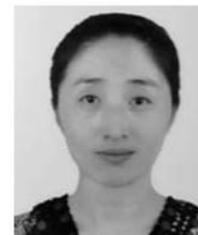


## PERSPECTIVE IN MEDICINAL CHEMISTRY

# Epidemiological Features of the 2019 Novel Coronavirus Outbreak in China

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**Abstract:** The fast-growing outbreak of the 2019 novel coronavirus (2019-nCoV), which originated from Wuhan locating in central China at the end of 2019, spread to multiple cities in merely a month. Although the mortality of this disease was lower than that of SARS, the incredible contagiousness was much higher than SRAS-CoV. Because of the tremendous clout of 2019-nCoV, it is essential to hold more details about it and monitor its future evolution. This mini review consequently summarizes the key elements of epidemiology features, providing updated relevant findings and novel insights related to 2019-nCoV.

**Keywords:** 2019 Novel Coronavirus (2019-nCoV), COVID-19, Epidemiology, Demographic features, Pathogenic molecular mechanism.

## 1. INTRODUCTION

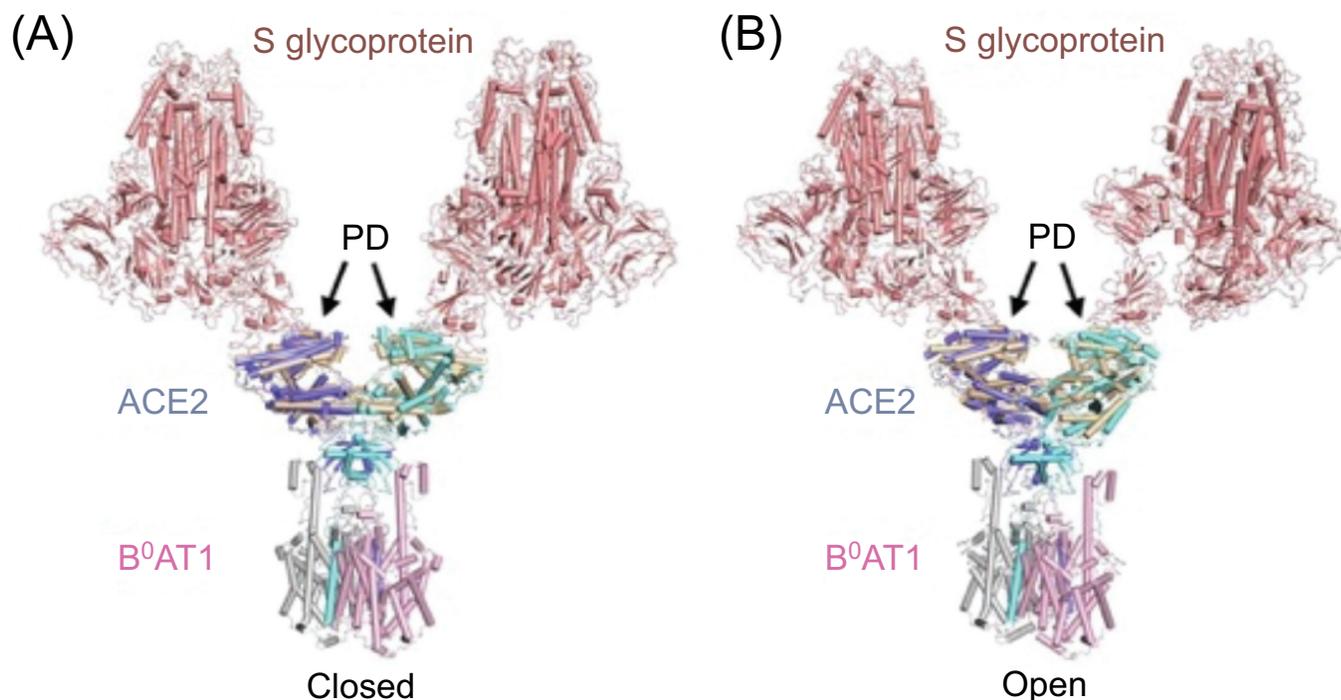
The 2019 novel coronavirus (2019-nCoV)-associated pneumonia (abbreviated as COVID-19) is currently raging in the world. The majority of the earliest cases were linked to the Huanan Seafood Wholesale Market in Wuhan city and the patients could have been infected through zoonotic or environmental exposures. However, the increasing number of cases were detected outside Wuhan without direct contact or exposure, together with the detection of infection in household cluster cases reported in *The Lancet* and the accumulating infections in health-care workers caring for patients with 2019-nCoV indicate human-to-human transmission. By 3 May, 2020, a total of 82880 confirmed cases, 4633 fatal cases have been identified in China, and there were more than 3 million confirmed cases in 211 countries and regions around the world, with a cumulative death of more than 210,000 cases. Though it appeared that the fatality rate of 2019-nCoV was lower than that of SARA-CoV and MERS-CoV, it served as the third coronavirus to emerge in the human population in the past two decades with an alarming rate of transmission, has put global public health institutions on high vigilance. On Jan 30, 2020, the World Health Organization (WHO) declared it to be a Public Health Emergency of International Concern. Shortly thereafter, WHO made the assessment that it can be characterized as a pandemic.

