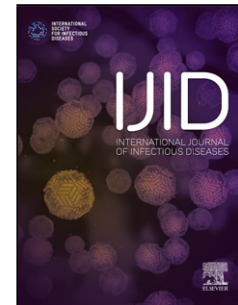


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Insight into 2019 novel coronavirus — an updated intrim review and lessons from SARS-CoV and MERS-CoV

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Highlights

The COVID-19 had a high R_0 , a long incubation period, and a short serial interval.

- The COVID-19 had a general low CFR, but much higher in patients with comorbidities.
- The spike protein binding to ACE2 may explain the high R_0 of COVID-19.
- Autopsy showed more exudative lesions, and less fibrosis and consolidation.
- Remdesivir, chloroquine, tocilizumab, and convalescent plasma may be effective.

Abstract:

Background: The rapid spread of the coronavirus disease 2019 (COVID-19), caused by a zoonotic beta-coronavirus entitled 2019 novel coronavirus (2019-nCoV), has become a global threat. Awareness of the biological features of 2019-nCoV should be updated in time and needs to be comprehensively summarized to help optimize control measures and make therapeutic decisions.

Methods: Based on recently published literatures, official documents and selected up-to-date preprint studies, we reviewed the virology and origin, epidemiology, clinical manifestations, pathology and treatment of 2019-nCoV infection, in comparison with severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV) infection.

Results: The genome of 2019-nCoV partially resembled SARS-CoV and MERS-CoV, and indicating a bat origin. The COVID-19 generally had a high reproductive number, a long incubation period, a short serial interval and a low case fatality rate (much higher in patients with comorbidities) than SARS and MERS. Clinical presentation and pathology of COVID-19 greatly resembled SARS and MERS, with less upper

respiratory and gastrointestinal symptoms, and more exudative lesions in post-mortems. Potential treatments included remdesivir, chloroquine, tocilizumab, convalescent plasma and vaccine immunization (when possible).

Conclusion: The initial experience from the current pandemic and lessons from the previous two pandemics can help improve future preparedness plans and combat disease progression.

Keywords: 2019-nCoV; COVID-19; SARS-CoV-2; SARS-CoV; MERS-CoV.

Introduction

In late December 2019, a pneumonia outbreak of unknown etiology took place in Wuhan, Hubei province, China, and spread quickly nationwide. Chinese Center for Disease Control and Prevention (CCDC) identified a novel beta-coronavirus called 2019-nCoV, now officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Gorbalenya et al., 2020), that responsible for the pandemic. This was the third zoonotic coronavirus breakout in the first two decades of 21st century that allowing human-to-human transmission and raising global health concerns. Chinese government had taken immediate, transparent and extraordinary measures, and reached initial achievements to control the outbreak. As of 11 March 2020, the pandemic caused accumulated 80955 confirmed cases and 3162 deaths in China, 37364 confirmed cases and 1130 deaths in 113 other countries worldwide. World Health Organization (WHO) deeply concerned the unprecedented swift global spread and severity of the outbreak, and by ignorance and inaction of some countries. Therefore, WHO announced the COVID-19 can be characterized as a pandemic (WHO, 2020a).

Biological features of 2019-nCoV and experiences combating COVID-19 should be updated in time and needs to be comprehensively summarized to help optimize control measures and make therapeutic decisions. What's more, the 2019-nCoV demonstrated partial resemblance with SARS-CoV and MERS-CoV, in phylogenetic analysis, clinical manifestations and pathological findings. Scientific advances from the SARS and MERS outbreaks can provide valuable insight into rapid understanding and control measures of the current pandemic. We searched literatures and guidelines in Pubmed, Web of Science, Embase, CNKI, Wanfang, VIP, preprint bioRxiv and medRxiv databases from the earliest available date to 11 March, 2020. Initial search terms were "2019-nCoV" OR "2019 novel coronavirus" OR "SARS-CoV-2" OR "COVID-19" OR "corona virus disease 2019" OR "NCP" OR "Novel coronavirus pneumonia". Further search words were above keywords, "SARS" OR "SARS-CoV" OR "severe acute respiratory syndrome", "MERS" OR "MERS-CoV" OR "middle east respiratory syndrome", in combinations of with "spike protein" OR "genome" OR "reproductive number" OR "incubation period" OR "serial interval" OR "fatality rate" OR "clinical characteristics" OR "pathology" OR "autopsy" OR "treatment".

