World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

CURRENT EPIDEMIOLOGY, DIAGNOSIS AND TREATMENT OF COVID-19

Md. Aqib Ali Faraz[1], Sowjanya Mendem[1]* and K. Sri Bharath[2]

[1]Department of Pharmacy Practice, MNR College of Pharmacy, Sangareddy, Telangana, India.
[2]Department of Pharmaceutics, MNR College of Pharmacy, Sangareddy, Telangana, India.

***Corresponding Author: Sowjanya Mendem**
Department of Pharmacy Practice, MNR College of Pharmacy, Sangareddy, Telangana, India.

Article Received on 12/06/2020 **Article Revised on 02/07/2020** **Article Accepted on 23/07/2020**

ABSTRACT

Novel Corona virus was first reported in Wuhan, Hubei Province of China, and was then classified as Severe acute respiratory syndrome corona virus-2 (Sars-CoV-2) by the International Committee on Taxonomy of Viruses. Elderly patients with comorbitdities were primarily at risk due to the virus, but it is also known to affect the younger populations. The rapid spread of virus across the globe demonstrated human to human transmission of the virus through droplets or direct contact. This spread was also made possible by asymptomatic carriers of the virus. As of January 30, 2020 7,734 cases were reported in China and the virus had spread to 19 other countries, including-Taiwan, Thailand, Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan, Singapore, Republic of Korea, UAE, United States, the Philippines, Canada, India, Australia, Germany, Finland and France. According to the Indian Council of Medical Research, Hospitals admitting suspected cases of COVID19 should collect nasal and throat swab samples in one VTM tube and transport them to the nearest testing laboratory in cold chain. Current coronavirus diagnostic tests include reverse transcription-polymerase chain reaction (RT-PCR), RT-PCR (rRT-PCR), real-time RT-PCR and reverse transcription loop-mediated isothermal amplification (RT-LAMP). The inhibition of cellular function and molecular pathways involved in the immune activation by Hydroxychloroquine (HCQ) and Chloroquine (CQ) enable their use in the treatment of Covid-19. Remdesivir is a recently FDA-approved drug for the treatment of Covid-19. It acts as a nucleoside analog with significant antiviral activity. As of July 2, 2020, the World Health Organization (WHO) reported 1,03,57,662 confirmed cases world wide and 05,08,055 deaths have been confirmed.

KEYWORDS: Covid-19, Epidemiology, prevention, diagnosis, treatment, Remdesivir.

INTRODUCTION

Novel Corona virus was first reported in Wuhan, Hubei Province of China, and was then classified as Severe acute respiratory syndrome corona virus-2 (Sars-CoV-2) by the International Committee on Taxonomy of Viruses. This virus belongs to the *Betacoronavirus* lineage, sub genus *Sarbecovirus*. The symptoms vary from a fever, cough, shortness of breath, leukopenia, pneumonia in both lungs, weakness, diarrhoea, tastlessness. Elderly patients with comorbitdities were primarily at risk due to the virus, but it is also known to affect the younger populations.[1] The Chinese Center for Disease Control and Prevention (CCDC) identified this infection as a novel coronavirus infection o January 7, 2020, the WHO announced a new name for the epidemic disease as 2019-new coronavirus disease on February 11.[2]

Earlier studies revealed a connection between a single local fish and wild animal market for most cases of infection, which could be due to possible animal-to human transmission, however, the rapid spread of virus across the globe demonstrated human to human transmission of the virus through droplets or direct contact. This spread was also made possible by asymptomatic carriers of the virus.[3] Presently, three single strand RNA (ssRNA) beta-coronavirus have been identified and include: severe respiratory syndrome (SARS) virus, Middle-East respiratory syndrome (MERS) virus, and SARS-CoV-2. SAR-CoV-2 was found to be 96% identical at the whole-genome level to a bat coronavirus, indicating that bats might be the intermediate host for the virus.[4]

