Review Article

The Continuing Pandemic Threat of COVID-19 - A Need for Public Enlightenment

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Abstract

A novel coronavirus 2019 now re-designated coronavirus disease 2019 (COVID-19) virus, emerged in Wuhan, China, on December 2019. Greater details about its origin and basis for high transmissibility remain largely unknown. The increasing incidence possibly linked to human-to-human transmission of the virus has resulted in rapid spread of the disease to 145 countries including Nigeria. To the best of our knowledge, the current review is one of the first locally published information on the novel COVID-19.We hereby describe the etiology, epidemiology, clinical management, and infection prevention and control of practices against COVID-19. This is to create more public awareness and sensitize health-care professionals on the urgent need for early recognition of suspect cases and practice of droplet and contact precautions to curtail the rapid spread of COVID-19.

Keywords: 2019-novel coronavirus, AFRICA, coronavirus disease 2019, EPIDEMIC, public health, Wuhan virus

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Introduction

The coronaviruses (CoVs) are a large family of RNA viruses that have been associated with illnesses that range from the common cold to more severe respiratory tract infection and rarely gastroenteritis.[1] The last two decades had witnessed the emergence of two previously unknown CoVs; Middle east respiratory syndrome CoV (MERS-CoV) and severe acute respiratory syndrome CoV (SARS-CoV).[2] Both SARS-CoV and MERS-CoV have emerged from animal reservoirs and both are highly pathogenic and associated with severe respiratory syndrome in humans.[2] Four other human CoVs (HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1) also induce mild upper respiratory diseases.

The World Health Organization (WHO) was alerted to several cases of pneumonia in Wuhan City, Hubei Province of China by December 31, 2019. Most patients worked at or lived around the local Huanan seafood (wet) market, where live animals were also on sale. By January 7, 2020 a novel CoV (2019-nCoV) was confirmed by the Chinese Centre for Diseases Control and Prevention as the cause of the pneumonia. This new virus was temporarily named "2019-nCoV."[3] Thereafter, the international committee on taxonomy of viruses assigned the name, SARS-CoV-2 to the virus due to its close genetic relatedness to the SARS CoVs. Finally, and more recently, the WHO has permanently designated the virus as CoV disease 2019 (COVID-19).

As at April 9, 2020, COVID-19 was affecting 210 countries and territories around the world. There were 1,684,281 cases globally out of which 81,907 were from China. The mortality so far is about 102,053 with 375,221 recovered cases.[4] In Africa, 52 of 54 countries have confirmed cases of COVID-19. The first report of COVID-19 in Nigeria was an index case that travelled into the country from Italy; subsequently, the number of cases has risen steadily to 288 confirmed cases on April 8, 2020, out of which 51 had recovered with a total of 7 deaths.[3] The

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genetic sequence of the first case from Nigeria clustered with the European clade thus confirming the patients' travel history.

As the virus rapidly spread to different countries and territories, on March 12, 2020, the WHO declared the COVID-19 a pandemic thus raising the alert as very high globally thereby calling on all countries to take urgent precautionary measures.[4] The first confirmed case on African soil (in Egypt) has raised more concerns due to the weak health-care systems and low level of preparedness in most developing nations especially the African subregion. The countries with ongoing community transmission at the moment are; Italy, China, Iran, France, Germany, Spain, Republic of Korea, and Japan.

Peculiarities of the COVID-19 are high transmissibility of the virus evidenced by the WHO estimated reproductive number (Ro) between 1.4 and 2.5.[5] The case fatality rate (CFR) from COVID-19 fluctuates based on age from country to country but the average estimate as at March 3, 2020 was 3.6%, which is currently lower than the CFR of 10% reported for SARS and 34% for MERS.[6] It is noteworthy to observe that the situation might change as the virus could mutate over time. Although all age groups are susceptible to the virus, older people, and individuals with pre-existing comorbidities such as hypertension and other cardiovascular diseases, diabetes, asthma, pregnancy, and other immunosuppressive states appear to be more vulnerable to becoming severely ill with the virus.[7]

The social media and other conventional outlets have allowed for rapid dissemination of inaccurate information on the COVID-19 outbreak, hence the need for verified information sharing. This review describes the etiopathogenesis and clinical management of COVID-19, with a view to enlighten the public and health-care professionals on modes of transmission/manifestations and importance of infection prevention and control (IPC) measures against the virus.

