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# Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures

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## Abstract:

By Feb 27<sup>th</sup>, 2020, the outbreak of COVID-19 caused 82623 confirmed cases and 2858 deaths globally, more than Severe Acute Respiratory Syndrome (SARS) (8273 cases, 775 deaths) and Middle East Respiratory Syndrome (MERS) (1139 cases, 431 deaths) caused in 2003 and 2013 respectively. COVID-19 has spread to 46 countries internationally. Total fatality rate of COVID-19 is estimated at 3.46% by far based on published data from Chinese Center for Disease Control and Prevention (China CDC). Average incubation period of COVID-19 is around 6.4 days, ranges from 0-24 days. The basic reproductive number ( $R_0$ ) of COVID-19 ranges from 2-3.5 at the early phase regardless of different prediction models, which is higher than SARS and MERS. A study from China CDC showed majority of patients (80.9%) were considered asymptomatic or mild pneumonia but released large amounts of viruses at the early phase of infection, which posed enormous challenges for containing the spread of COVID-19. Nosocomial transmission was another severe problem. 3019 health workers were infected by Feb 12, 2020, which accounted for 3.83% of total number of infections, and extremely

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burdened the health system, especially in Wuhan. Limited epidemiological and clinical data suggest that the disease spectrum of COVID-19 may differ from SARS or MERS. We summarize latest literatures on genetic, epidemiological, and clinical features of COVID-19 in comparison to SARS and MERS and emphasize special measures on diagnosis and potential interventions. This review will improve our understanding of the unique features of COVID-19 and enhance our control measures in the future.

**Keywords:** COVID-19, features, diagnosis and interventions

**Running title:** Unique epidemiological and clinical features of COVID-19

## 1. Introduction

In December of 2019, a cluster of patients with pneumonia of unknown cause was observed in Wuhan, China. A novel coronavirus was identified as the causative pathogen<sup>1-6</sup>, provisionally named as 2019 novel coronavirus (2019-nCoV) by the World Health Organization (WHO). On Feb 11, 2020, WHO named this novel coronavirus pneumonia as “COVID-19” (Corona Virus Disease 2019). Based on phylogeny, taxonomy, and established practice, the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses formally recognizes this virus as a sister to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and renamed it as SARS-CoV-2<sup>7</sup>. SARS-CoV-2 belongs to species of Severe Acute Respiratory Syndrome related Coronavirus (SARSr-CoV) and genus Betacoronavirus<sup>2</sup>. COVID-19 rapidly triggered a global health emergency alert and spread to 46 countries by Feb 27<sup>th</sup>, 2020. SARS-CoV-2 is the seventh member of the family of coronaviruses that infects humans. Like SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), SARS-CoV-2 is responsible for lower respiratory infection and can cause Acute Respiratory Distress Syndromes (ARDS). Other human coronaviruses (HCoV 229E, NL63, OC43, and HKU1) are responsible for upper respiratory infections and common cold<sup>8</sup>.

By Feb 27<sup>th</sup>, 2020, according to open data from China CDC as shown in table 1 and Fig 1, COVID-19 has caused 82623 confirmed cases and 2858 deaths globally. Total case fatality rate is 3.46% as showed in table 1. Because COVID-19 started from Wuhan, the capital city of Hubei province with a large population of nearly 14 million people, 58.3% cases are in Wuhan. 1932 health workers have been infected in Wuhan alone<sup>9</sup>, which overwhelmed the local health system and resulted in the highest case fatality rate (4.42 %). Excluding Hubei province, the rest of China has 13045 cases, 109 fatalities (0.84%). Outside of China, COVID-19

has spread to 46 countries and has caused 3664 infections and 67 fatalities (1.83%). Overall, case fatality rate of COVID-19 so far is much lower than either SARS (9.6%) or MERS (34.5%)<sup>10</sup>. Here we summarized common and discrete features of SARS-CoV-2 in comparison to its two predecessors (SARS-CoV and MERS-CoV) in genetics, epidemiology, clinical features, and further discussed challenges for diagnosis and special control measures for COVID-19.

