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COVID-19: Transmission, Laboratory Diagnosis and Treatment Options

Ebidor Ufoumanefe Lawani-Luwaji[1], Augustine Oziegbe Akhogba[2]

[1]Department of Medical Laboratory Science, College of Health Sciences, Niger Delta University, Wilberforce Island, Nigeria
[2]Federal Medical Centre, Yenagoa, Nigeria
Email: eb2kng@yahoo.com, austinooh@gmail.com

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-COV2) the virus responsible for the outbreak of the 2020 pandemic at the Wuhan city in China belongs to the coronavirus family. While the disease rages, scientists are striving to discover drugs and vaccines to combat the virus. Person to person transmission has been the major source of transmission in respiratory droplets from an infected or an asymptomatic infected person to another and indirectly by virus contamination of objects. There has been no evidence of vertical transmission or transmission through blood and blood products. The virus can be detected in clinical specimens by electron microscopy, cell culture, real-time RT-PCR and next-generation sequencing. Therapeutic approaches to combat the infection have been supportive and preventive aimed at transmission reduction, but no specific drug candidate at the forefront for therapy. The race towards developing a vaccine for the disease has led to the discovery of 115 potential candidates. Databases such as Google Scholar, PubMed, MEDLINE and NCBI were searched to summarise the current state of knowledge to the global outbreak.

Subject Areas

Infectious Diseases

Keywords

COVID-19, Transmission, Detection, Treatment Options, Vaccine

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-COV2) the causative agent of the 2020 pandemic belongs to the coronavirus family. Coronaviruses are principally known to cause enteric or respiratory diseases, but sometimes also cause hepatitis or neurologic ailments [1]. They belong to the order *Nidovirales* which are RNA positive sense viruses and the two genera in this order are coronaviruses and toroviruses. These viruses have a unique chemical structure and a strategic replication pattern. Representative members of the *Coronaviruses* are known to infect multiple animal species and man. The animal species include ducks, monkeys, chickens, mice, cats, dogs, birds, cattle and bats [2].

The earliest description of coronavirus disease was in 1931 with the first human coronavirus (HCoV), HCoV-229E isolated in 1965 from humans. Until the epidemic of SARS in late 2002, two human coronaviruses existed, HCoV-229E and HCoV-OC43. After the identification of the SARS virus, other HCoVs have been identified [3].

Coronaviruses are divided into three groups based on their genetic similarities and hosts. Group 1 and 2 coronaviruses have mammals as their hosts, with the human coronaviruses found in these categories. The coronaviruses in group 3 are exclusively isolated from avians hosts. For decades, the coronaviruses in the groups have been studied, but new strains have been emerging such as the severe acute respiratory syndrome (SARS) which is a SARS-COV coronavirus [4], middle east respiratory syndrome-coronavirus (MERS-CoV) and the more recent COVID-19 virus causing the 2020 pandemic. After the SARS epidemic in 2003, concerted efforts have led to the discovery of two other respiratory coronaviruses affecting humans**,** HCoV-NL63 and HCoVHKU1 [5] [6].

Also, three other coronaviruses were isolated in 2005 and 2006 and were thought to be precursors for the human SARS-CoV [7] [8]. The human coronaviruses in group 1 are HCoV-229E and HCoV-NL63, group 2 comprises HCoV OC43 and HCoV-HKU1, group 3 has no known human coronaviruses discovered yet while SARS-CoV is placed in group 2 [2].

Diverse coronaviruses from bats have been identified and are classified into both group 1 and 2 based on the phylogenetic relationship with other mammalian coronaviruses. It was proposed that the ancestors of several coronaviruses are the bat and studies on HCoV 229E and OC43 (the common cold HCOv) crossed from cattle and bays which are the animal reservoirs to humans [3].

With the outbreak of SARS and COVID-19 in 2003 and 2019, it seems likely that there will be more coronavirus species crossing in the future and there is a need for more research into the unknown coronaviruses.

2. COVID-19

The novel coronavirus COVID-19 disease was suggested to have been spread from the wet animal market to humans. Person to person transmission has been the major source of transmission of this zoonotic disease that was declared a pandemic by the World Health Organization in March 2020 [9]. The incubation period of the infection was initially assumed to be 14 days [10] but more recent developments show a reduced incubation period to about 5 days. It is believed that the incubation period depends on the immune status and age of the patient because it was shorter with the over 70 years than those below 70 years [11].

Common symptoms of COVID-19 usually begin with an onset of fever, cough and dyspnoea headache, fatigue, with sputum production in some patients [12]. Other symptoms include diarrhoea, haemoptysis, lymphopenia and dyspnoea [13].

Clinically, the features revealed by computerised tomography (CT) chest scan presents as pneumonia, but, there were also irregular features such as cardiac injury, respiratory distress syndrome, and occurrence of ground-glass opacification (GGO) that resulted in patients death [12] as shown in **Figure 1**. It is believed that GGO encouraged inflammation by inducing both localized and systemic immune responses [9].