Moreover, official documents and news released by National Health Commission of P.R. China, CCDC, CDC(USA) and WHO were accessed for up-to-date information on COVID-19. Only the articles in English or Chinese were considered.

In this review, we highlight the pandemic potential and pathological indications of emerging coronavirus, comprehensively and systematically summarize the up-to-date knowledge of the biological characteristics of 2019-nCoV, including virology and origin, epidemiology, clinical manifestations, pathology and treatment. Because of its natural structures and biological features to bind receptors on host cells, the spike protein of 2019-nCoV may played an essential role in disease spreading. We summarized all of the four available pathology studies of COVID-19 biopsy and autopsy, and compared the results with previous two deadly coronavirus diseases. New therapeutic measures are emerging one after another. Potential effective treatments were remdesivir, chloroquine, tocilizumab, convalescent plasma and vaccine immunization (when possible). Evidence-based medicine should always be advocated to guide our clinical decision.

Virology and origin

Coronavirus belongs to the subfamily Orthocoronavirinae in the family of Coronaviridae in the order Nidovirales, which mainly caused infections in respiratory and gastrointestinal tract. The 2019-nCoV is a novel enveloped beta-coronavirus which has a single stranded positive sense RNA genome(Zhu et al., 2020). Concerning the origin of the virus, several phylogenetic analysis suggested the bat to be the most probable animal reservoir. Based on genome sequencing, 2019-nCoV is about 89% identical to bat SARS-like-CoVZXC21, 82% identical to human SARS-CoV and about 50% to MERS-CoV(Chan et al., 2020; Lu et al., 2020). As both SARS-CoV and MERS-CoV were transmitted from bats to palm civets or dromedary camels, and finally to humans, there should be another animal representing as an intermediate host between bat and human. Pangolins were suggested as the possible intermediate hosts, because their genome had approximately 85.5%-92.4% similarity to 2019-nCoV, representing two sub-lineages of 2019-nCoV in the phylogenetic tree, one of which (GD/P1L and GDP2S) was extremely closely related to 2019-nCoV(Lam et al., 2020). Other research suggested 2019-nCoV was the recombinant virus of bat coronavirus and

snake coronavirus, by comparison in conjunction with relative synonymous codon usage bias among different animal species(Ji et al., 2020). The truth is yet to be discovered.

The spike surface glycoprotein of coronavirus plays an essential role in binding to receptors on host cells and determines host tropism. Spike protein(S-protein) of 2019-nCoV is reported to bind with angiotensin-converting enzyme 2 (ACE2), the same receptor of SARS-CoV to invade host cells; whereas MERS-CoV uses dipeptidyl peptidase 4 (DPP4) as the primary receptor(Wu et al., 2020). The amino acid sequence of S-protein in 2019-nCoV is 76.47% identical to that of SARS-CoV, with the same structural confirmation and electrostatic properties in the interaction interface. The residues at positions 442, 472, 479, 487, and 491 in S-protein are reported to be at receptor complex interface with ACE2. However, four of the five critical residues in the 2019-nCoV S-protein are not preserved except for Tyr491. The binding free energy for 2019-nCoV S-protein to bind with human ACE2, increases by 28 kcal mol⁻¹ compared to SARS-CoV S-protein (-50.6kcal mol⁻¹ vs. -78.6kcal mol⁻¹), due to the loss of hydrogen bond interactions by replacing Arg426 with Asn426(Xu et al., 2020a). Furin-like cleavage site was supposed to be cleaved by proprotein convertase furin at special viral envelope glycoproteins, thereby enhancing viral fusion with host cell membranes. Coutard and colleagues (2020) reported a furin-like cleavage site in the S-protein of 2019-nCoV, which is absent in other lineage b beta-coronaviruses. Another research team also discovered an “RRAR” furin recognition site by an insertion in the S1/S2 protease cleavage site in 2019-nCoV, instead of a single arginine in SARS-CoV. After quantifying the kinetics mediating the interaction via surface plasmon resonance, ACE2 is calculated to bind to 2019-nCoV ectodomain with ~15 nM affinity, which is approximately 10- to 20-fold higher affinity than ACE2 binding to SARS-CoV(Wrapp et al., 2020). In all, the binding affinity between 2019-nCoV S-protein and ACE2 is comparable or even stronger than SARS-CoV S-protein and ACE2. This may explain the rapid development and strong ability of human-to-human transmission in COVID-19.