## 2. Genetic biology of SARS-CoV-2

Full-length genome sequences of SARS-CoV-2 were obtained from early infected individuals related to a wild animal market in Wuhan by different research groups through next generation sequencing<sup>1,2,11</sup>. Full genomic length of this novel coronavirus ranges from 29891 to 29903 nucleotides (nt)<sup>2,4</sup>. All viral genome sequences obtained are extremely similar, showing more than 99.98% sequence identity. SARS-CoV-2 is 96.2% identical at the whole-genome level to a bat coronavirus isolate RaTG13 (GISAID accession no.EPI\_ISL\_402131) collected from Yunnan province, China, and is 88% identical to two bat-derived SARS-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, collected in 2018 in Zhoushan, eastern China<sup>1,2,11</sup>. The close phylogenetic relationship to RaTG13 suggests bats are probably natural hosts for SARS-CoV-2<sup>2</sup>. Human SARS-CoV-2 have a unique RRAR motif in the spike protein which is not found in coronaviruses isolated from pangolins, suggesting SARS-CoV-2 may not come directly from pangolins<sup>12</sup>. An evolutionary study<sup>13</sup> based on 86 genomic sequences from GISAID (<https://www.gisaid.org/>) showed three deletions were found in isolates from Japan, USA, and Australia, ninety-three mutations found over the entire genomes. Of note, eight mutations were found in the spike surface glycoprotein, especially three mutations (D<sup>354</sup>, Y<sup>364</sup>, and F<sup>367</sup>) located in the spike surface glycoprotein receptor-binding domain, which suggested SARS-CoV-2 may rapidly evolve to evade immune response and adapt to other hosts in the future.

SARS-CoV-2 share 79% nt sequence identity to SARS-CoV and around 50% to MERS-CoV<sup>2</sup>. However, the seven conserved replicase domains in ORF1ab (used for CoV species classification) of SARS-CoV-2 are 94.6% identical to SARS-CoV, implying the two belong to same species<sup>1,2</sup>. The receptor binding protein spike (S) gene of SARS-CoV-2 is highly divergent to all previously described SARS-CoVs with less than 75% nt sequence identity to except a 93.1% nt identity to RaTG13. Homology modelling revealed SARS-CoV-2 had a similar receptor-binding domain structure to that of SARS-CoV<sup>11</sup>. Further study showed SARS-CoV-2 uses the same cell entry receptor, ACE2, as SARS-CoV, not CD26 as MERS-CoV<sup>2</sup>. Structural analysis by Cryo-EM revealed SARS-CoVs protein binds ACE2 with 10-20 folds

higher affinity than SARS-CoV<sup>14</sup>, which suggests that SARS-CoV-2 may be more infectious to human than SARS-CoV.

### 3. Epidemiology of COVID-19

Transmission of infectious diseases must rely on three conditions: sources of infection, routes of transmission, and susceptible hosts. As the COVID-19 continues spreading, more epidemiologic features of SARS-CoV-2 have been revealed. Based on recently published literatures, we compared transmission features of SARS-CoV-2 with SARS-CoV and MERS-CoV in table 2. All three epidemics caused by these three coronaviruses are linked to wild animal markets. SARS and MERS are defined as zoonotic disease, and transmitted by intermediated hosts (palm civets and dromedary camels respectively)<sup>11</sup>. Recent studies showed pangolins<sup>15</sup> and snakes<sup>16</sup> at wild animal markets were likely to be intermediate hosts of SARS-CoV-2.

Human-to-human transmission was considered as a major transmission mode. According to the sixth version of the guidance for diagnosis and treatments for COVID-19 issued by the National Health Commission of China, SARS-CoV-2 was transmitted through respiratory aspirates, droplets, contacts, and feces, and aerosols transmission is highly possible. Chan JF et al.<sup>6</sup> reported that six familial members got COVID-19, but none of them had contacts with Wuhan markets or animals, although two had visited a Wuhan hospital. Based on data from China CDC, 58.3% of COVID-19 cases are in Wuhan, while rest of cases are imported from Wuhan. Wuhan is the capital of China's Hubei province, with over 14 million inhabitants, and is a major transportation hub, which increases person-to-person contacts and adds to the possibility of exporting cases to other locations. The early outbreak data largely followed the exponential growth before the implementation of quarantine strategies by governments on Jan 24<sup>th</sup>, 2020. The basic reproductive values ( $R_0$ ) of COVID-19 at the early stage were calculated between 2 and 3.5, indicating that one patient could transmit the disease to two to three other people<sup>17-20</sup>, which was higher than SARS and MERS. Phylodynamic analysis based on 52 genomic sequences of SARS-CoV-2 strains sampled in different countries publicly available at GISAID showed the estimated mean evolutionary rate was  $7.8 \times 10^{-4}$  subs/site/year (range  $1.1 \times 10^{-4}$ – $15 \times 10^{-4}$ ), which was in line with that of SARS and MERS, and the mean time of the most recent common ancestor (tMRCA) was 73 days<sup>21</sup>. With enforced implementation of isolation strategies,  $R_0$  was expected to decline in coming days. The mean incubation period was around 6.4 days (ranges from 0 to 24 days)<sup>19,22</sup>.