It is also vital to note that some COVID-19 patients had gastrointestinal distress and the possibility of an oro-faecal route as a potential means of transmission. Therefore, the identification of the virus in either urine or faecal samples could give a further means of identifying the virus [9].

2.1. Mode of Transmission

The evidence available from the progression of the disease shows transmission of COVID-19 is by both direct and indirect transmission. The virus is transmitted directly in respiratory droplets from an infected person to another or an asymptomatic infected person and indirectly by virus contamination of objects [9] [14]. There has been no evidence of vertical transmission as samples from cord blood, Amniotic fluid, breastmilk and neonatal throat swab tested negative

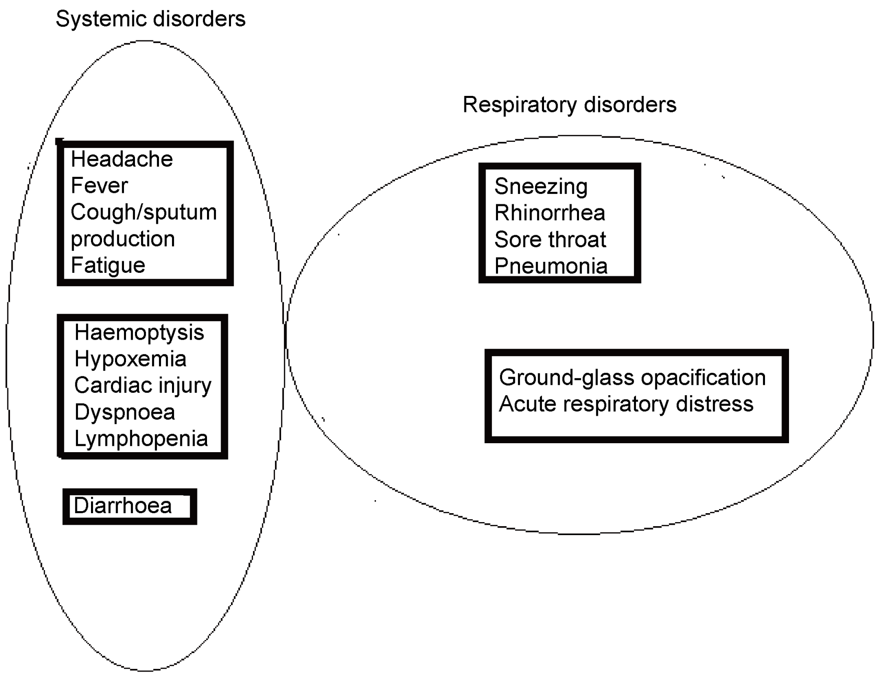

Figure 1. Some systemic and respiratory symptoms presented by COVID-19 patients.

to the virus. Also, it has not been proven to be transmitted through blood and blood products and there is the need for cautious assessment of donors [15].

2.2. Pathogenesis

The structure and genome of the virus could have a role to play in the pathogenetic mechanisms of COVID-19 disease [16]. The spikes on the protein envelop of the virus which mediates cell entry was seen to have structural similarities with the SARS virus though amino acid differences were noticed at some key residues [11].

Scientists in China revealed that the CoV2 virus requires the same receptor as the SARS virus to enter cells. This receptor is the angiotensin-converting enzyme 2 (ACE2), it has been shown that virus and host cell binding is an important factor for the pathogenesis of infection [11] [17].

The pathogenesis has been drawn from the previous SARS epidemic and influenza pandemic and with more studies going on around the world, the mechanism of the virus would be determined in subsequent months and the gap in knowledge filled. From a cell biology point of view and based on cells infected, the pathogenesis of COVID-10 can be divided into three stages or phases which match the diverse clinical phases of COVID-19 [18]. The first phase may be tagged as asymptomatic, which is usually 1 - 2 days after infection of contact with the virus. When the virus is inhaled into the nasal cavity, the first point of contact is the epithelial cells where they bind to and start replication. Some earlier studies have shown the angiotensin-converting enzyme 2 (ACE2) is the main receptor for both SARS-CoV and SARS-COV2 viruses [19] [20]. With limited innate immunity and local proliferation of the virus, detection is possible when swabs are taken from the nostrils. Though viral load may be reduced, asymptomatic individuals are infectious [21].

In Subsequent days, the virus replicates further in the respiratory tract as it and migrates downwards through the airways, triggering a strong innate response with clinical manifestation of the disease [21]. Clinical observation of infected patients revealed that approximately 80% exhibited a mild form of COVID-19 and the disease was limited to the upper respiratory tract. The third phase of the disease is the progression from mild to an acute respiratory disease (ARDS) with pulmonary infiltration and fatality at this stage varies noticeably with age [18].

Once the virus gets to and infects the lungs, they infect the alveoli and increased replication releases more virions, alveoli cells go through apoptosis and cell death [21]. ARDS is life-threatening because it prevents sufficient oxygen from entering the lungs and likewise circulation. This accounts for mortality seen in most acute lung injury and respiratory diseases [22].

