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A Review of the COVID-19 Pandemic and the Role of Medical Laboratory Scientists in containment

Isaiah Nnanna Ibeh[1], Seyi Samson Enitan[2]*, Richard Yomi Akele[3] and Christy Chinwe Isitua[4]

[1]*Department of Medical Laboratory Science, University of Benin, Benin City, Nigeria.*
[2]*Department of Medical Laboratory Science, Babcock University, Ilishan-Remo, Nigeria.*
[3]*Department of Medical Laboratory Science, Afe Babalola University, Ado-Ekiti, Nigeria.*
[4]*Department of Microbiology, Afe Babalola University, Ado-Ekiti, Nigeria.*

ABSTRACT

The Coronavirus Disease – 2019 (COVID-19) virus has infected more than one million people, leaving more than 50,000 people dead across the globe. The health system of many countries has been overwhelmed by the pandemic, with many losing a significant number of their health professionals in the fight against the virus. While doctors and nurses are so visible at the front lines and are being applauded for the gallant role they are playing in the recovery of hundreds of thousands of COVID-19 patients, the world knows little about those behind their successes, the Medical Laboratory Scientists (MLS). Medical laboratory science is the bedrock of diagnostic medicine and the role of the MLS in containing any pandemic cannot be overemphasized. An effective and timely diagnostics approach is fundamental and germane for the successful containment of any outbreak and the MLS are at the fore-front. They are the ones testing clinical specimens from infected and clinically recovered patients. As disease detectives, their role in the fight against the COVID-19 pandemic include, but not limited to: diagnosis, monitoring, confirmation of recovery, safety and efficacy testing of broad-spectrum antiviral agents, discovery and development of vaccines, validation of testing protocols and testing kits, offering of advisories to guide government policy on containment at all levels amongst others. The current pandemic requires a multidisciplinary approach and therefore the MLS should be fully integrated into the multidisciplinary team to effective contain the pandemic. The aim of this review therefore is to provide facts and figures about the COVID-19 pandemic, and to appraise the critical role of the Medical Laboratory Scientists in the fight against the pandemic.

Key Words*:* COVID-19, Virus, Pandemic, Medical Laboratory Scientists, Role, Containment

***Corresponding Author:** E-mail: enitans@babcock.edu.ng, Cell Phone: +2348065483761, ORCID: 0000-0001-5993-7920

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1. Introduction

The World Health Organization through its Director-General, Tedros Adhanom Ghebreyesus, officially declared the Coronavirus Disease – 2019 (COVID-19) a pandemic on March 11, 2020 [1]. The disease is spreading so fast that any count of confirmed cases and deaths quickly becomes out dated. So far, globally, the new coronavirus has infected more than one million people and leaving more than 50,000 people dead in about 180 countries [2]. Beyond animal to human transmission, the virus is now spreading from person-to-person regardless of geographical location [3-6].

In December 2018, the African Society for Laboratory Medicine convened a very timely meeting titled; "Preventing and Controlling the Next Pandemic: The Role of the Laboratory", a meeting that brought to bear the fact that the Medical Laboratory is strategically placed in a pivotal position in the prevention and controls of any outbreak be it an epidemic or a pandemic. Barely after a year the next pandemic is here with us; COVID-19 [7]. In the face of this pandemic, it becomes critical to revisit the role of the Medical Laboratory Scientist in the fight against the COVID-19 pandemic both at the present and in time to come. In this current review, we shall be looking at the history, etiology, pathogenesis and pathophysiology of the Coronavirus disease, as well as the role of the Medical Laboratory Scientists in containing the pandemic.

2. History of COVID-19 Pandemic

On December 31 last year, China alerted the WHO about the occurrence of several cases of unusual pneumonia caused by unknown virus among persons who had either visited or had consumed food from the live animal market in Wuhan City of China, the epicenter of the outbreak [8]. Since then, infection has spread to other Chinese cities, as well as internationally, resulting in the current pandemic. On January 5, Chinese officials ruled out the possibility that this was a recurrence of the severe acute respiratory syndrome (SARS), an illness that started in China and resulted in the deaths of more than 770 people globally in 2002-2003. On January 7, the WHO announced they had identified a new virus. The novel virus was named 2019-nCoV and was identified as member of the *Coronaviridae* family, which also includes SARS and MERS. China announced its first death from the virus on January 11 2020. It was the case of a 61year old man who had bought consumables from the seafood market. Following this development, Wuhan was placed under quarantine with effect from January 23 as rail and air departures were suspended. The Chinese officials reported the first death outside the Hubei province and Beijing cancelled events for the Lunar New Year, slated to commence on January 25. Meanwhile, as at January 23, 2020, the WHO said that the outbreak did not yet constitute a public emergency of international concern and there was "*no evidence*" of the virus spreading between humans outside of China [9, 10].

On January 30, the WHO declared the outbreak a global health emergency of international concern as the death toll in China jumped to 170, with 7,711 cases reported in the country, where the virus had spread to all 31 provinces and new cases were confirmed in Australia, Canada, Germany, Japan, Singapore, the US, the UAE and Vietnam [11, 12]. Li Wenliang, a doctor who was among the first to sound the alarm over the coronavirus, died on February 7 and

Hong Kong introduced prison sentences for anyone breaching quarantine rules [13, 14]. By February 9, the fatalities in China surpassed that of the 2002-2003 SARS epidemic, with 37,198 infections and 811 deaths recorded. The Chinese leader, President Xi Jinping made his first public appearance since the epidemic started, visiting a hospital in Beijing and urging assurance in the fight against the deadly virus. On February 11, the WHO announced that the new coronavirus would be called "COVID-19 virus" as deaths toll in China reached 1,016, with 42,638 infections recorded [15]. The first confirmed case of Coronavirus in Africa was recorded in Egypt on February 14, 2020 [16], while Nigeria announced its first COVID-19 case on 27th February, 2020 [17]. Both African countries have a total of 779 and 74 confirmed cases, respectively as at April 01, 2020. As the virus continue to spread globally like a wide fire, the WHO eventually declared the coronavirus outbreak a pandemic officially on March 11 2020 [1, 18]. Currently, the virus has spread to about 181 countries and territories. The total number of coronavirus cases has surpassed one million, leaving more than 50,000 dead globally [2]. The reported data clearly shows that COVID-19 is no longer a China problem, but a global one. Every country and people should therefore expect the disease and get prepared for it.

