

Epidemiology, Viral Pathogenesis, Host-Immune Response and Potential Vaccine Trial for the Treatment of SARS-CoV-2 Infection

Abbas Abel Anzaku^{1*}, Olasinbo Balogun¹, Akwashiki Ombugadu², Nneka Egbuchulam³, Ibrahim Yusuf⁴, Ifeanyichuku Odoh¹, Nurudeen Olalekan Oketade⁵, Akpason Esla Amre⁶

¹Department of Clinical Laboratory Services, Institute of Human Virology, Abuja, Nigeria; ²Department of Zoology, Federal University of Lafia, Nasarawa State, Nigeria; ³Research Unit, Initiative for Safe Use of Medicines, Nigeria; ⁴Department of Microbiology, Ahmadu Bello University, Zaria, Nigeria; ⁵International Research Centre of Excellence, Institute of Human Virology, Abuja, Nigeria; ⁶Department of Microbiology, Faculty of Science, Federal University of Lafia, Nasarawa State, Nigeria

ABSTRACT

Background: The current outbreak of COVID-19 caused by SARS-CoV-2 raised fundamental public health concerns as its emergence has been marked the third introduction of a highly pathogenic coronavirus into the human population after SARS-CoV and MERS-CoV in the twenty-first century. Recent advancement of SARS-CoV-2 infection revealed mechanism of immune evasion during the pathogenesis. Hence, this study reviewed available literature on epidemiology of SARS-CoV-2, viral pathogenesis, host immune response to the infection and potential vaccine trial for the treatment of the infection.

Methods: Systematic review technique was used for this study.

Results: This study provides an immunological insight into the SARS-CoV-2 infection for better understating of the virus and as well as the strategies for use in combating the disease.

Conclusion: This predictive view may help in designing an immune intervention or preventive vaccine for COVID-19 in the near future.

Keywords: Active healthy ageing; Quality of life; Older adults; Community care

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a highly transmissible infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in Wuhan, China in the late 2019 and eventually spread all over the world. In early 2020, the World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Concern (PHEIC) that requires a collaborative approach as it poses a risk to global public health population at risk of the infection (WHO, 2020). After the emergence of the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) in the twenty-first century, the outbreak of SARS-CoV-2 has been marked the third strain of the coronaviruses, spreading from

epidemic to a pandemic [1]. The full genome sequencing and phylogenic analysis indicated that SARS-CoV-2 is a β (beta) Coronavirus in the same subgenus as the SARS virus but in a different clad; It was similar to a bat Coronavirus thereby suggesting that the reservoir host maybe bats [2,3]. Currently, over 60.4M million populations are infected with SARS-CoV-2 and over 1.4 million deaths have been recorded around the world as reported by the WHO [4]. Africa CDC reported a total number of 2.14 million laboratory-confirmed cases with over 50,000 deaths in the whole of Africa. As at November 2020, the Nigerian Center for Disease Control (NCDC) reported a total of 66,805 laboratory-confirmed cases with at least 1,000 deaths (NCDC, 2020). Despite global efforts to curb the COVID-19 pandemic, the infection rate is at the increasing order due to poor infection control measures. This review intends to evaluate

Correspondence to: Abbas Abel Anzaku, Department of Clinical Laboratory Services, Institute of Human Virology, Abuja, Nigeria, Tel: 08038141859; E-mail: humbleabel2016@yahoo.com

Received: November 18, 2020; **Accepted:** December 02, 2020; **Published:** December 08, 2020

Citation: Anzaku AA, Balogun O, Ombugadu A, Egbuchulam N, Yusuf I, Odoh I, Oketade NO, et al. (2020) Epidemiology, Viral Pathogenesis, Host-Immune Response and Potential Vaccine Trial for the Treatment of SARS-CoV-2 Infection. J Infect Dis Prev Med. 8: 209.