Epidemiology

The pandemic escalated exponentially at the beginning of 2020, which might only be the tip of the iceberg due to delayed case reporting and deficiency in testing kits(Li et al., 2020). The onset of first cluster cases were reported an exposure history to the

Huanan seafood(wild animal) wholesale market in Wuhan. However, phyloepidemiologic analyses suggested that Huanan market was not the origin of 2019-nCoV. The virus was imported from elsewhere and boosted in the crowded market(Yu et al., 2020). The proportion of infected cases without an exposure history and in health care workers gradually increased. All of the evidence indicated the human-to-human transmission ability of 2019-nCoV, which may already be spread silently between people in Wuhan before the cluster of cases from Huanan market was discovered in late December. Person-to-person transmission may occur mainly through droplet or contact transmission. According to Guan's latest pilot study, 2019-nCoV was detected positive in the gastrointestinal tract specimens (stool and rectal swabs) as well as in saliva and urine, and even in esophageal erosion and bleeding site of severe peptic ulcer patients(Guan et al., 2020). Four important epidemiological parameters of 2019-nCoV were reviewed in comparison with those of SARS-CoV and MERS-CoV(shown in Table 1).

Reproductive number is an indication of the transmissibility of a virus, representing the average number of new infections generated by an infectious person in a totally naïve population. For $R_0 > 1$, the number of infected is likely to increase; for $R_0 < 1$, transmission is likely to decline and die out. The reproductive number updated along with the development of the outbreak and interventions. R_0 was estimated to be around 3 for SARS(Bauch et al., 2005) and < 1 for MERS(Bauch and Oraby, 2013). The preliminary R_0 of 2019-nCoV was reported as 2.24-3.58(Liu et al., 2020). Several research groups reported estimated R_0 of the outbreak depending on distinct estimation methods and the validity of underlying assumptions. Liu et al. (2020) reviewed all of the 12 references of an estimated R_0 ranged from 1.4 to 6.49, with a mean of 3.28 and a median of 2.79. In clinical studies, a 425-case study by 22 January 2020, reported an R_0 of approximately 2.2(95%CI, 1.4-3.9)(Li et al., 2020), while another 4021-case study by 26 January 2020, estimated 3.77(95%CI, 3.51-4.05) (Yang et al., 2020). The discrepancy may be due to sample number and different stages of the pandemic.

Incubation period is defined as the interval from initial exposure to an infectious agent to onset of any symptoms or signs it causes. A long incubation period may lead to a high rate of asymptomatic and subclinical infection. The first prediction of mean incubation period was 5.2 days (95%CI, 4.1-7.0 days), with the 95th percentile of the distribution at 12.5 days, based on 2019-nCoV exposure histories of the first 425 cases in Wuhan(Li et al., 2020). A 4021-case study reported 4.75 days (interquartile range:

