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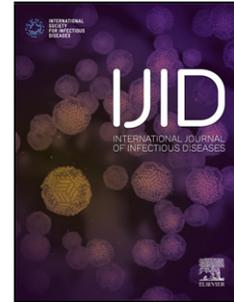
The SARS-CoV-2 Outbreak: What We Know

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Highlights

- the latest summary of the COVID-19 outbreak in China;
- there might be an oral-fecal transmission of the virus;
- aggregates and consolidates the epidemiology, clinical manifestations, diagnosis, treatments and preventions of this new type of coronavirus.

Abstract

There is a current worldwide outbreak of the novel coronavirus Covid-19 (coronavirus disease 2019; the pathogen called SARS-CoV-2; previously 2019-nCoV), which originated from Wuhan in China and has now spread to 6 continents including 66 countries, as of 24:00 on March 2, 2020. Governments are under increased pressure to stop the outbreak spiraling into a global health emergency. At this stage, preparedness, transparency, and sharing of information are crucial to risk assessments and beginning outbreak control activities. This information should include reports from outbreak site and from laboratories supporting the investigation. This paper aggregates and consolidates the epidemiology, clinical manifestations, diagnosis, treatments and preventions of this new type of coronavirus.

Key words: coronavirus; SARS-CoV-2; CoVID-19; Epidemiology; Clinical features; Diagnosis; Treatments; Managements strategies

Introduction

Coronaviruses (CoVs), a large family of single-stranded RNA viruses, can infect animals and also humans, causing respiratory, gastrointestinal, hepatic, and neurologic diseases[1]. As the largest known RNA viruses, CoVs are further divided into four genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus and delta-coronavirus[2]. To date, there have six human coronaviruses (HCoVs) been identified, including the alpha-CoVs HCoVs-NL63 and HCoVs-229E and the beta-CoVs HCoVs-OC43, HCoVs-HKU1, severe acute respiratory syndrome-CoV (SARS-CoV)[3], and Middle East respiratory syndrome-CoV (MERS-CoV)[4]. New coronaviruses appear to emerge periodically in humans, mainly due to the high prevalence and wide distribution of coronaviruses, the large genetic diversity and frequent recombination of

their genomes, and the increasing of the human-animal interface activities[5, 6].

In late December 2019, a number of local health authorities reported clusters of patients with pneumonia of unknown cause, which were epidemiologically linked to a seafood market in Wuhan, Hubei Province, China[5] The pathogen, a novel coronavirus (SARS-CoV-2), was identified by local hospitals using a surveillance mechanism for "pneumonia of unknown etiology" that was established in the wake of the 2003 SARS outbreak with the aim of allowing timely identification of novel pathogens[5, 7]. On 30 January 2020, the World Health Organization (WHO) declared that CoVID-19 is a "public-health emergency of international concern"[8]. The pandemic is escalating rapidly. We searched the associated literature in CoVID-19 to summarize the epidemiology, clinical characteristics, diagnosis and treatments and preventions of the infection of SARS-CoV-2.

Epidemiology

Scope of the CoVID-19 infection outbreak

Since December 2019, multiple cases occurring unexplainable pneumonia were successively reported in some hospitals in Wuhan city with a history of exposure to a large seafood market in Wuhan city, Hubei province, China. It has been confirmed to be an acute respiratory infection caused by a novel coronavirus. So far, this disease has rapidly spread from Wuhan to China's other areas, and 66 countries. And then, clustered cases and confirmed cases without a history of travel to Wuhan emerged as the advancing of this disease[9]. In addition, confirmed cases without clear exposure to the seafood market of Wuhan have been spread in many foreign countries[10].

According to National Health Commission of the People`s Republic of China, as of 24:00 on March 2, 2020, a total of 80, 302 CoVID-19 cases in China have been confirmed in 31 provinces (autonomous regions and municipalities), and Xinjiang Production and Construction Crops，including Hong Kong, Macao, and Taiwan, including 2947 (3.66%) deaths. At present, there are 30, 095 confirmed cases (6, 806 severe cases), 47, 260 (58.85%) discharged cases, and 587 suspected cases were recorded. It is worth mentioning that up to now, Tibet and Qinghai provinces have no new coronavirus infected patients[11]. As of 11 February, a total of 1,715 medical workers had been infected, of which 5 had died, with a crude case fatality rate of 0.3%. The number of confirmed cases has surpassed SARS in 2003.

