ISSN: 2635 - 2826

Journal of Clinical & Biomedical Research

SCIENTIFIC Research and Community

Research Article

Open Access

Lack of Robust Laboratory Testing Infrastructure in Nigeria: A Promoter of Community Transmission Outcome of COVID 19 Virus

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ABSTRACT

Background: An outbreak of unknown origin which broke out in China in December 2019 has become a global threat to human lives and economies. Coronavirus disease 2019 (COVID19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic by the World Health Organisation (WHO) due to its rapid global spread and concurrent of level devastation. Many countries are currently on lockdown to mitigate the spread while different treatment options have been proposed, but none has been approved by the appropriate authority. Currently, the disease has affected over 10 million people worldwide while claiming as many as 517,877 lives respectively.

Aim: To evaluate the inadequate COVID-19 testing capacity in Nigeria, probable causes and how it can promote community transmission of the disease

Methodology: Peer-reviewed published research articles containing information on COVID-19, the causative virus and other important details were systematically appraised and summarized. The reviewed studies comprise of cross-sectional and observational studies of wide range of outcome.

Findings: COVID-19 which first broke out in Wuhan City of China has now spread to about 216 countries, causing fatalities in large numbers. It has been reported that individuals with increased risk of severe outcomes include the elderly and those with underlying health conditions. The incubation period of the disease ranges from 1-14 days, during which the disease can be transmitted by both symptomatic and asymptomatic patients. Patients manifest with symptoms such as fever, dry cough, dyspnoea, etc., while the major causes of death include multi-targeted organ failure, acute respiratory distress syndrome (ARDS), shock, etc. The disease can be diagnosed by the detection of the nucleic acid of SARS-CoV-2 in patient samples via real-time reverse-transcription polymerase chain reaction (rRT-PCR). Since there is currently no approved therapeutics or vaccine for the disease, early detection and management of symptoms represent the best way of helping patients to recover in good time. While many countries are responding by scaling up their testing capacities, Nigeria has struggled to scale up her testing capacity to a reasonable extent, though not really enough in capacity and robustness, considering the large population size to cover in the country, and this therefore, may pose huge amount of threat of increased community transmission of the disease in our neighbourhood, if not corrected in time

Conclusion/recommendation: The leadership of Nigeria agency in-charge of disease control and prevention needs to scale up the testing capacity within the country, as soon as possible to reduce the risk of increased transmission of the disease, while reassuring the inhabitants of the hope and capacity of overcoming the outbreak. It is also very important that long-term development strategies be put in place to revamp the weak health care facilities in the country, with respect to provision of modern technological advanced medical equipment's and the training of manpower to cover the already existing shortage of expertise in molecular diagnosis and research outcome.

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Received: September 17, 2020; **Accepted:** September 29, 2020; **Published:** October 27, 2020

Keywords: Lack of Testing Facility, Covid 19 Pandemic, Nigeria, Community Transmission, Risk Factors, Large Population

Introduction

Coronavirus disease 2019 (COVI 19) was first discovered in China when a pneumonia of unknown origin broke out in Wuhan, Hubei Province, China, affecting a cluster of people linked to a large seafood and live animal market in the area [1]. A novel coronavirus (n-CoV), currently known as SARS-CoV-2, was identified in the respiratory samples of the pneumonia patients [2]. The infection has since spread around the world, and has been classified as a pandemic by the WHO [3]. It has affected over 10.7 million people and claimed as much as 517,877 lives as of 26 May 2020 [4].

With the pathogenesis of the disease currently unknown, it has been suggested based on the analysis of the structural features that the virus may be able to bind to the angiotensin-converting enzyme-2 (ACE2) receptor in humans to gain entry into humans [5]. COVID-19 patients experience symptoms akin to those of viral pneumonia such as dry cough, fever and dyspnoea. Some reports suggest that older age and the presence of underlying health problems contribute to the severity of illness, and the infection may cause mild, severe or critical illness. Furthermore, projected estimates from evidenced-based studies have revealed that about 80% of patients experienced mild illness, 14% present with severe illness while 5% suffer critical illness. [6].

However, despite causing definite irretrievable damage (loss of lives) to the society, COVID-19 has placed the global economy on a standstill. To curtail the transmission and spread of the disease, many of the affected countries have instituted some level of strategies such as complete lockdown and social distance measures. The entire educational, sports, commercial and spiritual institutions are closed in many of the affected countries. Industries, except those involved in essential services, are suffering long-term closure in many countries, while people in the tourism and transportation industries are faced with extreme difficulties. Also, productivity in the affected countries has gone sorely low, and this could increase the level of unemployment index in those countries. Besides, there is massive expenditure on the treatment and rehabilitation of the infected population as well as their families [7], even in the midst of slow production and scarce medical supply consumables across the world.

Nonetheless, in Nigeria, the disease has spread to almost all the states, affecting about 27,564 people and claiming at least 628 lives [8]. As of 3 July 2020, about 148,188 tests have been conducted in the country [8], a value that is underwhelming regarding the country's population size and the number of tests being conducted in other countries [9, 10]. The slow rate of COVID-19 testing in Nigeria has been a major concern as it puts the population at increased risk of asymptomatic transmission of the disease [11]. Also, in countries with corrupt economies, resource allocations are usually ineffective, and due to bribery or kickbacks, unqualified companies win government contracts and are awarded projects; the quality of education and health care also debilitates increasingly [12]. Considering these, as well as the level of corruption in Nigeria [13], the cause of the low/weak health care standard in the country may not be far away from being palpable.

Justification

Lack of adequate testing capacity has been reported to play a role in the widespread community transmission of COVID-19 [14]. In Nigeria, there is a slow rate of COVID-19 testing since the index case [8, 10], potentially pointing to the unavailability of sufficient testing facilities for the large population of the country [8, 9]. With large numbers of new cases emerging daily, it becomes difficult to pinpoint a particular source of the growing infection spread dynamics in the country.

However, COVID-19 transmission in Nigeria has now become a community transmission [4] outcome, hence; this study is aimed at evaluating the potential causes of the low diagnostic capacity in the country, and how it may have played a role in the community transmission of the disease within the country. Nevertheless, by creating this awareness through this medium, it is firmly believed that the fallout from this scholarly advocacy would effectively stimulate the leadership of the country to be more proactive, responsive and deliberate towards investing its resources appropriately, towards revamping the ill-equipped health sector in response to the on-going COVID-19 pandemic, and to subsequently prepare for future outbreaks of similar infectious diseases outcome any time and any day.

Methodology

Study Approach

This study involved the systematic evaluation of selected and published articles according to the sequence of systematic review as described by Aveyard [15]. According to Aveyard, a systematic review is an approach involving the extraction and presentation of the detailed summary of valid research evidence applicable to other studies, following critical assessment by a particular body of knowledge. The articles retrieved in this study were critically evaluated, analyzed, synthesized and presented after their findings were diligently extracted accordingly.

