

**INTERNATIONAL JOURNAL OF SCIENCE FOR GLOBAL SUSTAINABILITY****The Response of Nigerian Government to COVID-19: Patient Management and Diagnosis – A Mini-Review**

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ABSTRACT

A series of pneumonia cases of unknown cause has emerged in Wuhan, Hubei, China, in December 2019 with clinical manifestation highly related to pneumonia. Analysis of the respiratory tract sample of the infected patients by deep sequencing revealed a coronavirus named 2019 novel coronavirus (2019-nCoV), which is relatively considered as a deadly severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronaviruses are positive RNA viruses, non-segmented assigned to the family of Coronaviridae, and the order Nidovirales. They are widely distributed in humans and other mammals. Although coronavirus infection is mild, beta coronaviruses (SARS-CoV-2, MERS-CoV-2, and SARS-CoV) epidemic and pandemic have claimed the lives of people all over the world in the past two decades and presently. There is a scarcity of information on COVID-19 in Nigeria, there are less published information on how physicians are managing COVID-19, SARS-CoV-2 diagnosis, and its success and challenge. This research reviewed the current COVID-19 diagnostic techniques used in Nigeria, drugs used in patient management, and general management adopted by physicians. RT-qPCR is the standard diagnostic technique recommended by NCDC, while patient management is basically using a drug such as Lopinavir-ritonavir and vitamins. However serological tests can be used for supportive information. Hence, PCR-based diagnostic technique is adopted in Nigeria to test for COVID-19, but information about the challenge and success of using PCR in COVID-19 diagnosis is not available which is a new area of research.

Keywords: SARS-CoV-2; COVID-19; Molecular Diagnosis; Patient Management; NCDC

1.0 INTRODUCTION

Coronaviruses are positive RNA viruses, non-segmented assigned to the family of Coronaviridae, and the order Nidovirales. They are widely distributed in humans and other mammals. Although coronavirus infection is mild, beta coronaviruses (SARS-CoV-2, MERS-CoV-2, and SARS-CoV-2) epidemic and pandemic have claimed the lives of people all over the world in the past two decades and presently (Kumar, 2020). A series of pneumonia cases of unknown cause has emerged in Wuhan, Hubei, China, in December 2019 with clinical manifestation highly related to pneumonia. Analysis of the respiratory tract sample of the infected patient by Deep sequencing revealed a coronavirus named 2019 novel coronavirus

(2019-nCoV), which is relatively considered as deadly severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with the characteristics of flu-like symptoms, including cough, fever, and anhelation with the possibility of a high rate of transmission from human to human (Rothan & Byrareddy, 2020). Biophysical and crystal electron microscopy studies (CryoEM) have shown that the high rate of SARS-CoV-2 transmission is due to the high affinity (~15nM) of its spike protein with the human ACE2 receptor. DNA sequencing revealed the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in animals such as a bat (Walls et al., 2017). Therefore, the 2019-n-CoV was found to be