## 2. THE MOLECULAR STRUCTURE AND RECEPTOR OF 2019-nCoV

2019-nCoV is one type of zoonotic coronaviruses belonging to  $\beta$ -coronavirus cluster. The largest scale genetic analyses lately indicated that 2019-nCoV had evolved into two major types (designated L and S), and they differed in geographical distribution and proportion of the population. What is more, they could have great divergence at transmission and pathogenicity as well [1]. The homology between 2019-nCoV and bat coronavirus at the genetic level reached 90%, indicating that the virus is very likely to come from bats [2]. However, on the basis of current data, the origin of 2019-nCoV is still needed to be confirmed. What we are sure of was the spike glycoprotein (S glycoprotein) of 2019-nCoV on the virion surface mediates receptor recognition and membrane fusion via ACE2 (Angiotensin-converting enzyme), similar to SARS-CoV. S glycoprotein of 2019-nCoV has a part of the amino acid residue which has changed significantly compared with SARS-CoV, causing the affinity between ACE2 and the RBD (receptor binding domain in ACE2) of 2019-nCoV is more than 10 times higher than that with the RBD of SARS-CoV, which accounted for the quite effectively transmission of it. Furthermore, as the coronavirus, S glycoprotein is surface-exposed and mediates entry into host cells, and is the main target of neutralizing antibodies upon infection and the focus of therapeutic and vaccine design.

The team of Zhou obtained the complex of ACE2 with a transporter BOAT1 in the intestinal tract through co-expression, because ACE2, as a membrane protein, is difficult to obtain stably *in vitro*, and analyzed its three-dimensional structure using cryo-electron microscope platform. The complex exists as a dimer, with “open” and “closed” conformations following the transfer of the peptidase domain (PD) (Fig. 1).

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**Fig. (1).** Overall structure of the ACE2-B<sup>0</sup>AT1 complex [3]. (A) The complex existing as a dimer could combine two S glycoprotein simultaneously. (B) is same to (A), but with the open conformation.

### 3. THE PATHOPHYSIOLOGICAL PATHOGENESIS OF 2019-nCoV

ACE2 is mainly expressed in the epithelium of small intestine, blood vessel, especially in the main targeted organ lung, correlating to clinical features of patients. About the severe lung damage of new coronary pneumonia, some scholars put forward the theory of "cytokine storm" to explain the sudden aggravation. Actually, "cytokine storm" was a calling designed for immune system to respond quickly, but also causing damage to the body, including vessels and organ tissues, increasing vascular permeability with leakage of plasma, especially in lung. The immune response also triggers the release of nitric oxide, which further dilutes blood and destroys vessels. All factors contribute to the hypotension of dangerous levels, hypoxia of tissue and multi-organ dysfunction. Innated and acquired immune responses enable containment of virus in most of the patients with mild disease, while cytokine dysregulation, viral cytopathic effect, abnormal immune response and autoimmune mechanism may lead to more severe disease and death. Therefore, "cytokine storm" was regarded as the main pathophysiological pathogenesis of 2019-nCoV [4].