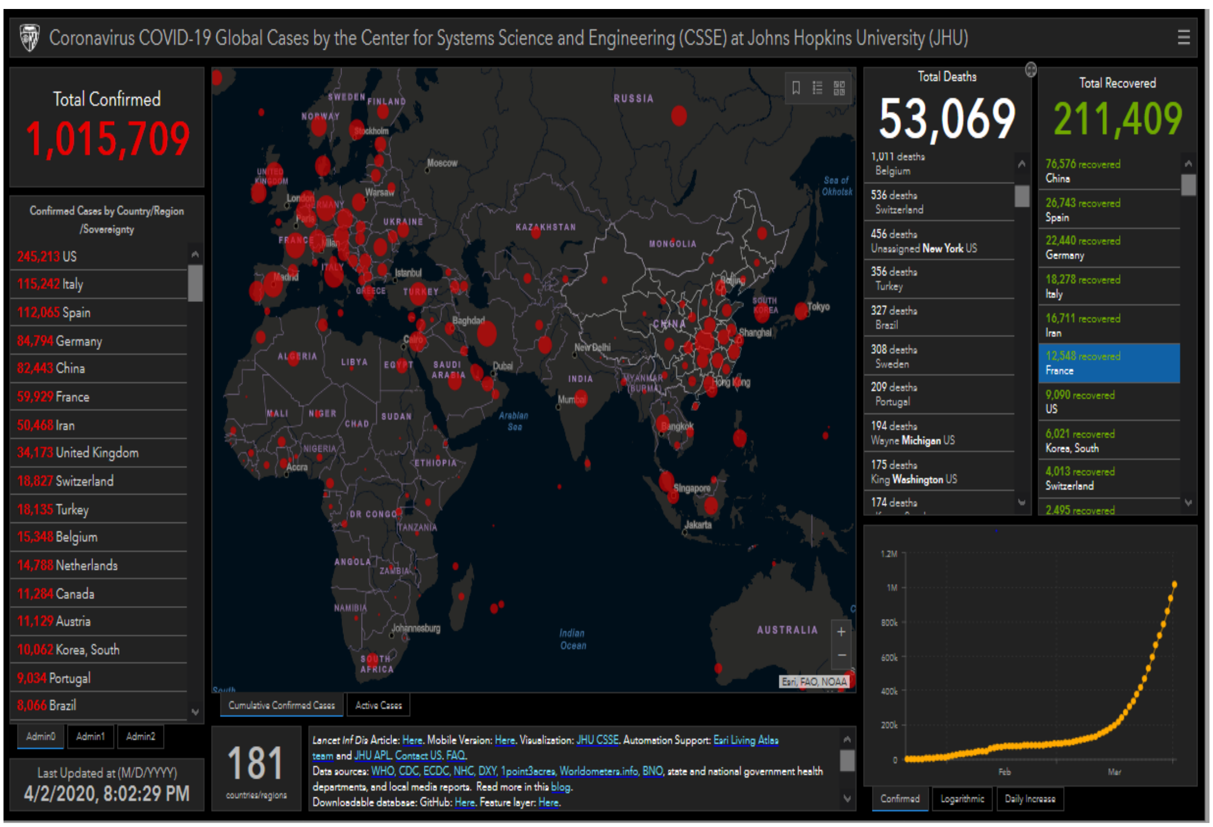

Fig. 1: COVID-19 Global Cases by Johns Hopkins CSSE as at April 02, 2020

3. Etiology of COVID-19 Pandemic

A new strain of coronavirus called the COVID-19 virus (also known as, *the Severe Acute Respiratory Syndrome Coronavirus 2, SARS-CoV-2*) has been implicated as the culprit of this weird pneumonia that started in Wuhan megacity of China [19]. It is an enveloped non-segmented positive sense single-stranded RNA virus in the family *Coronaviridae*. The virus pathogenicity has been linked to the envelop which promotes viral assembly and release. In appearance, the virus looks like a crown under the electron microscope (Figure 2), hence the name, "*Corona"*. Like other coronaviruses, the COVID-19 virus genome is about 400-500nm in size and encodes structural proteins (e.g spike glycoprotein and accessory proteins), as well as non-structural proteins such as RNA-dependent RNA polymerase, helicase, papain-like protease and 3-chymotrypsin-like protease [20, 21].

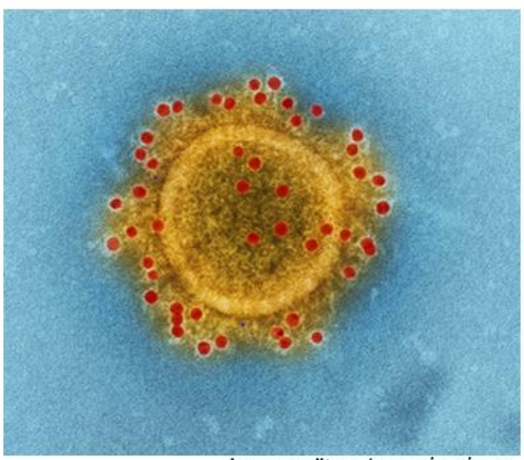

Image credit: *proteogenix.science*

Fig. 2: Coronavirus as seen under the electron microscope

4. Transmission of COVID-19 Virus

Although, the first cases of the COVID-19 were linked to consumption of seafood animals, as well as bats and snakes, the ongoing human-to-human transmission is mainly through respiratory droplets from infected individuals, contact with contaminated objects and surfaces and social activities like hand-shaking, hugging and kissing [22, 23]. The virus is spread in droplets or droplet nuclei released from the nose and mouth of an infected person when they sneeze or cough. A single cough may produce about 3,000 droplets, while a sneeze can generate as many as 10,000 droplets. Once the virus becomes airborne, it may remain suspended in the air for up to 8 hours depending on the prevailing environmental conditions such as temperature and relative humidity [24]. Anyone within two (2) meters of the cough or sneeze of an infected person may take in the respiratory droplets into his or her airway and become infected. Otherwise, the viral particle drops about 10 feet after been discharged from an infected person and may fall on other's people clothing and surfaces around them.