Similar to SARS and MERS, nosocomial transmission was a severe problem to COVID-19, and even worse. A recent retrospective study<sup>9</sup> indicated that a total of 1716 health workers were infected, accounting for 3.84% of total cases. Nosocomial infections extremely burdened the health system and hindered early infected individuals from getting immediate medical supports, therefore resulting in high case fatality rate in Wuhan as shown in table 1. In Wuhan alone, 1080 health workers were infected, in return case fatality rate of Wuhan is the highest. Wang D et al.<sup>23</sup> reported that among 138 hospitalized patients with COVID-19, 41% of patients were suspected to be infected via hospital-related transmission, 26% of patients received ICU care, and mortality was 4.3%. A lot of respiratory treatments for critically ill patients are deemed as high-risk factors for nosocomial transmission, such as intubation, manual ventilation by resuscitator, noninvasive ventilation, high-flow nasal cannula, bronchoscopy examination, suction and patient transportation, etc<sup>24</sup>. Unexpectedly, a large portion of nosocomial transmissions occurred through contacts between clinicians and visitors with no or mild symptoms of COVID-19 at the early phase of this outbreak. Similarly, presymptomatic transmission occurred through familial<sup>25-27</sup> and social gatherings<sup>27</sup>, such as banquets, church activities, sports, cruise traveling, and so on.

Vertical transmission was sporadically reported in some media but not yet proved. Chen et al.<sup>28</sup> investigated nine pregnant women with COVID-19 in their third trimester who underwent caesarean section. SARS-CoV-2 was tested in the amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from six pregnant women with COVID-19 pneumonia, and got all negative results. None of the neonates has clinical signs of infection. This result suggested no intrauterine fetal infections occurred as a result of COVID-19 infection during the late stage of pregnancy. Previous studies also showed no evidence of perinatal infection of SARS-CoV or MERS-CoV during pregnancy<sup>29</sup>. However, a neonate born to a pregnant woman with COVID-19 pneumonia tested positive for SARS-CoV-2 infection 36 hr after birth at Wuhan Tongji Hospital<sup>28</sup>. It is reasonable to assume that a newborn could be infected, either in utero or perinatally, and thus newborns should be placed in isolation to avoid exposure to any source of infection.

In terms of susceptible populations, all groups were generally susceptible to COVID-19 regardless of age or gender<sup>9</sup>. Patients aged from 30 to 79 accounted for 86.6 % of all cases<sup>9</sup>. The median age of the patients was 47 years<sup>30</sup>.

Unlike SARS and MERS, patients diagnosed as COVID-19 have presented with high viral loads even when those have no fever or mild symptoms<sup>31</sup>. High titers of SARS-CoV-2 were detected in travelers who recently visited Wuhan and have no

fever or mild symptoms in the United States<sup>31</sup> and Germany<sup>32</sup> and other places<sup>33</sup>. A study showed high viral loads were detected in upper respiratory specimens of patients with COVID-19, and viral shedding pattern of patients resembles that of patients with influenza<sup>33</sup>. This suggests SARS-CoV-2 may stay around for some time like influenza viruses.

