ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue –2, April - 2020, Page No. : 15 - 23

Rise of New Pandemic Covid-19, Etiology, Clinical Features, Treatment: A Narrative Review

[1]Dr. Venkatesh Balaji Hange, Postgraduate Student, Department of Oral And Maxillofacial Surgery, K.D. Dental College & Hospital, Mathura, Uttar Pradesh.

[2]Dr.Shrey Srivastava[2], Postgraduate Student, Department of Oral And Maxillofacial Surgery, K.D. Dental College & Hospital, Mathura, Uttar Pradesh.

[3]Dr.Shishir Mohan Devki, Head of Department, Department of Oral And Maxillofacial Surgery, K.D. Dental College & Hospital, Mathura, Uttar Pradesh.

[4]Dr. Hasti Kankariyam Professor, Department of Oral And Maxillofacial Surgery, K.D. Dental College & Hospital, Mathura, Uttar Pradesh.

Corresponding Author: Dr. Venkatesh Balaji Hange, Postgraduate Student, Department of Oral And Maxillofacial Surgery, K.D. Dental College & Hospital, Mathura, Uttar Pradesh.

Citation this Article: Dr. Venkatesh Balaji Hange , Dr.Shrey Srivastava, Dr.Shishir Mohan Devki, Dr. Hasti Kankariya, "Rise of New Pandemic Covid-19, Etiology, Clinical Features, Treatment : A Narrative Review ", IJMSIR- April - 2020, Vol – 5, Issue -2, P. No. 15 – 23.

Type of Publication: Review Article

Conflicts of Interest: Nil

Introduction

Corona viruses are positive strand RNA viruses that cause disease in humans, and domestic and companion animals. They are most notorious for causing the Severe Acute Respiratory Syndrome in 2002–2003. All corona viruses follow the same basic strategy of replication. Corona viruses all encode 15–16 replicase related proteins, 4–5 structural proteins and 1–8 group-specific or accessory proteins. Corona viruses are readily transmitted across species. This mechanism has been seen when SARS-corona virus crossed species from bats to intermediate hosts, such as palm civets, and then to humans. It also demonstrates the vast number of animals, including humans, which have been infected with viruses closely associated to bovine corona virus.(1) The corona virus belongs to a family of viruses that may cause various symptoms such as pneumonia, fever, breathing difficulty, and lung infection. These viruses are common in animals worldwide, but very few cases have been known to affect humans.(2)

In 31 December 2019, in Wuhan City, Hubei Region, China, 27 patients of unexplained aetiology pneumonia were recorded. Such patients most notably showed clinical symptoms of dry cough, dyspnea, fever, with bilateral pulmonary infiltrations on the imaging. Reports were mostly traced to Wuhan's Huanan Seafood Wholesale Market, which sells fish and a multitude of live animal species, which include chickens, bats, marmots and snakes.(3) On 8 January 2020, the Chinese Center for Disease Control and Prevention officially recognized the new corona virus as the causative pathogen of COVID-19.(Li et al. 2020) after identified from throat swab samples conducted by

the Chinese Centre for Disease Control and Prevention (CCDC) on 7th January 2020.(4)The 2019-nCoV has features typical of the corona virus family and was classified in the beta corona virus 2b lineage. The 2019-nCoV has close similarity to bat corona viruses, and it has been postulated that bats are the primary source.(5)As of March 24, 2020, COVID-19 has been recognized in 196 countries., with a total of 395,583 laboratory-confirmed cases ,103,736 recovered and 12,234 deaths. Till this date 519 laboratory-confirmed cases, 40 recovered and 10 deaths were reported by Indian Council Of Medical Reserch in India. To date, majority of cases 96% (262,623) reported with mild symptoms (flu-like symptoms) including fever ,dry cough & sore throat and 4% (12,222) serious or critically ill patients with pneumonia ,chest tightness ,chest pain , and shortness of breath out of 274,845 active cases.

The mortality rate of COVID-19 is about 3.4% globally ,by WHO as of March 3 by WHO director Dr.Tedros Adhanom ghebreyesus during media briefing.