3.0-7.2 days) (Yang et al., 2020). Another 88-exported-case study calculated the mean incubation period to be 6.4 days (95%CI, 5.6–7.7 days), using known travel histories to and from Wuhan and symptom onset dates (Backer et al., 2020). All these literatures lay the foundation to set 14 days as the medical observation period if any exposure occurred. A latest study collected 1099 cases from 552 hospitals in 31 provinces in China and declared a median incubation period of 3.0 days, ranging from 0 to surprisingly 24.0 days. An adjustments in screening and control policies may be needed. The 2019-nCoV generally has a longer incubation time than SARS-CoV (4.0 days, 95% CI 3.6-4.4 days) (Lessler et al., 2009) and MERS-CoV (range 4.5-5.2 days) (Park et al., 2018).

Serial interval is the interval from illness onset in a primary case to illness onset in the secondary case. The mean serial interval was estimated at 7.5 days (95% CI, 5.3-19 days) using contact tracing data from early Wuhan cases in 2019-nCoV pandemic, which was shorter than the 8.4-day mean serial interval reported for SARS (Lipsitch et al., 2003) and 12.6-day for MERS (Cowling et al., 2015). Another estimation of the mean serial interval from 26 infector-infectee pairs was surprisingly 2.6 days, which was shorter than the median incubation period, suggesting a substantial proportion of secondary transmission before illness onset (Nishiura et al., 2020).

The CFR in early studies of COVID-19 involving relatively small samples of confirmed cases in Wuhan, varied from 4.3% to 14.6% (Chen et al., 2020a; Huang et al., 2020; Wang et al., 2020a), but that may not be able to reflect the truth. The CFR in Wuhan was undoubtedly higher than CFR outside of Wuhan. The reported CFR ranged 1.4%-3.06% in large nationwide case studies (Guan et al., 2020; Yang et al., 2020). Prognosis factors such as male, elderly patients aged ≥ 60 years, underlying disease, severe pneumonia at baseline and a delay from onset to diagnosis >5 days substantially elevated the CFRs (Yang et al., 2020). CFRs in patients with cardiovascular disease, diabetes, hypertension and respiratory disorders were as high as 10.5%, 7.3%, 6.0% and 6.3%, respectively. According to WHO announcement, SARS accounted for 8096 cases and 774 death, with a CFR of 9.6% (WHO, 2004). MERS-CoV infection were responsible for 2229 cases and 791 death, with a crude CFR of 35.5% (WHO, 2018). A study of 44672 cases conducted by CCDC reported a CFR of 2.3% nationwide, with a CFR of 2.9% in Hubei province compared to 0.4% in other parts of China (Wu and McGoogan, 2020). Despite a gradually stable CFR around 3, the prognosis and outcome of COVID-19 was also extraordinarily destructive and causing more death

because of its enormous infected population. We can see a family close relative clustering phenomenon of severe and death cases. Genome sequencing and linkage analysis of ACE2 gene polymorphism may help determine individual susceptibility to 2019-nCoV and provide early-warning detection mode of severe COVID-19 in clinical practice.

Clinical manifestations

Clinical presentation of COVID-19 greatly resembled viral pneumonia such as SARS and MERS. Most cases are mild cases(81%), whose symptoms were usually self-limiting and recovery in two weeks(Wu and McGoogan, 2020). Severe patients progressed rapidly with acute respiratory distress syndrome (ARDS) and septic shock, eventually ended in multiple organ failure.

General information of four inpatient case studies with relatively comprehensive data were summarized in supplementary table 1. The 2019-nCoV was more likely to infect elderly men with comorbidities. Males were more susceptible to 2019-nCoV infection, same as SARS-CoV and MERS-CoV studies(Badawi and Ryoo, 2016), due to X chromosome and sex hormones' role on innate and adaptive immunity(Jaillon et al., 2019). Chronic underlying diseases (mainly hypertension, cardio-cerebrovascular diseases and diabetes) may increase the risk of 2019-nCoV infection(Guan et al., 2020), which is similar to MERS-CoV infection(Badawi and Ryoo, 2016). Smoking may be a negative prognostic indicator for COVID-19(Chen et al., 2020a; Guan et al., 2020).