#### 4. Clinical features of COVID-19

The full spectrum of disease severity as shown in the guidelines for diagnosis and treatments for COVID-19<sup>44</sup> issued by the National Health Commission of China had been updated for 6 times by Feb 19<sup>th</sup>, 2020. COVID-19 is now classified as 4 levels based on the severity of symptoms: mild, moderate, severe, and critical. Mild patients only present mild symptoms without radiographic features. Moderate patients present with fever, respiratory symptoms, and radiographic features. Severe patients meet one of three criteria: (1) dyspnea, RR>30 times/min, (2) oxygen saturation <93% in ambient air, (3) PaO<sub>2</sub>/FiO<sub>2</sub><300 mmHg. Critical patients meet one of three criteria: (1) respiratory failure, (2) septic shock, (3) multiple organ failure. The largest epidemiology study done by China CDC<sup>9</sup> showed among 44672 confirmed cases, 86.6% of confirmed patients were aged 30-79 years, 80.9% were considered mild/common pneumonia, 13.8% were severe cases, 4.7% were critical cases. Case fatality rate for critical patients was 49%. Patients with comorbidities (cardiovascular disease, diabetes, chronic respiratory disease, hypertension, cancers) had higher case fatality rates (10.5%, 7.3%, 6.5%, 6.0%, 5.6% respectively) than those without comorbidities (0.9%). This indicated comorbidities were high risk factors for COVID-19 patients.

Clinical symptoms of severe and critical patients with COVID-19 resembled most of SARS and MERS as listed in table 3, including fever, dry cough, myalgia, fatigue, dyspnea, anorexia, diarrhea, ARDS, arrhythmia, acute kidney injury, various degrees of liver damage, and septic shock. Common symptoms of hospitalized patients with COVID-19 included fever (98.6%), fatigue (69.6%), and dry cough<sup>23,46</sup>, diarrhea<sup>47</sup>. Less common symptoms included muscle ache, confusion, headache, sore throat, rhinorrhoea, chest pain, sputum production<sup>47</sup>, and nausea and vomiting<sup>46</sup>. Severe complications included acute respiratory distress syndrome, RNAemia, acute cardiac injury, and multiple organ failure<sup>47</sup>. The median time from first symptom to dyspnea was 5.0 days, to hospital admission was 7.0 days, and to ARDS was 8.0 days<sup>23</sup>. A few patients had symptoms such as nasal congestion, runny nose, sore throat, myalgia and diarrhea<sup>44</sup>. Most patients had a good prognosis according to the guidelines for diagnosis and treatments for COVID-19<sup>44</sup>. Wang D et al.<sup>23</sup> reported that age and comorbidity may be risk factors. A recent study showed that renal damage was



caused by virus and antiviral drugs<sup>48</sup>. Meanwhile, SARS-CoV-2 might cause various degrees of liver damage<sup>49</sup> and damages in testicular tissue<sup>48</sup>. Mild patients showed only low fever, mild fatigue, and no pneumonia. Severe patients usually had dyspnea/hypoxemia one week after the onset. Critical patients could quickly progress to ARDS, shock, metabolic acidosis, coagulation dysfunction and multiple organ functional failure, etc<sup>44</sup>. Dyspnea, abdominal pain, and anorexia were also more common in critically ill patients<sup>23</sup>. It had to be noted that severe and critically ill patients might present moderate to low fever, even without obvious fever<sup>44</sup>.

Laboratory features of COVID-19 included Lymphopenia with depletion of CD4 and CD8 lymphocytes, prolonged prothrombin time, elevated lactate dehydrogenase<sup>23</sup>, elevated D-Dimer, elevated alanine transaminase, C-reactive protein, and creatinine kinase<sup>47</sup>. ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNF $\alpha$ , compared with non-ICU patients<sup>47</sup>. Patients who received ICU care had numerous laboratory abnormalities that suggested COVID-19 might be associated with cellular immune deficiency, coagulation activation, myocardia injury, hepatic injury, and kidney injury as showed in table 3. Laboratory abnormalities were similar to those previously observed in patients with MERS-CoV and SARS-CoV infection<sup>23,50</sup>. Most patients had elevated C reactive protein, erythrocyte sedimentation rate, and normal procalcitonin. In severe cases, D-dimer increased and peripheral blood lymphocytes progressively decreased. Severe and critically ill patients had elevated inflammatory factors<sup>44</sup>. In the nonsurvivors, the neutrophil count, D-dimer, blood urea, and creatinine levels continued to increase<sup>23</sup>.

X-ray and chest computed tomographic scans showed bilateral patchy shadows or ground glass opacity in the lungs of moderate and severe patients<sup>46</sup>. It had to be noted that majority of COVID-19 patients with mild/moderate symptoms can quickly transit into severe or critical statuses if without immediate care<sup>51</sup>. These virus- carriers with no or mild symptoms can fool health workers and could be huge challenges for controlling this epidemic.