Internationally, confirmed cases have been reported in 66 countries and 6 continents and another Diamond Princess. Outside of China, a total of 10415 cases of CoVID-19 have been reported from 66 countries, with 168 deaths. The epidemics in the Republic of Korea, Italy, Iran and Japan have been became the greatest concern of WHO[12]. According to the European Centre for Disease Prevention and Control (ECDC)[13], the latest daily risk assessment on COVID-19, March 2, they ECDC have now considered the risk moderate to high level. The case fatality rate of the currently reported cases in China is less than 4%, which implies that so far, this novel coronavirus does not seem to cause the high fatality rates previously observed for SARS-CoV and MERS-CoV, 10% and 37%, respectively [14]. According to the latest data, a total of 36167 cases were reported in Hubei, China, that gives a cumulated attack rate (CAA) of 0.11% (the permanent resident population of Hubei is about 59, 170, 000). However, when compared to the influenza virus of pH1N1, which shared the same transmission route, have a 50 times higher CAA, this data showed the importance of the intense quarantine and social distancing measures the Huibei government have taken.

Host and reservoir

Wild animals and bats are considered as the natural reservoir hosts and play a crucial role in transmitting various viruses, including Ebola, Nipah, Coronavirus and others [6, 15]. SARS-CoV-2 is the seventh member of the family coronaviruses, which is the beta-CoV with over 70% similarity in genetic sequence to SRAS-nCoV[16]. Like SARS-CoV, MERS-CoV, and many other coronaviruses, SARS-CoV-2 likely originated in bats, but it requires further confirmation whether pneumonia infected by the SARS-CoV-2 is transmitted directly from bats or through an intermediate host[9, 17, 18].Recent research has found that the virus is 96% identical at the whole-genome level to a bat coronavirus, which means bats is the most possible host of the SARS-CoV-2[17, 18]. Also, Ji and colleagues [19] demonstrated that snack as possible virus reservoir for human infection. And Zhu et al [16] indicated that bats and minks maybe the two potential hosts of the novel coronavirus, while the minks may be the intermediate hosts of this virus. Subsequently, studies have shown that pangolins are potential intermediate hosts, but in general, intermediate hosts may have multiple hosts[20]. For many viruses, one of the key steps in the emergence process is the jump from animals to humans. Thus, identifying the source of the virus will help control its spread[18].

Route of transmission

Chan and his colleagues [21] reported a case of five patients in a family cluster, which confirmed Person-to-person transmission of CoVID-19. Health officials have identified evidence of transmission along a chain of 4 "generations" (a person who originally contracted the virus from a nonhuman source infected someone else, who infected another individual, who then infected another individual), suggesting sustained human-to-human transmission[22, 23]. Up to present, the main infection source was the patients who with pneumonia infected by the SARS-CoV-2. Respiratory droplet transmission is the main route of transmission, and it can also be transmitted through aerial droplets and contact[9]. However, we also should attach importance to asymptomatic cases which may play a critical role in the transmission process[24]. Recently, new coronavirus was detected in the feces of confirmed patients in Wuhan, Shenzhen and even the first case in the United States, indicating that the virus can replicate in the digestive tract and exist, suggesting the possibility of fecal-oral transmission[25], but it is not certain that eating virus-contaminated food causes infection and transmission. There were also views that viruses in feces may be re-transmitted by aerosol formation of virus-containing droplets, requiring further investigation. At present, there is no evidence for aerosol transmission of CoVID-19. WHO also believes that further evidence is needed to assess the possibility of aerosol transmission[23]. In addition, it has been reported that the mother was diagnosed with a new type of coronavirus pneumonia, and the newborn was positive for viral nucleic acid in pharynx swabs after 30 hours of birth[26], suggesting that the new type of coronavirus may cause neonatal infection through mother-to-child transmission, which of course needs to be confirmed by more scientific studies[27].

WHO has published their estimation of R_0 to be 2.0-2.5 using early information[28]. Li *et al.*[7] analyzed data on the first 425 confirmed cases in Wuhan and found that the R_0 to be 2.2, without specifying their modelling method Jonathan Read and his colleagues[16] from Lancaster University who used a deterministic Susceptible-Exposed-Infected-Recovered (SEIR) metapopulation transmission model to determine the R_0 to be around 3.1. Majumder and his colleagues[29] used Incidence Decay and Exponential Adjustment (IDEA) model to estimate the R_0 to be 2.0-3.3 (The study did not published yet, available at SSRN). Recently, a large group of researchers from multiple institutes led by Jianhong Wu from York University[30] proposed a more general

deterministic SEIR compartmental model using more parameters, and arrived at a much higher R_0 number of 6.47. A recent research[31] on the Diamond Princess cruise ship outbreak, at a loosen intervention and quarantine condition, showed the R_0 was 2.28, and if reduce the R_0 by 25% and 50%, the estimated cumulative cases would be reduce from 1514 to 1081 and 758, also proved that intense quarantine and social distancing measures should be taken to control the outbreak. While Estimates from the SARS-CoV outbreak in 2003 reported an R_0 of 3[32], which means SRAS-CoV-2 has a similar ability to spread as SRAS-CoV, or higher spreading ability than SRAS-CoV, so that the SARS-COV-2 outbreak caused more than 90000 cases in 66 countries all over the world in less than 2 months, that's times of the SARS-COV outbreak[33, 34].