Copyright: © 2020 Anzaku AA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

the molecular epidemiology of SARS-CoV-2 infection, viral pathogenesis, host immune response to the infection and potential vaccine trial for the treatment of the infection thereby providing valuable recommendations based on recent research progress of COVID-19 response.

EPIDEMIOLOGY OF SARS-COV-2

COVID-19 pandemic is considered one of the major pandemics to human population as it began from Wuhan City, Hubei Province of China (Original epicenter of COVID-19) and spread around the globe within a short time [5], stated that each country at various time points is at a different stage of the pandemic, thereby, complicating the actual epidemiology of the disease. The African continent is the least affected region by the COVID-19 pandemic to date. As at 31th July 2020, WHO reported 559,446 confirmed cases and at least 12,769 deaths from 54 Africa [6]. The African continent is the last one and least affected by COVID-19 pandemic to date [7].

Several major factors such as late arrival of the pandemic, weak diagnostics including inadequate COVID-19 testing, lack of essential medical supplies and a small susceptible population will significantly affect and change the epidemiology of COVID-19 in the continent.

MOLECULAR CHARACTERIZATION AND GENETIC MAKEUP OF SARS-COV-2

Just like the two other strains of coronaviruses (SARS-CoV and MERS-CoV), SARS-CoV-2 is an enveloped virus with a positive-sense single-stranded RNA genome (26e32 kb); SARS-CoV-2 infection was classified as a β CoV of group 2B by the WHO [8]. Four coronavirus genera (a, b, g, d) have been identified so far, with human coronaviruses (HCoV) detected in the coronavirus (HCoV-229E and NL63) and β coronavirus (MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1) genera. The first isolate of the viral genome of SARS-CoV-2 had 89% nucleotide homology with bat SARS-CoV and 82% with that of human SARS-CoV [9]. Following this similarity level with other SARS-CoVs, the new virus was officially named SARS-CoV-2 by the WHO and CoV study group of the International Committee on Taxonomy of Viruses on 30th January 2020 [10] members of the coronaviridae family [11] approximately 67% of SARS-CoV-2 RNA are mainly located within the 1st ORF and translates the pp1a and pp1ab polyproteins which encode sixteen non-structural proteins (NSP). The remaining ORFs code structural and accessory proteins while part of the genome encodes Nucleocapsid (N) protein, Spike (S) glycoprotein, Matrix (M) protein, and small Envelope (E) protein [12]. According to [13] the phylogenetic tree demonstrates the virus' ability to undergo immunologic pressure and increase the frequency of mutations in the genetic sequence of coronavirus among people from different countries; which can, in turn, increase virulence and transmissibility of the virus. There is a slight variation between the Open Reading Frames (ORFs) of coronaviruses across

The S protein is a trimetric, cell-surface glycoprotein consisting of two subunits (S1 and S2), where the S1 subunit is responsible for receptor binding [14] in the same vein reported that S surface protein plays key roles in the viral life cycle and host

defense as it is responsible for receptor binding, host range, membrane fusion, hemagglutination and is a target for eliciting host neutralizing antibodies (Figure 1) below shows SARS-CoV-2 viral structure.

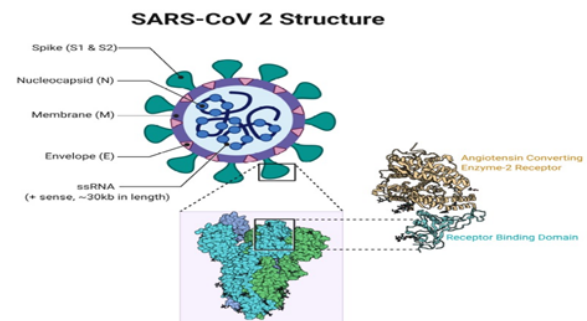


Figure 1: Virology of SARS- CoV-2 [7].