Strategy and Search Items

Researchers, on searching through Google and other valuable websites, tends to discover global views and emerging perspectives about a topic of interest, which makes room for the determination of keywords that is related to the topic being researched [16]. Hence, a quick search was made on Google to discover various keywords and different ways to describe the topic. Different keywords were combined to search various electronic databases such as WHO, Pub Med, Science Direct, Medscape, CDC, NCDC, Lancet, Science Direct, Elsevier, Acata and BBC respectively. The abstract of each retrieved article was perused to determine its focus as well as its relevance to the topic under review. Boolean operators and truncations were combined with different keywords to expand the scope of the search.

Inclusion Criteria

Published research articles which have been peer-reviewed, and contain details on COVID-19 infection, SARS-CoV-2, the disease progression, diagnosis, spread and containment strategies, as well as the curtailment interventions and challenges, were included in this review. Excluded from the review were articles which did not meet the above criteria. The article must have been written in very clear English Language.

Methodological Quality of Included Articles

The articles included in this review were individually appraised for source reliability, generalizability, validity, design framework and simplicity of information.

Findings

The various information's extracted from the articles from different data base were grouped into themes for easy analysis and synthesis. The various themes are follows (1) SARS-CoV-2 and COVID-19, (2) Epidemiology, (3) Pathogenesis and clinical manifestations, (4) Treatment, management and control, (5) Diagnosis, COVID-19 testing around the world, as well as (6) COVID-19 testing in Africa. However, it is firmly expected that the interesting fall outs from the various themes would be used to generate a very strong evidence based discussion on the subject matter. Thus, recommendations would be provided as a way forward outcome.

SARS-CoV-2 and COVID-19

COVID-19 is the pandemic disease that has affected a large number of the world's population and economies, causing illness in millions of people and a huge number of deaths around the world [17, 18]. Coronaviruses (with the largest known RNA genomes of 30-32 Kilobases) belong to the Coronaviridae family of viruses

within the Nidovirales order (which comprises other families such as Arteriviridae, Mesoniviridae, and Roniviridae) [19, 20]. The Coronaviridae family comprises the Coronavirinae and the Torovirinae subfamilies, and the former is further subdivided into four genera, the alpha, beta, gamma, and delta coronaviruses. Beforehand, the viruses were arranged into these genera based on serology, but phylogenetic clustering has become the basis for virus grouping [20]. The causative virus SARS-CoV-2 is an enveloped, single-stranded, non-segmented, positive-sense RNA virus which belongs to the beta coronavirus genus of viruses, with a genome size of 29.9 kb [20, 21]. Beforehand, there have been six identified human-susceptible coronaviruses. They include the α-coronaviruses (HCoV-229E and HCoV-NL63) and β-coronaviruses (HCoV-HKU1 and HCoV-OC43), all of which have low pathogenicity and causes mild respiratory symptoms akin to a common cold. However, the other two known β-coronaviruses, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) result in severe respiratory tract infections which are potentially fatal [22].

Moreover, it was found that SARS-CoV-2 shares about 79.5% genomic sequence similarity with SARS-COV and 96.2% similarity with the bat coronavirus RaTG13. The mammal bat has been suspected to be the natural host for SARSCoV-2 based on virus genome sequencing results and evolutionary analysis, and it has been suggested that the virus can be transmitted via unknown intermediate hosts from bats to humans. It has also been discovered that SARS-CoV-2 could utilize the angiotensin-converting enzyme 2 (ACE2) receptor in human tissues (the same receptor used by SARS-CoV) to gain entry and cause COVID-19 in humans [23].

Epidemiology

A respiratory tract infection epidemic broke out in Wuhan, Hubei Province, China in December 2019, and a majority of the patients were reportedly linked to a large seafood and live animal market in the area [24, 25]. As of 7 January 2020, the World Health Organisation (WHO) announced that a novel coronavirus (nCoV) had been isolated in China from samples obtained from these patients, and other respiratory pathogens such as SARS-CoV, MERS-CoV, avian influenza, adenovirus and influenza were ruled out as the causes of the epidemic by laboratory tests [2].

As of 3rd July 2020, the world had recorded 10,710,005 cases of the disease and a consequent 517,877 number of deaths across 216 countries, in the different continents of the world save for Antarctica [4, 18]. In the United States, over 2.6 million confirmed cases of COVID-19 and about 127,858 deaths have been recorded as of 3rd July 2020, and this represents the highest number of cases recorded by a single country [4]. Furthermore, as of March 16th, 2020, the highest percentage of deaths was recorded in adults aged 85 years or older (10% - 27%), while adults aged between 65-84 years recorded 3% - 11% deaths. Also, 1% - 3% of deaths was recorded in adults aged between 55-64 years and adults aged between 20-54 years recorded less than 1%. However, no death attributable to COVID-19 had been reported in persons aged 19 years or younger in the United States [26]. Thus, the reasons for this, are still immunologically unclear, even as scientist across the globe are still working assiduously to unravel the best clinical reason for this outcome.

However, according to the data from China, older adults, especially those with serious underlying health conditions, are faced with a higher risk of severe COVID-19-associated illness and deaths than younger individuals. While a larger number of COVID-19 cases reported in China were mild (81%), roughly 80% of deaths occurred in adults aged 60 years and older. Whereas, only one person aged ≤19 years died (0.1% death) [27]. Overall, China had recorded 85,278 cases and 4,648 deaths as of 3rd July 2020, and has been able to put the disease transmission under control [4]. A high number of cases has also been recorded in different countries around the world regardless of their healthcare capacity, including the United Kingdom, Italy, Spain, France, Germany, Russian Federation, Turkey, Iran and so on [4].

Furthermore, on the contrary, the number of cases reported in Africa is still relatively low compared to those reported in other continents [4]. The index case of COVID-19 in Africa was recorded in Egypt on 15 February 2020 [28], and by 28 February, the index case in Sub-Saharan Africa was recorded in Nigeria [29]. The disease has since spread to every country in Africa as of 26th May, 2020, with Lesotho being the last to record an infection [4, 30]. According to the Nigeria Centre for Disease Control (NCDC) as of 3rd July 2020, COVID-19 has spread to 36 states in the country, with Cross River being the only state yet to report a case of the infection [8]. Africa Centres for Disease Control also reported as of 3rd July 2020, that the continent had recorded a total of 414,011 number cases of the infection, 10,260 deaths and 195,729 recoveries. Whereas, 5,445,710 cases have been reported in the America, and 2,737,869 cases have been reported in Europe as of 3rd July 2020 [31, 4].

Several outbreak reports (especially those involving severe diseases) have noted relatively low prevalence among the paediatric population. However, some case reports (including a recent news report from Chicago) have revealed severe disease in children, but such reports have been infrequent and have often been associated with comorbidities [32]. Laboratory-confirmed cases of COVID-19 for which patient age was known, reported between February 12th and April 2nd in the United States was 149,082, and only 2,572 cases (1.7%) involved children less than 18 years [33]. A report from China revealed that most children infections were believed to come from close contact with family members [34]. A relatively high percentage of COVID-19 cases involving children under 18 years tends to be less symptomatic or asymptomatic, and as a result, may have caused missed infections and could probably also be a reservoir of transmission [33, 34].