Currently, seven human CoVs (HCoVs) have been reported and are named as: Human coronavirus NL63 (HCov-NL63) and Human coronavirus 229E (HCov-229E) belong to the alpha-coronavirus genus. Human coronavirus OC43 (HCoV-OC43), Human coronavirus (HCoV-HKU1), SARS-CoV, SARS-CoV-2 and Middle East respiratory syndrome coronavirus (MERS-CoV), belong to the *beta-coronavirus* genus. Mild respiratory disease in humans is caused by HCoV-229E, HCoV-

NL63, HCoV-HKU1 and HCoV-OC43 strains of coronavirus.[5]

The average incubation period of the 8,866 nationwide cases in China (as of January 26) was found to be at 4.75 days. After January, the average time between the onset and initial diagnosis in confirmed patients in China was found to be 4.6 days. Also, it was found that the time between the onset of severe illness and initial diagnosis was 8 days. Symptoms of Covid-19 generally include, fever, fatigue, and dry cough. Atypical symptoms include expectoration, headache, hemoptysis, nausea, vomiting, and diarrhoea. Loss of smell and taste (chemosensory dysfunction) was also found to be closely associated with the infection and is typically recovered within 2 to 4 weeks after the first infection. Certain asymptomatic patients reported symptoms like mild fatigue, low fever, and were mostly recovered within a week.[6]

Coronavirus can be spread by sneezing, cough droplets and physical contact with the infected. The virus is reported to infect a person at a distance of about 6 ft radius and can survive for about 2 hours to a few days in the cough/sneeze droplets on the surface or the ground. Infection is spread rapidly when a healthy person comes in contact by touching these surfaces or objects.[7]

EPIDEMIOLOGY

The first 4 cases of COVID-19 were reported on 29 December, 2019, in the Wuhan city, Hubei Province, China.[8] In between December 18, 2019 and December 28, 2019 five patients were hospitalized with the complaint of respiratory distress syndrome. One of these five patients succumbed to death, and this was the first reported death due to COVID-19.[9] By January 22, 2020, there were a total of 571 cases of COVID-19 reported in 25 provinces of China.[10] As of January 30, 2020 7,734 cases were reported in China and the virus had spread to 19 other countries, including-Taiwan, Thailand, Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan, Singapore, Republic of Korea, UAE, United States, the Philippines, Canada, India, Australia, Germany, Finland and France. A total of 90 cases had been reported in these countries.[11]

By February 27, 2020 82,623 cases were confirmed globally and 2858 deaths were reported. According to 6th version of guidance for diagnosis and treatment for COVID-19 by National Health Commission of China human to human transmission was the major means of transmission of the virus. They concluded that the virus was transmitted through respiratory aspirates, droplets, feces, and aerosols transmission.[12] A Research on early transmission dynamics of the virus recorded Median age of patients up to 59 years, starting from 15 years of age to 89 years, the majority (59 per cent) were male. Most of the adult patients were between 35 and 55 years of age.[13],[15] Various studies of COVID-19 have calculated the frequency of basic replication (R_0) to be between 2.6 and 4.71. The total incubation time of COVID-19 was calculated to be 4.8 ± 2.6, ranging from 2 to 11 days and 5.2 days (95% confidence interval, 4.1 to 7).[14] (These indicators have been briefly illustrated in Table.1). The latest guidelines from the Chinese health authorities suggested an average incubation time of 7 days, varying from 2 to 14 days.[15] During the time of preparation of this manuscript, as of July 2, 2020 the World Health Organization (WHO) reported 1,03,57,662 confirmed cases world wide and 05,08,055 deaths have been confirmed. We can observe that within a span of 4 months the number of confirmed cases has increased by 125 times and has reached over 20 countries.[16]

Table 1. Epidemiological indicators of COVID-19.

Indicators	Description
Age	Cases range between 35 and 55 years of age. Median age of patients was up to 59 years.
Sex of the patients	Majority of the patients were male compared to females
Incubation time	The total incubation time of COVID-19 was calculated to be 4.8 ± 2.6, ranging from 2 to 11 days and 5.2 days (95% confidence interval, 4.1 to 7). Average incubation time of 7 days, varying from 2 to 14 days.
Reproduction and replication rate (R_0)	Between 2.6 and 4.71.