## 5. Challenges for diagnosis of COVID-19

Diagnosis of COVID-19 has been facing difficulties because laboratory detections and radiographic images are not always in agreement with clinical features and contact histories of patients<sup>71</sup>. Laboratory detections included genomic sequencing, RT-PCR, and serological methods (such as Enzyme-linked immunoassay, ELISA). Additionally, because manifestations of the novel coronavirus pneumonia were diverse and changed rapidly, judging by

radiographic images for early detection and evaluation of disease severity and follow-up of patients were heavily depended on experience<sup>51</sup>. As a result, clinically suspected patients, with a history of exposure, fever, and positive findings on chest CT, had to receive rapid diagnosis with molecular technologies<sup>72</sup>.

Genomic sequencing was a way for identifying disease associated pathogens<sup>2,11</sup> at the beginning of the outbreak of COVID-19. But it was too complicated and expensive for a large scale of detections. RT-PCR methods based on spike gene and N gene developed by several companies and China CDC were widely used for detecting viral RNA, and were considered a gold standard<sup>2,11,44,73</sup>. However, this method had its limitations, such as short detection window from nasopharyngeal swabs, false sampling, cross-contamination of samples, inconsistency of sample collections and preparations.

RT-PCR methods generated false-positive or false-negative results<sup>72,74</sup>, which caused troubles for isolating sources of infections and determining hospitalization days. According to current guidelines for diagnosis and treatments for COVID-19, if one is tested by RT-PCR negative for twice, he/she is considered the cured and should be discharged. However, some of cured and discharged patients later have been tested positive by RT-PCR<sup>75</sup>. Presumably, many factors mentioned above could lead to “false negative” in these cases. On the other hand, a proportion of patients with fever or pneumonia were wrongly isolated together with other confirmed patients with COVID-19 in general medical wards because RT-PCR could produce false positive results due to sample contaminations or other reasons. These patients turned out to be infected by influenza or other pneumonia associated pathogens. A recent large diagnostic study<sup>72</sup> showed 316 patients were confirmed infected with multiple respiratory pathogens including common human coronavirus (5 cases), influenza A virus (2), rhinovirus (12), and influenza A H3N2 (12), respiratory syncytial virus (7), influenza B virus (6), metapneumovirus (4). In addition, RT-PCR methods could generate inconsistent results. A fluorescence-based quantitative PCR kit urgently distributed by the China CDC was designed to detect NP and ORF1ab regions on the SARS-CoV-2 genome. Sometimes, the results from the two pairs of primers did not agree with each other<sup>72</sup>. Besides technical difficulties, deletions and mutations in genome of SARS-CoV-2 occurred during viral evolution may also contribute to false results generated by RT-PCR.

Enzyme-linked immunoassay (ELISA) was highly recommended and expected to improve detection rate for COVID-19<sup>72</sup> because sampling blood was much less stringent than sampling nasal or oral swabs for detecting viruses, and antibodies allows much longer detection window than viruses. Furthermore, ELISA had a



quick turnaround time and relatively low costs. The strength of ELISA methods could make up of the shortages of RT-PCR<sup>74</sup>. ELISA method based on SARSr-CoV Rp3 nucleocapsid protein was successfully developed to detect IgM and IgG against SARS-CoV-2 in early COVID-19 cases<sup>2</sup>. A caveat is that this ELISA method may generate false positive results as N protein is the most conservative viral protein among human  $\beta$ -coronavirus genus<sup>76</sup>. Antigens used in ELISA may react with antibodies against 4 other human coronaviruses that occurred in common colds. S protein is the most diverse protein and may be good candidate for ELISA development<sup>2</sup>.

Differential diagnosis is also critical for confirming cases of COVID-19. Winter usually has higher prevalence of flu and other pathogens associated pneumonia. In all, diagnosis of COVID-19 has to be based on comprehensive understanding of epidemic history, clinical features, radiographic features, and laboratory detection<sup>44</sup>.

## 6. Potential interventions

Isolation is still the most effective means of containing COVID-19<sup>77</sup>. Effective surveillance is the prerequisite for blocking the source of infections. Many methods are applied to recognize source of infections (laboratory confirmed patients, suspected infected persons, and closely contacted persons), including community registration, tracing suspected carrier by cell phones. Those evaluated at moderate/high risk of exposure are encouraged to report conditions daily. General medical wards were used to collectively monitor and treat mild patients<sup>72,78</sup>.