### 4. THE CLINICAL FEATURES OF 2019-nCoV

According to 1099 cases reported by Guan *et al.*, most of the cases manifested symptoms of fever (87.9%) and cough (67.7%) in 4-5 days after infection (The median incubation was 4 days, range from 1 to 21 days). Nevertheless, the rate of infection without fever was notably higher than that of SARS (1%) or MERS (2%), therefore, only focus on the fever status about suspected cases would lead to a missed diagnosis. In addition, it was common that patient was admitted with an abnormality on chest X-ray. 76.4 % of 840 cases statistics showed signs of pneumonia, 59% were ground-glass opacity and 46% had bilateral patchy shadows and 82.1% had lymphopenia, and 36.2% had thrombocytopenia. The severity of the disease is related to the viral load and immune function of human body. Most patients recovered by the autoimmune function, only a few patients were seriously ill or died [5].

### 5. DEMOGRAPHIC FEATURES OF 2019-nCoV PATIENTS

Highest incidence was observed among adults  $\geq 60$  years. According to the research of CDC, including 72314 cases, 30-79 years old patients dominated confirmed cases. This age group occupied 89.9% confirmed cases in Wuhan, 88.6% in Hubei province and 86.6% in the entire country [6]. A similar age distribution was observed in the suspected patient. However, age-gender pattern differed between Wuhan, the source of the outbreak, and other regions. The high incidence of subpopulation outside Wuhan tended to be younger than that in Wuhan.

Overall, males (51.4%) experienced a higher incidence than females. The higher prevalence of ACE2 receptors, to which the virus binds, in the lungs of Asian males could have contributed to this gender difference. Significant gender difference was only found outside Wuhan [6]. However, Guan, *et al.* [5], did not observe a significant statistical difference in gender ( $P>0.05$ ).

Furthermore, patients diagnosed with severe pneumonia were significantly older, and had a higher proportion of males, in comparison to those with mild pneumonia and non-pneumonia. Notably, those patients with underlying diseases have significantly higher risk of severe pneumonia and negative outcome. According to 1099 cases reported by Guan, *et al.*, 25.2% of patients had at least one underlying disease (such as hypertension, and chronic obstructive pulmonary disease), 15.74% (173/1099) of patients were critically ill, potential complications were significantly more common in severe cases [5]. Conversely, children might be less likely to become infected or, if infected, may show milder symptoms.

## 6. THE TRANSMISSIBILITY AND MORTALITY OF 2019-nCoV

It is obvious that this outbreak spreaded *via* “human to human” transmission and almost everyone was susceptible to be infected, whether there was an opportunity to be infected again for the people rescued from 2019-nCoV remains unknown. The ratio of asymptomatic infected cases was not clear yet. But, it was relatively rare and was not the main driver of transmission in China. Epidemiological investigations show that most medical staff may be infected within the family instead of hospital, what’s more, infected medical workers were rarely seen outside Wuhan. So far, there were no reports about super-spread event in any medical institution. Hence, nosocomial transmission was not the characteristic of propagation of 2019-nCoV in China.

The transmissibility of 2019-nCoV is quite effective. The number of infectious cases shed an exponential growth in the past few weeks. Since the outbreak occurred, several groups devoted to the estimates of the basic reproduction number ( $R_0$ ).  $R_0$  is an index that reflects the ability of the virus to transmit, defined as the average number of secondary infections can generate in a fully susceptible population. The  $R_0$  value of the 2019-nCoV was blocked between 2.0 and 4.0. An estimate of  $R_0=2.0$  based on 425 early reported patients is likely an underestimation given the serious delay in case confirmation during the early phase [7]. Subsequently, a study of a family cluster published on January 24, 2020 in *The Lancet*, showed estimated  $R_0$  value 3.6 to 4.0 [8]. On January 31, a modeling study in *The Lancet*, estimating the  $R_0$  value to be 2.68 [9]. The latest study which showed estimated  $R_0$  value obtained from mathematical modeling study using five independent methods was 3.39 [10]. No matter which, it was a very high number indicative of a very fast rate of spread. Additionally, the routes of transmission might have contributed considerably to the rapid spread of 2019-nCoV. Conventional routes of transmission of SARS-CoV, MERS-CoV and highly pathogenic influenza consisted of the respiratory droplets and direct contact. However, according to Zhong’s pilot experiment, fomites transmission might have played a role in the rapid transmission of 2019-nCoV [5]. What is worse, the ability to transmit through lacrisert or aerosol produced from medical intervention required to be further surveyed, and equal protection should be taken into account.