associated with contact with a local seafood market that illegally sold animals such as poultry, bats, marmots, and snakes in Wuhan, and according to recent studies, bats or snakes are the potential natural reservoir of 2019-n-CoV. The incubation period of the virus based on data from the hospitalized patient is 3 to 7 days with mild symptoms and asymptomatic accounting for 80%, 15% are severe symptoms, needing oxygen, and 5% are critical infections, needing ventilators (Hu et al., 2020). The infection of SARS-CoV-2 is mediated by the spike protein receptor-binding domain (RBD) of the spike protein. It is still unknown if SARS-CoV-2 infects any immune cells because only a small percentage of lung resident monocytes/macrophages express the ACE2 receptor (Tortorici & Veessler, 2019). Other receptors may exist, or another cellular entry mode is utilized such as antibody-dependent enhancement. Scientists are carrying out research to find treatment for COVID-19 (Hoffmann et al., 2020). The research revealed that there are 30 drugs including western medicines, natural products, and traditional Chinese medicines with the potential of treating COVID-19. Clinical trials of some of those drugs demonstrate efficacy against SARS-CoV-2 (Zumla et al., 2016). Antivirals including lopinavir/ritonavir, chloroquine phosphate, interferon α (IFN- α), ribavirin, remdesivir, and arbidol are among the guideline given by the National Health Commission (NHC) for the Prevention, Diagnosis, and Treatment of SARS-CoV-2 infection (Senanayake, 2020). Interestingly, on 8th April 2020, the world research and development of the COVID-19 vaccine have shortlisted 115 vaccines in which 37 were not yet confirmed, and 78 are shown to be effective in protection against COVID-19, and most are at the preclinical stage (Kulkarni et al., 2018). Some of the candidate vaccines that are currently under clinical development are mRNA-1273 from Moderna, Ad5-nCoV from CanSino Biologicals, INO-4800 from Inovio and LV-SMENP-DC, and pathogen-specific aAPC from Shenzhen Geno-Immune Medical Institute. Nevertheless, there is another vaccine development company that is working on the development of other novel vaccines. Even though there are efforts made to develop vaccines and therapeutic drugs, but preclinical evidence has proven the potential of many drugs and vaccines, however, larger scale clinical trials are still required (F. Wang et al., 2020).

Before the report of the COVID-19 outbreak in Africa, WHO identified a strong link between the continent and China and has sent out guidelines on preparedness for the outbreak. Nigeria is one of the thirteen top countries identified with high risk for COVID-19 importation based on either direct link or high travel volume to and from China (Omaka-Amari et al., 2020). On the 27th of February 2020, the first case of COVID-19 in Nigeria identified in Lagos from an Italian visiting Lagos, Nigeria. Since then, 54,000 cases were discovered in Nigeria with 1000 cases of death (1st of September 2020). (Otuonye et al., 2020) investigated clinical report of COVID-19 patient in Lagos, and stated that out of 154 patients investigated, most survived the disease with symptoms, with more males (74.7) than females, the common symptoms observed in those individuals are fever, breathing difficulty, dry cough, and malaise. Death and cases of COVID-19 in Nigeria rise steadily to date since the discovery of the first case in Lagos. The government has acted by advocating for complete to partial lockdown in the country, physical distancing, banning public gatherings (going to church, mosque, and schools), to minimize the spread of the virus (Elimian, 2020). Also, some clinical activities were brought to halt to reduce the spread of the virus. In Nigeria, there have been complaints about the shortage of medical equipment and personal protective equipment (PPE), this is supported by evidence from health workers who got infected due to lack of sufficient equipment. The Nigerian government under NCDC established a preparedness group before the importation of the virus into the country, where screening for travellers was carried out at the point of entry. Based on lessons learned from the EVD outbreak, the NCDC strengthened the National Reference Laboratory with diagnostic capacity for epidemic-prone pathogens. Through this process, the NCDC supported 22 of the 32 states to establish emergency operation centers (EOC) and trained rapid response teams in all the 36 states (Ihekweazu & Agogo, 2020).

Furthermore, provision of public health advisories was done by NCDC such as sharing the case definition, contact tracing, case management, strengthen five laboratories for diagnosis and preventive information with networks of national and subnational public health workers (11;26(4):444–8., n.d.). The

NCDC developed guidelines for self-isolation, recommended PPE, health care delivery recommendation, SARS-CoV-2 case definition, a business guide for COVID-19, infection prevention, national COVID-19 guide case management, dead body management, the use of face mask, and testing strategy for COVID-19 within 2 months of the start of the pandemic in Nigeria (Oleribe et al., 2020). Besides, NCDC reported that the National Reference Laboratory Abuja is equipped human resources and technical capacities that is needed for the diagnosis of COVID-19. There is scarcity of information on COVID-19 in Nigeria, there are less published information on how physicians are managing COVID-19, SARS-CoV-2 diagnosis, its success, and challenge. This study aims at reviewing the current diagnostic techniques used in the diagnosis of COVID-19 and its success in Nigeria, drugs used in patient management, and general management adopted by physicians.