Therapeutics of COVID-19 primarily include symptomatic treatments and antiviral therapies. Early supportive interventions are critical for treating mild patients including nutrient supplements, oxygen therapy, Chinese herbal medicine, antibacterial therapy. Patients infected with COVID-19 are mostly middle-aged and elderly generally with low resistance to infection<sup>72</sup>. Supportive treatments are necessary for patients with mild symptoms at the early stage of infection. For critically ill patients, high-flow oxygen therapy, extracorporeal membrane oxygenation, glucocorticoid therapy and administration of convalescent plasma are applied<sup>44,79</sup>. There are several suggested antiviral treatments: lopinavir/ritonavir, ribavirin, interferon- $\alpha$ , chloroquine phosphate, and abidor. It is not recommended to use three or more antiviral drugs above simultaneously<sup>44,80,81</sup>. Combinational use of lopinavir, ritonavir and ribavirin in the treatment of SARS was reported to be associated with better outcome<sup>82</sup>. It was previously reported that Chloroquine could inhibit SARS-CoV<sup>83</sup> and was

tested for treating COVID-19 in clinical trials in China. Recently, several studies suggested remdesivir effectively inhibit RNA viruses (including SARS/MERS-CoV/2019-nCoV) infection<sup>81,84,85</sup>. Remdesivir was used on the first patient in the United States and showed promising results<sup>31</sup>. Currently, three clinical trials were registered for testing remdesivir on the treatment of COVID-19 (<http://clinicaltrials.gov>). In addition, a pan-coronavirus fusion inhibitor EK1 targeting the HR1 domain of human coronavirus spike was reported to have the potential to treat COVID-19<sup>86</sup>. Convalescent sera were used for treating critically ill patients and show some effects<sup>87</sup>.

Recent report indicated that transmission may occur from individuals with no symptoms or from convalescents<sup>72,88</sup>. It is likely that SARS-CoV-2 will stay around for some time and even coevolve with its hosts. Due to uncertainty of clinical spectrum of virus carriers, vaccination is highly recommended for susceptible populations, especially for those with comorbidities (cardiovascular disease, diabetes, chronic respiratory disease, hypertension, cancers). Vaccines based on S protein, T cell epitopes and RBD (receptor binding domain) have been studied for SARS and MERS<sup>86,89-91</sup>. Recently, an oral vaccine based on yeast expressed S protein developed by a group of scientists in Tianjing University of China provoked a lot of interests after it was reported by Jingyun News. However, it needs to be further tested in clinical trials. On Feb 24<sup>th</sup>, 2020, Moderna, a pharmaceutical company in the United States announced that its experimental mRNA COVID-19 vaccine, known as mRNA-1273, was ready for human testing and the initial batch of the vaccine were shipped to U.S. government researchers from the National Institute of Allergy and Infectious Diseases (NIAID). We have reasons to believe that vaccines would be a way to prevent viral infection because convalescent sera could improve conditions of critically ill patients<sup>87</sup>. In addition to the protective and therapeutic measures mentioned above, psychological interventions were expected to be helpful for infection control<sup>92</sup>.

## 7. Conclusion

Latest literatures and official data from China CDC revealed the epidemic of COVID-19 caused more infections and deaths than either SARS or MERS by far, despite of the fact that its case fatality rate is much lower. SARS-CoV-2 appears to be more infectious than SARS-CoV or MERS-CoV based on  $R_0$  values calculated at the early stage of this outbreak. Majority of infected individuals with no or mild symptoms can release viruses and spread viruses to others, which is extremely challenging for preventing the spread of COVID-19. Therefore, intense surveillance is vital for preventing sustained transmission. Active interventions including nutrition supplement, symptomatic treatment, and antiviral treatment

are critical for mild patients as well as severe patients. Finally, prophylactic vaccination is highly demanded for future prevention of emerging coronavirus related epidemics or pandemics.

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### **Authors' contributions**

Qingsong Qin Conceived, wrote, and revised the paper. Yixuan Wang, Yuyi Wang, and Yan Chen equally contribute to writing. All authors approved the final version of the manuscript before submission.

### **Conflict of interests**

The authors declare that they have no conflict of interests.