Studies have shown that the virus is capable of surviving for a varied period of time depending on the surfaces: human hands (5-10 minutes), Paper (3-4 hours), Copper (4 hours), fabrics (6-12 hours), metal surface (12 hours), cardboard (up to 24 hours), and up to 72 hours on plastic and stainless steel [24, 25]. The virus remains on these surfaces for the stipulated periods waiting to be picked up by people's hands when they touched such surfaces and then touch their eyes, ears, nose or mouth, from there the virus can find its way into the respiratory tract of the victim, where it then initiates an infection. China in the middle of the pandemic commenced disinfecting and isolating used banknotes as the WHO warned that banknotes may serve as vehicle for the spread of COVID-19 virus. In fact, there are some evidences that the virus is also shed for longer period in fecal matter, so poor toilet hygiene is a predisposing factor to COVID-19 [26]. Being heat labile, the virus does not tolerate the sunlight. It gets inactivates at temperature 26-27^{o}C *in vitro*, hence the climate of each geographical region affects its transmissibility. The viral envelope is sensitive to organic solvent, hence the use of alcohol-based sanitizer for prevention and control [27].

5. Pathogenicity and Replication of COVID-19 Virus

The Type-2 alveolar cells (pneumocytes) in the respiratory tract are the predilection sites for the COVID-19 virus. The virus uses a host cell entry receptor called the Angiotensin Converting Enzyme Type 2 (ACE-2) found on these cells to infect humans. These cell entry receptors are also found in the epithelial cells of the gastrointestinal tract of humans and are also used by the SARS virus [20, 28]. When an individual is exposed to the COVID-19 virus from the respiratory droplets of an infected person, the virus attaches to the host's receptor site (ACE-2) via its surface spike glycoprotein (Adhesion stage) and penetrate into the host's cell through fusion. The dissolution of the viral capsid in order to release the viral nucleic acid into the host's cell is the uncoating stage. This process is mediated by the protease enzyme and it is optimum at 37^{o}C and in the presence of Mg^{2+} and Ca^{2+} ions. After this process, the virus integrates itself (*i.e.*, nucleic acid) into the host genome and the entire synthetic activity of the host cell is short down and re-directed towards the synthesis of the viral molecules. After the release of viral nucleic acid, there is total disappearance of the viral nucleic acid as it cannot be demonstrated. However, a host of synthetic activity takes place in the host cell [20].

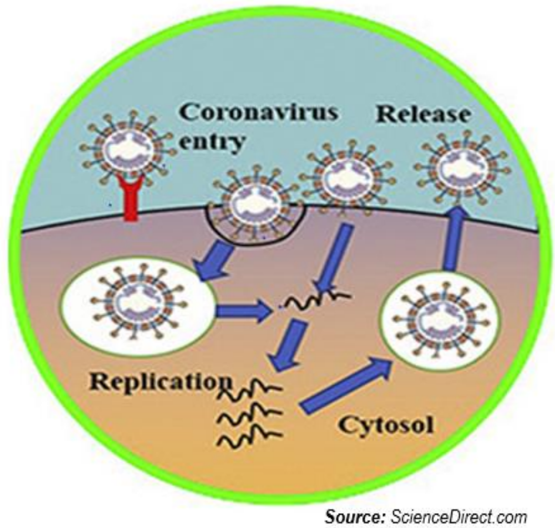

Fig. 3: Schematic diagram illustrating life cycle of COVID-19 virus

Meanwhile, in the cytoplasm, the single stranded viral RNA genome is first transcribed into a single stranded messenger RNA (*ssmRNA*) using the enzyme *transcriptase*. The *ssmRNA* then moves to the ribosome where it is then translated into two polyproteins (*pp1a and pp1ab*) and structural proteins. Autoproteolytic cleavage of polyproteins then produces number of non-structural proteins including *RNA-dependent RNA polymerase*, *helicase* and nonstructural protein 3, 4, and 6. The latter are thought to be responsible for anchoring the coronavirus replication/transcription complex through recruitment of intracellular endoplasmic reticulum membranes to form double membrane vesicles abbreviated as DMV [20].

RNA-dependent RNA polymerase (*RdRp*) and *helicase* localize to double membrane vesicles drive the production of *subgenomic RNAs* (*sgRNAs*) from which the structural and accessory proteins are produced in the next phase of translation. Once synthesized, transmembrane structural proteins "S", "M", and "E" are inserted, and folded into the endoplasmic reticulum (ER) and then transported to the Endoplasmic reticulum-Golgi intermediate compartment (*ERGIC*). The nucleocapsid is formed by the combination of the viral genomic RNA and nucleocapsid "N" protein in the cytoplasm (Assembly stage). Following the final assembly of the virion in the intermediate compartment, vesicles containing the virus particles then fuse with the host's cell plasma membrane and the mature virions are release via smooth-walled vesicles by exocytosis and the cycle continues, until all the cells are infected [20, 29].

6. Pathophysiology of COVID-19

Early in infection, the virus invades two types of cells in the lungs: mucus-producing (Goblet) cells and ciliated cells. Mucus keeps the lungs from drying out and protect them from pathogens. Cilia on the other hand, beat the mucus towards the exterior of the nasopharynx, clearing debris, including viruses out of the lungs. It is likely that the cilia cells are the preferred hosts of COVID-19 virus. When these cells die, they slough off into the airways, filling them with debris and fluid which is characterized with dry cough and shortness of breath and ultimately pneumonia in both lungs. The immune cells recognize the virus and flood into the lungs. The lungs tissue becomes inflamed and damaged due to hypersensitivity.

