OPEN ACCESS

Katalyst Publishing Group

Research Article

Journal of Current Trends in Pharmaceutical Sciences

Epidemiology, Virology, Pathogenesis and Treatment of Novel COVID-19

Farouk S. Nas[1], Muhammad Ali[2*], Lurwan Mu'azu[3] and Muhammad S. Abdallah[4]

[1]Department of Biological Sciences, Bayero University Kano, Nigeria

[2]Department of Microbiology, Federal University Gusau, Nigeria

[3]Department of Biological Sciences, Federal University Gusau, Nigeria

[4]Desert Research Monitoring and Control Centre, Yobe State University Damaturu, Nigeria

Received Date: 24 May, 2020
Accepted Date: 01 June, 2020
Published Date: 10 June, 2020

***Corresponding author:** Muhammad Ali, Department of Microbiology, Federal University Gusau, Nigeria, E-mail: alimuhd4real@gmail.com

Citation: Muhammad Ali (2020) Epidemiology, Virology, Pathogenesis and Treatment of Novel COVID-19. J Cur Tre Pharm Sci 1: 104.

Abstract

In December 2019, a pneumonia associated with the corona virus disease 2019 (COVID-19) emerged in Wuhan, Hubei Province, China. It is highly contagious and has been quickly spread to many other parts of China and some other countries within a month since the first report emerged. As of May 12, 2020, total of 4,088 848 cases of confirmed infections and 283,153 deaths have been reported worldwide. The Symptoms of COVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. Based on the laboratory confirmed cases, typical signs and symptoms include: fever, dry cough, fatigue, sputum production, shortness of breath, sore throat, headache, myalgia or arthralgia, chills, nausea or vomiting, nasal congestion, diarrhea, and hemoptysis, and conjunctival congestion. Potential therapeutic strategies against COVID-19 involve the use of broad-spectrum antibiotics, anti-malarial and anti-viral drugs. Currently, there may be many promising vaccines for COVID-19, but more laboratory and clinical evidence still should be explored. The paper was aimed to review epidemiology, virology, pathogenesis and treatment of novel covid-19.

Keywords: COVID-19, Corona Virus, Epidemiology, Pathogenesis, Vaccines

Introduction

The coronavirus belongs to a family of viruses that may cause various symptoms such as fever, lungs infections and difficulty in breathing [1]. These viruses are common in animals worldwide, but very few cases have been known to affect humans. The World Health Organization (WHO) used the term 2019 novel coronavirus to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China on 29 December 2019 [2-4]. The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) [4]. And the current reference name for the virus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was reported that a cluster of patients with pneumonia of unknown cause was linked to a local Huanan South China Seafood Market in Wuhan, Hubei Province, China in December 2019 [5].

As of May 12, 2020, 84,451 cases of confirmed infections and 4,644 deaths have been reported in Chinese mainland [6]. Outside of China, there had been 4,004,397 confirmed cases and 278,509 death from the rest of the world were reported as of May 12, 2020 [7]. The outbreak of COVID-19 raised intense attention not only within China but internationally [8]. Due to the rapid spread of SARS-CoV-2 through human-to-human transmission, the cases currently continue to rise. SARS-CoV-2 extracted from patients with pneumonia in Wuhan is an enveloped single stranded RNA-type beta-coronavirus [9]. The genome sequences of SARS-CoV-2 shared 79.5% sequence identity to severe acute respiratory syndrome-related coronaviruses (SARS-CoV) [10,11]. In addition, the spike (S) protein of SARS-CoV-2 and SARS-CoV enters human alveolar epithelial cells through binding angiotensin converting enzyme 2 (ACE2) receptors [10]. COVID-19 can be diagnosed by either chest CT radiography or a laboratory testing.

Challenges in treating COVID-19 Coronavirus disease (COVID-19) present a global challenge, particularly in the rapid increase of critically ill patients with pneumonia and absence of definitive treatment. The mortality appears to be around 2%; early published data indicate 25.9% with SARS-CoV-2 pneumonia required ICU admission and 20.1% developed acute respiratory distress syndrome [12]. There is presently no vaccine or specific anti-viral drug regime used to treat critically ill patients. The management of patients mainly focuses on the provision of supportive care, e.g., oxygenation, ventilation, and fluid management. Combination treatment of low-dose systematic corticosteroids and anti-virals and atomization inhalation of interferon have been encouraged as part of critical COVID-19 management [13].