Etiology

CoVs are large, enveloped, positive sense, single stranded RNA viruses belonging to the *Coronaviridae* family.[1] The *Coronaviridae* family consists of two subfamilies: Coronavirinae and Torovirinae. Members of the subfamily Coronavirinae are subdivided into four genera; alpha, beta, delta, and gamma. The alpha and beta are the most common genera known to cause human infections. All CoVs share a common morphology and possess a single-stranded RNA genome of up to 30 kb in length. The club-shaped surface glycoprotein of the virus gives it a "crown-like" or corona appearance and is important for binding to host cell receptors. It also serves as a major determinant factor for host range restriction.[2]

CoVs virions contain three major structural proteins: the very large (200 K) glycoprotein S (for spike) that forms the bulky (15–20 nm) peplomers found in the viral envelope, an unusual transmembrane glycoprotein (M) and the internal phosphorylated nucleocapsid protein (N).[8] In addition, there is a minor transmembrane protein E, and some CoVs contain a further envelope protein with both hemagglutination and esterase (HE) functions. The CoV genome contains 7–14 open reading frames (ORFs) starting from the 5'-end, Gene 1, which comprises two-thirds of the genome, is about 20–22 kb in length. It consists of two overlapping ORFs (1a and 1b), collectively functioning as the viral RNA polymerase (Pol). The order of the other four structural protein genes is 5'-S (spike)–E (envelope)–M (membrane)–N (nucleo capsid)-3'. These genes are interspersed with several ORFs encoding nonstructural proteins and the HE glycoprotein, when present.[8]

Pathogenesis

The COVID-19 outbreak has been primarily linked with exposure to the Huanan seafood market in Wuhan city with subsequent possibility of human to human spread.[9,10] The source of the COVID-19 is still unknown and no specific animal association has been identified so far. However, research is ongoing with many considerations including possible intermediate animal vectors (such as palm civets, bat species, camels, cats, mice, and raccoon dogs) and several avian hosts being implicated as potential source of the virus.[11-13] The virus reportedly spreads through droplet nuclei from human to human and could be transmitted in hospitals and family settings, including travellers to other geographical regions.[14-16] Contact with contaminated surfaces and fomites has also been implicated in the spread of COVID-19 virus. The detailed mechanism of COVID-19 transmission remains largely unknown.[17] Asymptomatic infections have been associated with viral shedding making it more difficult for IPC.[18] The viral receptor for COVID-19 is speculated to be Angiotensin converting enzyme 2 (ACE2) which is also the receptor for SARS-CoV and is expressed on a wide variety of body tissues.[11,12,19] The ACE2 receptor is a membrane protein that is expressed abundantly on lungs, heart, kidney, and small intestine as well as other tissues. Other proteins, such as CD209 L (L-SIGN), DC-SIGN, and L SECtin, also support the entry of COVID-19 into cells, but cannot by themselves confer susceptibility to a cell lacking ACE2.