More cells are destroyed and slough off into the lungs, further blocking them, thereby increasing the severity of the pneumonia. Increased scarring of the lungs potentially results in respiratory failure. Patients that get to this stage of infection develop lung fibrosis, suffer permanent lung damage or even die [29].

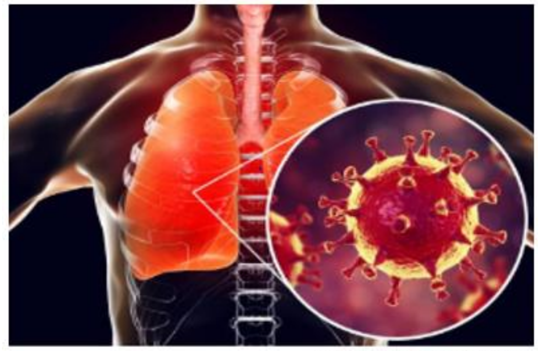

Image credit: Shutterstock

Fig. 4. Coronavirus infects the Type-2 alveolar cells of the respiratory tract causing pneumonia-like symptoms

There are clinical and laboratory evidence of lesions in lungs of COVID-19 patients. The virus creates holes in the lungs, making them to look like honeycomb-like. This is most likely due to the over-reactive immune response earlier mentioned, which affects both infected and healthy tissues and creates scars that stiffen the lungs. Patients may therefore require ventilators to aid breathing. The inflammation also results in more permeable alveoli (the thin interface, where the lungs replace carbon dioxide in the blood with oxygen inhaled).

Increased permeability causes fluid to leak into the lungs which decreases the lungs' ability to oxygenate blood, and in severe cases, floods them leading to breathing difficulty, which can be very fatal. Excessive immune reaction due to the presence of the virus can also cause another type of damage due to over-production of cytokines (like IL-1B, IL-6, IL-8, CCL2, CXCL10, CCL2, CCL3, CCL5 etc) by activated leucocytes, resulting in a cytokine storm, characterized by widespread inflammation in the body, increase in blood vessel permeability and escape of fluid. This makes it difficult for oxygenated blood to reach the rest of the body, resulting in multiple organ failure [20, 29].

7. Pathogenesis and Clinical Manifestations of COVID-19

The period that lapses between the disappearance of the COVID-19 viral particle within the infected host cell and the reappearance of its off spring within same cell is termed "latency". It is also referred to as "dormancy" because there is no expression of symptoms at this stage. On the other hand, the period that lapses between the disappearance of the COVID-19 viral particle within the host cell and the re-appearance of its off spring in the clinical specimens of the host is termed "Incubation" and is characterized by symptoms. The virus has an incubation period which ranges from 0-14 days (with an average of 4.1 days) post-exposure. Interestingly, an incubation period of up to twenty-one (21) days has been recorded in some patients [20, 30].

On day 0, the virus comes into contact with the epithelial surface of nasopharynx of the host. On day 1-2 the virus localized in the epithelium tissue where it replicates and start shielding into the lymph nodes by day 3-4. This results into viremia where the infection spread into different organs through the blood stream from the lymph nodes by day 5-7. Viral shedding in infected persons may last up to 28 days or more [31].

The disease is associated with atypical pneumonia characterized with high fever (45%), sore throat (30%), dry cough (65-80%), chest pain and difficulty in breathing (20-40%), diarrhea (10%) amongst other clinical manifestations [32, 33]. In the first 72 hours (Day 1-3) post-exposure, the virus first multiple in the throat, and the infected person may show symptoms similar to common cold. There could be slight sore throat, but no fever and tiredness. By Day 4, The sore throat is a little more pronounced with hoarse voice. There is slight loss in appetite, with mild diarrhea. The body temperature is around 36.5^{o}C. In addition to sore throat and hoarse voice, Day 5 is characterized with slight fever (36.5 to 36.7^{o}C), body weakness and joint pain. By Day 6, the patient present with cough accompanied by mucus or dry cough, sore throat with painful swallowing, as well as diarrhea and vomiting. Day 7 is characterized with pronounced fever (37.4 to 37.8^{o}C) amongst other signs and symptoms. By Day 8-9, the fever is more intense (38^{o}C or higher), the dry cough is more severe and persistent, with breathing difficulty, as well as chest pain [29, 34].

8. Risk Factors of COVID-19

The virus is believed to be more infectious than its counterparts (SARS and MERS). International travel, as well as lack of proper entry screening at airports and seaports are largely responsible for the importation of the COVID-19 virus from the epi-centre (Wuhan, China) to other countries of the world. Identified risk factors include: recent travel to any high risk country during the past 14 days, direct and close contact or exposure to an infected COVID-19 patient. The elderly, the immunocompromised, as well as those with underlying condition including asthma, diabetes, obesity, hypertension, liver and kidney problem are at greater risk of the disease [32, 35].

9. The Role of Medical Laboratory Scientists in containing the COVID-19 Pandemic

The Medical Laboratory Scientist (MLS), also referred to as the Clinical Laboratory Scientist or Biomedical Laboratory Scientist, is a vital healthcare detective, uncovering and providing laboratory information from laboratory analyses that assist physicians in patient's care [36]. These health professionals use different biomedical instrumentation and technology, computers, and methods requiring manual dexterity to perform laboratory testing on clinical specimens including blood, urine, feces, semen, aspirates amongst others [37, 38].

Laboratory testing encompasses such disciplines as clinical chemistry, medical microbiology (Virology, Bacteriology and mycology), hematology/blood group serology, immunology, histopathology, and molecular biology. Medical laboratory science professionals generate accurate laboratory data that are needed to aid in detecting infectious pathogens like bacteria or viruses, cancer, heart attacks, diabetes, as well as drug poisoning. In addition, they monitor testing quality and consult with other members of the healthcare team for a better health outcome of the patient [39, 40]. This implies that a Medical Laboratory Scientist is a "disease detective," helping to pinpoint the etiology of disease through the examination and analysis of blood, tissue and other body fluids. He/she also monitor disease and treatment progression, as well as develop vaccines to combat infectious diseases.