2.3. Laboratory Diagnosis

COVID-19 can be detected from clinical specimens by electron microscopy, cell culture, real-time RT-PCR and next-generation sequencing through the World Health Organization warned against the isolation of virus from patients [23].

Samples for COVID-10 detection are an oropharyngeal swab specimen for nucleic acid testing referred to as nucleic acid amplification testing. Other samples such as stool, blood can also be used, but the preferred sample since the outbreak of the pandemic is the oropharyngeal swab. The viral nucleic acid is extracted from the samples and used or can be stored at a temperature of −80˚C [24].

The one-step reverse transcription loop-mediated isothermal amplification (RT-LAMP) has been the detection method used, which is grounded on PCR technology. This method has been shown to have many advantages and used in the diagnosis of several diseases including the zika virus [25].

2.4. Treatment Options Available

Therapeutic approaches to combat the infection have been supportive, prevention which are aimed at transmission reduction [26]. To date, no single drug has been discovered to treat COVID-19 but there are several drug candidates at the forefront for therapy. Majorly, repositioning of old drugs has been the way forward in COVID-19 therapy since information about the safety, drug interactions and side effects of such old drugs are available. The old drug chloroquine, used for malaria treatment, has shown to have apparent effectiveness and adequate safety against COVID-19 related pneumonia in clinical trials in China [27]. Also, clinical trials with chloroquine and hydroxychloroquine on respiratory viral load in France showed a reduction in viral load and this reduction was profound with azithromycin [28]. Divergent results have been seen with the use of lopinavir/ritonavir for COVID-19 therapy. It was effective for the treatment of an index case reported in Korea [29], but in a randomised trial, lopinavir-ritonavir was linked with only supportive care and had no benefit for critically ill patients neither did it improve on mortality [13]. Several other drugs are undergoing trials such as arbidol, favipiravir and remdesivir [30] [31]. Others are tocilizumab (Actemra), Interferon β 1a (SNG001) [32]. With no existing precise therapy or vaccine for COVID-19, there is an urgency to repurpose or develop novel drugs to help put an end to the pandemic. The race towards developing a vaccine for the disease has led to the discovery of 115 potential candidates. Out of the 115 vaccine candidates, 78 have shown promising results. Notable amongst these candidates are those developed by Moderna (mRNA-1273), CanSino Biologicals (Ad5-nCoV), Inovio (INO-4800) while Shenzhen Geno-Immune Medical Institute is developing both LV-SMENP-DC and pathogen-specific aAPC. Presently, the University of Oxford vaccine also designed using recombinant DNA techniques to produce a SARS-CoV-2 antigen has been tested on 500 volunteers with plans to further trials [33]. Other vaccine developers have specified plans to begin human testing later in the year [34].

2.5. Preventive Measures

According to the World Health Organisation and the Centre for Disease Control

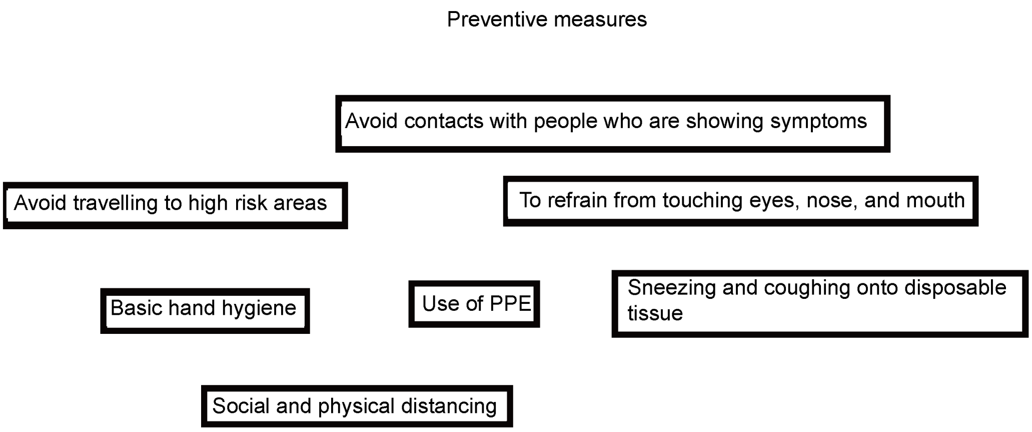

Figure 2. Some preventive measures against COVID-19.

and Prevention (CDC) US, preventive measures by individuals will reduce the spread of the disease [35]. The non-pharmaceutical methods are shown in **Figure 2**.

The non-pharmacological methods are shown above and adherence to these guidelines is effective in preventing the spread of COVID-19.

3. Conclusion

Several lives have been lost because of the COVID-19 pandemic and economies of countries struggling. With no definitive treatment and vaccine available, hand hygiene, physical and social distancing is the non-pharmacological method of staying safe.

Conflict of Interest

The authors declare no conflict of interest.

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