CoVs have been shown to generally infect the respiratory, gastrointestinal, hepatic, and central nervous systems of human, livestock, birds, bat, mouse, and many other wild animals.[11,13] Bats are probably the major natural reservoirs of alphacoronaviruses and betacoronaviruses (including COVID-19).[11,19] Detailed information about pathogenesis is very scanty hence the need for additional studies to gain further insights about its origin and tropism. Following infection, the incubation period has been reported to be about 4–14 days but could be as long as 24 days.[20] In trying to unravel the possible pathogenesis, *in vitro* inoculation of the COVID-19 onto surface layers of human airway epithelial (HAE) cells resulted in cytopathic effects and cessation of cilium beating of the cells, thus confirming its pathogenicity along the respiratory tract.[13]

Clinical Features

The most common presentations in cases from the current outbreak are; fever or cough while many patients present with shortness of breath in addition to other manifestations which include, muscle ache, confusion, headache, sore throat, sneezing, hemoptysis, chest pain, diarrhea, nausea, and vomiting.[9,10,14,16] Other COVID19 patients have reported diarrhea, disturbances of smell and taste, including anosmia, hyposmia, ageusia, and dysgeusia. Radiological findings include bilateral pneumonia, multiple mottling and ground-glass opacity with or without consolidation, and pneumothorax.[9,10,14,16] Clinical manifestations are generally nonspecific with an average of 8 days from illness to onset of dyspnea.[10] In pregnancy, CoVs could lead to poor obstetric outcomes including maternal morbidity and eventually death.[14] The effect on the unborn fetus is yet to be described in details.

Complications included acute respiratory distress syndrome (ARDS), hypoxemic respiratory failure, sepsis, septic shock, anemia, acute cardiac injury, and secondary infection.[10,15] Mortality has been found to be higher in elderly patients aged 60 years and above, patients with comorbid conditions; asthma, diabetes, hypertension, and other cardiac diseases. Patients with mild infections recover within 2 weeks while patients but severe illnesses might last about 3–6 weeks.

Treatment

Infected persons should be categorized into mild, moderate, or severe illness as this will determine the degree of supportive care to be instituted. Severe illness occurs in about 20% of COVID-19-infected person and they present with severe pneumonia, ARDS, hypoxemic respiratory failure, sepsis, and septic shock. About 80% of individuals present with mild illnesses and may not require hospital admission except there is a concern for rapid deterioration hence, may be discharged home and offered home care as described subsequently.

Asymptomatic or Mild Illness

Asymptomatic or mild illnesses may not require hospital admission. Although, the WHO recommends that suspected cases should be isolated and monitored in the hospital setting as there are reports of clinical deterioration during the 2nd week of illness.[13-15] However, home care may be offered to patients who have mild disease with no comorbid conditions, in certain situations such as limited resources and capacity to meet the health-care services demand, unavailable or unsafe in-patient care. Safety of the patient's home environment should be assessed along with careful clinical judgment when making this decision. Throughout the period of the home care, there should be a communication link with a health-care provider who would review the patient's health for progression of status. Infected persons and their household should be educated on personal hygiene, IPC practices and safe care of the infected person. The following recommendations are often required for home based care of mild CoV illnesses.

1. Patient should be placed in a well-ventilated single room
2. Number of caregivers should be limited and no visitors permitted
3. Other members of the household should stay in a different room or if not possible, they should maintain at least a distance of 1 m from the patient
4. Movement of the patient should be limited as well as limiting shared space
5. A tightly fitted medical mask should be worn by caregiver when in the same room as the patient
6. Individuals at risk of severe disease should not come close or provide care to the patient
7. Hand hygiene after contact with patient or their immediate environment
8. Patients should be assisted to perform regular hand hygiene as needed
9. Practice of respiratory hygiene by all particularly the ill patient, i.e., covering mouth during coughing or sneezing using medical masks, flexed elbow followed by hand hygiene. Materials used to cover mouth should be discarded
10. Direct contact with body fluids especially respiratory or oral secretions and faeces should be avoided
11. Frequently touched surfaces should be disinfected daily with regular householddisinfectant containing cleaners or diluted bleach as CoVs is known to persist on inanimate surfaces such as metal, glass, or plastic for up to 9 days[5,8]
12. Toilet surfaces and bathrooms should be cleaned and disinfected daily as above
13. Bedspreads, towels, and clothes should be washed regularly with regular laundry soap and water or machine washed at 60°C–90°C with common household detergents and dried thoroughly
14. Protective clothing and disposable gloves should be used when cleaning or handling surfaces, linen, or clothing soiled with body fluids
15. All symptomatic patients should stay at home till symptoms are resolved and/or Reverse transcription-polymerase chain reaction (RT-PCR) tests are negative
16. Members of the household should be considered as contacts and monitored closely for symptoms of COVID-19.