2.0 Molecular Pathogenesis SARS-CoV-2

Coronaviruses are large RNA genome viruses with an enveloped positive-strand RNA. The genomes of all coronavirus are similarly arranged with the replicase locus which encoded within the 5' ends, and the 3' end genome of coronavirus encodes the structural proteins (Brian & Baric, 2005). The structural proteins of the SARS-CoV-2 that mediate infection are spike (S), small membrane (E), membrane (M), and nucleocapsid (N) and internal (I) protein encoded N gene. The nucleocapsid proteins form a complex with the SARS-CoV-2 genome which will then lead to the formation of a helical capsid structure located in the viral envelope (Muhammed, 2020). The spike structural protein which is a 3D polypeptide is made up of the receptor-binding domain (RBD), which is subdivided into S1 and S2 sub-unit. The

RBD is responsible for the binding of spike protein to angiotensin-converting enzyme receptor 2 (ACE2) (Figure 1) (Walls et al., 2017). The replicase gene of the SARS-CoV-2 is encoded by the 5' ends of the coronavirus genome containing two very large open reading frames (ORFs), in which ORF1a and ORF1b, which accounts for about two-thirds of the genome. The replicase translated to polyproteins (pp) 1a and 1ab, with pp1ab, expressed via a translational frameshift encoded near the end of orf1a (V'kovski et al., 2020). The SARS-CoV-2 binds to the angiotensin-converting enzyme receptor (ACE2) of human airway epithelia which results in its entry into the host. The virus release RNA into the cytoplasm, the ORF1a, and ORF1b of the RNA is translated into polyprotein 1a (pp1a) and polyprotein 1ab (pp1ab). The ORF1a encodes the enzyme protease that cleaves the polyproteins into non-structural proteins (nsps) which form the RNA replicase-transcriptase complex that is needed for structural protein synthesis. The replicase complex executes the formation of negative-sense RNA (Cevik et al., 2020). Upon fragmentation of the negative-sense RNA into 7-9 sub-genomic RNA through discontinuous transcription, after which fragments that encode spike, membrane, nucleocapsid, and envelope protein are formed, in which the proteins are formed after translation in the rough endoplasmic reticulum, and then they pass through the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) into the Golgi apparatus where sortation and assembly take place. Finally, viral protein and genomic RNA are then assembled as virion in the Endoplasmic reticulum and Golgi and then released outside the cell as a vesicle (Muhammed, 2020).