DIAGNOSIS

Rapid and precise identification of COVID-19 is important for monitoring of an outbreak in a Nation. Using a random-access approach, diagnosis can be done more easily than with batch-wise testing.[17] The SARS-CoV-2 positive-sense, the single-stranded RNA genome is 30 kb in size and codes 9,860 amino acids.[18] According to the Indian Council of Medical Research, Hospitals admitting suspected cases of COVID19 should collect nasal and throat swab samples in one VTM tube and transport them to the nearest testing laboratory in cold chain.

Current coronavirus diagnostic tests include reverse transcription-polymerase chain reaction (RT-PCR), RT-PCR (rRT-PCR), real-time RT-PCR and reverse transcription loop-mediated isothermal amplification (RT-LAMP). RT-LAMP has equal sensitivity to rRT-

PCR, is highly sensitive, and used for MERS-CoV detection. Three new RT-PCR assays targeting RNA-dependent polymerase (RdRp)/Hel, spike (S), and nucleocapsid (N) genes of SAR-CoV-2 were developed.[19] The COVID-19-RdRp / Hel assay was highly sensitive and accurate for detection of SARS-CoV-2 RNA in vitro and in COVID-19 patient specimens among the three novel assays.[18] Real-time RT-PCR is widely used in diagnostic virology.[20] Shortly after the onset of symptoms, positive SARS-CoV-2 RT-PCR level was observed, with a slowly decreasing trend thereafter.[21]

The Hologic Panther Fusion (PF) method allows for rapid, fully automated processing of diagnostic specimens including removal of RNA, amplification of target sequences, and detection of PCR amplicons in around 3.5 hours in real-time.[17]

Serological tests are currently being established for widespread use. But it presents with the following challenges: firstly, assessing the sensitivity and specificity of tests, especially during the acute infection phase; secondly, ensuring the test does not detect cross-reactivity with other viral pathogens resulting in false-positive results; third, understanding antibody kinetics.[22]

Viral RNA detection from oral swabs used for diagnosis of Covid-19 is not ideal. The virus can occur in patients' anal swabs or blood when the detection of oral swabs is negative. In later stages of infection, the intestinal infection was observed in patients infected with SARS-CoV and MERS-CoV.[23]

The present laboratory test is time-consuming, and the diagnosis is hindered by a shortage of consumer kits. For the negative RT-PCR reports, COVID-19 infection should be tested with standard chest computerized tomography (CT) for patients with symptoms like fever, sore throat, fatigue, coughing or dyspnea.[19]

PREVENTION

Preventive approaches focus on patient isolation and careful management of the virus, including adequate steps to be taken during the diagnosis and clinical treatment of an infected patient. Physical contact and airborne precautions should be followed during specimen processing, and the induction of sputum should be avoided.

The WHO and other organizations have issued the following general recommendations.

- Avoid close contact with subjects suffering from acute respiratory infections.
- Wash your hands frequently, especially after contact with infected people or their environment.
- Avoid unprotected contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands.
- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immunocompromised should avoid public gatherings.

Health care staff who tend to infected individuals should safety measures that include EPPs such as N95 or FFP3 masks, eye protection, gowns, and gloves that avoid virus transmission.[24]

TREATMENT

The inhibition of cellular function and molecular pathways involved in the immune activation by Hydroxychloroquine (HCQ) and Chloroquine (CQ) enable their use in the treatment of Covid-19. Chloroquine analogues are weak diprotic bases that can penetrate the cell and concentrate in endosomes and lysosomes, leading to elevated intra-vesicular pH which results in the prevention of endosome trafficking and eventually prevents the viral fusion into the cell. The drugs are also observed to interfere with the glycosylation of the ACE-2 receptor, which prevents SARS-CoV-2 receptor binding, thereby preventing the infection. A dose of 400mg of HCQ, given twice daily for 1 day, followed by 200 mg twice a day for 4 days is recommended for treatment.[24]