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Table 1 : The global distribution of mortality of COVID-19 ( by 2-27-2020 )

|                                     | <b>Number of confirmed cases</b> | <b>Percentage of total cases</b> | <b>Number of deaths</b> | <b>Fatality rate</b> |
|-------------------------------------|----------------------------------|----------------------------------|-------------------------|----------------------|
| <b>Wuhan</b>                        | 48137                            | 58.3%                            | 2132                    | 4.42%                |
| <b>Rest of Hubei</b>                | 17777                            | 21.5%                            | 550                     | 3.09%                |
| <b>Hubei</b>                        | 65914                            | 79.8%                            | 2682                    | 4.07%                |
| <b>Rest of China</b>                | 13045                            | 15.8%                            | 109                     | 0.84%                |
| <b>China</b>                        | 78959                            | 95.6%                            | 2791                    | 3.53%                |
| <b>International (46 countries)</b> | 3664                             | 4.43%                            | 67                      | 1.83%                |
| <b>Total</b>                        | 82623                            | 100%                             | 2858                    | 3.46%                |

**Table 2: epidemiological characteristics of SARS-CoV, MERS-CoV, and SARS-CoV-2.**

|                                   | SARS-CoV   | MERS-CoV   | SARS-CoV-2   |
|-----------------------------------|--|--|--|
| <b>Estimated <math>R_0</math></b> | 2~5 <sup>34,35</sup>   | <1 <sup>34</sup>   | 2.68 (95% CI, 2.48 to 2.86) <sup>19</sup>  |
| <b>Host of virus</b>              | natural host: chinese horseshoe bats <sup>36</sup><br>intermediate host: masked palm civet <sup>11</sup><br>terminal host: humans <sup>11</sup>  | natural host: bats <sup>11</sup><br>intermediate host: dromedary camels <sup>11</sup><br>terminal hosts: humans <sup>11</sup>  | natural host: bats <sup>11</sup><br>intermediate host: pangolins <sup>15</sup><br>terminal hosts: humans <sup>11</sup>   |
| <b>Virus transmission mode</b>    | person-to-person transmission through droplets <sup>37</sup> ,<br>opportunistic airborne transmission <sup>38</sup> ,<br>nosocomial transmission <sup>39</sup> ,<br>sporadic zoonotic transmission,<br>aerosol transmission <sup>40</sup> ,<br>fecal-oral transmission <sup>36</sup> . | respiratory transmission <sup>41</sup> ,<br>sporadic zoonotic transmission <sup>38</sup> ,<br>nosocomial transmission <sup>39</sup> ,<br>via aerosols <sup>40</sup> ,<br>limited human to human transmission <sup>42</sup> . | person-to-person transmission through respiratory droplets, contact and fomites <sup>34</sup> ,<br>zoonotic transmission <sup>43</sup> ,<br>nosocomial transmission <sup>9</sup> ,<br>fecal-oral transmission, and aerosol transmission is highly possible <sup>44</sup> . |
| <b>Median incubation</b>          | 4.6 days (95% CI, 3.8–5.8 days) <sup>38</sup>  | 5.2 days (95% CI, 1.9–14.7) <sup>38</sup>  | 6.4 days (range, 0 to 24.0 days) <sup>45</sup>   |

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period

|                           |                               |                                   |                                |
|---------------------------|-------------------------------|-----------------------------------|--------------------------------|
| <b>Case-fatality rate</b> | worldwide (WHO): 9.6%         | worldwide (WHO): 34.5%            | Wuhan, China:3%. <sup>34</sup> |
|                           | mainland China:6.4%           | South Korea: 20.4%. <sup>19</sup> |                                |
|                           | Hong Kong: 17%. <sup>19</sup> |                                   |                                |

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**Table 3: clinical, laboratory and radiologic characteristics of SARS-CoV, MERS-CoV, and SARS-CoV-2.**