Keywords: Novel coronavirus, pneumonia, COVID-19, 2019-nCoV, SARS-CoV-2 ,pneumonia ,Infectious diseases, Evidence-based medicine.

Literature Search

This narrative review discusses the relevant literature, including updated studies, Case series , protective measure ,treatment guidelines and the implications for practice with respect to (novel Corona virus, nCoV) infection. We performed a literature search using ProQuest, MEDLINE, and PUBMED. The search terms used wer COVID-19, Corona viruses, outbreak, “respiratory illness”, “transmission”, and “infection control and management”. After reading the article titles and abstracts, full text, we included 20 articles based on the quality of the studies.

Virology

There are seven strains of human CoVs, which include 229E, NL63,nOC43, HKU1, Middle East respiratory syndrome (MERS) CoV, severe acute respiratory syndrome (SARS) CoV, and 2019 novel coronavirus (nCoV), responsible for the infection with special reference to the involvement of the respiratory tract (both lower and upper respiratory tract), e.g., common cold, pneumonia, bronchiolitis, rhinitis, pharyngitis, sinusitis, and other system symptoms such as occasional watery and diarrhea. (6)

Corona viruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms.(2) According to recent research, similar to SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), SARSCoV-2 is zoonotic, with Chinese horseshoe bats (Rhinolophus sinicus) being the most probable origin (Chan et al. 2020; Lu et al. 2020) and pangolins as the most likely intermediate host (The Chinese Preventive Medicine Association 2020). (4)

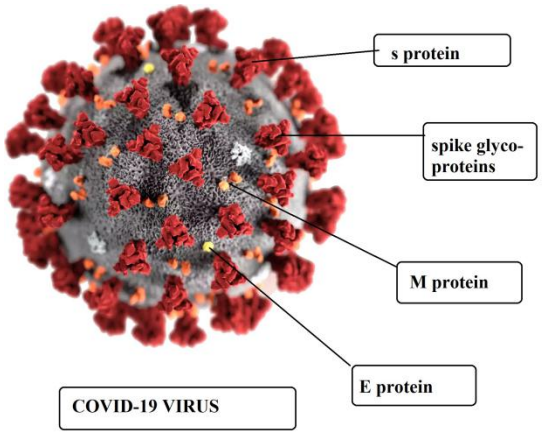

Fig. 1: Illustration showing structure of corona virus , COVID-19 .

Corona viruses (CoVs) have a single-stranded RNA genome (size range between 26.2 and 31.7 kb, positive sense) protected by an enveloping membrane. The form is either pleomorphic or spherical (Figure 1) but is distinguished by club-shaped glycoprotein projections on its surface (diameter 80–120 nm). Of all RNA viruses, the RNA genome of CoV is among the largest.(7) A most significant structural proteins of CoV are spike (S) protein (trimeric), membrane (M) protein, envelop (E) protein, and nucleocapsid. Some of the viruses such as beta CoVs also have hemagglutinin esterase (HE) glycoprotein.(8).

Mode of Transmission

CoVs have been defined as a novel respiratory tract virus in the samples collected from the individuals who present symptoms of respiratory tract infection in 1962.This is a huge family of viruses that are widespread in several different animal species, which include camels, cows, cats, and bats. Animal CoVs will occasionally cause illness and, as a result, spread to humans through epidemics such as MERS, SARS, and COVID-19.(9)Many domestic and wild animals, including camels, cattle, cats, and bats, may serve as hosts for corona viruses. It is considered that, generally, animal corona viruses do not spread among humans .However, there are exceptions, such as SARS and MERS, which are mainly spread though close contact with infected people via respiratory droplets from cough or sneezing. With regard to COVID-19, early patients were reported to have some link to the Huanan Seafood Market in Wuhan, China, suggesting that these early infections were due to animal-to-person transmission.(2)(10)

In addition, there may be risk of fecal-oral transmission, as researchers have identified SARS-CoV-2 in the stool of patients from China and the United States (Holshue et al. 2020). However, whether SARS-CoV-2 can be spread through aerosols or vertical transmission (from mothers to their newborns) is yet to be confirmed (Chen, Guo, et al. 2020; WHO 2020c; Zhu et al. 2020).(4) There is likely an intermediate host between bats and humans, and preliminary data suggest it is the pangolin (a scaly anteater), an endangered and commonly trafficked mammal in which recombination of the bat and pangolin coronaviruses could have occurred.(11)