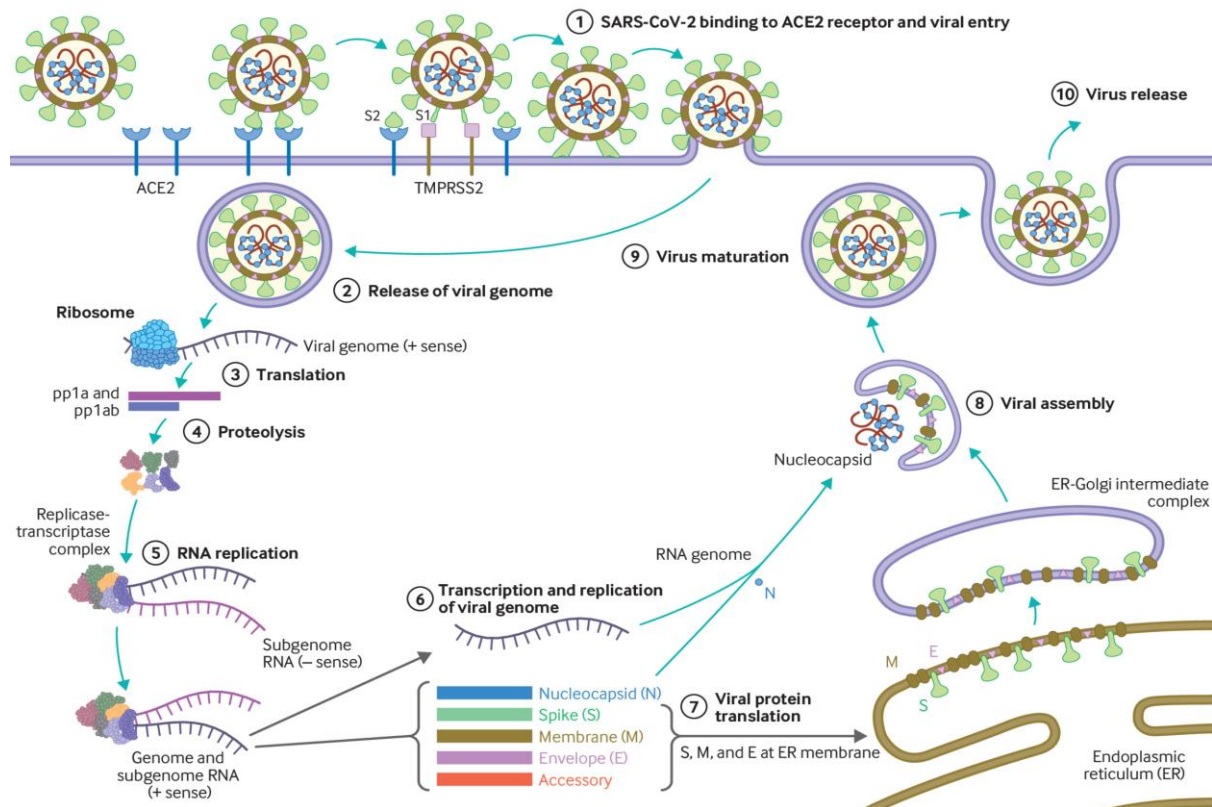


Figure 1. An overview of SARS-CoV-2 pathogenesis. Figure adapted with permission from (Cevik et al., 2020)

3.0 Diagnosis of COVID-19 in Nigeria

Accurate molecular diagnostic tests are necessary for confirming a diagnosis of COVID-19. Direct detection of SARS-CoV-2 nucleic acids in respiratory tract specimens informs patient, healthcare institution, and public health-level decision-making. The number of available SARS-CoV-2 nucleic acid detection tests is rapidly increasing (Hanson et al., 2020). According to a declaration by WHO, tracking SARS-CoV-2 infection, apprehension of its epidemiology, case management data, reducing the transmission of the virus is not possible without legit diagnostic technique for COVID-19. Suspects of the disease and people who have been in contact with them are strongly recommended for the diagnosis by the apex health organization ((WHO), n.d.). Testing for COVID-19 is important for causative virus identification (Ibeh et al., 2020). Serological screening (this method is not good for acute diagnosis of the disease), molecular techniques, and virus isolation and culture is a tool used in COVID-19 diagnosis. Testing COVID-19 by serological technique is associated with limitations such as lack of sensitivity and less understanding of the immunologic progression of the virus. The danger of using the serological technique is that after 9 to 11 days, that is the best

time that antibodies are detected in plasma, the risk of viral transmission will be high. Genetic relationship of SARS-CoV-2 with other coronaviruses make the technique less specific, with high cross-reactivity possibilities and can easily give false-positive result (C. Wang et al., 2020). That is why the call to stop the use of the serological technique for COVID-19 diagnosis (Umaru, 2020). Isolation of SARS-CoV-2 from patients and culture is not a good strategy for detection of the virus, this is because there is a need for level 3 and 4 biosafety facilities, in which there is no availability such facilities in Nigeria (*Laboratory testing for coronavirus disease (COVID-19) in suspected human cases.* 2020, 2020). The use of specialized Vero cells for culturing is time-consuming (taking up to 3 to 5 days for the cytopathic effect to take place). A quicker diagnosis of COVID-19 using this technique is not possible. That is why the technique of real-time reverse transcription PCR (sensitive and selective proven with the low false-positive result) is globally used and it was set as the standard for the diagnosis of COVID-19 (Corman et al., 2020). Evaluation of other fast, sensitive, and selective techniques (CRISPR-Cas9-assay, multiplex isothermal amplification linked to microarray detection, loop-assisted isothermal amplification,) of SARS-CoV-2