Remdesivir is a recently FDA-approved drug for the treatment of Covid-19. It acts as a nucleoside analog with significant antiviral activity. As an inhibitor of RNA-dependent polymerase RNA (RdRp), it can inhibit multiple coronavirus replication in respiratory epithelial cells. In a rhesus monkey infected with MERS-CoV, treatment with Remdesivir 24 hours before an infection can fully prevent symptoms, strongly inhibit viral replications in the respiratory tract and prevent pulmonary lesions from developing. The administration of Remdesivir 12 hours after infection offers direct clinical benefits, reducing clinical symptoms, replication of the lung virus, and lesions of the lungs. Recent cases of Remdesivir have been effective in treating COVID-19. The New England Journal of Medicine published the entire course of the first patient's recovery in the USA.[26] A study by Jienchi Dorward et al concluded insufficient evidence for the clinical use of Lopinavir/Ritonavir.[27] Favipiravir (FPV) is a prodrug and a novel RNA-dependent RNA polymerase (RdRp) inhibitor, proved to be effective in the treatment of influenza and Ebola virus. A study by Wang et al proved a reduction in SAR-CoV-2 infection by treatment with FPV and Remdesivir. Overall, the studies on the role of antivirals in the treatment of Covid-19 are not conclusive.[28] Recently, the ICMR has approved for the emergency public use of

Lopinavir-Ritonavir combination in patient with moderate to severe degrees of the infection.[29]

For more than a century, Convalescent plasma therapy (CP), a traditional adaptive immunotherapy, has been applied to the prevention and treatment of many infectious diseases. During the past two decades, CP therapy has been successfully used with acceptable effectiveness and protection in the treatment of the SARS, MERS, and 2009 H1N1 pandemic. A useful donor source of CP may be patients who have recovered from COVID-19 with a high neutralizing antibody titer. Studies have shown the safety, accessibility, and betterment in Covid-19 patients due to CP therapy. Patients receiving CP exhibited a rapid increase of lymphocyte count and a decrease of C- reactive protein (CRP), with the absorption of lung lesions on CT. Plasma therapy has no serious adverse reactions, with the only risk being the transmission of a potential pathogen.[30]

CONCLUSION

This study gives a brief picture of the current scenario of the COVID-19 outbreak, exploring origin, epidemiology, diagnosis and treatment of novel corona virus. Conclusions can be drawn from the rate of spread of the virus in a span of over 7 months, considering it a Public health emergency. Since, a specific treatment is yet to be formulated, we recommend the scholarly community around the world to invest more amount of work and research in order to provide a reliable ways and methods to mange this public health emergency and minimize its impact.

CONFLICT OF INTEREST: None declared.