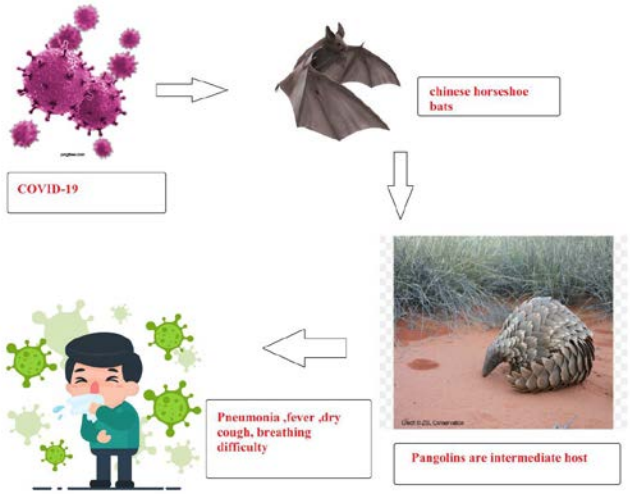

Figure 2 : Illustrates of 2019 Novel Corona virus showing bats as a supposed principal carrier , pangolin as intermediate host , transmitting COVID-19 to human through animal to human transmission.

Clinical Features

Study by Carlos del Rio et.al. , In overall, the clinical appearance featured fever in 83% to 98% of patients, dry cough in 76% to 82%, and fatigue or myalgia in 11% to 44%. Additional symptoms have been documented, like headache, sore throat, stomach pain, and diarrhea. Abnormal laboratory observations reported were lymphopenia (70 per cent), extended prothrombin time (58 per cent) and elevated lactate dehydrogenase (40 per cent). Chest radiographs are distinguished by bilateral patchy infiltrates and CT

scans appear to show ground-glass infiltrates.(11) Wu Z, McGoogan JM, surveys of hospital patients, primarily in Wuhan, China, show that the average age is 50 years, with a small overrepresentation of men; roughly 25% of patients have a serious condition necessitating intensive care, and nearly 10% need mechanical ventilation.(12) Patients with mild symptoms were reported to recover after 1 week while severe cases were reported to experience progressive respiratory failure due to alveolar damage from the virus, which may lead to death. Cases resulting in death were primarily middle-aged and elderly patients with pre-existing diseases(tumor surgery, cirrhosis, hypertension, coronary heart disease, diabetes, and Parkinson's disease).(6)(13).

WHO diagnostic criteria based on symptoms and travel.

Clinical Features

Acute respiratory infection (ARI) ,Fever or measured temperature ≥38C° ,Cough Onset within the last ~10 days ,Requires hospitalization .

Epidemiological Risk :- History of travel from Hubei Province , Healthcare workers who have worked in an environment where patients with ARI are being cared for , Unexpected clinical course follows despite treatment, including rapid deterioration , Close contact (within 2 metres for over 15 minutes) with confirmed COVID-19 infection , Present in healthcare facilities and hospitals in countries where COVID-19 has been reported , All of the above occurring within 14 days prior to symptom onset.(14)

Chen N, Zhou M et.al. ,Approximately one-fourth to one-third of hospitalized patients in Wuhan had serious medical problems, such as acute respiratory distress syndrome, arrhythmia, and shock, and were therefore shifted to the intensive care. (15) For patients with suspected infection, the following procedures have been suggested for diagnosis: performing real-time fluorescence (RT-PCR) to detect the positive nucleic acid of SARS-CoV-2 in sputum, throat swabs, and secretions of the lower respiratory tract samples .(2)

Treatment & Management

A total of 233 trials are registered till date in the Chinese Clinical Trial Registry (dated Feb 24, 2020, keywords 2019-nCov and COVID-19). Among the pharmacotherapeutic agents evaluated, some of the highlighted agents, which are being evaluated, are high-dose Vitamin C, favipiravir, adalimumab, dihydro-artemisinin piperaquine, leflunomide, dipyridamole, chloroquine or hydroxychloroquine, suramin sodium, lopinavir/ritonavir and arbidol (umifenovir) tablets, and IFN-alpha 2b .(6)