diagnosis is ongoing (Ai et al., 2020). The molecular basis of COVID-19 diagnosis by PCR is that it is sensitive and selective for detection of a gene sequence encoding RNA dependent RNA polymerase (RdRP), nucleocapsid, membrane, spike, and envelop protein (Feng et al., 2020). Furthermore, (Li et al., 2020) reported that enzyme-linked immune assay, nested RT-PCR, droplet digital PCR, nanoparticle-based amplification, portable bench size top analyser, Immunofluorescence assay, chemiluminescence immunoassay, lateral flow assay, microarray, and microfluidic chip, and sequencing, are additional techniques that can be used for the diagnosis of COVID-19. But Nigerian government through NCDC has directed the use of quantitative real-time reverse transcriptase-polymerase chain reaction (RT-qPCR) as the standard method for testing COVID-19 in Nigeria (Figure 2), but the serological test can be used to provide supportive information. A variety of samples can be used from the patient for the test such as nasopharyngeal and swab, ambulatory patients, and sputum (if produced) and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease. The best sample that gives good results is the one obtained from lower respiratory materials. However,

difficulty in sample collection is the main challenge (Enitan et al., 2020). There is limited information about the diagnosis strategies adopted by the Nigerian government, its success, and challenges. Therefore, this is a new area of research to find more data on how Nigeria is testing for the disease and the challenges they are facing. This will serve as a guide for the government to know if they need a new diagnostic technique in the future or a better PCR technique (redesigning of the current technique). (Feng et al., 2020) reported that the specificity of the RT-PCR depends on the choice of target. This is because the gene coding for enveloping protein (E gene) is highly conserved in coronaviruses, cross-reaction of a gene coding for nucleocapsid protein (N gene) might occur with the N gene of another coronavirus. The S gene coding for spike protein can be differentiated within CoVs (SARS-CoV-2 from SARS-CoV-2). During the early period of the pandemic, WHO made different molecular diagnostic tools available in different parts of the world. The RT-PCR protocol (designed with primers for E gene, N gene, and RdRP) from Germany is the most sensitive. In Nigeria, there is no information regarding the type of gene their PCR is targeting. Therefore, this is a new area of research.