Clinical information of the above four selected inpatient case studies were summarized in supplementary table 2. Onset of symptoms were usually mild and nonspecific, presenting by fever, dry cough and shortness of breath. Very few COVID-19 patients had prominent upper respiratory tract and gastrointestinal symptoms (eg, diarrhea) (Guan et al., 2020; Huang et al., 2020), compared to 20–25% of patients with MERS-CoV or SARS-CoV infection developed diarrhea(Assiri et al., 2013). However, only 43.8% of COVID-19 patients had an initial presentation of fever, and developed to 87.9% following hospitalization(Guan et al., 2020), compared to as high as 99% and 98% frequent in SARS-CoV and MERS-CoV infection(Badawi and Ryoo, 2016). Those patients without fever or even asymptomatic may be left un-quarantined as silent infection source, if the surveillance methods focused heavily

on fever detection. Moreover, the onset of symptoms may help physicians identifying patients with poor prognosis. Patients admitted to the ICU were more likely to report pharyngeal pain, dyspnea, dizziness, abdominal pain and anorexia(Wang et al., 2020a).

In terms of laboratory findings, a substantial decrease in the total number of lymphocytes could be used as an index in the diagnosis of 2019-nCoV infection, indicating a consumption of immune cells and an impairment to cellular immune function(Chen et al., 2020a). Non-survivors developed more severe lymphopenia over time(Wang et al., 2020a). Initial proinflammatory plasma cytokine concentrations were higher in COVID-19 patients than in healthy adults. ICU patients had even higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNF α compared to non-ICU patients(Huang et al., 2020). There were numerous differences in laboratory findings between patients admitted to the ICU and those not, including higher white blood cell and neutrophil counts, higher levels of D-dimer, creatine kinase, and creatine in ICU patients(Wang et al., 2020a).

Typical chest CT manifestation of COVID-19 pneumonia were initially small subpleural ground glass opacities that grew larger with crazy-paving pattern and consolidation. After two weeks of growth, the lesions were gradually absorbed leaving extensive opacities and subpleural parenchymal bands in recovery patients. However, Guan et al. (2020) demonstrated that patients with normal radiologic findings on initial presentation consisted of 23.9% and 5.2% of severe and non-severe cases respectively, which add the complexity to disease control.

Pathology

Autopsy or biopsy studies would always be the key to understand the biological features of 2019-nCoV. Histological examinations of two patients underwent lung lobectomies for adenocarcinoma, revealed edema, proteinaceous exudate, focal hyperplasia of pneumocytes with only patchy inflammatory cellular infiltration without prominent hyaline membranes. Since both patients didn't develop symptoms of COVID-19 pneumonia at the time of surgery, these changes likely represent an early phase of the lung pathology of COVID-19 pneumonia. Qian and his colleagues (2020) first reported the pathological characteristics of a patient who died from COVID-19. General observation from raw eyes showed less fibrosis and consolidation, instead

more exudative lesions in COVID-19 than SARS. Microscopic examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates, indicating ARDS. Interstitial mononuclear inflammatory infiltrates were dominated by lymphocytes. Multinucleated syncytial cells with atypical enlarged pneumocytes showed viral cytopathic-like changes, without obvious intranuclear or intracytoplasmic viral inclusions. Results from flow cytometric analysis demonstrated that the counts of peripheral CD4⁺ and CD8⁺ T cells were substantially reduced, while their status were hyper-activated. It indicated the severe immune injury in later stage of COVID-19, but not by virus direct destruction(Xu et al., 2020b). Based on the public database and single-cell RNA-Seq technique, pathological studies revealed that male donors had a higher ACE2-expressing cell ratio than their female counterparts. The only Asian male specimen has five more times as much as ACE2 expressing on the white and African American donors. This might explain why the 2019-nCoV and previous SARS-CoV pandemic were concentrated in the Asian population and a heightened susceptibility of male patients, although more evidence was needed to draw such conclusion(Yu et al., 2020).