Worthy of note here, is that behind every accurate and reliable laboratory result, is a dexterous and proficient Laboratory Scientist. Therefore, the role of the Medical Laboratory Scientist in the fight against the COVID-19 pandemic include, but not limited to: diagnosis, monitoring, confirmation of recovery, safety and efficacy testing of broad-spectrum antiviral agents, vaccine discovery and development, validation of testing protocols and testing kits, offer advisories to guide government policy on containment and promote health advocacy at all levels amongst others [38, 41].

9.1 Diagnosis

Accurate diagnosis in a timely fashion is very critical to the containment of any disease outbreak, hence the role of medical laboratory scientists in the control of the COVID-19 pandemic. Besides, the detection of the COVID-19 virus in suspected cases, they also have the responsibility of identifying underlying conditions (such as diabetes, multiple myeloma, liver disorder, kidney disorder etc) that may complicate the prognosis of confirmed cases [42-44].

Following the onset of a cluster of acute pneumonia cases which occurred in Wuhan, China in December 2019, the Scientists at the Viral Research Institution in China quickly swung into action and identified the etiology as a β-coronavirus, formerly named 2019-nCoV and now COVID-19 virus [8]. The complete genomic sequencing of the novel virus was done to distinguish it from other related viruses (such as coronavirus 229E, coronavirus HKU1, coronavirus NL63 and coronavirus OC43) that present with similar acute respiratory syndrome [8, 45]. Genetic similarity among infectious agents, makes laboratory diagnosis very crucial and this is an exclusive duty of a Medical Laboratory Scientist [46].

Presently, the gold-standard for the laboratory diagnosis of COVID-19 is nucleic acid detection in nasal swab, throat swab or other respiratory tract specimen using the Real time polymerase chain reactions (RT-PCR) or a qPCR which may be confirmed using Next generation sequencing – NGS [8, 33]. The Stop TB Partnership and Global Drug Facility (GDF) has developed a new test for the detection of COVID-19 virus, using the Xpert Express COVID-19 virus cartridge which has received emergency use authorization (EUA) from the United States Food and Drug Administration (FDA) on 21 March, 2020. The cartridge can be used on any of the currently available GeneXpert system running on a software version 4.7 or higher in recommended Biosafety Level Laboratory (e.g BSL-2). The Xpert Express can provide rapid detection of the COVID-19 virus in about 45-50 minutes [47].

Several serologic methods are also being developed (which will require validation) on the bases that Immunoglobin M (IgM) and Immunoglobin A (IgA) are detectable within the 4 days of infection and IgG at about 14th day of infection [48]. If these are detectable, a ELISA test will be valuable in detection of infection and the progression of the disease as a high IgM levels may help detect active infection, while a fourfold increase in IgG titer confirms infection. A combination of qPCR/RT PCR with IgM ELISA has the potential for an increased detection rate. The RT-PCR is appropriate for acute phase of the disease when antibodies are yet to be produced against the virus. The RT-PCR test specifically probe for the presence of viral RNA genome in patient's specimen in the absence of any clinical symptom, during the incubation period. This method affords early diagnosis and therefore early treatment to prevent the onset of resulting lung fibrosis.
The COVID-19 Rapid Diagnostic Test (RDT) Kits on the other hand, use the principle of immunochromatography to probe for the presence of COVID-19 antibodies in patient's serum. Such antibody test is appropriate for convalescent phase of the disease. Following the declaration of the disease a pandemic, Scientists have been able to produce rapid diagnostic tests that can specifically identify the presence of antibodies against the virus in the patient's serum. The COVID-19 Rapid Diagnostic Test (RDT) Kits uses the principle of immunochromatography to probe for the presence of COVID-19 antibodies in patient's serum. Such antibody test is appropriate for convalescent phase of the disease. The COVID-19 rapid test kits are much needed in resource-limited settings without facility for molecular testing such as the RT-PCR. The rapid test kits produce result in 15 minutes against the 2 hrs of RT-PCR. When properly validated, their usage will reduce the waiting time for treatment of patients who turned up in emergency rooms and medical clinics with pneumonia-like symptoms [49, 50].

As disease detectives, diagnostic preparedness is very critical. An effective and timely diagnostics approach is fundamental and germane for the successful containment of any outbreak. From lessons learnt from previous outbreaks, poor diagnostic preparedness has contributed significantly to delays in the identification of recent outbreaks for multiple pathogens, including, Lassa fever, Ebola, Yellow fever and Zika, primarily due to poor local diagnostic capacity [51].

Figure 5: Images of a COVID-19 Rapid Test Cassette and Blood Sample Positive for COVID-19

An estimated three months' delay was documented during the 2013–2016 Ebola epidemic in West Africa between the index case detection and the identification of the causative agent; post-outbreak analyses suggest that diagnosing 60% of patients within 1 day instead of 5 days could have reduced the attack rate from 80% to nearly 0% [52]. Diagnostics information coupled with appropriate interventions eventually led to the containment of the outbreak, however, the delays had resulted in the loss of thousands of lives and billions of dollars in the cost of response [53].

Diagnostic preparedness is multi factorial as it encompasses availability of diagnostic methods and kits, adequate training and knowledge on the part of professionals, rapid response to outbreaks and emergency situations, so also biosafety practices and logistic matters. WHO had tied successes in the fight against the HIV/AIDS pandemic to the development of effective screening and testing of individuals. Recalling that outbreaks can be so overwhelming giving no time for preparation after its onset, it calls for preparedness beforehand. One can never be over prepared for an outbreak haven that no one can perfectly predicts what comes up next even though epidemiological indicators may occasionally be suggestive. The rate of spread of the COVID 19 has been unprecedented further buttressing the great need for diagnostic preparedness on the part of the Medical Laboratory Scientists [53].