REFERENCES

1. Zhang LP, Wang M, Wang Y, Zhu J, Zhang N. Focus on a 2019-novel coronavirus (SARS-CoV-2). Future Microbiology. 2020 May.
2. Abd El-Aziz TM, Stockand JD. Recent progress and challenges in drug development against COVID-19 coronavirus (SARS-CoV-2)-an update on the status. Infection, Genetics and Evolution, 2020 Apr 19: 104327.
3. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. International journal of antimicrobial agents, 2020 Feb 17: 105924.
4. Huang J, Song W, Huang H, Sun Q. Pharmacological therapeutics targeting RNA-dependent RNA polymerase, proteinase and spike protein: from mechanistic studies to clinical trials for COVID-19. Journal of Clinical Medicine, 2020 Apr; 9(4): 1131.
5. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, Giridharan B, Ganesan S, Venugopal A, Venkatesan D, Ganesan H, Rajagopalan K. COVID-19: A promising cure for the global panic. Science of The Total Environment, 2020 Apr 4: 138277.
6. Guo G, Ye L, Pan K, Chen Y, Xing D, Yan K, Chen Z, Ding N, Li W, Huang H, Zhang L. New Insights of Emerging SARS-CoV-2: Epidemiology, Etiology, Clinical Features, Clinical Treatment, and Prevention. Frontiers in Cell and Developmental Biology. 2020 May 22; 8: 410.
7. Ali I, Alharbi OM. COVID-19: Disease, management, treatment, and social impact. Science of the Total Environment, 2020 Apr 22: 138861.
8. A. Du Toit, Outbreak of a novel coronavirus, Nat. Rev. Microbiol, 2020; 18: 123.
9. L.L. Ren, Y.M. Wang, Z.Q. Wu, Z.C. Xiang, L. Guo, T. Xu, et al., Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study, Chinese Med J, 2020.
10. H. Lu, Drug treatment options for the 2019-new coronavirus (2019-nCoV), Biosci. Trends, 2020.
11. M. Bassetti, A. Vena, D. Roberto Giacobbe, The Novel Chinese Coronavirus (2019-nCoV) Infections: challenges for fighting the storm, Eur. J. Clin. Invest, 2020; e13209.
12. Wang, Y, Wang, Y, Chen, Y, Qin, Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol, 2020; 92: 568– 576.
13. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med, 2020.
14. Liu T, Hu J, Kang M, Lin L, Zhong H, Xiao J, et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV), 2020.
15. Adhikari, S., Meng, S., Wu, Y. et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis Poverty, 2020; 9: 29.
16. WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. Covid19.who.int. 2020 [cited 2 July 2020]. Available from: https: //covid19.who.int/
17. Cordes AK, Heim A. Rapid random access detection of the novel SARS-coronavirus-2 (SARS-CoV-2, previously 2019-nCoV) using an open access protocol for the Panther Fusion. Journal of Clinical Virology, 2020 Apr; 125: 104305.
18. Chan JF, Yip CC, To KK, Tang TH, Wong SC, Leung KH, Fung AY, Ng AC, Zou Z, Tsoi HW, Choi GK. Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel real-time reverse transcription-PCR assay validated in vitro and with clinical specimens. Journal of Clinical Microbiology, 2020 Apr 23; 58(5).
19. Zhai P, Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of COVID-

19. International Journal of Antimicrobial Agents, 2020 Mar 28: 105955.
20. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DG. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Eurosurveillance. 2020 Jan 23; 25(3): 2000045.
21. Tang Xiao A, Xin Tong Y, Gao C, Zhu L, Jie Zhang Y, Zhang S. Dynamic Profile of RT-PCR Findings from 301 COVID-19 Patients in Wuhan, China: A Descriptive Study. Yi and Gao, Chun and Zhu, Li and Jie Zhang, Yu and Zhang, Sheng, Dynamic Profile of RT-PCR Findings from, 2020 Feb 29; 301.
22. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, Wang YY, Xiao GF, Yan B, Shi ZL, Zhou P. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerging microbes & infections, 2020 Jan 1; 9(1): 386-9.
23. Winter AK, Hegde ST. The important role of serology for COVID-19 control. The Lancet. Infectious Diseases, 2020 Apr 21.
24. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). InStatpearls [internet] 2020 Mar 8. StatPearls Publishing.
25. YAVUZ S, ÜNAL S. Antiviral treatment of COVID-19. Turkish Journal of Medical Sciences, 2020 Apr 21; 50(SI-1): 611-9.
26. Cao YC, Deng QX, Dai SX. Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. Travel Medicine and Infectious Disease, 2020 Apr 2: 101647.
27. Dorward J, Gbinigie K. Lopinavir/ritonavir: A rapid review of effectiveness in COVID-19.
28. Cai Q, Yang M, Liu D, Chen J, Shu D, Xia J, Liao X, Gu Y, Cai Q, Yang Y, Shen C. Experimental treatment with favipiravir for COVID-19: an open-label control study. Engineering, 2020 Mar 18.
29. Bhatnagar T, Murhekar MV, Soneja M, Gupta N, Giri S, Wig N, Gangakhedkar R. Lopinavir/ritonavir combination therapy amongst symptomatic coronavirus disease 2019 patients in India: Protocol for restricted public health emergency use. Indian Journal of Medical Research, 2020 Feb 1; 151(2): 184.
30. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, Zhou M, Chen L, Meng S, Hu Y, Peng C. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proceedings of the National Academy of Sciences, 2020 Apr 28; 117(17): 9490-6.