Pathological manifestations of SARS and MERS infected patients may shed lights to control current 2019-nCoV pandemic. Histology examination demonstrated a considerably higher viral load of SARS-CoV RNA in lung and small bowels than other organs of the body, suggesting an reason for manifestation of pneumonia and diarrhea in SARS patients. Living 2019-nCoV was also detected positive in stool specimens and rectal swabs of infected patients, indicating possible transmission route of oral-faecal transmission. Proper handling with the infected corpse and disposal of human excreta of infected patients were of great importance(Nicholls et al., 2003). Thrombi were seen in all six autopsies of SARS-CoV infected patients, with even huge thrombus formation in part of pulmonary vessels. Coagulation function disorders were reported in most of the severe COVID-19 patients, by elevated levels of D-Dimer and prolonged prothrombin time, some of whom ended in disseminated intravascular coagulation(Chen et al., 2020a; Huang et al., 2020; Wang et al., 2020a). This may explain some sudden death of clinical recovery patients and serve as an indication for disease severity. In an autopsy study, the only one patient without usage of corticosteroids demonstrated increased CD3⁺ lymphocyte than five other specimen treated by corticosteroids(Pei et al., 2005). It suggested an inhibition of immune system

and a careful usage of corticosteroids in COVID-19 treatment. Much is to be discovered in more 2019-nCoV autopsies.

Treatment

There are currently no vaccine or specific effective antiviral therapies for COVID-19 in general. Thus there is an urgent need for global surveillance of COVID-19 patients. New therapeutic drugs are emerging one after another. However, double-blinded randomized controlled trials with larger sample size are needed to determine the safety and efficacy of these new drugs and guide clinical decision. Medical interventions can be divided into four major categories: general treatment, coronavirus specific treatments, antiviral treatments and others.

General treatments included nutritional interventions, immuno-enhancers and Chinese medicine. Interferon, intravenous gamma-globulin and thymosin were believed to boost our immune system to fight with SARS-CoV and MERS-CoV as well as 2019-nCoV. Chloroquine, an old Chinese medicine for treatment of malaria and autoimmune disease, had demonstrated remarkable inhibition in the spread of SARS-CoV by interfering with ACE2 in Vero E6 cell lines (Vincent et al., 2005). Wang et al. (2020b) demonstrated that chloroquine functioned at both entry and post-entry stages of the 2019-nCoV infection in Vero E6 cells, as well as an immune-modulating activity that enhanced antiviral effect in vivo. Recent multicenter clinical trials conducted in China have also reported obvious efficacy and acceptable safety in COVID-19 patients by reducing exacerbation of pneumonia, improving radiological findings, promoting a virus negative conversion, and shortening the disease course (Gao et al., 2020).

Due to the indispensable role of the S-protein in coronavirus, therapies and vaccine exploration targeting S-protein-ACE2 interaction may be very promising. Previous therapies targeting SARS-CoV and MERS-CoV may accelerate the development of treatment of COVID-19 because of their structure resemblance and genome similarities. The human monoclonal antibody could efficiently neutralize SARS-CoV and inhibit syncytia formation between S-protein and ACE2 expressing cells (Sui et al., 2004). Appropriate modification of the monoclonal antibody may be effective for treatment of COVID-19. What's more, potential therapies targeting the renin-angiotensin system, to increase ACE2 expression and inhibit ACE may be

developed to treat COVID-19 in the future. Hoffmann et al. (2020) reported a cellular protease TMPRSS2 for 2019-nCoV priming upon entrance into cells and viral spread in the infected host cells. The serine protease inhibitor camostat mesylate against TMPRSS2, can efficiently blocked 2019-nCoV-S-protein-driven cell entry, which could be a promising treatment for 2019-nCoV infection.