Nonetheless, premature births were observed in some pregnant women with COVID-19 infection [35, 36]. According to some studies, most neonates born to COVID-19 positive mothers tested negative, though some presented with respiratory symptoms and eventually recovered. Some neonates also tested positive for the infection but eventually recovered as well [37, 38, 39]. As a result, vertical transmission of the disease cannot be ruled out. It has been reported that the risk of contracting COVID-19 infection among children is higher in those younger than 1 year, than in older children [40].

Table 1: NCDC report on laboratory-confirmed COVID-19 cases in Nigeria, as well as the recoveries, deaths and day(s) since last reported case as of 15th September 2020

S/N	STATES	CONFIRMED CASES		DISCHARGED CASES		DEATHS		TOTAL ACTIVE CASES	TOTAL SAMPLES TESTED	DAYS SINCE LAST REPORTED CASE
		TOTAL	NEW	TOTAL	NEW	TOTAL	NEW			
1	Lagos	18,696	33	15,245	0	204	1	3,247	116,836	0
2	FCT	5,451	4	1,684	0	75	0	3,692	53,417	0
3	Oyo	3,221	0	2,102	0	39	0	1,080	21,241	2
4	Plateau	3,142	27	2,088	47	31	0	1,023	27,754	0
5	Edo	2,610	0	2,427	7	103	3	80	15,629	3
6	Kaduna	2,296	17	2,182	21	33	0	81	17,699	0
7	Rivers	2,208	0	2,118	0	59	0	31	20,244	1
8	Delta	1,791	0	1,629	0	49	0	113	9,683	2
9	Ogun	1,754	6	1,697	17	28	0	29	12,178	0
10	Kano	1,732	0	1,626	0	54	0	52	64,207	2
11	Ondo	1,584	0	1,490	0	35	0	59	7,318	2
12	Enugu	1,232	0	1,088	0	21	0	123	4,476	1
13	Ebonyi	1,034	0	997	0	30	0	7	5,795	6
14	Kwara	1,002	0	794	0	25	0	183	5,436	1
15	Katsina	843	0	457	0	24	0	362	17265	1
16	Abia	828	0	792	0	8	0	28	6,543	3
17	Osun	805	0	763	0	17	0	25	3,912	1
18	Gombe	773	0	677	0	24	0	72	15,611	1
19	Borno	741	0	703	0	36	0	2	11,232	15
20	Bauchi	680	0	656	0	14	0	10	7,858	1
21	Imo	546	0	216	0	12	0	318	3,588	4
22	Benue	467	0	401	0	9	0	57	3,243	3
23	Nasarawa	447	1	298	0	12	0	137	3,391	0
24	Bayelsa	393	0	370	0	21	0	2	1,788	5
25	Jigawa	322	0	308	0	11	0	3	2,876	61
26	Ekiti	303	1	267	0	5	0	31	5,736	0
27	Akwa Ibom	286	0	251	0	8	0	27	2,409	2
28	Niger	244	0	216	0	12	0	16	1,837	11
29	Anambra	232	1	184	0	19	0	29	1,494	0
30	Adamawa	230	0	196	0	15	0	19	2,0592	6
31	Sokoto	159	0	142	0	17	0	0	2,921	15
32	Taraba	95	0	73	0	6	0	16	750	4
33	Kebbi	93	0	84	0	8	0	1	856	18
34	Cross River	83	0	74	1	9	1	0	1,140	12
35	Zamfara	78	0	73	0	5	0	0	404	26
36	Yobe	72	0	59	0	8	0	5	643	3
37	Kogi	5	0	3	0	2	0	0	243	74
Total		27,564	454	11,069	268	628	12	15,867		

The states, including FCT, are arranged in descending order based on the number of confirmed cases [8].

Pathogenesis and Clinical Manifestations

In the first stage of infection within 1 to 2 days (asymptomatic stage), inhaled viral particles likely penetrate the epithelial cells of the nasal cavity (mainly via the ACE2 receptor) and replicate within the cells [41, 42]. Local propagation of the virus occurs but is followed by a limited innate immune response. The virus can be detected by nasal swabs at this stage, and though the viral burden may be low, these persons are infectious [43].

In the second stage, as viral propagation takes place, the virus moves along the conducting airways down the respiratory tract and triggers a more robust immune response from the innate immune system. The virus (SARS-CoV-2), as well as the early markers of the innate immune response, can be detected by nasal swabs or sputum, and the disease (COVID-19) manifests clinically at this point. The subsequent clinical course of the infection may be predicted by analyzing the level of interferon gamma-induced protein 10 (CXCL10) or other cytokines associated with innate response [44]. Mild disease, mostly restricted to the upper respiratory tract and conducting airways, occurs in about 80% of the infected patients, and these patients may be observed at home with conservative symptomatic therapy [45].

Uninterestingly, roughly 20% of infected individual's progress to the third stage where some persons will develop pulmonary infiltrates, and some will present with severe disease [45]. The virus eventually gets to the lungs and infects the type II cells of the alveoli (tiny air sacs in the lungs); these type II cells are preferential targets of SARS-CoV and influenza than type I cells [46, 47]. As SARS-CoV multiplies within these type II cells, viral particles are released in large numbers and thus, the type II cells undergo apoptosis and die [48]. The released viral particles go on to infect other type II cells in adjacent alveolar units, and such areas of the lung (s) will likely lose most of their type II cells, resulting in the triggering of secondary pathways for epithelial regeneration [49]. The abnormal wound healing process may result in more severe scarring of the lung (s) and fibrosis, than other forms of acute respiratory distress syndrome (ARDS). Also, a robust innate and adaptive immune response and epithelial regeneration will be required for recovery from the disease [43]. The elderly population is particularly at risk of severe outcomes of the disease because of their weakened immune response, and diminished ability to repair the damaged epithelium. The reduced mucociliary clearance associated with the elderly population may also allow the virus to more readily disseminate to the gas exchange units of the lung(s) [50]. However, significant knowledge gaps exist in the pathogenesis of COVID-19, that need to be filled in over the next couple of months.

The WHO and the US Centers for Disease Control and Prevention estimates the incubation period for SARS-CoV-2 to range from 2 to 14 days [51, 52], with a median incubation period of about 5 days [53]. During this incubation period, an infected individual can potentially transmit the disease to a healthy individual [54]. The disease is transmitted mainly via contact with respiratory droplets containing the virus [55], and can be spread by both symptomatic and asymptomatic individuals [56].