Epidemiology of Covid-19

On 29 December 2019, the first four cases of an acute respiratory

syndrome of unknown etiology were reported in Wuhan City, Hubei Province, China among people linked to a local seafood market ("wet market") [2]. Research is underway to understand more about transmissibility, severity, and other features associated with COVID-19 [3]. It appears that most of the early cases had some sort of contact history with the original seafood market [2,10]. Soon, a secondary source of infection was found to be human-to-human transmission via close contact. There was an increase of infected people with no history of exposure to wildlife or visiting Wuhan, and multiple cases of infection were detected among medical professionals [2,10]. It became clear that the COVID-19 infection occurs through exposure to the virus, and both the immunosuppressed and normal population appear susceptible. Some studies have reported an age distribution of adult patients between 25 and 89 years old. Most adult patients were between 35 and 55 years old [14], and there were fewer identified cases among children and infants [14,15]. A study on early transmission dynamics of the virus reported the median age of patients to be 59 years, ranging from 15 to 89 years, with the majority (59%) being male [2]. It was suggested that the population most at risk may be people with poor immune function such as older people and those with renal and hepatic dysfunction (Li et al., 2020)[2]. The COVID-19 has been found to have higher levels of transmissibility and pandemic risk than the SARSCoV, as the effective reproductive number of COVID-19 is estimated to be higher than the reported effective reproduction number of SARS at this early stage [13]. The average incubation duration of COVID-19 was estimated to be 4.8 ± 2.6, ranging from 2 to 11 days [13] and 5.2 days (95% confidence interval, 4.1 to 7) [2]. The latest guidelines from Chinese health authorities stated an average incubation duration of 7 days, ranging from 2 to 14 days [6].

Table 1 below represents the number of confirmed COVID-19 cases as of 12th May, 2020. On 12th May, 2020, there were 4,088 848 confirmed cases and 283,153 deaths reported globally [16]. The countries with higher number of confirmed cases and death according to situation report by World Health Organization as of May 12th 2020 is presented in Table 2

Table 1: Number of confirmed COVID-19 cases as of 12th May, 2020

Region	Confirmed cases	Total death
Globally	4,088 848	283,153
Africa	46,829	1,449
Americas	1,743,717	104,549
Eastern Mediterranean	274,027	9,138
Europe	1,755,790	157,880
South-East Asia	105,901	3,597
Western Pacific	161,872	6,527

Table 2: Countries with highest number of confirmed COVID-19 cases as of 12th May, 2020

Country	Confirmed cases	Total death
United States of America	1,298,287	78,652
Russia	232,243	2 116
Spain	227,436	26,744
The United Kingdom	223,064	32,065
Italy	219,814	30,739
Germany	170,508	7,533
Brazil	162,699	11,123
Turkey	139,771	3,841
France	137,491	26,600
Iran	109,286	6,685

The Signs, Symptoms, Progression and Severity of COVID-19

According to World Health (2020), the Symptoms of COVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. As of 12th May, 2020 and based on 4,088,848 laboratory confirmed cases, typical signs and symptoms include: fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), and hemoptysis (0.9%), and conjunctival congestion (0.8%). People with COVID-19 generally develop signs and symptoms, including mild respiratory symptoms and fever, on an average of 5-6 days after infection (mean incubation period 5-6 days, range 1-14 days).

Most people infected with COVID-19 virus have mild disease and recover. Approximately 80% of laboratory confirmed patients have had mild to moderate disease, which includes non-pneumonia and pneumonia cases, 13.8% have severe disease (dyspnea, respiratory frequency ≥30/minute, blood oxygen saturation ≤93%, PaO_2/FiO_2 ratio <300, and/or lung infiltrates >50% of the lung field within 24-48 hours) and 6.1% are critical (respiratory failure, septic shock, and/or multiple organ dysfunction/failure). Asymptomatic infection has been reported, but the majority of the relatively rare cases who are asymptomatic on the date of identification/report went on to develop disease. The proportion of truly asymptomatic infections is unclear but appears to be relatively rare and does not appear to be a major driver of transmission [4].

Individuals at highest risk for severe disease and death include people aged over 60 years and those with underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer. Disease in children appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported amongst individuals aged less than 19 years. A very small proportion of those aged under 19 years have developed severe (2.5%) or critical disease (0.2%) [17].