There are no effective antiviral treatment for coronavirus infection, even the strong candidates as lopinavir/ritonavir and abidol exhibited no remarkable effect on clinical improvement, day 28 mortality or virus clearance(Chen et al., 2020). Expectation and attention were shifted to “remdesivir” which may be the most potential wide-spectrum drug for antiviral treatment of 2019-nCoV. Remdesivir is an adenosine analogue, which incorporates into novel viral RNA chains and results in pre-mature termination. It is currently under clinical development for the treatment of Ebola virus infection(Mulangu et al., 2019). Wang et al. (2020b) revealed that remdesivir were highly effective and safe in the control of 2019-nCoV infection in Vero E6 cells and Huh-7 cells. A successful appliance of remdesivir on the first 2019-nCoV infected case in the United States when the his clinical status was getting worsen, were recently released(Holshue et al., 2020). Animal experiments also showed superiority of remdesivir over lopinavir/ritonavir combined with interferon- β , by reducing MERS-CoV titers of infected mice and improving the lung tissue damage(Sheahan et al., 2020). The effectiveness and safety of remdesivir can be expected by the clinical trial lead by Dr Bin Cao.

The 2019-nCoV infection is associated with a cytokine storm triggered by over-activated immune system(Huang et al., 2020; Xu et al., 2020b), similar to SARS and MERS. The aberrant and excessive immune responses lead to a long-term lung function and structure damage in patients survived from ICU. Ongoing trials of IL-6 antagonist tocilizumab, which shown effective against cytokine release syndrome resulting from CAR-T cell infusion against B cell acute lymphoblastic leukemia, may be expanded to restore T cell counts and treat severe 2019-nCoV infection(Le et al., 2018). The available observational studies and meta-analysis of corticosteroid treatment suggested impaired antibody response, increased mortality and secondary infection rates in influenza, increased viraemia and impaired virus clearance of SARS-CoV and MERS-CoV, and complications of corticosteroid therapy in survivors(Zumla et al., 2020). Therefore, corticosteroid should not be recommended for treatment of 2019-nCoV, or use on severe patient with special caution. A review

on convalescent plasma for treatment of SARS-CoV and severe influenza infection, suggested a reduction in hospital stay and mortality rate, especially when administered early after symptom onset (Mair-Jenkins et al., 2015). However, another study demonstrated no significant improvement of convalescent plasma transfusion on survival of Ebola virus infected patients. Possible reasons may be the unknown levels of neutralizing antibodies in convalescent plasma and transfusion timing (van Griensven et al., 2016). In terms of vaccine, if any cross-reactive epitopes were identified between 2019-nCoV and SARS-CoV, previous vaccine for SARS-CoV might be re-utilized to facilitate 2019-nCoV vaccine development. We recommend an influenza and *Streptococcus pneumoniae* vaccination for prophylaxis, especially in elderly adults (Chen et al., 2020b). Both pandemic viruses result in similar respiratory symptoms and hard to distinguish. The 2019-nCoV pandemic initiated in flu season which easy to develop a combination infection of 2019-nCoV and influenza or *Streptococcus* infection. Vaccination against influenza and *Streptococcus pneumoniae* in vulnerable elderly people with comorbidities are highly cost-effective, which is demonstrated to associate with reductions in the risk of hospitalization and death from all causes during influenza seasons (Nichol et al., 2003).

Conclusion

In conclusion, it still remains a challenging task to fight the 2019-nCoV of unknown origin and mysterious biological features, and to control an outbreak of COVID-19 with such a high R_0 , a long incubation period and a short serial interval, by limited treatment and prevention measures. Lessons learned from the MERS and SARS outbreaks can provide valuable insight into how to handle the current pandemic. The successful public health outbreak response tactics of Chinese government, such as hand hygiene, wearing masks, isolation, quarantine, social distancing, and community containment, can be copied by other countries according to their national situation. As the pandemic is still ongoing and expanding, experiences and research literatures from China and other countries will increase. The 2019-nCoV should be monitored of any possible gene variation of antigenic drift or antigenic conversion, to avoid another round of outbreak. Another lessons from this pandemic will be awe for nature and love for life.