9.2 Monitoring

Laboratory monitoring of COVID-19 patients is another crucial role of a Medical Laboratory Scientist in containing the pandemic. It is the duty of the MLS to carry out tests that will assist in monitoring the disease progression, as well as the prognosis of the patient following initiation of antiviral therapy, as well as to detect post recovery complications which may arise in the future. It is very important to determine when a patient can actually be said to have recovered fully. The Medical Laboratory Scientists play a significant role in confirming the state of recovered patient before he or she is allowed to reunite with the community to avoid a silence spread of the disease due to carrier status.

There are laboratory tests that can be used to ascertain that a patient has fully recovered and no longer shedding the virus post-treatment. Usually, MLS determine the viral load and leukocytes count of the patient before and after treatment. Viral load and leukocytes (Total/Differential) Count are important indices of the virologic and immunologic responses of the COVID-19 patient, respectively.

Patients who have clinically recovered from COVID-19 are discharged after confirmation of negative viral status usually by at least two consecutive polymerase chain reaction (PCR) tests [54, 55]. Sadly, it has been reported that some recovered COVID-19 patients turned positive again after they were discharged from the hospitals [56-58]. The reason for this development is unclear and requires further investigation. The probable explanation could be that, either the patients were not properly treated, or that they were not adequately tested to ensure that they have achieved complete viral clearance before been discharge from the hospitals [54]. One wonders why a hospital would discharge a patient who have not fully recovered? The overburdened healthcare system is said to be putting pressure on doctors to discharge people who may not have fully recovered to free up beds for newly infected patients.

Experts in this regard, are now calling for some more stringent hospital discharge protocols to avoid a re-occurrence of such incidence [59].

Lymphopenia with an increase in neutrophils as a result of down regulation of the lymphocytes is common in COVID-19 patients [32, 60]. COVID-19 Patients that cleared infection had been reported to have their numbers of CD3+, CD4+, CD8+ T cells and B cells significantly restored close to normal levels, compared to those who failed to clear infection. The recovered patients had a higher count of leukomonocytes compared to others [55].

Other abnormal laboratory diagnostic features that the Medical Laboratory Scientists also watch out for in COVID-19 patient include: a lower serum albumin, a decrease in hemoglobin concentration and absolute lymphocytes count, accompanied with increase in serum C-reactive protein, D-Dimer, Lactate dehydrogenase, Ferritin, Interleukin-6 (IL-6) and higher erythrocyte sedimentation rate (ESR). In severe case of the disease, serum liver enzymes (*Alanine aminotransferase* and *Aspartate aminotransferase*), bilirubin, Creatinine, blood urea nitrogen (BUN), procalcitonin and cardiac biomarkers are elevated. These abnormalities are however resolved with treatment success [51, 53].

Furthermore, the role of the Medical Laboratory Scientists in a pandemic situation goes beyond just testing to know who is infected and who is clean, the dynamics of the spread of the disease, its pathogenesis, genetic evolution, prevention and control measures must also be investigated [61]. The MLS play a critical role in disease surveillance [62]. They conduct periodic pathogenicity and immunogenicity studies to detect the emergence of new serotypes of the COVID-19 virus due to mutation, as well as test for the development of herd immunity in the community. The transmissibility of the virus might change and it can also learn new ways to evade the immune defense of the host. It is the duty of the MLS to identify any possible change in the spread dynamics of the virus, as well as strategies used by the virus to circumvent the host's defense system. It is also the responsibility of the MLS to detect and monitor the presence of herd-immunity in a community [63].

The term *"herd immunity"* refers to the fact that the risk of infection among susceptible individuals in a population is reduced by the presence of adequate numbers of immune individuals. People who have been immunized serve as a protective barrier for other individuals who have not been immunized, provided that the number of immunized individuals has reached a certain level, usually 80% or higher. Reaching and maintaining that level provides communal protection or *"herd immunity"* to unimmunized individuals in the population [63, 64].

The effect of "*herd immunity"* is reflected in the dramatic decreases in the incidence of disease, even when all susceptible individuals have not been vaccinated (No COVID-19 vaccine at the moment). As the herd-immunity increases, the incidence of disease automatically decreases. The threshold of immunity needed for this indirect protection, however, depends on many factors, including the: transmissibility of the virus, nature of the immunity, and the distribution of the immunized individuals in the geographical location. However, individuals protected by herd immunity remain susceptible to infection upon exposure and this can lead to a fresh outbreak of disease when a group of susceptible individuals accumulate in a given community. Herd immunity can simply be determined by conducting a seroprevalence study of the COVID-19 in a given community. Currently, Scientists are requesting for the plasma of patients who have recovered fully from the COVID-19 to understudy the nature of antibodies produced, whether long lasting, short lived or intermediate [65].

9.3 Control

Beyond diagnosis and monitoring, the Medical Laboratory Scientists also play a vital role in the control of any disease outbreak. They are involved in all aspects of infection control program, particularly in the community and hospital's infection surveillance system. They support the infection control program to effectively and efficiently use laboratory services for epidemiologic purposes. They provide support for sterilization and disinfection in the facility including biological monitoring of sterilization [66]. Help develop policies and procedures on handling health hazards within and outside the hospital environment. Take the needed action when a commercial product is suspected to be contaminated. Test hospital personnel and environment for possible infection or contamination. Provide advice on specimen collection, transport and handling to prevent a possible outbreak [46, 67]. They put in place plans for containment of all the specimens that has been sent to the Laboratory for analysis as these may carry potential deadly pathogens that may trigger the next pandemic if not well contained. It is the statutory role of the MLS to ensure the biosafety of the laboratory environment even as they carry out their daily routines. In fulfilment of this it is required that any work done on COVID-19 virus must be carried out in Biosafety Level 3 (BSL-3) facility or at least a BSL-2 as required by International Standard Organization [68, 69]. They also provide advice on judicious used of antimicrobial agents, including antiviral agents used in the treatment of COVID-19 patients. They make laboratory test results available in an organized, easily accessible, and timely manner for better patient clinical outcome, thus flattening the curve of the disease [70]. They don't just turn out laboratory results, but also monitor the same for unusual findings and alert the clinician promptly as the need arises [71].