|                   | SARS-CoV  | MERS-CoV  | SARS-CoV-2  |
|-------------------|---|---|---|
| Clinical features | <p>1. persistent fever, chills/rigor, myalgia, dry cough, headache, malaise and dyspnea<sup>38</sup>.</p> <p>2. sore throat, rhinorrhea, sputum production, nausea and vomiting, watery diarrhea<sup>52,53</sup> and dizziness were less common<sup>38</sup>.</p> <p>3. severe cases: accelerated breathing, shortness of breath, or obvious respiratory distress<sup>54</sup>.</p> <p>4. organ failure including Liver</p> | <p>1. begins with fever, cough, chills, sore throat, myalgia, arthralgia, followed by dyspnea and rapid progression to pneumonia within the first week<sup>57-60</sup>.</p> <p>2. gastrointestinal symptoms, including diarrhea, vomiting<sup>57-62</sup>, and abdominal pain<sup>57</sup>.</p> <p>3. severe cases: ARDS, acute renal failure and even multiple organ failure<sup>63</sup>, including Liver function damage<sup>64</sup>.</p> <p>4. 21% of cases had no/mild symptoms, while 46% had severe disease or died<sup>65</sup>.</p> | <p>1. fever, dry cough, myalgia, fatigue, dyspnea, anorexia<sup>23</sup>. Fever and cough were the dominant symptoms, diarrhea is uncommon<sup>45</sup>.</p> <p>2. multiple organ failure, including renal damage<sup>48</sup>, liver damage<sup>49</sup>, and testicular tissue damage<sup>48</sup>.</p> <p>4. mild patients: low fever, mild fatigue, and no pneumonia<sup>44</sup>.</p> <p>5. severe patients: dyspnea or hypoxemia one week after the onset<sup>44</sup>.</p> <p>6. critical patients: ARDS, facial shock etc<sup>44</sup>. Dyspnea, abdominal pain, and anorexia were also common<sup>23</sup>.</p> <p>7. 80.9% were considered mild/common pneumonia,</p> |

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|                     |   |   |   |
|---------------------|---|---|---|
|                     | damage <sup>55</sup> .<br><br>5. 11.1% severe respiratory illness, 61% mild symptom <sup>56</sup> .   |   | 13.8% were severe cases, 4.7% were critical cases.  |
| Laboratory features | <p>1. lymphopenia, DIC, elevated LDH, CK<sup>38</sup>. White blood cell count is generally not high<sup>54</sup>.</p> <p>2. CD4 and CD8 T-lymphocyte counts fell in the early course, it was associated with adverse clinical outcome<sup>66</sup>.</p> <p>3. thrombocytopenia, prolonged APTT, elevated D-Dimer, ALT<sup>50</sup>.</p> | <p>1. similar to SARS, common laboratory findings include leukopenia<sup>57,58,62,67</sup>, elevated LDH, AST, thrombocytopenia, and lymphopenia<sup>57</sup>.</p> <p>2. several cases: viral RNA in blood, urine, and stool but at much lower viral loads<sup>58,68</sup> compared to SARS.</p> <p>3. Elevated liver enzymes<sup>69</sup>, which may be related to liver injury.</p> | <p>1. depressed total lymphocytes, prolonged PT, elevated levels of LDH<sup>23</sup>, AST, ALT<sup>45</sup>, blood urea, creatinine<sup>23</sup>.</p> <p>2. most patients have elevated CRP and erythrocyte sedimentation rate and normal procalcitonin<sup>44</sup>.</p> <p>3. severe cases: D-dimer increases and peripheral blood lymphocytes progressively decreased<sup>44</sup>.</p> <p>4. critically ill patients: elevated inflammatory factors<sup>44</sup>.</p> <p>5. nonsurvivors: the neutrophil count, D-dimer, blood urea, and creatinine levels is very high<sup>23</sup>.</p> |
| Radiologic features | <p>1. the predominant involvement of lung periphery and the lower zone. Absence of pleural effusion<sup>38</sup>.</p> <p>2. ground-glass opacification and</p>  | <p>1. bilateral hilar infiltration, unilateral or bilateral patchy densities or infiltrates, ground-glass opacities, and small pleural effusions<sup>38</sup>.</p> <p>2. lower lobes are</p>  | <p>1. bilateral distribution of patchy shadows and ground glass opacity was a typical hallmark of CT scan for NCIP<sup>23</sup>.</p> <p>2. radiologic abnormality occurs in a substantial proportion of patients on initial presentation<sup>45</sup>. Pleural</p>  |

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lobe thickening<sup>70</sup>. affected with more effusion is rare<sup>44</sup>.  
 rapid radiographic  
 progression than  
 SARS<sup>38</sup>.

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ARDS=acute respiratory distress syndrome. PT=prothrombin time. AST=aspartate aminotransferase. ALT=alanine aminotransferase. LDH=lactate dehydrogenase. CK=creatinine kinase. CRP=C-reactive protein. DIC=disseminated intravascular coagulation. APTT=activated partial thromboplastin time.

### Figure

Fig 1. Case numbers and fatality rates of COVID-19 in Wuhan and other areas.