As of 12th May, 2020, 283,153 of the 4,080,848 laboratory confirmed cases have died which indicated that the crude fatality ratio (CFR) is 6.9%. The overall CFR varies by location and intensity of transmission. Mortality increases with age, with the highest mortality among people over 80 years of age (CFR 21.9%). The CFR is higher among males compared to females (4.7% vs. 2.8%). By occupation, patients who reported being retirees had the highest CFR at 8.9% while patients who reported no comorbid conditions had a CFR of 1.4%, patients with comorbid conditions had much higher rates: 13.2% for those with cardiovascular disease, 9.2% for diabetes, 8.4% for hypertension, 8.0% for chronic respiratory disease, and 7.6% for cancer [4].

Virology of Coronavirus

Coronaviruses are enveloped viruses with a positive sense single-stranded RNA genome (26e32 kb) [18]. Four coronavirus genera (α, β, γ, δ) have been identified so far, with human coronaviruses (HCoVs) detected in α coronavirus (HCoV-229E and NL63) and β coronavirus (MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1) genera [19]. The genome of SARS-CoV-2 is similar to that of typical CoVs and contains at least ten open reading frames (ORFs). The first ORFs (ORF1a/b), about two-thirds of viral RNA, are translated into two large polyproteins. In SARS-CoV and MERS-CoV, two polyproteins, pp1a and pp1ab, are processed into 16 non-structural proteins (nsp1-nsp16), which form the viral replicase transcriptase complex [20]. Those nsps rearrange membranes originating from the rough endoplasmic reticulum (RER) into double-membrane vesicles where viral replication and transcription occur [21,22]. The other ORFs of SARS-CoV-2 on the one-third of the genome encode four main structural proteins: spike (S), envelope (E), nucleocapsid (N) and membrane (M) proteins, as well as several accessory proteins with unknown functions which do not participate in viral replication (Figure 1).

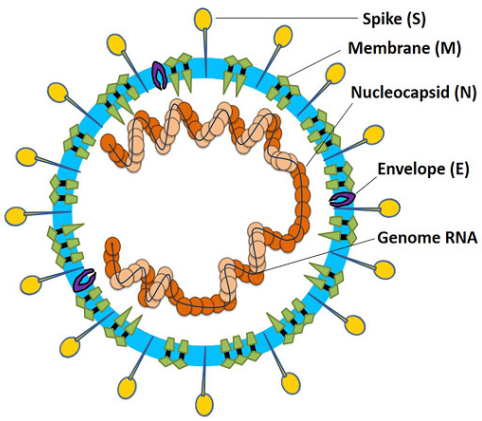

Figure 1: Molecular structure of Corona virus [23].

Pathogenesis of Coronavirus

Coronaviruses 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 [4,5]. Other than SARS-CoV-2, there are six known coronaviruses in humans: HCoV-229E, HCoV-OC43, SARS-CoV, HCoVNL63, HCoV-HKU1, and MERS-CoV [6,9,17,23]. After the virus enters the body, it needs the help of special receptor called Angiotensin Converting Enzymes 2 (ACE 2) [24]. The ACE 2 is present on the surface of alveolar cells in the lungs. There are 3 types of alveolar cells; the type 1, 2 and 3. The type 1 is responsible for gas exchange; type 2 is responsible for producing 'surfactant" which is a mixture of proteins and fats that reduce surface tension of the alveoli, while type 3 cells are macrophages (the immune cells). The ACE 2 is found on type 2 cells. The corona virus envelop contains protein (it also expressed other poly-proteins, nucleoproteins, and membrane proteins, such as RNA polymerase, 3- chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins) called spikes that help the virus bind to the ACE 2 [25,26]. On binding with ACE 2, the genetic materials of the virus enters the cell and the cell is harnessed to produce viral proteins, thus the virus multiplies and the cell dies which resulted in the production or release of specific inflammatory mediators by the type 2 cells [27]. The mediators stimulate the existing immune cells 'macrophages' and secrete chemical substances called cytokines. Three types of cytokines are produced namely; Interleukin 1 (IL1), Interleukin 6 (IL6) and Tumor necrosis factor (TNF- α) which reaches the blood stream and causing symptoms associated with Covid 19.

