg/L was reported above the normal range (0–10 mg/L). High sedimentation levels for erythrocytes and D-dimer were also observed [5]. The major pathogenesis of COVID-19 as a respiratory system attacking virus was extreme pneumonia, RNAaemia, combined with ground-glass opacity incidence, and acute cardiac injury [5]. In patients with COVID-19 infection with IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNÿ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA, significantly high blood levels of cytokines and chemokines were reported. Some of the severe cases admitted to the intensive care unit displayed high levels of pro-inflammatory cytokines, including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα, which were reasoned to encourage severity of the disease [40].

Table 1. Reaction mix from Taq Man fast virus master mix.

Reagents	For a single rxn (µl)
H_2O (RNase free)	8.5 ml
4x Reaction mix*	5 ml
Forward primer (10 µM)	1 ml
Reverse primer (10 µM)	1 ml
Probe (10 µM)	0.5 ml
RNA sample	4 ml
Final rxn volume	20 ml

Table 2. The temperature of the RT-PCR for both monoplex assays can be conducted under the same conditions.

Temperature (°C)	Time (Minute : Second)	No. of cycles
50	5:00	1
95	0:20	
95	0:05	40
60	0.35	

Recent updated treatment scenario of infected patients by COVID-19

There are appropriate guideline lines of treatment for the coronavirus infected patients is unknown but at present scientists are trying to develop new drugs or treating with the existing drugs to control the coronavirus. There are several procedures of treatment mentioned in this paper.

Treatment Guideline Scenario 1: HIV vaccine failed to kill the coronavirus and the scientists are trying to control this virus by applying different types of Antiviral drugs but the proper result they can't get yet now.

Treatment Guideline Scenario 2: Treatment after coronavirus infection must be supportive for sign and symptom control, the patient received antipyretic therapy to control the body temperature consisting of 650 mg of acetaminophen or paracetamol for every 4 hours total dose per day is 3900 mg (approximately 4 g) as needed and 600 mg of ibuprofen every 6 hours. COVID-19 infected patients also received 600 mg of guaifenesin (as expectorant) that helps for drainage of the mucus or sputum from the lungs for his continued cough and approximately 6 liters of normal saline for the hospitalized patients for regular rinsing of the nose to prevent infection with coronavirus. In addition, there were alterations in hepatic function measures: levels of alkaline phosphatase (68 U per liter), alanine aminotransferase (105 U per liter), aspartate aminotransferase (77 U per liter), and lactate dehydrogenase (465 U per liter) for hospitalized patients.

Treatment Guideline Scenario 3: Interferon Alpha-2B is an antiviral or antineoplastic drugs (BID, atomization inhalation), Lopinavir plus ritonavir (0.5 g BID, orally) as antiviral therapy and also moxifloxacin (400 mg once daily, in IV form) to prevent secondary infection; in case of serious shortness of breathing and hypoxia methylprednisolone (80 mg BID, in IV form).

Treatment Guideline Scenario 4: Oseltamivir therapy and along with oxygen therapy. Treatment Guideline scenario 5: Blood plasma from recovered patients could help treat the new coronavirus affected patients. Because recovered patient's blood plasma contain specific antibody that could destroy the coronavirus. Treatment Guideline scenario 6: Bruce Aylward, an assistant director-general of the World Health Organization (WHO) said at a press conference they found in lab experiments, remdesivir blocks the activity of the new coronavirus in cells. It's also effective against MERS and SARS, which are also coronaviruses, in cells.

Along with the above treatment laboratory analysis of a complete blood count such as RBC, WBC, hemoglobin, serum ferritin, hematocrit and platelets etc., blood chemical analysis, coagulation factors testing, assessment of liver functions and renal function, and measures of electrolytes balance, C-reactive protein, procalcitonin, lactate dehydrogenase, and creatine kinase are carried out [41].

At present different top pharmaceutical companies are trying to develop new vaccine against COVID-19 [42].

Results and Discussion

It is considered that this virus first transmitted from the animal. In the case of SARS and this coronavirus outbreak, bats were considered the original hosts of the coronavirus. They then infected other animals via their poop or saliva, and the unwitting intermediaries transmitted the virus to humans [43]. For diagnosis and detection of the COVID-19 at present CT scan, immune identification technology (Point-of-care Testing (POCT) of IgM/IgG, Enzyme-linked Immunosorbent Assay (ELISA)) and RT-PCR (Nucleic acid detection) are used by the maximum healthcare institute and by the Hospital.

We found some common complications from coronavirus infected

patients. Those are difficulties in breathing, fever, rhinorrhoea, myalgia, cough, dyspnoea, chest pain, or diarrhoea. Yet now no specific out come from the treatment we can't get that the infected patients have been curried by the treatment. Globally different healthcare based organization till now trying to disclose new treatment guidelines for the COVID-19. Recent a data published they said that transfusions of blood products containing antibody obtained from survivors have contributed to a 50% reduction in death among severely ill patients [44,45].

The major pathogenesis of COVID-19 as a respiratory system attacking virus was extreme pneumonia and damages the alveoli of the lung that is responsible for Oxygen (O_2) and Carbon-di-Oxide (CO_2), RNAaemia, combined with ground-glass opacity incidence, and acute cardiac injury [46,47].

Conclusion

The diagnosis of the disease was complicated at the time of the initial phase of coronavirus outbreak because of verities of symptoms and no specific diagnosis testing procedure and also treatment against the virus. The term COVID-19 has been introduced to patients without clear radiological sings who have laboratory confirmed symptomatic cases. Better understanding of the disease spectrum is needed as SARS-CoV-2 infection was observed in 8.9% of patients before developing viral pneumonia or viral pneumonia. In accordance with earlier studies, we observed that COVID-19's clinical properties resemble those of SARS-CoV. The main symptoms were fever, cough, alveolar damage, breathing problem, desquamation of pneumocystis and also hyaline membrane formation and GI symptoms were rare, indicating a disparity in viral tropism relative to SARS-CoV, MERS-CoV and periodic or seasonal influenza. Now scientists disclose the genetic sequences of the COVID-19, we think these genetic sequences will help to identify the origin of the virus. At present there are no specific treatment procedures to control the coronavirus but antivirus drugs are using to control this contagious disease. Our findings reports will help the general peoples and also physician to understand the disease pattern. Transmission patterns, treatment scenario, pathogenesis and genetic sequences of the coronavirus.

Conflict of Interest

The corresponding authors declare the review was conducted without any financial supports from any persons or institute. The authors also declare that they have no conflict of interests with the other Co-authors.

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