TRANSMISSION ROUTE OF SAR-COV-2 INFECTION

Several literatures on the virus have revealed that human-to-human transmission is the major route of transmission of SARS-CoV-2 [15]. SARS-CoV-2 transmission normally occurs through respiratory droplets. Other routes of transmission such as surface transmission, aerosolization in a confined space, or spread from asymptomatic individuals have been reported, though the significance of their role in contributing to overall transmission is yet to be fully clarified [14]. Patient can transmit the infection up to 2 weeks after having recovered from symptoms of the disease [16]. Transmission through fecal-oral means is reported to be unlikely [17,18]. Respiratory droplets can be generated by sneezing (40,000 droplets), coughing (3,000 droplets), or talking (about 600 droplets per minute). They can also be produced by medical procedures like intubation and bronchoscopy or by the use of oxygen masks and nebulizers.

After infection with SARS-CoV-2, the virus binds to the host receptor expressed by host cells and synthesize with the cell membrane; the lung epithelial cells are the primary target of the virus [15]. Human-to-human transmission of SARS-CoV occurs by the binding between the receptor-binding domain (RBD) of virus spikes and the cellular receptor which has been identified as angiotensin-converting enzyme 2 (ACE2) receptor [19].

SARS-COV-2 VIRAL ATTACHMENT AND PENETRATION MECHANISMS

Coronaviruses in general exhibit specific genes in ORF1 downstream regions that encode proteins for viral replication, nucleocapsid, and spikes formation [20]. The glycoprotein spikes on the outer surface of coronaviruses are responsible for the attachment and entry of the virus to host cells. The RBD is loosely attached among viruses that enable the virus to infect multiple hosts [21]. ACE-2 is a special receptor protein situated on the surface of the biological membrane of the cells of the heart, lungs, arteries, intestine, and the renal tissues and is vital in the regulation of blood pressure; unfortunately, this receptor serves as a pathway for SARS-CoV-2 viral penetration the human cells [22]. The virus's outer surface is hydrophilic with a

lipophilic side on the inside which is why it could be destroyed by detergents [23]. The SARS-CoV-2 invasion into human cells is facilitated by the transmembrane spike glycoprotein that forms homotrimers expanded from the viral external; the S protein contains two functional variants accountable for binding to the human cell receptor (S1 variant) and fusion of the viral and cellular membranes (S2 variant). For many CoVs, S is hewed at the border between the S 1 and S2 variants which remain non-covalently bound in the perfusion conformation [24]. The distal S1 variant comprises the RBD and contributes to the stabilization of the pre-fusion state of the membrane-anchored S 2 variant that comprises the fusion apparatus [25] as shown in Figure 2 below.

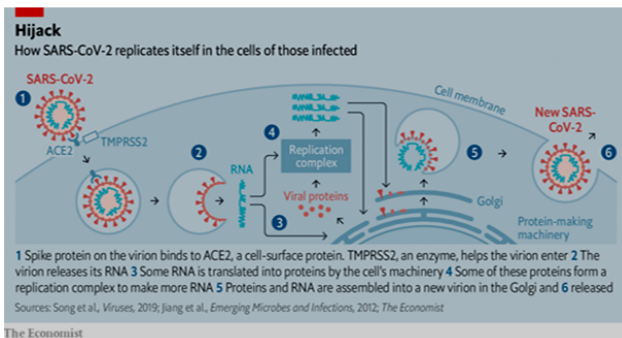


Figure 2: Attachment of SARS-CoV- 2 to ACE-2 receptor and replication [26].

PATHOGENESIS AND DISEASE CHARACTERIZATION

The severe symptoms of SARS-COV-2 infection are associated with an increasing number and rate of fatalities especially in the epidemic region of China. Patients with COVID-19 show clinical manifestations including fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia [27] reported that though infection in children has been observed to be less common and less severe than in adults, COVID-19 virus infects people of all ages. Patients can have high number of leukocytes, abnormal respiratory manifestations and increased level of plasma pro-inflammatory cytokines. The main pathogenesis of COVID-19 infection as a respiratory system targeting virus in Figure 3 was severe pneumonia, RNAemia, combined with the incidence of ground-glass opacities, and acute cardiac injury sounds of both lungs, and a body temperature of 39.0 °C.