Clinical manifestations

A wide range of clinical manifestations are seen in patients with SARS-CoV-2 from mild, moderate, to severe and rapidly progressive and fulminant disease. And most of the patients with SARS-CoV-2 were normal and mild, and their mortality was lower than SARS-CoV and MERS-CoV.

Incubation Period

In recent publications, the mean incubation period of CoVID-19 was a little bit different. Wang et al, with 138 cases, reported that the median durations from first symptoms to dyspnea, hospital admission, and Acute severe respiratory syndrome (ARDS) were 5 days (range, 1-10), 7 days (range, 4-8), and 8 days (range, 6-12), respectively[35]. And Li et al, with 425 confirmed cases, instructed that the mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days. In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproductive number was estimated to be 2.2 (95% CI, 1.4 to 3.9)[7]. While Guan et al[36] , with 1099 patients, reported that the estimated mean incubation period of SARS-CoV-2 infection was 3.0 days (range, 0 to 24.0), which was shorter than the two researches above (3.0 days vs 5 days and 5.2 days). The median incubation period of CoVID-19 ARD was 3.0 days and it had a relatively lower fatality rate than SARS and MERS[35]. While the estimated mean incubation period of SARS-CoV infection was 4.6 days (95% CI, 3.8–5.8 days)[37] and 95% of illness onset occurred within 10 days[38]. The mean time from symptom onset to hospitalization was between 2 and 8 days, but was shorter toward the later phase of the epidemic. The mean time from symptom onset to need for invasive mechanical ventilation (IMV) and to death was 11 and 23.7 days, respectively[39].

Symptoms

Symptom of CoVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death A study of 41 patients[14] who were initially diagnosed with the outbreak (the diagnosis date was up to 2 January) found that the most common symptoms were fever (98%), cough (76%), myalgia or fatigue (44%), and atypical symptoms included sputum (28%), headache (8%), hemoptysis (5%) and diarrhea (3%). About half of the patients had dyspnea (the median from onset to dyspnea was 8 days). Lymphocytopenia was observed in 63% of patients. All patients had pneumonia. Complications included acute respiratory distress syndrome (29%), acute heart injury (12%), and secondary infections (10%); 32% of patients require to be treated in the ICU. An analysis of 1099 confirmed cases (up to 29 January)

conducted by NanShan Zhong's team[40], found that the most common symptoms were fever (87.9%) and cough (67.7%), diarrhea (3.7%) and vomiting (5.0%). 25.2% of the patients had at least one underlying disease (such as hypertension, chronic obstructive pulmonary disease). Lymphocytopenia was observed in 82.1% of patients. On admission, 50% of the patients presented ground-glass shadow on chest CT. A retrospective study[35] of 138 hospitalized patients from January 1 to 28 found that patients receiving treatment in the ICU were older, more likely to have underlying diseases, and more likely to have dyspnea, and the median length of stay was 10 days [35]. Recent studies indicate that patients≥60 years of age are at higher risk than children who might be less likely to become infected or, if so, may show milder symptoms or even asymptomatic infection[7]. Epidemiology Working Group for NCIP Epidemic Response of the Chinese Center for Disease Control and Prevention[41], with a total of 72314 patients, reported that there were 44672 (61.8%) confirmed cases, and 889 asymptomatic cases (1.2%) among the total number of the patients. Among confirmed cases, most were aged 30-79 years (86.6%), and considered mild/mild pneumonia (80.9%).

Diagnosis

Clinical Diagnosis

The SARS-CoV-2 infected cases have symptoms like fever, fatigue, dry cough, dyspnea etc., with or without nasal congestion, runny nose or other upper respiratory symptoms[1, 25]. Despite the atypical symptoms were reported, Guan *et al.*[40] pointed out that fever is still the typical symptom of SARS-CoV-2 infection.

a) Physical examination

Patients with mild symptoms may not be present positive signs. Patients in severe condition may have shortness of breath, moist rales in lungs, weakened breath sounds, dullness in percussion, and increased or decreased tactile speech tremor, etc.

b) CT imaging examination

The imaging finding vary with the patient`s age, immunity status, disease stage at the time of scanning, underlying diseases, and drug interventions.