Currently, there are hundreds of Medical Laboratory Scientists working in more than twenty (20) research laboratories worldwide in desperate search for cure and vaccine in the fight against the COVID-19 pandemic. Different safety and efficacy testing of broad-spectrum antiviral agents and candidate vaccines are ongoing with near success. The WHO and FDA have promised to remove all the bottle-necks in testing and certification. The role of the MLS in validating testing protocols and testing kits cannot be overemphasized. The MLS working in the *In vitro* Reference Laboratory of the Medical Laboratory Science Council of Nigeria (MLSCN) are carrying out tests of accuracy and specificity to validate the effectiveness and performance of the new COVID-19 rapid diagnostic test kits that have flooded the Nigeria market [72]. In addition to the above roles, we also have high-power MLS providing advisories to guide government policy on containment of the pandemic. Some of them are members of the COVID-19 Containment Task force at different levels. These and many more are the crucial role of the Medical Laboratory Scientists in containing the current pandemic.

10. More on the pathogenesis of

COVID -19

While there is a lot yet to be learned concerning the pathogenesis of COVID -19, we examine here critically the issue of cytokine storm as a major immune-compromising event which incapacitates the individual's immune response mechanism leading to less effective cellular immune response and bizar humoral immune response coordination. The implications are many including the inability of the body to fight its own fight, poorly regulated pro-inflammatory cytokines which may be associated with high inflammation and rise in body temperature, fluid accumulation, excessive cellular and tissue damage cascading to a whole lot of events that favor the survival and multiplication of virus in the body in association with body pains, fatigue and dry cough e.t.c as the storm escalates. Assuming the above observation is true then the most effective line of treatment will include the following:

- Secure/restore the integrity of the immune system
- Hit the virus directly
- Prevent bacterial infection
- Restore fluid dynamics
- Prevent spread of infection from the index case
- Assist respiration in severe cases (ventilators needed)

Different countries may develop or adapt varied intervention tools, the valid considerations being the efficiency/effectiveness of the tools, cost, sustainability and cultural values.

11. Suggestions

Individuals, Corporate organizations, Local government, State governments and the Federal government should set aside funds for testing and treatment centers that should adopt the Nigerian approach. A lot of donations have been announced but no funds may be dedicated for this purpose because of the obvious gaps in the healthcare delivery system in Nigeria.

For the treatment of COVID-19 patients, we suggest the following:

- Tried and tested immune boosters including Manna, Immunovit, Berries e.t.c.
- Mefloquine or chloroquine (hydroxychloroquine)
- Azythromyzin
- If Manna is used, then Zinc sulphate should not be added. After 3 days, if no remarkable improvement, treatment can be reviewed.

Manna boost the immune system and provides energy and essential trace elements. It is therefore suitable for the seriously debilitated patients. In one of our studies, Manna improved response of HIV patients to highly active anti-retrovirals (Lamivudine, Zidovudine and Nevirapine) [73].

12. Action Protocol/Case Definition

- **Suspected case:**
  - ✓ High temperature, fever, cough (dry or productive), headache, runny nose.
  - ✓ Handheld infrared thermometer for determining temperature.
  - ✓ Case taken aside for questioning concerning his or her medical history, recent travels/ movements.

- **Probable case**
  - ✓ Presence of 3-5 of the vital signs, history of recent visit to epi-centers of COVID-19 (China, USA, Italy, Spain, United Kingdom e.t.c).

- ✓ Serological test for IgM, IgG, IgA.

- **Confirmed case**
  - ✓ Presence of relevant antibodies
  - ✓ Presence of relevant antigens
  - ✓ RNA amplication using PCR
  - ✓ RNA sequencing and blasting to confirm identity with the standard (COVID -19 probe).
  - ✓ Contact tracing becomes very relevant.
  - ✓ Two-three weeks after recovery, test should be repeated including stool antigen test.

As required for all infectious agents, diagnostic procedures must be carried out by medically qualified personnel (e.g Medical Laboratory Scientists) in levels 2-4 biosafety laboratories, with their Personal Protective Equipment (PPE) (International best practice- IBP) in order to prevent unnecessary spread of the virus among health workers and the public through droplets or aerosols.

In Nigeria, the south eastern states have adopted two basic approaches; formation of a Taskforce or Inter-Ministerial Committees. The action plans are similar, drawing extensively from WHO and CDC directives and guidelines (International Best Practices – IBP).

Since COVID-19 shows tropism for nasopharyngeal cells (especially the ACE-2 receptor bearing cells), all factors that weaken the integrity of these cells will promote infection, such as smoking, aging, alcoholism and other drug abuses. Those with underlying diseases e.g renal diseases, liver cirrhosis, diabetes e.t.c will succumb faster.

13. Options

Several treatment options are in the public domain. One can easily goggle very rich information on the trials going on. However, we will not shy away from making our own suggestion as follows:

1. Boost the immune system so that the body can fight its fight efficiently and courageously (There are so many reported immune boosters out there including the "Manna", which has shown positive effect against HIV).
2. Introduce anti-viral agents (Orthodox or traditional medicines).

The commonly reported orthodox treatment include hydroxychloroquine, azithromycin, some highly active anti-retrovirals (HAART). With regards to the use of African traditional medicine (ATM), there are a plethora of items that are reported to have anti-viral activities such as hot lemon with bicarbonate, alkaline drinks, Intercede Health products are in the market including Immunivit-IHP and Detox Tea which are immune boosters. There are over twelve standardized African traditional medicine (ATM) products that are associated with anti-viral activities. The Federal government should provide enabling environment for identifying and testing our indigenous products for their potentials as intervention tools in COVID-19 pandemic and any other disease outbreak. It is high time we stopped depending on foreign medicament to solve our health problems in Nigeria and Africa in general.