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Table 1. Epidemiology characteristics of COVID-19, SARS and MERS

	COVID-19	SARS	MERS
Original location	Wuhan, China	Guangdong, China	Jeddah, Saudi Arabia
Total cases (global)	85403+	8096	2229
Total death (global)	1753+	774	791
Healthcare worker cases(%)	3.8	21	18.6
Reproductive number	3.28	3.0	<1.0
Incubation period (days)	4.75-6.4	4.0	4.5-5.2
Serial interval (days)	2.6-7.5	8.4	12.6
Case-fatality rate (%)	3.0	9.6	35.5
CFR with comorbidities (%)	73.3	46.0	60.0

Supplementary Table 1. General information of 2019-nCoV inpatients

Studies	Huang et al.	Chen et al.	Wang et al.	Guan et al.
Collecting time(year of 2020)	January 22	January1-22	January 1-28	January 29
Number of cases	41	99	138	1099
Location	Wuhan	Wuhan	Wuhan	Mainland China
Mean Age (yrs)	49	55.5	56	47
Sex ratio (male: female)	73%:27%	68%:32%	54.3%:45.7%	58.1%:41.9%
Exposure history (%)	66	49	8.7	71.8
Underlying diseases (%)	32	50	NA	23.2
Diabetes (%)	20	13	10.1	7.4
Hypertension(%)	15	NA	31.2	14.9
Cardio-cerebrovascular disease(%)	15	40	19.6	3.9
Malignancy(%)	NA	1	7.2	0.9
Prognosis				
Remain hospitalization(%)	17	58	61.6	93.6
Discharged(%)	68	31	34.1	5.8
Died(%)	15	11	4.3	1.36

Supplementary Table 2. Clinical information of 2019-nCoV inpatients

Studies	Huang et al.	Chen et al.	Wang et al.	Guan et al.
Symptoms				
Fever (%)	98	83	98.6	87.9
Cough (%)	76	82	59.4	67.7
Myalgia (%)	44	11	34.8	14.8
Fatigue (%)		NA	69.6	38.1
Shortness of breath (%)	55	31	31.2	31-55
Headache(%)	8	8	6.5	13.6
Diarrhea (%)	3	2	10.1	3.7
Examinations				
Lymphopenia (%)	63	35	70.3	82.1
Leukopenia (%)	25	9	NA	33.7
Prolonged prothrombin time (%)	NA	5	58	NA
Aspartate aminotransferase elevation (%)	37	35	NA	22.2
Lactate dehydrogenase elevation (%)	73	76	39.9	41
Pneumonia in CT (%)	100	100	100	76.4
Progression (time from onset of symptoms)				
Hospital admission(days)	7	NA	7	NA
Dyspnea (days)	8	NA	5	NA
ARDS(days)	9	NA	8	NA
Mechanical ventilation (days)	10.5	NA	NA	NA
Admission to ICU(%)	15	23	26.1	5
Complications				
ARDS(%)	29	17	61.1	3.4
Acute cardiac injury(%)	12	NA	7.2	NA
Secondary infection(%)	10	NA	NA	NA
Acute kidney injury (%)	7	3	3.6	0.5
Shock(%)	7	4	30.6	1
Treatments				
Antiviral therapy(%)	93	76	89.9	35.8
Antibiotic treatment(%)	100	71	Most	57.5
Systematic corticosteroids(%)	22	19	44.9	18.6
Immunoglobulin(%)	NA	27	NA	13
CRRT(%)	7	9	1.5	0.8
Non-invasive ventilation or high-flow nasal cannula(%)	24	13	14	5.1
Invasive ventilation (%)	5	4	12	2.2
ECMO(%)	5	3	2.9	0.5

(ECMO=extracorporeal membrane oxygenation. CRRT=continuous renal replacement therapy.)