Potential Therapeutic Strategies Against COVID-19

To date, no specific antiviral treatment has been confirmed to be effective against COVID-19. Regarding patients infected with COVID-19, it has been recommended to apply appropriate symptomatic treatment and supportive care [3]. Initially, interferons-a nebulization, broad spectrum antibiotics, and anti-viral drugs were used to reduce the viral load [28-30], however, only remdesivir has shown promising impact against the virus [31]. Remdesivir only and in combination with chloroquine or interferon beta significantly blocked the SARSCoV-2 replication and patients were declared as clinically recovered [30,32]. Various other anti-virals are currently being evaluated against infection. Nafamostat, Nitazoxanide, Ribavirin, Penciclovir, Favipiravir, Ritonavir, AAK1, Baricitinib, and Arbidol exhibited moderate results when tested against infection in patients and in-vitro clinical isolates [30,32,33]. Several other combinations, such as combining the antiviral or antibiotics with traditional Chinese medicines were also evaluated against SARSCoV-2 induced infection in humans and mice [33]. Recently in Shanghai, doctors isolated the blood plasma from clinically recovered patients of COVID-19 and injected it in the infected patients who showed positive results with rapid recovery [34]. In a recent study, it was identified that monoclonal antibody (CR3022) binds - with the spike RBD of SARS-CoV-2. This is likely due to the antibody's epitope not overlapping with the divergent ACE2 receptor-binding motif. CR3022 has the potential to be developed as a therapeutic candidate, alone or in combination with other neutralizing antibodies for the prevention and treatment of - COVID-19 infection [35].

Vaccines for Covid-19

Effective SARS-CoV-2 vaccines are essential for reducing disease severity, viral shedding and transmission, thus helping to control the coronavirus outbreaks. There are several vaccination strategies against SARS-CoV, MERS-CoV tested in animals, including a live attenuated virus, viral vectors, inactivated virus, subunit vaccines, recombinant DNA, and proteins vaccines [36]. These studies are in progress, but it requires months to years to develop the vaccines for SARS-CoV-2. Currently, there may be many promising targets for SARS-CoV-2, but more laboratory and clinical evidence still should be explored. The WHO is working with Chinese scientists

to launch more than 80 clinical trials on potential treatments for SARS-CoV-2. Traditional Chinese medicine seems to have some effects in the supportive treatments [37,38]. Madagascar Covid organic herbal medicine made from Artesemia plant has been used for the treatment of the disease and has been used for several African countries such as Madagascar, Tanzania, Comoros, Senegal, Guinea Bissau, Nigeria, Chad and Equatorial Guinea. According to World health Organization (WHO), as of 22nd May 2020, there are about 10 candidate vaccines in clinical evaluation and about 114 candidate vaccines in pre-clinical evaluation [39].