14. Relevant Questions

There are a couple of gamine questions about the COVID-19 seeking urgent answers and such answers yet lies in the laboratory. These answers are potential determinants of the immediate feature of this pandemic. These questions include:

- Will infection with COVID -19 confer a long lasting immunity?
- Will serum therapy be useful?
- Does Immunity to COVID -19 involve the short and long term memory cells?
- Are the short term memory lymphocytes being very active in the acute phase thus, adequately treated cases can become sero-negative as quickly as possible?
- In contrast can the long term memory lymphocytes confer lasting immunity, but antagonize sero-conversion as is the case with HIV?
- What are the likely surrogates for the diagnosis of COVID-19?
- What are the sensitivity, validity and reliability of the new COVID-19 RDTs that have just been released into the market?
- Can a patient who had just recovered from COVID 19 be re-infected. If yes, how soon?
- What are the challenges facing COVID-19 vaccine discovery, development and certification?
- How efficient are the decontaminating agents currently in use in our hospital settings?
- What are the factors that makes the COVID-19 virus more infectious than SARS and MERS?
- Are there ongoing mutations in the virus that may cause some other havoc in the nearest feature? What are the after marks of the current outbreak?
- What are the dynamics of immune response to this infection and the disease as a whole?
- Are there genetic explanations for the COVID-19 susceptibility and disease progression among the whites compared to the blacks?

These and so many more are the questions staring the Medical Laboratory Scientists in the face as a result of the COVID-19 pandemic which calls for further studies and immediate actions tailored at answering them if the Medical Laboratory Scientists will not be failing in their obligations. The outbreak is on a speed lain, so also must responses assume a faster speed in a chase after it.

Breaking the cycle of transmission remains the standard procedure. Other possible mechanisms of COVID-19 evasion of the human immune response such as: antigenic variation (change in membrane proteins or epitopes) mimicry of host cells, encouraging the production of non-neutralizing antibodies which may aid the multiplication of the virus should be investigated.

15. Conclusions

No doubt the COVID-19 is now a pandemic and the virus is really testing the resilient of our health delivery system. Medical laboratory science is the bedrock of diagnostic medicine and the role of the MLS in containing any pandemic cannot be relegated to the background, not now or in the future. They are at the frontlines testing potentially infectious clinical specimens from patients. It is important for the Medical Laboratory Scientists to be regarded as professionals in their own right by patients, other co-operating parties in the health care system and by the governments too. To the Medical Laboratory Scientists, being professional means creating and maintaining flow and efficiency in the laboratory by way of general knowledge, a well-defined framework, structure and organisation in the fight against the pandemic. The first priority in diagnostic medicine is generation of reliable test results. In doing this, quality awareness by the MLS is of primary importance. The MLS develop methods for the control of all stages in analysis processes. They validate methods of analysis and secure optimum procedures supported by guidelines and instructions. MLS are careful and accurate about their work and understand the significance of their profession for the better outcome of the patient. They are aware that it is important to deliver "the right answer at the right time." To this effect, we hereby submit that, in addition to mobilizing doctors and nurses, Governments at all levels, should also see the need to effectively mobilize the Medical Laboratory Scientists because of the very critical role they play in stemming the tide of COVID-19 pandemic. There should be capacity building (in form of training, re-training and certification) for the Medical Laboratory Scientists, especially now and periodically to ensure continuing quality performance of laboratory testing and monitoring of infectious diseases. The current pandemic requires a multidisciplinary approach and therefore the MLS should be fully integrated into the multidisciplinary team to effective contain the pandemic. Clinical practice involves teamwork and no one single professional group has a monopoly of knowledge or skills. Thus, there will always be need to work together as a team for the best possible outcome for the patients. Medical Laboratory Scientists are conscious of the fact that maintenance of flow and efficiency in the work and maintenance of a professional image depend on a common work effort and everybody doing their job. Therefore, the Government should play the role of unbiased referee in fostering industrial harmony in the health sector, by not promoting one professional body at the expense of the other. To effectively contain the pandemic, we call on the Federal government to allow other laboratories (Public and Private) test for the coronavirus. It is very critical for testing of the virus be decentralized to unbundle the workload on the Nigeria Centre for Disease Control, which has the singular responsibility of testing and confirming COVID-19 cases in the country. This will no doubt increase the turnaround time for testing for the virus. It is so important to avoid losing probable cases to the community and reduce waiting time for confirmation. As at the time of writing this review, there are only five molecular laboratories testing for the virus, mainly concentrated in the southern region of the country with the exception of National Reference Laboratory in Abuja (FCT), others are ongoing projects. This does not speak well for the country as the giant of Africa. We therefore call on the government to make judicious use of the funds and donations that have been made available by well-meaning individuals and corporate bodies to fast track the completion of the ongoing molecular laboratory projects. The NCDC should also allow the use of validated rapid screening kits at either public or private laboratories with biosafety level 2 or 3. This would mean adjusting the algorithm to allow those who are positive to screening have confirmatory testing with PCR platforms. Furthermore, adequate isolation centres for a probable explosion of the Covid-19 infection in Lagos, Abuja, Kano and elsewhere should be put in place. The government in addition, should revisit the welfare package of the health workers (the MLS in particular), grant them life insurance, increase their hazard allowances, and also provide them with the required personal protective equipment (PPE) to safe guard their lives as they charge on against the monster called COVID-19. The MLSCN on the other hand, must ensure that our laboratory protocols for COVID-19 diagnosis and monitoring are consistent with global best practice, create a reliable system for management of COVID-19 test results and ensure that positive specimens and contaminated items used for testing and monitoring are proper handled and disposed thereafter according to standard health care waste management practices to prevent a possible laboratory fall-out of another infectious pathogen that may trigger the next pandemic. Finally, the MLSCN should continue to update testing algorithm, protocol and guidelines for COVID-19 testing. Standard Operating Procedures (SOPs) on laboratory waste management, sample collection, transportation and testing should be developed, circulated and updated periodically as the need arises.

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