The signs and symptoms manifested by COVID-19 patients resemble those of viral pneumonia, and the infection may be mild, severe or critical. Estimates have revealed that 80% of patients experience mild illness, 14% manifest severe illness, and only about 5% suffer critical illness. The severity of the illness is associated with the elderly and those with underlying health challenges [6]. In areas with low endemicity, large-scale screening may reveal more of the less symptomatic or asymptomatic patients [57]. Preliminary analysis of case series has revealed that the most common symptoms include fever, cough, myalgia, dyspnoea and fatigue. However, some other symptoms include anorexia, sore throat, sputum production, dizziness, chest pain, headache, confusion, rhinorrhoea, haemoptysis, diarrhoea, nausea/vomiting, and abdominal pain, but these symptoms are less common [58, 59, 60].

Furthermore, estimates have shown that about 90% of patients usually experience more than one symptom, and 15% presents with fever, cough, and dyspnoea [45]. However, COVID-19 has not caused pronounced upper respiratory tract or gastrointestinal symptoms in large numbers of patients when compared to the cases of SARS, MERS, and influenza [58, 59]. Within 1 to 2 days before the onset of breathing difficulties and fever, some patients may present with diarrhoea or nausea [60]. Besides, most children may present with signs of pneumonia on chest imaging, but they generally experience mild symptoms, without pneumonia or fever or no visible symptoms at all [61, 62, 63].

Treatment, Management and Control

Although no specific antiviral therapy has been approved for COVID-19, and there are no vaccines currently available for its prevention, several approaches such as hydroxychloroquine (200 mg every 12 hours), chloroquine (500 mg every 12 hours), and lopinavir/ritonavir (400/100 mg every 12 hours) have been proposed. The current treatment is mainly based on managing the manifested symptoms; patients with severe infection usually require oxygen therapy as the major treatment intervention. However, for cases of respiratory failure refractory to oxygen therapy, mechanical ventilation may be required, whereas individuals with septic shock are essentially managed with haemodynamic support [64].

Notably, the WHO conceded that preventing exposure to the virus is the central public health method for controlling the outbreak. Hence, they advised the general public to regularly wash hands frequently with soap and water for at least 20 seconds, or use a hand sanitizer that contains at least 60% alcohol, avoid using unwashed hands to touch the eyes, nose, and/or mouth, avoid close contact with sick people, wear a face mask when leaving home, disinfect frequently touched surfaces daily, seek medical advice promptly when symptoms (such as cough, fever, or dyspnea) appear, and cough/sneeze into a folded elbow or a disposable tissue and dispose of the tissue immediately [65, 66].

Notwithstanding, the inhabitants of endemic areas are advised to be watchful for potential symptoms, stay home as much as possible, and when it is imperative to leave home, one should practice social distancing (maintain at least 6 feet distance from other persons) [67]. Also, it is strongly advised that high-risk individuals (such as those who have come in close contact with suspected or confirmed cases), as well as international travellers (including travel on a cruise ship) should observe increased perceptional measures. These include observing self-quarantine for at least 14 days from the time of the last exposure, maintaining social distance from other persons and self-monitoring for the manifestation of symptoms [68]. For newly confirmed cases, contact tracing measures should also be carried out to detect and test individuals with whom they may have come in contact [69]. The WHO has also advised health workers to follow established

occupational safety and health procedures, wear and dispose of personal protective equipment (PPE) properly, self-monitor for symptoms and when ill, self-isolate and make the illness known to the managers [70].

Different Methods of Diagnosis of Covid 19 Virus

Nucleic Acid Amplification Tests (NAAT) for SARS-CoV-2

The standard diagnostic approach for COVID-19 is based on the detection of unique viral RNA sequences by nucleic acid amplification tests (NAAT) such as real-time reverse-transcription polymerase chain reaction (rRT-PCR), and nucleic acid sequencing is used for confirmation when necessary [71]. rRT-PCR is widely used for infectious diseases due to its high sensitivity and specificity. Together with automated sample processing and the availability of high-throughput thermocyclers [72], numerous samples can be analysed within a short time [73]. Viruses may be detected for longer durations and in early periods of illness via PCR assays [74], and the assays can also be carried out on chemically inactivated specimens [73]. Another important advantage of rRT-PCR assays is that both nucleic acid amplification and analysis are done concurrently in a closed system; this minimizes the risk of amplification product contamination that may cause false-positive results [75].

There are some molecular targets within the make-up of coronaviruses that can be used for PCR assays [76, 77, 78, 5]. These comprise structural proteins, including nucleocapsid (N), helicase (Hel), envelope glycoproteins spike (S), envelope (E) and transmembrane (M) [78, 5, 79]. Besides these structural proteins encoding genes, there exist species-specific accessory genes that are necessary for viral replication, and they include hemagglutinin-esterase (HE), RNA-dependent RNA polymerase (RdRp), and open reading frames ORF1a and ORF1b [77, 78, 5]. There is a possibility of cross-reaction with other endemic coronaviruses, as well as a potential genetic drift of SARS-CoV-2 especially as the virus evolves within new populations, which could lead to false results. To avoid such occurrences, it is necessary to incorporate at least two of the molecular targets in the assay [80]. A number of these molecular targets have been used by various investigators in different countries for rRT-PCR assays. In the United States, two nucleocapsid protein targets [N1 and N2] have been selected by the CDC as the two-target assay has shown to be performing well [81]. Another study in Hong Kong, China also adopted two targets for their rRT-PCR assay, first using the nucleocapsid target for screening and then the open reading frame 1b target for confirmation [82]. However, the WHO recommends the use of the envelope (E) gene for the first-line screening and the RdRp gene for the confirmatory assay [77]. Some other countries have also utilized other genetic targets to detect the virus but there has not been any indication that any one of these sequence regions used is advantageous over the other in diagnostic testing. Nonetheless, in the ideal design, the effects of genetic drift are mitigated with the inclusion of at least one conserved region and one specific region [80]. However, the use of this method is very expensive and this poses a big challenge [83].

Rapid Diagnostic Tests

To detect SARS-CoV-2 antigens and/or antibodies more rapidly, immunoassays (also known as rapid point-of-care immunoassays) have been developed and they are generally lateral flow assays. These assays have been designed to detect antigens such as SARS-CoV-2 or to detect antibodies (IgM and IgG) such as those against COVID-19 infections [80].

Rapid Antigen Lateral Flow Assays

Theoretically, these assays are advantageous as they produce test results within a reasonably short time and the associated low-cost detection of SARS-CoV-2. But based on the experience gotten from the diagnosis of influenza (Flu) viruses with this method, these assays are likely to have the problem of poor sensitivity [80]. Monoclonal antibodies specific for SARS-CoV-2, as well as several other rapid antigen assays, are being developed [84]. However, due to the disparity of viral loads in COVID-19 patients, there is concern that antigen detection may miss some cases as a result of low infectious burden or sampling variability [80].

Serology

This is an indirect measure of infection that measures the host response to an infection rather than measure the level of the infection, it is best utilized retrospectively. Serological methods have proven to be beneficial in confirming COVID-19 infection, and are rapidly being developed [85]. In the past, serology played a crucial role in the epidemiology of SARS [86] and some other coronavirus outbreaks [87]. Rapid lateral flow assays for antibodies (both IgM and IgG) will certainly play an important role in COVID-19 and should assist in the determination of burden of infection, the basic reproduction number, the role of asymptomatic infections, and the overall mortality. However, it takes weeks for the body to develop specific IgG responses, and IgM responses are usually non-specific. As a result, serology detection may not likely be essential in active case management, but may be relevant in other aspects such as the diagnosis/confirmation of late COVID-19 cases, or to ascertain the immunity of health workers as the outbreak progresses [80].