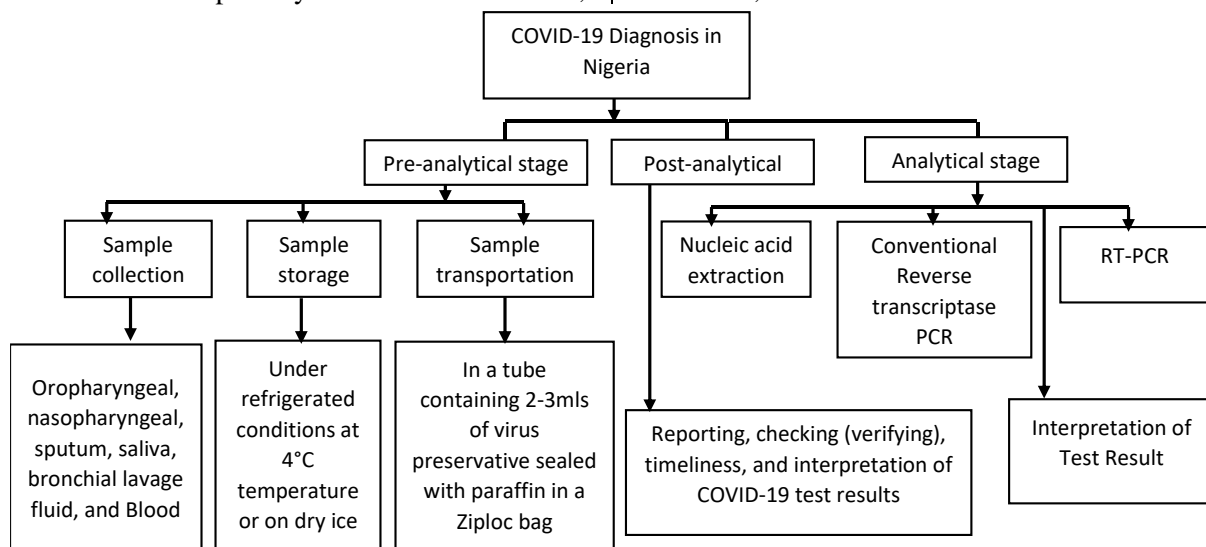


Figure 2. An overview of the process of COVID-19 diagnosis adapted in Nigeria

4.0 COVID-19 Management in Nigeria

Currently, there are no registered drugs to treat COVID-19 disease, and a vaccine is not available, the management is based on supportive therapy and treating the symptoms to prevent respiratory failure (Shanmugaraj et al., 2020). Most of the data available for pharmacological treatments are derived from medications used

during the SARS-COV and MARS-COV pandemics or from *in vitro* observations (Yang et al., 2020). The current clinical management for COVID-19 in countries such as the US, China, and India includes infection prevention, control measures, and supportive care which includes supplemental oxygen and mechanical ventilatory support.

Recent reports have suggested that Chloroquine/Chloroquine phosphate or Hydroxychloroquine (HCQ), usually used for treating malaria have an apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China (Gao et al., 2020). The recommended dose of chloroquine phosphate is 500 mg (300 mg for chloroquine) bd p. o. <= 10 days. Hydroxychloroquine on the other hand has been used by U.S clinicians in different dosing pattern 400 mg BD on day one, then daily for 5 days; 400 mg BD on day one, then 200 mg BD for 4 days; 600 mg BD on day one, then 400 mg daily on days 2 - 5 (Dong et al., 2020). The U.S food and drug administration (FDA) has also approved a drug called remdesivir for the treatment of COVID-19 in certain situations, the was used to treat an American patient in Snohomish County, Washington in 2020, who was infected with SARS-CoV-2 (Holshue et al., 2020), and his condition improved dramatically and discharged within 24 hours after admission (Harmon A, 2020). Gilead is currently providing the compound to China to conduct a pair of trials in infected individuals with and without severe symptoms (Johnson CY, 2020). On 17 March 2020, remdesivir was provisionally approved for use for COVID-19 patients in a serious condition in the Czech Republic. On 18 March 2020, the first Italian 79-year-old COVID-19 patient was successfully treated with remdesivir in Genoa. The dosing regimen is IV 200 mg on day one, followed by 100 mg every day until day five or ten (NP, 2020).

In Nigeria, COVID-19 patients are managed with chloroquine/hydroxychloroquine and vitamins, and the outcome of this treatment is generally positive. There is no progression in the severity of the disease and many patients were discharged home as a result they recovered from the virus. Lopinavir-ritonavir is another drug used for COVID19 treatment in Nigerian Hospitals, but shown to have no benefit over standard care in hospitalized patients (Bowale et al., 2020). However, there is less published information on how Nigeria is managing the current pandemic, this is a new area of research (gathering data on how Nigeria successfully fight the SARS-CoV-2 pandemic).

5.0 CONCLUSION

COVID-19 has affected the economy and the healthcare system worldwide, availability of data on how Nigeria is managing the cases of COVID-19, the diagnosis, challenges in diagnosis and management, and success will guide physicians, scientists, and researchers to improve on the management, diagnosis, and treatment to find a long-lasting solution for the disease in Nigeria. The standard protocol recommended by NCDC for the clinical diagnosis of COVID-19 in Nigeria is RT-qPCR. Even though there are less severe cases in Nigeria, patient management practice in Nigeria is basically using a drug such as Lopinavir-ritonavir and vitamins. However, there is a scarcity of information on diagnosis and patient management in Nigeria.

Conflict of Interest

The authors declared that there is no conflict of interest.

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