Moderate or Severe Illness

For persons with moderate or severe illness, supportive therapy, and monitoring should be instituted early. Supplemental oxygen therapy should be given and flow rate titrated to obtain SpO_2 ≥90% in nonpregnant adults and children without emergency signs while the target should be ≥92%–95%[13] in pregnant patients and ≥94% for children with emergency signs such as central cyanosis, severe respiratory distress, obstructed or absent breathing, shock, convulsions, or coma. Oxygen should be delivered via disposable, single use, oxygen delivering interfaces such as nasal cannula, simple face mask,

or mask with reservoir bag. Contact precautions should also be employed while handling contaminated oxygen interfaces. Fluids should be administered cautiously to patients with severe illness with no evidence of shock as aggressive fluid administration might worsen oxygenation.[9]

Empiric antimicrobials should be given to all patients with severe illness within an hour of identification of sepsis despite the suspicion of COVID-19 infection. Choice of antimicrobials should be based on the clinical diagnosis of community-acquired versus healthcare-associated pneumonia, local susceptibility data, and treatment guidelines. This antimicrobial can be de-escalated based on microbiology results and clinical judgment. The use of corticosteroids in the treatment of inflammation and cytokine-induced lung injury in CoVID-19 is controversial.[17] High-dose corticosteroids have been associated with secondary infections and delayed viral clearance.[14] The WHO advises against its routine use except for other reasons justifying its inclusion in the treatment plan.[9] Infected persons with severe illness must be closely monitored for signs of deterioration such as sepsis or rapidly progressive respiratory failure. Other comorbid conditions present must be identified and addressed appropriately. Communication should be maintained with the patient and family members about prognosis while offering support.

Case Management of the Coronavirus Disease 2019

A high index of suspicion is required in making a diagnosis. The WHO released a document that has nine sections which provide guidance on clinical management. The first section centers on patient recognition and sorting by triage. In order to do this, there is need for a case definition.[16]

Case Definitions

The WHO's Global Surveillance for Human Infection with the 2019-nCoV (COVID-19) provides information on the case definitions for surveillance of the infection.[17] This can be classified as; suspected, probable, or confirmed cases. This has so far been adopted by the Nigerian Centre for Disease Control NCDC, Surveillance Case Definitions for COVID-19 (Version 2).

Suspected case

Any person (including severely ill patient) presenting with fever, cough, or difficulty:

AND

Who within 14 days before onset of illness had any of the following exposures:

1. History of travel to and more than 24 h transit through any high-risk country* with widespread community transmission of SARS-coV2

   OR

2. Close contact with a confirmed case of COVID-19

   OR

3. Exposure to a health-care facility where COVID-19 case(s) have been reported.

A probable case

Any suspect case:

1. For whom testing for COVID-19 is indeterminate test results

   OR

2. For whom testing was positive on a pan-CoV assay
   OR

3. Where samples were not collected before the demise of a suspect case.

A confirmed case

Any person with laboratory confirmation of SARS-CoV-2 infection with or without signs and symptoms.

Health-care Worker Infection

Any health-care worker with moderate to severe respiratory illness reporting recent contact (<14 days) with patients with recent history of travel abroad and respiratory symptoms will be considered a suspect case.

Close contact by NCDC is living in the same household, had face-to-face contact or was in a closed environment with a case, a health-care worker or other person providing direct care or a laboratory worker handling COVID-19 infected-specimens, contact in an aircraft sitting within 2 seats (in any direction) of the case, crew members serving the section of the aircraft where the COVID-19 case was seated. An entire section or all passengers of an aircraft might be considered as close contacts, if the severity of symptoms or movement of the case is extensive.[21] Countries with ongoing community transmission as at March 17, 2020 are; China, Republic of Korea, Spain, Italy, Iran, Japan, France, and Germany.