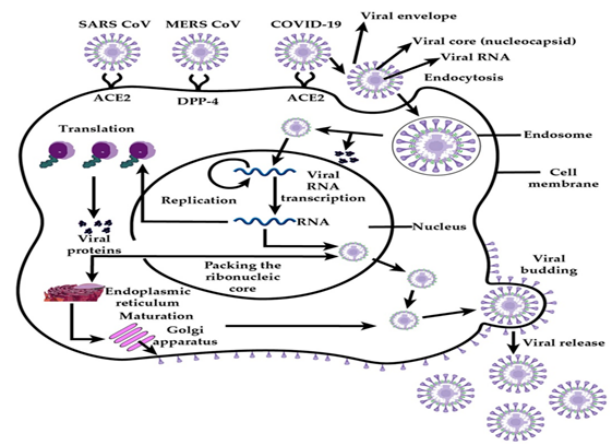


Figure 3: Pathogenesis of SARS-CoV- 2 [28].

HOST IMMUNE RESPONSE TO SARS-COV-2 INFECTION

Previous studies have suggested that SARS-CoV predominantly infects airway and alveolar epithelial cells, macrophages and vascular endothelial cells. During the early stage of infection with SARS-CoV-2, a vigorous type I Interferon (IFN) response could lead to appropriate adaptive immune responses that eventually trigger viral clearance; while severe cases are linked to delayed or absence of type I interferon response; instead, the initial response recruits neutrophils, monocytes and macrophages to the lung, which is associated with increased immunopathology as shown in Figure 4. Humoral immune response, especially the production of neutralizing antibody, plays a protective role by controlling the infection at a later phase and prevents re-infection in the future [29].

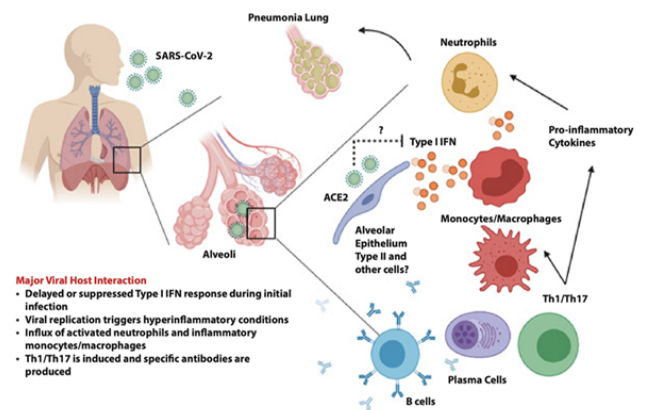


Figure 4: SARS-CoV- 2 viral-host interaction.

The influx of myeloid cells into the lungs is accompanied by a cytokine storm, with an increase in the level of serum pro-inflammatory cytokines, such as IL-1, IL-6, IL-12 and TNFα, which increase vascular permeability and decrease lung function. IL-6 can signal through direct binding to the IL-6 receptor on lymphocytes; it can also bind to soluble IL-6 receptor and bind to endothelial cells to stimulate vascular effects of the disease, and can change the expression of inflammatory mediators in the liver (Moore and June, 2020). In SARS-CoV-2 infection, both increases in monocytes and neutrophils in the lungs and higher

serum pro-inflammatory responses (cytokine storm) are associated with disease severity [20]. Antibodies against the IL-6 receptor, such as tocilizumab and sarilumab and antibodies against IL-6 itself, such as siltuximab, are in clinical trials; the goal is to decrease the effects of the cytokine storm in more advanced disease.