A recent paper reported by Zhonghua Jie He He Hu Xi Za Zhi ,shows an inhibitor effect of remdesivir (a new antiviral drug) and chloroquine (an old antimalarial drug) on the growth of SARS-CoV-2 in vitro, and an early clinical trial conducted in COVID-19 Chinese patients, showed that chloroquine had a significant effect, both in terms of clinical outcome and viral clearance, when comparing to controls groups Chinese experts recommend that patients diagnosed as mild, moderate and severe cases of COVID-19 pneumonia and without contraindications to chloroquine, be treated with 500 mg chloroquine twice a day for ten days.(16)

Gautret et al. (2020) ,Hydroxychloroquine (an analogue of chloroquine) has been demonstrated to have an anti-SARS-CoV activity in vitro. Hydroxychloroquine's clinical safety profile is superior than that of chloroquine (during long-term use) and requires higher regular doses and has less complaints about drug-drug interactions. Initial findings suggest the synergistic effect of the mixture of hydroxychloroquine with

azithromycin.Azithromycin has been shown to be active in vitro against Zika and Ebola viruses and to prevent severe respiratory tract infections when administrated to patients suffering viral infection.Oral hydroxychloroquine sulfate 200 mg, three times per day during ten days were given.(17)

lopinavir, a human immunodeficiency virus (HIV) type 1 aspartate protease inhibitor, have a inhibitory activity against SARS-CoV ,Ritonavir is combined with lopinavir to increase its plasma half life through the inhibition of cytochrome P450. An open-label study published in 2004 suggested, by comparison with a historical control group that received only ribavirin, that the addition of lopinavir–ritonavir (400 mg and 100 mg, respectively) to ribavirin reduced the risk of adverse clinical outcomes (acute respiratory distress syndrome [ARDS] or death) as well as viral load among patients with SARS.(18)

B.Cao, Y. Wang, D. Wen et.al. , A randomized, controlled, open-label study involving hospitalized adult patients with identified SARS-CoV-2 infection resulting respiratoryCovid-19 disease and oxygen saturation (Sao2) of 94 per cent or less when breathing ambient air or a proportion of partial oxygen pressure (Pao2) to fraction of inspired oxygen (Fio2) of less than 300 mm Hg was performed.Patients were randomly allocated a 1:1 ratio to accept either lopinavir–ritonavir (400 mg and 100 mg, respectively) twice daily for 14 days, in addition to standard therapy ,or standard care alone.lopinavir–ritonavir led to a median time toclinical improvement that was shorter by 1 day than that observed with standardcare (hazard ratio, 1.39; 95% CI, 1.00 to 1.91).

Gastrointestinal adverse events were more common in the lopinavir–ritonavir group, but serious adverse events were more common in the standard-care group.In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit.(19)

remdesivir was used in the first case reported from the United States of America, seemed successful, controlled studies with more cases areneeded.In-vitro studies have shown that viral RNA transcription was terminated with remdesivir in early stage.There are publications demonstrating that remdesivir has a strong antiviral activity in epithelial cell cultures against SARS-CoV, MERS-CoV and related zoonotic bat CoVs.(9)

Drug	Dosage	Mode of administration	Duration of treatment
IFN-α	5 million U or equivalent dose each time, 2 times/day	Vapor inhalation	No more than 10 days
Lopinavir/ritonavir	200 mg/50 mg/capsule, 2 capsules each time, 2 times/day	Oral	No more than 10 days
Ribavirin	500 mg each time, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir	Intravenous infusion	No more than 10 days

Chloroquine phosphate	500 mg (300 mg for chloroquine) each time, 2 times/day	Oral	No more than 10 days
Arbidol	200 mg each time, 3 times/day	Oral	No more than 10 days

Table 1: Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-induced Pneumonia, The 6th ed. (20)

Sheahan TP, Sims AC et.al. Remdesivir might be the best available medicine for the treatment of 2019-nCoV.Animal studies have shown that, relative to the control group, Remdesivir can dramatically reduce the virus titer of mice diagnosed with the Middle East Respiratory Syndrome (Mers)-CoV, reduce lung tissue damage and its effectiveness is superior than that of the Lopinavir / Ritonavir treatment group combined with interferon-β .(20)(22).