These case definitions were based on the available information and may be revised with the accumulation of new information.

Laboratory Diagnosis

Specimen collection and transport

Blood cultures should be collected for bacterial causes of pneumonia and sepsis preferably prior to the institution of antimicrobial therapy. However, antimicrobial therapy should not be delayed to collect blood cultures.

To make a diagnosis of COVID-19, appropriate specimen should be collected rapidly. The best time for specimen collection is yet to be determined. However, as in other viral respiratory tract infections, it is likely that respiratory specimens collected early after the onset of the illness would yield higher virus concentrations. Either specimens from the upper respiratory or lower respiratory tract (URT and LRT) can be collected. However, LRT specimen is preferred as it

is more likely to test positive. Examples of URT specimen which is collected include nasopharyngeal or oropharyngeal swabs, nasopharyngeal aspirate or nasal wash (specimen should not be collected from the nostrils or tonsils).[16,17] LRT specimens which can be collected include expectorated sputum, endotracheal aspirate, and bronchoalveolar lavage. Sputum induction should be avoided due to higher risk of aerosol transmission.

Appropriate personal protective equipment (PPE) should be worn during specimen collection (Droplet and contact precautions are needed during URT specimen collection while airborne precautions are important for LRT specimens). Specimen from the URT should be collected using a sterile Dacron or rayon swab with aluminum or plastic shafts (cotton tipped swabs or swabs with calcium alginate should not be used) and placed in a viral transport media while employing the triple package system.[16] Specimens can be stored at 4°C for up to 72 h, or at -70°C or lower if RNA extraction is delayed. Extracted RNA can be stored at −70°C or lower.[21] There might be dual infections with other respiratory viruses, hence both URT and LRT specimens should be tested for other respiratory viruses while LRT specimens should be tested for bacterial pathogens as well.[16] Clinical specimens should be processed in a certified Class II biosafety cabinet while following at least biosafety Level 2 guidelines. Viral RNA can also been detected in the blood, plasma and faces of infected persons.[9-12]

At the moment serological diagnostic tests are not in routine use.[22] However, acute and convalescent (probably 2–4 weeks after the acute phase of the illness) sera can be collected and stored for future use when serological tests become available. Urine specimen can also be considered for storage and future use. RT-PCR and next generation sequencing are used in detection of the viral nucleic acid and genomic sequences, respectively. Several in-house molecular assays have been developed to target some COVID-19 virus genes such as ORF 1ab, ORF1b-nsp,[23] nucleocapsid protein (N), envelope protein (E), spike protein among others with varying protocols.[24]

Viral Culture can be done using Vero E6 cells, special-pathogen-free HAE cells.[12] Other ancillary tests include complete blood count which might reveal anemia, leukocytosis or leukopenia with lymphopenia, with or without thrombocytopaenia. Liver function abnormality may be seen especially elevated aspartate aminotransferase in many of the patients.[10,18,19] Chest computerized tomography (CT) images among infected individuals differ in patients in intensive care unit (ICU) and that of non-ICU patients as it shows bilateral multiple lobular with subsegmental areas of consolidation and bilateral ground-glass opacity with subsegmental areas of consolidation, respectively.[10,25,26]