Although 2019-nCoV is highly contagious, the mortality of it was relatively low. Most cases were admitted as mild subgroup and normal subgroup which would be rescued ultimately, around 20% cases were severe subgroup, with high risk of ARDS, multi-organ dysfunction and death. Besides, the 80-year-old group had the higher risk, as well as the group with underlying complications, such as diabetes, cardiovascular diseases, chronic respiratory diseases, and so on. Collectively, the pathogenicity of 2019-nCoV appeared to be relatively mild. Among 44672 confirmed cases, a total of 1023 fatal cases indicated the crude case fatality rate (CFR) of 3.3%. The largest scale survey of 72314 cases estimated overall adjusted CFR to be 2.3%. No matter which, it was lower than those of SARS-CoV (9.2%) [11] and MERS-CoV (34.4%) [12]. Nonetheless, this rate would make it many times more severe than typical seasonal influenza, putting it somewhere between the 1957 influenza pandemic (0.6%) and the 1918 influenza pandemic (2%).

## 7. DEVELOPMENT OF TREATMENT AND THE CONTROL MEASURES OF 2019-nCoV IN CHINA

It is expected that serum antibodies from cured patients and traditional Chinese medicine will work against 2019-nCoV. Biomedical researchers are initiating countermeasure development for 2019-nCoV using SARS-CoV and MERS-CoV as prototypes. Broad-spectrum antivirals, such as remdesivir, have shown promise against MERS-CoV in animal models and are being assessed for 2019-nCoV. Additionally, more than 70 promising vaccine candidates were developed in the past few months, and up to 6 promising vaccine candidates had already entered clinical trials. Drawing on libraries of compounds that have already been tested for other epidemic and applying new screening technique including machine learning accelerated drug discovery. However, presently, none of specific drugs or vaccines against 2019-nCoV have proven effective through clinical phase trials.

Comprehensive nonpharmaceutical interventions have been taken by China to effectively avoid the spread of the virus and mitigate the impact of it, providing an important experience for the global response to 2019-nCoV. Greatly progress was made by China in this outbreak, including the improving epidemic information monitoring, promptly isolation and treatment of infectious sources, speeding up the standard of suspected cases, close contact managements, highly focusing on the prevention of the central of concentrated outbreaks and nosocomial infections, strengthening community prevention and control. Of which, source-tracing and isolation of close contacts for 14 days are productive and medical treatment for free. It is an important tool to accomplish timely reporting of infectious sources and effective application of control measures. Thanks to the effective prevention and control measures taken by the Chinese government and endeavors from all sectors of society, the epidemic situation of 2019-nCoV in China has been leveled off.

However, 2019-nCoV pandemic is far from over, and many countries are still in the early stages of the outbreak. What's worse, the virus will persist for a long time and is prone to relapse. The specific vaccine may be the only feasible way to end the epidemic. The world needs to accelerate work on treatments and vaccines of 2019-nCoV. Besides driving international collaboration, data sharing, giving aids to those countries severely suffering from 2019-nCoV and helping some African, Asian and Latin American countries get ready are crucial to save lives and slow the global circulation of the virus.

We should pay great respect to all people, especially doctors and nurses who are fighting in the front line of such epidemic situation as well as the struggling scientists. Deep thanks to all our compatriots, overseas Chinese and all the friends of the global villages that have helped us fight against the epidemic situation.

## CONSENT FOR PUBLICATION

Not applicable.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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