Favipiravir became authorised for the treatment of novel influenza in China from 15 February 2020.The medication is undergoing a major clinical trials in the treatment of COVID-19.Favipiravir is a new breed of RNA-dependent polymerase (RdRp) inhibitor.In contrast to its anti-influenza function, favipiravir is capable of preventing the replication of the virus.flavi-, alpha-, filo-, bunya-, arena-, noro-, and other RNA viruses.Favipiravir is transformed into an active phosphoribosylated state (favipiravir-RTP) in cells and is identified as a substrate by viral RNA polymerase, hence hindering the activity of RNA polymerase. Therefore, favipiravir may have potential antiviral action on SARS-CoV-2, which is a RNA virus.(20)A randomized controlled trial on favipiravir for the treatment of COVID-19 implemented by the National Infectious Diseases Clinical Medical Research Center and the Shenzhen's ,Third People's Hospital obtained favorable outcomes on 14 February. Early tests of a sum of 80 patients (including the experimental group and the control group) revealed that favipiravir had a far more potent antiviral activity than lopinavir / ritonavir .(21)

IFN-α is a broad-spectrum antiviral that is usually used to treat hepatitis, though it is reported to inhibit SARS-CoV reproduction in vitro.which can be used to treat HBV. based on the preliminary outcomes of clinical studies. Among adults, the specific approach in administering IFN-α is vapor inhalation at a dosage of 5 million U (and 2 mL of sterile water for injection), 2 times a day.Drugs for the 2019-new coronavirus identified using testing the existing broad-spectrum antiviral drugs by using standard assays, which have been used to treat other viral infections .by this methods one , can measure the effects of these drugs on the cytopathy, viral production and plaque formation of living cells and/or pseudocoronaviruses. (22)Given the practical constraints on substantially increasing the global availability of ECMO services in the next few months, it is important to emphasise the other evidence-based treatment options that can be(Table 3) provided for patients with severe ARDS from COVID-19 .(23)

Therapy	Implementation
High-flow nasal oxygen	Might prevent or delay the need for intubation
Tidal volume	Use 6 mL/kg per predicted bodyweight

	(can reduce to 4 mL/kg per predicted bodyweight)
Plateau airway pressure	Maintain at <30 cm H20 if possible Positive
end-expiratory pressure	Consider moderate to high levels if needed
Recruitment manoeuvres	Little value
Neuromuscular blockade	For ventilator dyssynchrony, increased airway pressure, hypoxaemia
Prone positioning	For worsening hypoxaemia, PaO2:FiO2 <100–150 mm Hg
Inhaled NO	Use 5–20 ppm
Fluid management	Aim for negative fluid balance of 0·5–1·0 L per day
Renal replacement	therapy For oliguric renal failure, acid-base management, negative fluid balance
Antibiotics	For secondary bacterial infections
Glucocorticoids	Not recommended
Extracorporeal membrane oxygenation	Use EOLIA trial criteria3

Table 2: Therapeutic options for severe acute respiratory distress syndrome related to coronavirus disease 2019 , ppm=parts per million.(23)

Conclusion

The latest outbreak of COVID-19 was deemed a pandemic by W.H.O. As of 24 March 2020, COVID-19 was reported in 196 countries, with a total of 395,583 laboratory-confirmed outbreaks, 103,736 recovered and 12,234 fatalities. Up to this date, 519 laboratory-confirmed cases have been reported, 40 managed to recover and 10 fatalities have been reported by the Indian Council of Medical Reserch. Until now, no effective antiviral drug or vaccine has been identified for the treatment of COVID-19. Most of the drug choices come from prior experience in the treatment of SARS, MERS or some other new influenza virus.Effective symptomatic intervention remains a gold standard in the treatment of COVID-19. Scientists and researchers are performing numerous trials around the world. We expect to see conclusive drug treatment and vaccine against COVID-19 in the anytime soon, until then prevention is the gold standard approach against the novel corona virus.