Imaging

For any region of the world, the local procedures for infection prevention and control should be utilised for all imaging examinations to avoid transmission. The results from imaging examinations may differ from patient to patient due to factors such as disease stage at the time of scanning, immune status, patient's age, underlying diseases and drug interventions [88].

During the early stage of pneumonia cases, chest X-ray examination may reveal multiple small patchy shadows and interstitial changes which are more pronounced in the periphery of the lungs. But the X-ray image in severe cases may show infiltrating shadows, bilateral multiple ground-glass opacity, as well as pulmonary consolidation, with infrequent pleural effusion [88, 89].

However, pulmonary lesions are more clearly revealed by a chest computed tomography (CT) scan than in an X-ray image. With clear details, CT scan reveals ground-glass opacity, as well as segmental consolidation in bilateral lungs especially in the periphery of the lungs. Also, severely infected children may show multiple lobar lesions in both lungs. [90].

Other Diagnostic Tools

Virus culture is not recommended as a diagnostic routine [71, 80]. However, when necessary, blood and sputum cultures may be conducted to rule out other organisms that cause respiratory tract infections such as adenovirus, influenza, parainfluenza, rhinovirus, respiratory syncytial virus, SARS-CoV, etc., as well as bacterial infections such as mycoplasma pneumonia, chlamydia pneumonia, etc. [55].

Certain blood abnormalities can serve as markers to indicate

the presence of the infection. The most common blood markers include leukocytosis, leukopaenia, lymphopenia, and elevated liver transaminases. Other markers include neutrophilia, thrombocytopaenia, renal impairment, as well as decreased levels of albumin and haemoglobin [58, 59, 60].

Covid-19 Testing Around the World

In the United States (US), a country with a population size of over 330 million people [9] and that has recorded over 2.6 million cases of COVID-19 as of 26 May 2020 [4], over 36.4 million tests have been carried out as of 27 May 2020 [10]. As of 3 July 2020, the US received 50,000 samples from the United Kingdom (UK) for analysis as the samples could not be processed in British laboratories due to operational issues [91]. However, the UK with a population size of over 67 million people [9], and around 284,900 cases of COVID-19, had carried out over 10.3 million tests as of 3 July 2020 [10], and had set a target of 100,000 tests per day [92]. Nonetheless, Canada with over 105,000 cases of COVID-19, had conducted over 2.8 million COVID-19 tests on her population [10] of over 37 million people as of the same date [9].

As of 3 July 2020, Russia with a population size of over 145 million people [9] and over 674,000 cases of COVID-19, had carried out over 20.4 million tests and had the highest number of COVID-19 tests across Europe [10]. As of 21 March 2020, Russia had delivered 100,000 COVID-19 testing kits to 13 different countries and helped to detect the index cases in Belarus, Armenia, Kyrgyzstan and Uzbekistan [93]. In the same vein, Italy with about 241,000 cases of COVID-19, had carried out over 5.6 million tests [10] on her population of over 60 million people [94] as of 3 July 2020. A report from Italy explained that the mass COVID-19 testing in Vò town helped eradicate the infection from the town [95]. Whereas, Spain (with about 297,000 cases) had carried out over 5.4 million tests on her population of over 46 million people as of the same date [9].

Also, over 9.5 million COVID-19 tests have been conducted in India, a country that has recorded about 672,644 cases of COVID-19 [10] and has a population size of over a billion people [9] as of 3 July 2020. Also, about 3.5 million tests had been conducted in the United Arab Emirates (UAE) that has about 50,857 cases of COVID-19 [10] with a population of over 9 million people [9] as of 3 July 2020.

However, several other countries across Europe, America, Asia and Oceania had conducted a huge number of tests, ranging from hundreds of thousands to millions [10] as of 3 July 2020.

Covid 19 Testing in Africa

The African country with the highest number of COVID-19 cases is South Africa with over 177,000 cases and population size of around 59 million people [9]. The country had been able to conduct about 1.7 million tests [10] as of 3 July 2020. The second highest testing country in Africa is Morocco with around 748,449 tests, and had confirmed about 13,822 cases [10] in the country with a population size of around 36 million people [9] as of 3 July 2020. Ghana (with over 19,000 cases) and Uganda (with about 927 cases) had conducted about 307,133 and 205,312 tests [10] in their populations of over 30 million [9] and 45 million [9] respectively as of 3 July 2020. However, Nigeria with a population size of over 200 million (largest in Africa) [9], had conducted just about 148,188 tests and confirmed 27,564 cases [8] as of the same date.

Discussion

According to the reported figures indicating the extent of COVID-19 in Nigeria and other African countries, there is a relatively low level of spread. However, this can be attributed to the low levels of testing in the regions. With a population size of over 200 million people [9], Nigeria had conducted just about 27,564 tests as of July 3 [8]. Whereas, Botswana whose population is just around 1% Nigeria's population, had conducted over 45,000 tests; South Africa (about a quatre of Nigeria's population) had conducted over 1.7 million tests; and Morocco (about 18% of Nigeria's population) had conducted over 748,000 tests as of July 3, all representing the very few countries in Africa with promising testing capacities. This is a stark contrast from the thousands and millions of tests conducted in many countries of Europe, America and Asia, and whose statistics on the spread of the virus tend to reveal more of the reality of the outbreak [96, 9, 10].

The slow rate of COVID-19 testing in Nigeria owes largely to the lack of adequate testing capacity in the country. As of 15 April 2020, the NCDC reported that Nigeria had a total of 11 activated testing centres around the country, while 4 were still in progress [97]. This implies that at that time, Nigeria had 1 testing centre for every 18 million people based on the nation's population as estimated by World Population Review [9]. Sequel to the fact that 11 testing centres were distributed across the 36 states of Nigeria, as well as the capital city [98], Samples obtained from states in which there are no testing centres, will have to be transported to others states for testing. Hence, effective diagnosis and the number of samples tested per day at that time could be massively affected by the shortage of testing labs, and perhaps such other factors as transportation hazards and delays, sample mismanagement, as well as temperature change.

It was suggested by the head of WHO that the detection, isolation and treatment of cases will prevent extreme outcomes of COVID-19 [99]. Several countries have conducted a large number of tests to help discover the disease burden within their territories, and as well, isolate the infected population to reduce the rate of spread [10]. However, this has not been the case in Nigeria, and the current situation puts the entire Nigerian population at increased risk as potential carriers of the virus are living freely and making contacts with more people every day, without even knowing they are infected.