LABORATORY DIAGNOSIS FOR COVID-19

Molecular techniques and Antibody testing (serology Immunoassay) are used for the diagnosis of SARS-CoV-2 infection, however molecular testing such as Nucleic Acid Amplification Test (NAAT) which involves real-time Reverse Transcription-PCR (RT-PCR) assay remain the most reliable diagnostic method. Immune identification technology (Point-Of-Care (POC) diagnostics of IgM/IgG, Enzyme-Linked Immunosorbent Assay (ELISA), Gene-Xpert and blood culture are other diagnostic methods used for COVID-19 testing. The two commonly used nucleic acid detection technologies for SARS-CoV-2 are real-time quantitative polymerase chain reaction (RT-qPCR) and high-throughput sequencing. The authoritative identification method for SARS-CoV-2 is virus blood culture and high-throughput sequencing of the whole genome. However, the application of high-throughput sequencing technology in clinical diagnosis is limited because of its equipment dependency and high cost. So RT-qPCR is the most common, effective and straightforward method for detecting pathogenic viruses in respiratory secretions and blood.

CANDIDATE VACCINES TRIAL FOR SARS-COV-2 INFECTION

Till date, there is no precise antiviral therapy against COVID-19 although there are other supportive treatments. Previously, different strains of SARS-CoV were used to produce inactivated vaccines which efficiently reduced the viral load in animal models [30,31] noted that while the conventional medicines are focused on treatment of infectious disease with clinical symptoms, vaccines are intended for use in persons without symptoms in order to prevent the manifestation of diseases.

Cheung et al. produced a potential DNA vaccine candidate expressing an antigenic peptide from the SARS-CoV N protein with a single-chain-timer (peptide-b2m-MHC I) approach that induces SARS-CoV-specific T-cells with cytotoxicity to N protein-expressing cells. Antigenic peptides act as useful agents in the studies of SARS-specific immunity and immunopathogenesis and candidates for vaccine development. The major antigens in these T-cell-targeting vaccines are focused on the S or N proteins of SARS-CoV. Due to the low immunogenicity of single peptide vaccinations, many different strategies have been developed to elicit effective T cell responses and efficient protection by T-cell-based vaccines. DNA vaccines encoding N or S gene segments that cover the immunodominant T-cell epitopes have been developed in mouse models. However, there are few vaccines in the pipeline against SARS-CoV-2. The mRNA-1273 based vaccine prepared by the US National Institute of Allergy and Infectious Diseases against SARS-CoV-2 reported a progressive outcome of the experimental COVID-19 vaccines as it generates immune response after a successful trial. The mRNA-1273

which was designed to protect against SARS-CoV-2 was generally well tolerated and prompted neutralizing antibody activity in a healthy individual [32].

The mRNA vaccine against SARS-COV-2 is based on a relatively new genetic method that does not require growing the virus in the laboratory but carried out directly in the body that received the vaccine [33].

The US National Library of Medicine (2020) reported a clinical trial for DNA vaccine ChAdOx1 nCoV-19 against Coronavirus which was initially developed to prevent MERS (72) and was based on adenovirus vaccine vector and SARS-COV-2 spike protein. The vaccine was modified to inhibit viral replication and genetic code that transmits instructions for the production of viral Spike protein perhaps to exclude has been added, allowing the adenovirus to produce this protein after vaccination [34].

Currently, there is relatively low data indicating Africans' involvement in COVID-19 clinical trials, however, traditional medicine has been used to manage COVID-19 patients with a recommendation by some governments requiring treatment protocols that have not been validated through clinical trials [35].

STRATEGIES IN COMBATING COVID-19

To combat the impact of COVID-19 on global health, strategies such as expanding access to COVID-19 diagnostics and organizing trainings on infection control practices, tracking and reporting COVID-19 data and impact and accelerating discovery of potential therapies are strongly recommended. In addition, preparing for mass vaccination and building global collaboration with health agencies even in resource limited settings will help strengthen efforts to curb COVID-19 [36-47].

Furthermore, scientists across all regions should participate in ongoing anti-viral drug evaluations and vaccine clinical trials. This will provide better data on the universal safety and effectiveness of these biological products.

Bio-informatics analyses of SARS-CoV-2 isolates are also critical. This will help determine the previous structural protein events and possible future mutation using specialized software. Ser-surveys and molecular testing of animal models to detect and identify possible reservoir and intermediate hosts of SARS-CoV-2 and the transmission mode of SARS-CoV-2 is paramount.