Chest X-ray examination In the early stage of pneumonia cases, chest images show multiple small patchy shadows and interstitial changes[14], remarkable in the lung periphery[21]. Severe cases can further develop to bilateral multiple ground-glass opacity, infiltrating shadows, and pulmonary consolidation, with infrequent pleural effusion. While *Chest CT scan* Pulmonary lesions are shown more clearly by CT than *X-ray examination*, including ground-glass opacity and segmental consolidation in bilateral lungs, especially in the lung periphery. In children with severe infection, multiple lobar lesions may be present in both lungs. A study of CT scans of 21 patients with SARS-CoV-2 infection showed that three (21%) with normal CT scans, 12 (57%) with ground-glass opacity only, and six (29%) with ground-glass opacity and consolidation at presentation[42] Another study of 41 patients with confirmed SARS-CoV-2 infection was reported to have bilateral lung involvement on chest radiographs[14]. Overall, the imaging findings reported for CoVID-19 are similar to those reported with SARS[43, 44] and MERS[45, 46], not surprising as the responsible viruses are also coronaviruses.

Laboratory Diagnosis

It mainly should be distinguished from other known viral virus of pneumonia, such as influenza viruses, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, SARS-CoV, etc.;

and also, from mycoplasma pneumonia, chlamydia pneumonia, and bacterial pneumonia. In addition, it should be distinguished from non-infectious diseases, such as vasculitis, dermatomyositis, and organizing pneumonia[9]. So, laboratory diagnosis is necessary. Identification of CoVID-19 mainly includes virus isolation and viral nucleic acid detection. According to the traditional Koch`s postulates, virus isolation is the "gold standard" for virus diagnosis in the laboratory[47] A variety of specimens (such as swabs, nasal swabs, nasopharynx or trachea extracts, sputum or lung tissue, blood and feces) should be retained for testing in timely manner, which gives a higher rate of positive detection of lower respiratory tract specimens[47].

Viral nucleic acids can also be used for early diagnosis, which is the most important thing. So, we should detect SARS-CoV-2 nucleic acid: accurate RNA detection of SARS-CoV-2 is with diagnostic value[47]. The full gene sequence of SARS-CoV-2 has now been obtained and samples can be collected from the upper respiratory tract (oropharyngeal and nasopharyngeal) and lower respiratory tract (endotracheal aspirate, expectorated sputum, or bronchoalveolar lavage) of patients suspected SARS-CoV-2 infection for diagnosis by real time RT-PCR method[48] Also, in the early stage of the disease, the total number of leukocytes decreased or keeps normal, with decreased lymphocyte count or increased or normal monocytes also indicated the diagnosis of CoVID-19[9].

Treatments and Preventions

At present, there is no vaccine or antiviral treatment for human and animal coronavirus, so that identifying the drug treatment options as soon as possible is critical for the response to the CoVID-19 outbreak. WHO has announced that a vaccine for SARS-CoV-2 should be available in 18 months, but achieving this will require funding and public interest to be maintained even if the threat level falls[49]. The mainstay of clinical management is largely symptomatic treatment, with organ support in intensive care for seriously ill patients[50].

The general strategies include bed rest and supportive treatment, including antiviral therapy [51], antibioics application, immunomodulating therapy[52], organ function support, respiratory support, bronchoalveolar lavage (BAL), blood purification and extracorporeal membrane oxygenation (ECMO)[53].

Novel coronavirus infection is a new communicable disease with an emergent outbreak that affects all populations[54]. SARS-CoV-2 infection has been classified as category B infectious disease legally but managed as category A infectious disease by Chinese government. It is paramount to implement infection control practices by infection source controlling, transmission route blocking, and susceptible population protection. The unprecedented flurry of activity by WHO and other global public health bodies has mainly focused on preventing transmission, infection control measures, and screening of travelers[50].

Conclusions

How easily the virus is transmitted between persons, and how it affects individual persons and potentially vulnerable population subgroups, such as the elderly or those with chronic health conditions? What is the source of the virus? And how can it spread around the world in such a short time? At the moment, we know relatively little about CoVID-19, except that it is a highly pathogenic human pathogen, possibly a zoonotic agent. Now that a pandemic has occurred, it is critical that countries around the world take steps to stop transmission and save lives. In addition,

we should actively study its origin, tropism, and pathogenesis with the aim of providing some guidance in dealing with this rapidly spreading epidemic. Challenges remain in several key areas, including the recent cases of people who have tested positive for the virus. Can these cured patients be transmitted to others? All these suggest that we should develop more detailed criteria for the prevention and control of the virus, and more stringent criteria for discharge of patients after treatment.

Contributors

All authors contributed to the conception of the Review. Di Wu, Tiantian Wu and Qun Liu contributed the literature search, data traction and data synthesis, created the tables, and wrote the manuscript. All authors contributed to the interpretation of the data and revision of the manuscript.

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Ethical Approval

None.

Conflicts of interests

We declare no conflicts interests.

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