Looking into the roots of the diagnostic problems in Nigeria, a lot can be attributed to the leadership of the country. Several epidemics occur in Nigeria almost every year and the country had always responded to wade them out [100]. The recent Ebola, Monkeypox and Lassa fever epidemics in the country were effectively contained by prompt responses which involved large finances and commitment of government and her relevant agencies. According to Azuonwu [101], the Nigerian government made a prompt financial commitment to tackle Ebola during the 2014 outbreak [101], even the government as at then took visible responsibility and pro-activeness in good time. However, the post-outbreak response from the leadership has not been outstanding. Despite the responses to the previous outbreaks and the emergency responses to COVID-19, Nigeria only has 28 active PCR facilities for COVID-19 testing in 19 out of the 36 states in the country as reported by the NCDC on 26 May 2020 [102]. This would potentially be a palpable setback to overall testing of huge population of Nigeria, even when the rural areas must be certainly be left out in the scheme of things.

Critically, African health ministers agreed to the Abuja Declaration of 2001 to allocate at least 15% of their national budgets towards rejuvenating their health care systems [103]. However, despite

Nigeria's position in Africa, her health expenditure as a percentage of her Gross Domestic Product (% of GDP) is 3.76 as of 2017. In other words, Nigeria's health expenditure is 3.76% of her total expenditure as of 2017, a value apparently underwhelming when compared to those of other African countries. Sierra Leone boasts of 13.42%, South Sudan – 9.76%, Malawi – 9.65%, Liberia – 8.16%, South Africa – 8.11%; only 9 African countries have below Nigeria's 3.76% of GDP as of 2017 [104]. The high level of corruption in Nigeria has only worsened the situation. Corruption, which has been defined by the World Bank as the "abuse of public office for private gain" [105] has crippled the economy of Nigeria as well as the health system. Some common corrupt practices in Nigeria include bribery, inequitable political considerations, diversion of budget allocations, failure of contractors and suppliers to deliver and not being held accountable, theft or diversion of drugs/supplies for personal use or private sector benefits, use of public equipment and facilities to attend to private patients, unnecessary referrals to private facilities, absenteeism, unofficial payments demanded from patients for services, as well as theft of user fee revenue [106]. The diversion of health budget allocations means that even the little percentage of the country's budget allocated to health care is not fully invested in the sector, and all these have contributed to the backwardness of health care delivery services in the country.

Furthermore, the lack of adequate testing capacity in Nigeria can also be attributed to the high cost of setting up PCR laboratories as well as its high cost of running and maintenance. Extensive personnel training and expertise are required for the operation of RT-PCR machines [107], and the machines are expected to be used with uninterrupted power supply as they are very delicate and sensitive [108]. However, with limited expertise and the country being faced with acute electricity problems for years [109], these tend to increase the burden of rapidly scaling up testing within the country.

As reported by the WHO, a strong health system has a well-remunerated and trained workforce, strong finance structure, adequate and highly maintained facilities, vaccines and technologies, logistics for medicines and a reliable and regularly updated health information system. With appropriate governance, all these ensure that health service delivery is accessible and timely [110]. However, this is hardly the case in Nigeria where there is a predominance of poor remuneration of the health workforce, inequitable distribution of health workers, gross under-supply of several health facilities, lack of regular clinical training across several health centres, as well as very challenging working conditions, usually due to the shortage of power supply and inadequate call rooms and meals [111, 112]. These are followed by distrust, dissensions and frequent conflicts among different professional groups in the health sector, where other health workers have claimed that the Nigerian health system is structured to mainly favour the physicians [113, 114]. Many freshly out of school health care professionals find it difficult to get internship and horsemanship positions, and this difficulty extends to the employment stage as there are not enough job positions [115]. All these have resulted in a massive brain drain of Nigeria's health professionals to other countries (especially to Europe and America) [115].

As the aforementioned abnormalities in the health sector have persisted over the years, coupled with the cost, time and resources required to set up standard health care facilities [83], emergency responses during outbreaks that involve the establishment of facilities become burdensome; COVID-19 outbreak is a perfect illustration of this scenario. Long-term establishment plans are less burdensome to execute because the country will always have time to do international businesses, accumulate internally generated revenues, taxes, grants and fines, all yielding funds to power the ongoing projects [116]. But in emergency cases like COVID-19 outbreak, with lockdowns in major countries and cities, diminishing economic activities and downsizing economic capacities,it becomes a problem for the country to effectively scale-up the health care infrastructure to meet the required standards to combat the outbreak [117]. Besides, the increasing rate of infection of health workers in Nigeria is only but reducing the available workforce in the country [118].

A study in Chicago revealed a cluster of 16 cases of confirmed or probable COVID-19 emanating from non-household contacts with one infected person. This study pointed out the lack of laboratory testing for probable cases as the first of three limitations that had promoted the transmission [119]. Another study reported that timely and accurate laboratory testing of samples from cases being investigated represents an important aspect of response, which supports decisions on strategies of infection control and patient management at health facilities [120]. The WHO also explained that to halt the spread of COVID-19, it is required of every territory to find and test every suspected case to promote prompt and effective isolation and appropriate care for confirmed cases, as well as prompt contact-tracing of close contacts of all confirmed cases to rapidly identify, quarantine and medically monitor them for the virus incubation period of 14 days [14].

Hence, the inadequate COVID-19 testing capacity in Nigeria [10] means that a lot of cases are probably unidentified, thereby potentially resulting in the unforeseen transmission of the infection in different areas of the country. As a result, curtailing the disease transmission becomes more challenging and community transmission of COVID-19 is inadvertently promoted. Hence, the lockdown efforts in the country, despite the resulting increase in hardship, become undermined and less effective due to the lack of adequate testing and isolation of confirmed cases.

Conclusion and Recommendation

Despite the massive efforts being made around the world towards curtailing the spread of COVID-19, the high rate of spread in higher equipped countries and territories does not give hope to countries with weaker health infrastructure. With cases and deaths increasing daily, many countries are scaling up their testing capacities to test as many people as possible to ensure early detection, isolation and treatment of new cases to prevent further transmission. However, a handful of countries are struggling to meet up with the testing demands, and Nigeria is the case study in this review. Political and socio-economic challenges, as well as corruption, have ensured that health care in Nigeria has remained below standard. This puts the inhabitants of the country at increased risk of infection as the low testing capacity means that many asymptomatic carriers of the SARS-CoV-2 are living freely in the country and making contacts with more people, potentially increasing the rate of transmission. Hence, the leadership of Nigeria faces an uphill task of having to scale up the testing capacity in the country as soon as possible to instil some hope and trust into the inhabitants. Based on the present challenges in the health sector, the scholars wishes to make the following recommendations:

1. The government should invest massively to scale up the testing capacity for COVID-19 in the various states to a reasonable level.
2. The government should increase the percentage of the national

budget allocated to the health sector.

3. All projects being awarded should be monitored to completion.
4. There is also a need for improvement in the educational and employment sectors, proper remuneration of health workers and the development of standard research institutes to:

a. Provide a sufficiently skilled healthcare workforce, enough to cater for the country's population healthcare demands.
b. Decrease the looming brain drain of health workers to other countries.