Conclusion

The coronavirus belongs to a family of viruses that may cause various symptoms such as pneumonia, fever, breathing difficulty, and lung infection. Challenges in treating COVID-19 Coronavirus disease (COVID-19) present a global challenge, particularly in the rapid increase of critically ill patients with pneumonia and absence of definitive treatment. However, the potential therapeutic strategies against COVID-19 involve the use of broad-spectrum antibiotics, anti-malarial and anti-viral drugs. Currently, there may be many promising vaccines for COVID-19, but more laboratory and clinical evidence still should be explored.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Wuhan Municipal Health and Health Commission (WMHC) (2020) Briefing on the Current Pneumonia Epidemic Situation in Our City.
2. Li Q, Guan X, Wu P, Wang X, Zhou L, et al. (2020) Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 382: 1199-1207.
3. Centre for Disease Control and Prevention (CDC). 2019 Novel coronavirus, Wuhan, China. 2020.
4. World Health Organization (WHO). Novel Coronavirus–China. 2020.
5. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020 382: 727-733.
6. National Health Commission of the People's Republic of China (NHC). Feb 12: Daily briefing on novel coronavirus cases in China.
7. World Health Organization (WHO). Novel coronavirus (2019-nCoV) situation report-22.
8. 8. Wang C, Horby P W, Hayden F G, Gao F (2020) A Novel Coronavirus Outbreak of Global Health Concern. Lancet 395: 470-473.
9. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395: 507-513.
10. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, et al. (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579: 270-273.
11. Wu A, Peng Y, Huang B, Ding X, Wang X, et al. (2020) Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. Cell Host Microbe 27: 325-328.
12. Lai CC, Shi TP, Ko WC, Tang HJ, Hsueh PR (2020) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents 55:105924.
13. Liu Y, Li J, Feng Y (2020) Critical care response to a hospital outbreak of the 2019-nCoV infection in Shenzhen, China. Crit Care 24:56
14. Medical expert group of Tongji hospital. Quick guide to the diagnosis and treatment of pneumonia for novel coronavirus infections (third edition). Herald Med. 2020.
15. Wang C, Wang X (2020) Prevalence, nosocomial infection and psychological prevention of novel coronavirus infection. Chin General Pract Nurs 18:2-3.
16. World Health Organization (WHO) (2020) Coronavirus disease (COVID-19) Situation Report-113. Data as received by WHO from national authorities by 10:00 CEST.
17. Lu R , Zhao X, Li J, Peihua Niu, Bo Yang, et al. (2020) Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395: 565-574.
18. Su S, Wong G, Shi W, Jun Liu, Alexander C K Lai, et al. (2016) Epidemiology, Genetic recombination, and pathogenesis of coronaviruses, Trends Microbiol 24: 490-502.
19. Perlman S, Netland J (2009) Coronaviruses post-SARS: Update on replication and pathogenesis. Nat Rev Microbiol 7: 439-450
20. Fehr AR and Perlman S. Coronaviruses: an overview of their replication and pathogenesis, Methods Mol. Biol. 1282 (2015) 1e23,
21. Masters PS (2006) The molecular biology of coronaviruses. Adv. Virus Res. 66: 193-292.
22. Knoops K, Kikkert M, Worm SH, Jessika C Zevenhoven-Dobbe, Yvonne van der Meer, et al. (2008) SARS-coronavirus replication is supported by a reticulovesicular network of modified endoplasmic reticulum. PLoS Biol 6: e226.
23. Li AZ, Manman Geng, Yizhao Peng, Liesu Meng, Shemin Lu, et al. (2020) Molecular immune pathogenesis and diagnosis of COVID-19. Journal of Pharmaceutical Analysis 10: 102-108.
24. Wang N, Shi X, Jiang L, Zhang S, Wang D, et al. (2013) Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4. Cell Res 23: 986-993.
25. Wu F, Zhao S, Yu B, Chen Y-M, Wang W, et al. (2020) A new coronavirus associated with human respiratory disease in China. Nature 579: 265-269.
26. Zhou P, Yang X, Wang X, Hu B, Zhang L, et al. (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579: 270-273.
27. Xu X, Chen P, Wang J, Feng J, Zhou H, et al. (2020) Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci 63: 457-460
28. Ng CS, Kasumba DM, Fujita T, Luo H (2020) Spatio-temporal characterization of the antiviral activity of the XRN1-DCP1/2 aggregation against cytoplasmic RNA viruses to prevent cell death. Cell Death Differ.
29. Wang BX, Fish EN (2019) editors. Global virus outbreaks: Interferons as 1st responders. Seminars in immunology. Elsevier 43:101300.
30. Wang M, Cao R, Zhang L, Yang X, Liu J, et al. (2020) Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 30: 269-271.
31. Agostini ML, Andres EL, Sims AC, Graham RL, Sheahan TP, et al. (2018) Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. MBio 9:e00221-e318.
32. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, et al. (2020) First case of 2019 novel coronavirus in the United States. N Engl J Med 382: 929-936.

33. Sheahan TP, Sims AC, Leist SR, Schäfer A, Won J, et al. (2020) Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun 11:1-14.
34. Derebail VK, Falk RJ (2020) ANCA-associated vasculitis-refining therapy with plasma exchange and glucocorticoids. Mass Medical Soc 382: 671-673.
35. Tian X, Li C, Huang A, Xia S, Lu S, et al. (2020) Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody. bioRxiv 9: 382-385.
36. Graham RL, Donaldson EF, Baric RS (2013) A decade after SARS: strategies for controlling emerging coronaviruses. Nat Rev Microbiol 11(12):836-848.
37. Li G, Clercq ED (2020) Therapeutic options for the 2019 novel coronavirus (2019-nCoV). Nat Rev Drug Discov
38. Liu J, Manheimer E, Shi Y, Gluud C (2004) Chinese herbal medicine for severe acute respiratory syndrome: a systematic review and meta-analysis. J Altern Complement Med 10: 1041-1051.
39. World Health Organization (2020) Draft landscape of COVID-19 candidate vaccines.