Specific anti-coronavirus disease 2019 therapy

At the moment, there is no Food and Drug Administration approved drug used in the treatment of COVID-19. However, several drugs are being investigated for their activity against the virus with some of them showing promising results. One of the drugs is Remdesivir, an adenosine analogue which has demonstrated antiviral activity against a wide range of RNA viruses including SARS-Cov and MERS-CoV. It acts by incorporating into the nascent viral RNA chains which results in a premature termination.[27] Chloroquine, which is an antimalarial and autoimmune disease drug and recently reported as a potential broad spectrum antiviral drug has also showed significant activity against the virus. It blocks the viral infection by increasing the endosomal pH needed for virus/cell fusion. Its immunomodulatory effect may also have a synergistic contribution to its antiviral activity *in vivo*.[27] However, human trials will be needed to determine its effect on the virus *in vivo*. Lopinavir-ritonavir combination treatment and interferon beta which have showed promising results in MERS-CoV in animal models are being investigated for their activity against COVID-19. Several randomized controlled trials (RCT) are also underway to evaluate the effect of different drugs in COVID-19-infected patients.[28] Such as severe 2019-nCoV Remdesivir RCT in Beijing, China, which is on-going and mild/moderate 2019-nCoV Remdesivir RCT which is yet to commence.[29]

Complications should be prevented based on the surviving sepsis bundle by reducing the days of mechanical ventilation, reducing the incidence of ventilator associated pneumonia in mechanically ventilated patients; reducing the incidence of venous thromboembolism, catheter-associated blood stream infections, pressure ulcers, stress ulcers, and gastrointestinal bleeding and ICU-related weakness.[16]

Discharge criteria include being afebrile for at least 3 days, significant improvement in respiratory symptoms, 2 consecutive negative URT and LRT specimens which were at least 24 h apart. Home isolation for 14 days after discharge should be suggested if necessary.[16,30]

Infection Prevention and Control Practices

On identification of a suspected or probable case of COVID-19 infection, there is a need for the implementation of appropriate IPC practice. Suspected patients are given medical masks at triage and placed in an isolation room. A distance of at least 1 m should be maintained between suspected patients and other patients. The patient is also instructed to cover the nose and mouth during coughing or sneezing into flexed elbows or tissues and perform hand hygiene upon contact with respiratory secretions.[16]

Droplet precautions are also employed such as the use of medical mask when within 1–2 meters of a suspected patient. Patients should be nursed singly or grouped together with those with same etiological or clinical diagnosis in an airborne infection isolation room where available with spatial separation.[16,31,32] If not available, patients can be placed in well ventilated rooms with air flow of at least 160 L/s per patient or in negative pressure ventilation with at least 12 air changes per hour and controlled direction of air flow when

using mechanical ventilation. Eye protection such as goggles should be worn when providing care in close contact. The patient movement should also be limited and masks must be worn when outside their rooms.

Contact precautions should also be applied to prevent direct or indirect transmission from contaminated equipment and surfaces. PPE should be worn when entering and removed on leaving a room. Disposable or dedicated equipment should be used for each patient and if not possible, they should be cleaned and disinfected between patient uses. Health-care providers should not touch their eyes, nose or mouth with potentially contaminated gloved or ungloved hands. Hand hygiene should be performed at all times including the "5 moments" apply before and after use of PPE.[16]

Airborne precautions, such as the use of N95 respirators, should only be employed along with standard and contact precautions when performing aerosol generating procedures such as open suctioning of the respiratory tract, intubation, bronchoscopy of cardiopulmonary resuscitation.[16]

The patient should be preferably managed in single rooms with limited access to visitors. Equipment should be single use when possible, dedicated to the patients and disinfected between uses. All precautions should continue until patient is asymptomatic.

Conclusion

Considering the increasing incidence of the COVID-19, and how its mode of transmission as well as the mechanisms of action seems to differ from the previously known members of the *Coronaviridae* family, it is important that studies should be intensely focused on gaining better insight into the pathogenesis of the virus. Although there have been few reports of drugs inhibiting the activities of the virus *in vitro* and *in vivo*, there is an urgent need for the discovery of novel vaccine or therapeutic targets for COVID-19. At present, a huge amount of funding has been committed for vaccine platforms, with four candidates in varied developmental stages, there is unlikely to be a viable vaccine for at least another 12–18 months.

In addition, there is an urgent need for development of rapid molecular based point of care test kits to facilitate early confirmation of suspected cases.

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Conflicts of interest

There are no conflicts of interest.

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