5. The policymakers and the health professionals of the country need to co-operate together to create a long-term blueprint for the improvement of the sector and provide key indicators of performance.
6. Rules and regulations against corrupt practices, with appropriate punishments, should be made tougher to help reduce corruption in the health sector and the country at large.

Acknowledgement: We are eternally grateful to Prof. S D Abbey, Prof. G.N Wokem and Dr Azuonwu Good luck for their moral support and encouragement. We are also grateful to ICT Department of the Rivers State University for their technical support, during gathering of online resources of the work.

Conflict of Interest: No report of conflict of interest among authors was reported to the best of my knowledge.

References

1. Zhu N, Zhang D, Wang W, Xingwang Li, Bo Yang et al (2019) A Novel Coronavirus from Patients with Pneumonia in China. The New England Journal of Medicine, 382: 727-733.
2. World Health Organisation (2020) Novel Coronavirus – China https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/.
3. WHO (2020) Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: Interim guidance.
4. World Health Organisation (2020) Coronavirus disease (COVID-19): Situation report – 165 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200703-covid-19-sitrep-165.pdf?sfvrsn=b27a772e_2.
5. Lu R, Zhao X, Li J, Peihua Niu, Bo Yang et al (2020) Genomic characterization and epidemiology of 2019 novel coronavirus:541 implications for virus origins and receptor binding Lancet 30: 30251-8.
6. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020) the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China [Chinese]. Chinese Center for Disease Control and Prevention Weekly 41: 145–51.
7. Chakraborty I, Maity P (2020) COVID-19 outbreak: Migration, effects on society, global environment and prevention. Science of the Total Environment 728: 1-7.
8. Nigeria Centre for Disease Control (2020). An update of COVID-19 outbreak in Nigeria. https://ncdc.gov.ng/diseases/sitreps/?cat=14&name=An%20update%20of%20COVID-19%20outbreak%20in%20Nigeria.
9. World Population Review (2020). Total Population by Country 2020. https://worldpopulationreview.com/countries/.
10. Worldometer (2020). Reported cases and deaths by country, territory, or conveyance. https://www.worldometers.info/coronavirus/?utm_campaign=homeAdvegas1?%22%20%5Cl%20%22countries%3Ca%20href=.
11. WHO (2020) Q&A on coronaviruses (COVID-19) https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-coronaviruses.
12. Mirzayev E (2020) How Corruption Affects Emerging Economies https://www.investopedia.com/articles/investing/012215/how-corruption-affects-emerging-economies.asp.
13. The Guardian (2019) Corruption as Nigeria's death agent https://guardian.ng/opinion/corruption-as-nigerias-death-agent/.
14. WHO (2020) COVID-19 strategy update. https://www.who.int/docs/default-source/coronaviruse/covid-strategy-update-14april2020.pdf?sfvrsn=29da3ba0_6.
15. Aveyard H (2010) Doing a literature review in health and social care. (2nd edn), Open University Press, Maidenhead, UK.
16. Tod A, Palfreyman S, Burke L (2004) Evidence-based practice is a time of opportunity for nursing. British Journal of Nursing, 13: 211-216.
17. Menickella B (2020) COVID-19 worldwide: The pandemic's impact on the economy and markets.https://www.forbes.com/sites/brianmenickella/2020/04/08/covid-19-worldwide-the-pandemics-impact-on-the-economy-and-markets/#5a428fd428c3.
18. World Health Organisation (2020) Coronavirus disease (COVID-19) pandemic. https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
19. Weiss SR, Leibowitz JL (2011) Coronavirus pathogenesis. Advances in Virus Research, 81: 85-164.
20. Fehr AR, Perlman S (2015) Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol 1282: 1-23.
21. Wu A, Peng Y, Huang B, Xiao Ding, Xianyue Wang et al (2020) Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe 27: 325-8.
22. Yin Y, Wunderink RG (2018) MERS, SARS and other coronaviruses as causes of pneumonia. Respirology 23: 130-7.
23. Zhou P, Yang XL, Wang XG, Hu B, Zhang L et al (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579: 270-273.
24. World Health Organisation (2020) Pneumonia of unknown cause – China. https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/.
25. Hui DS, Azhar EI, Madani TA, Christian Drosten, Alimuddin Zumla et al (2020) The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - the latest 2019 novel coronavirus outbreak in Wuhan, China. International Journal of Infectious Diseases 91: 264-266.
26. CDC (2020) Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19)UnitedStateshttps://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w.
27. Zhonghua Liu Xing Bing Xue Za Zhi (2020) Novel Coronavirus Pneumonia Emergency Response Epidemiology Team the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China 41: 145-151.
28. Makoni M (2020) Keeping COVID-19 at bay in Africa. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30219-8/fulltext#articleInformation.
29. The Guardian (2020). Nigeria confirms first coronavirus case in sub-Saharan Africa. https://www.theguardian.com/world/2020/feb/28/coronavirus-found-in-sub-saharan-africa-as-who-says-spread-could-get-out-of-control.
30. Shaban AR (2020) Coronavirus in Africa: 119,454 cases; 3,592 deaths; 48,607 recoveries.https://www.africanews.

com/2020/05/27/coronavirus-in-africa-breakdown-of-infected-virus-free-countries/.