CONCLUSION

Understanding SARS-CoV-2, its mode of transmission and viral mechanism of actions are critical to COVID-19 infection prevention control. Hence, accelerated effort to develop novel antiviral drugs and candidate vaccines to curb the disease is critical. Regular practices of infection prevention control as a measure to curtail community transmission of COVID-19 should be embraced.

ACKNOWLEDGEMENTS

Not applicable.

FUNDING

No funding was received.

AUTHORS' CONTRIBUTION

AAA conceptualized and drafted the manuscript, OB, AO, IY, NE, critically reviewed manuscript and validated resource material, IO, NOO. All authors read and approved the final manuscript.

COMPETING INTEREST

All authors have declared that there are no conflicts of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

REFERENCES

- Li Z, Yi Y, Luo X, Xiong N, Liu X, Li S, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol.* 2020;10:1002.
- Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel Coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223):514-523.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterization and epidemiology of 2019 novel Coronavirus: implications for virus origins and receptor binding. *Lancet.* 2020; 395(10224):565-574.
- Ted Regencia and Joseph Stepansky, Tamila Varshalomidze. Global coronavirus death toll top 100,000: live updates. *News/US and Canada.* 2020.
- Lone SA, Ahmad A. COVID-19 pandemic- an African perspective. *Emerg Microbes Infect.* 2020;9(1):1300-1308.
- Coronavirus in africa breakdown of infected virus free countries. *Africanews.* 2020.
- The last continent to face up COVID-19, Africa 'needs to wake up. *EURACTIV.* 2020.
- Hui DS, IA E, Madani TA, Ntoumi F, Kock R, Dar O, et al., The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health: The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis.* 2020; 91: 264-266.
- Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J Virol.* 2020;94:127-220.
- Chan JF, Kok KH, Chu H, To KK, Yuan S, Yuen KY. Genomic characterization of 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020; 9(1): 221-236.
- Song Z, Xu Y, Bao L, Zhang L, Yu p, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses.* 2019; 11(1): 59.
- Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol.* 2019;17 (3): 181-92.
- Shen Z, Xiao Y, Kang L, Ma W, Shi L, Zhang L, et al. Genomic diversity of SARS-CoV-2 in coronavirus disease 2019 patients. *Clin Infect Dis.* 2020;71(15): 713-720.
- Jaimes JA, Millet JK, Stout AE, Andre NM, Whittaker GR. A tale of two viruses: the distinct spike glycoproteins of feline coronaviruses. *Viruses.* 2020;12(1): 83.
- Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al., A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res.* 2020;7: 4.
- Guo GJ, Wang C, Luo F, Yu F, Zhang W, Chen H, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020;395(10226): 809-815.
- Gracia P V, Luo C, Malpassi R E. Perinatal transmission with SARS-CoV-2 and route of pregnancy termination: a narrative review. *J Matern Fetal Neonatal Med.* 2020;1-5.
- Vivanti A J, Vauloup-Fellous C, Prevot S, Zupan V, Suffee C, Do J, et al. Transplacental transmission of SARS-CoV-2 infection. *Nature Communication.* 2020;11: 3572.
- P. Wu, X. Hao, E.H.Y. Lau, J.Y. Wong, K.S.M. Leung, J.T. Wu, et al., Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020, *Euro Surveill.* 25 (2020).
- Boheemen SV, Graaf MD, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. *M Bio.* 2012;3(6): 473-512.
- Boheemen SV, Graaf MD, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. *M Bio.* 2012;3(6): 473-512.
- Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A Pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579 (7798): 270-273.
- Xu X, Chen P, Wang J, Feng J, Zhou H, Li X. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modelling of its spike protein for risk of human transmission. *Sci China Life Sci.* 2020;63(3): 457-60.
- J.K. Millet, G.R. Whittaker. Host cell entry of Middle East respiratory syndrome coronavirus after two-step, furin-mediated activation of the spike protein. *Proc Natl Acad Sci U S A.* 2015;111(42):15214-15219.
- MA, Veesler D. Structural insights into coronavirus entry. *Adv Virus Res.* 2019;105: 93-116.
- Understanding SARS-CoV-2 and the drugs that might lessen its. 2020.
- Bamidele JO, Daniel OJ. Epidemiology of Coronavirus Disease (COVID-19) in Nigeria. *Annals of Health Research.* 2020;6(2): 125-132.
- Docea AO, Tsatsakis A, Albulescu D, Cristea O, Zlatian O, Vinceti M, et al. A new threat from an old enemy: Reemergence of coronavirus (Review). *Int J Mol.* 2020;45: 1631-1643.
- Gorse GJ, Donovan MM, Patel GB. Antibodies to coronaviruses are higher in older compared with younger adults and binding antibodies are more sensitive than neutralizing antibodies in identifying coronavirus-associated illnesses. *J Med Virol.* 2020;92(5): 512-517.
- See RH, Zakhartchouk AN, Petric M, Lawrence DJ, Mok CP, Hogan RJ, et al. Comparative evaluation of two severe acute respiratory syndrome (SARS) vaccine candidates in mice challenged with SARS coronavirus. *J Gen Virol.* 2006;87(3): 641-50.
- Kamal AM, Mitrut P, Docea AO, Soşoi S, Kamal KC, Mitrut R, et al. Double therapy with pegylated Interferon and Ribavirin for chronic hepatitis C. A pharmacogenetic guide for predicting adverse events. *Farmacologia.* 2017;65(6):877-884.
- Jackson LA. Experimental COVID-19 Vaccine Safe, Generates Immune Response. *N Engl J Med.* 2020.
- Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines - a new era in vaccinology. *Nat Rev Drug Discov.* 2018;17:261-279.