References

1. Stanley Perlman and Jason Netland ,Coronaviruses post-SARS: Update on replication and pathogenesis ,Nat Rev Microbiol. 2009 June ; 7(6): 439–450. doi:10.1038/nrmicro2147
2. Sasmita Poudel Adhikari, Sha Meng, Yu-Ju Wu, Yu-Ping Mao, Rui-Xue Ye, Qing-Zhi Wang, Chang Sun,Sean Sylvia, Scott Rozelle, Hein Raat and Huan Zhou1,Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review ,Infectious Diseases of Poverty (2020) 9:29 ,https://doi.org/10.1186/s40249-020-00646-x.
3. Lu H, Stratton CW, Tang Y (2020) Outbreak of Pneumonia of Unknown Etiology in Wuhan China: the Mystery and the Miracle. J Med Virol jmv.25678
4. L. Meng1, F. Hua , and Z. Bian ,Coronavirus Disease 2019 (COVID-19): Emerging and Future Challenges for Dental and Oral Medicine
5. DaweiWang, Bo Hu, Chang Hu, Fangfang Zhu et.al. ,Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected

Pneumonia inWuhan, China ,JAMA. doi:10.1001/jama.2020.158

6. Prajapat M, Sarma P,Shekhar N, Avti P, Sinha S, Kaur H, et al. Drug targets for corona virus: A systematic review. Indian J Pharmacol 2020;52:56-65.
7. Yang H, Bartlam M, Rao Z. Drug design targeting the main protease, the Achilles' heel of coronaviruses. Curr Pharm Des 2006;12:4573-90.
8. Hilgenfeld R. From SARS to MERS: Crystallographic studies on coronaviral proteases enable antiviral drug design. FEBS J 2014;281:4085-96.
9. Sahin AR, Erdogan A, Mutlu Agaoglu P, Dineri Y, Cakirci AY, Senel ME, et al. 2019 Novel Coronavirus (COVID-19) Outbreak: A Review of the Current Literature. EJMO 2020;4(1):1-7.
10. Liu T, Hu J, Kang M, Lin L, Zhong H, Xiao J, et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV). 2020; doi: https://doi.org/10.1101/2020.01.25.919787
11. Carlos del Rio, Preeti N. Malani ,COVID-19—New Insights on a Rapidly Changing Epidemic ,JAMA Published online February 28, 2020 E1-E2.
12. Wu Z,McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. Published February 24, 2020. doi:10.1001/jama.2020.2648
13. Li T, Wei C, Li W, Hongwei F, Shi J. Beijing Union Medical College Hospital on "pneumonia of novel coronavirus infection" diagnosis and treatment proposal (V2.0). Med J Peking Union Med Coll Hosp. 2020. http://kns.cnki.net/kcms/detail/11.5882.r.20200130.1430.002.html.Accessed 2 Feb 2020.
14. Centers for Disease Control and Prevention (2020) 2019 Novel Coronavirus.https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html.
15. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, et al. 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 395(10223):507–513.
16. Zhonghua Jie He He Hu Xi Za Zhi ,Multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia. Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia ,Mar 12;43(3):185-188. doi: 10.3760/cma.j.issn.1001-0939.2020.03.009.
17. Gautret et al. (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents –In Press 17 March 2020 –DOI : 10.1016/j.ijantimicag.2020.105949
18. Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax 2004; 59: 252-6.
19. B. Cao, Y. Wang, D. Wen ,A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19 ,Th e new england journal o f medicine ,DOI: 10.1056/NEJMoa2001282.

20. Liying Dong, Shasha Hu, Jianjun Gao ,Discovering drugs to treat coronavirus disease 2019 (COVID-19) ,Drug Discoveries & Therapeutics. 2020; 14(1):58-60 ,DOI: 10.5582/ddt.2020.01012 .
21. News.http://www.szdsyy.com/News/0a6c1e58-e3d0-4cd1-867a-d5524bc59cd6.html (accessed February 22, 2020). (in Chinese).
22. Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun. 2020 ; 11:222.
23. Michael A Matthay, J Matthew Aldrich, Jeffrey E Gotts ,Treatment for severe acute respiratory distress syndrome from COVID-19.