34. Calina D, Oana A, Petrakis DD, Egorov AM, Ishmukhametov AA, Gabibov AG. Towards effective COVID-19 vaccines: Updates, perspectives and challenges (Review). *Int J Mol.* 2020;3-16.
35. Madagascar: artemisia, l'arme (controversée) de Rajoelina contre le Covid-19. *La Afrique Tribune.* 2020.
36. Coronavirus Disease 2019 (COVID-19). *African Dise Cont Prev.* 2020.
37. Docea, AO, Tsatsakis A, Albulescu, D, Cristea O, Zlatian O, Vinceti M, et al. A new threat from an old enemy: Reemergence of coronavirus (Review). *Int J Mol.* 2020;45(6):1631-1643.
38. Tatar G, Tok TT. Structures and Functions of Coronavirus Proteins: Molecular Modeling of Viral Nucleoprotein. *Int J Virol Infect Dis.* 2017;2(1):001-007.
39. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill.* 2020; 25(3):2000045.
40. Wuhan Municipal Health and Health Commission's Briefing on the Current Pneumonia Epidemic Situation in Our City. WHO. 2020.
41. Xiaowei Li, Manman Geng, Yizhao Peng, Liesu Meng, Shemin Lu. Molecular immune pathogenesis and diagnosis of COVID-19. *J Pharm Anal.* 2020; 10(2):102-108.
42. Lone SA, Ahmad A. COVID-19 pandemic- an African perspective. *Emerg Microbes Infect.* 2020;9(1):1300-1308.
43. Funk S. bpmmodels: Methods for analyzing the sizes and lengths of chains from branching process models. 2020.
44. ClinicalTrials.gov: A Study of a Candidate COVID-19 Vaccine(COV001). US National Library of Medicine. 2020.
45. Bamidele JO, Daniel OJ. Epidemiology of Coronavirus Disease (COVID-19) in Nigeria. *Annals of Health Research.* 2020;6(2): 125-132.
46. A second COVID-19 case is confirmed in Africa. WHO.2020.
47. COVID-19 dashboard. CDC. 2020.