31. Africa Centres for Disease Control (2020) Coronavirus Disease 2019 (COVID-19): Latest updates on the COVID-19 crisis from Africa CDC. https://africacdc.org/covid-19/.
32. Cennimo DJ (2020) Coronavirus Disease 2019 (COVID-19). https://emedicine.medscape.com/article/2500114-overview#a5.
33. CDC (2020) Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020 https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm.
34. Qiu H, Wu J, Hong L, Yunling Luo, Qifa Song et al. (2020) Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohortstudy.https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30198-5/fulltext.
35. Zhu H, Wang L, Fang C, Sicong Peng, Lianhong Zhang et al. (2020) Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Translational Pediatrics, 9: 51-60.
36. Xiaotong Wang, Zhiqiang Zhou, Jianping Zhang, Fengfeng Zhu, Yongyan Tang et al. (2020) A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. Clinical Infectious Diseases, 71: 844-846.
37. Schwartz DA (2020). An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Archives of Pathology & Laboratory Medicine In-Press.
38. Zeng L, Xia S, Yuan W, Kai Yan, Feifan Xiao et al. (2020). Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China 174: 722-725.
39. Chen H, Guo J, Wang C, Fan Luo, Xuechen Yu et al. (2020). Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet, 395: 809-815.
40. Dong Y, Mo X, Hu Y, Xin Qi, Fang Jiang et al. (2020). Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics [Epub ahead of print].
41. Yushun Wan, Jian Shang, Rachel Graham, Ralph S. Baric, Fang Li (2020) Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. Journal of Virology 94: e00127-20.
42. Hoffmann M, Kleine-Weber H, Schroeder S, Nadine Krüger, Tanja Herrler et al. (2020) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell, 181: 271-280.
43. Mason RJ (2020). Pathogenesis of COVID-19 from a cell biology perspective. European Respiratory Journal, 55: 2000607.
44. Tang NL, Chan PK, Wong CK, K. To, A Wu et al. (2005) Early enhanced expression of interferon-inducible protein-10 (CXCL-10) and other chemokines predicts adverse outcome in severe acute respiratory syndrome. Clin Chem, 51: 2333-2340.
45. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. JAMA, 323: 1239-1242.
46. Mossel EC, Wang J, Jeffers S, Karen E. Edeen , Shuanglin Wang et al. (2008) SARS-CoV replicates in primary human alveolar type II cell cultures but not in type I-like cells. Virology, 372: 127-135.
47. Weinheimer VK, Becher A, Tonnies M, Gudrun Holland, Jessica Knepper et al. (2012) Influenza A viruses target type II pneumocytes in the human lung. Journal Infectious Diseases, 206: 1685-1694.
48. Qian Z, Travanty EA, Oko L, Karen Edeen, Andrew Berglund et al. (2013). Innate immune response of human alveolar type II cells infected with severe acute respiratory syndrome-coronavirus. American Journal of Respiratory Cell and Molecular Biology, 48: 742-748.
49. Yee M, Domm W, Gelein R, Karen L de Mesy Bentley, R Matthew Kottmann et al. (2017) Alternative progenitor lineages regenerate the adult lung depleted of alveolar epithelial type 2 cells. American Journal of Respiratory Cell and Molecular Biology, 56: 453-464.
50. Ho JC, Chan KN, Hu WH, Wah Kit Lam, Ling Zheng et al. (2001) The effect of aging on nasal mucociliary clearance, beat frequency, and ultrastructure of respiratory cilia. The American Journal of Respiratory and Critical Care Medicine, 163: 983-988.
51. World Health Organization (2020). Novel coronavirus (2019-nCoV) situation report - https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200126-sitrep-6-2019--ncov.pdf.
52. Centers for Disease Control and Prevention (2020). Coronavirus disease 2019 (COVID-19): symptoms. https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html.
53. Li Q, Guan X, Wu P, Xiaoye Wang, Lei Zhou et al. (2020) Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. The New England Journal of Medicine, 382: 1199-1207.
54. Yu P, Zhu J, Zhang Z, Yingjun Han (2020) A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. The Journal of Infectious Diseases Vol 221: 1757–1761
55. Jin Y, Cai L, Cheng Z, Hong Cheng, Tong Deng et al. (2020) A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Medical Research 7, Article number: 4.
56. Shen K, Yang Y, Wang T, Dongchi Zhao, Yi Jiang et al. (2020) Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World Journal of Pediatrics, Epub ahead of print. 16: 223-231.
57. Chang D, Lin M, Wei L, Lixin Xie, Guangfa Zhu et al. (2020) Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China 323:1092-1093.
58. Huang C, Wang Y, Li X, Lili Ren, Jianping Zhao et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 395: 497-506.
59. Chen N, Zhou M, Dong X, Jieming Qu, Fengyun Gonget al. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet vol 395: 507-513.
60. Wang D, Hu B, Hu C, Fangfang Zhu, Xing Liu et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA, 323: 1061-1069.
61. Chen ZM, Fu JF, Shu Q,Ying-Hu Chen,Chun-Zhen Hua et al. (2020) Diagnosis and treatment recommendations for

pediatric respiratory infection caused by the 2019 novel coronavirus. World Journal of Pediatrics, vol 16: 240-246.

62. Shen KL and Yang YH (2020) Diagnosis and treatment of 2019 novel coronavirus infection in children: a pressing issue. World Journal of Pediatrics, 16: 219–221.
63. Wang XF, Yuan J, Zheng YJ, Chen J, Bao YM et al. (2020) Clinical and epidemiological characteristics of 34 children with 2019 novel coronavirus infection in Shenzhen [in Chinese]. 58: E008.
64. Cascella M, Rajnik M, Cuomo A, Scott C. Dulebohn, Raffaela Di Napol (2020) Features, Evaluation and Treatment Coronavirus (COVID-19) [Updated 2020 Apr 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/.
65. Centers for Disease Control and Prevention (2020) How to Protect Yourself & Others. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fprepare%2Fprevention.html.
66. World Health Organization (2020) Coronavirus disease (COVID-19) advice for the public. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public.
67. Centers for Disease Control and Prevention (2020) Public Health Recommendations for Community-Related Exposure. https://www.cdc.gov/coronavirus/2019-ncov/php/public-health-recommendations.html.
68. Centers for Disease Control and Prevention (2020) Public Health Recommendations after Travel-Associated COVID-19 Exposure. Available at: https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html.
69. European Centre for Disease Prevention and Control (2020) Contact tracing: Public health management of persons, including healthcare workers, having had contact with COVID-19 cases in the European Union – second update, 31 March 2020. Stockholm: ECDC.
70. World Health Organization (2020) Coronavirus disease (COVID-19) outbreak: rights, roles and responsibilities of health workers, including key considerations for occupational safety and health. Available at: https://www.who.int/publications-detail/coronavirus-disease-(covid-19)-outbreak-rights-roles-and-responsibilities-of-health-workersincluding-key-considerations-for-occupational-safety-and-health.
71. World Health Organization (‖2020)‖ Laboratory testing for coronavirus disease 2019 (‖COVID-19)‖ in suspected human cases: interim guidance, https://apps.who.int/iris/handle/10665/331329.
72. Peirce J (2002) High-Throughput Thermocyclers. Available at: https://www.the-scientist.com/technology-profile/high-throughput-thermocyclers-52525.
73. Raabe V, Koehler J (2017) Laboratory diagnosis of Lassa fever. Journal of Clinical Microbiology 55: 1629-1637.
74. Trappier SG, Conaty AL, Farrar BB, Dave D. Auperin, Joseph B. McCormick et al.(1993) Evaluation of the polymerase chain reaction for diagnosis of Lassa virus infection. American Journal of Tropical Medicine and Hygiene 49: 214 -221.
75. Loeffelholz MJ, Tang YW (2020) Laboratory diagnosis of emerging human coronavirus infections - the state of the art. Emerg Microbes Infect 9: 747-756.
76. Chu DKW, Pan Y, Cheng SMS, Hui KPY, Krishnan P, Liu Y et al.(2020) Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia.66: 549-555.
77. Corman VM, Landt O, Kaiser M, Richard Molenkamp, Adam Meijer et al. (2020) Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 25: 10.2807/1560-7917.ES.2020.25.3.2000045.
78. Cui J, Li F, Shi ZL (2019) Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 17: 181-192.
79. Chan JF, Yip CC, To KK, Tommy Hing-Cheung Tang, Sally Cheuk-Ying Wong et al. (2020) Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel real-time reverse transcription-polymerase chain reaction assay validated in vitro and with clinical specimens. J Clin Microbiol, 4: 00310-20.
80. Tang YW, Schmitz JE, Persing DH, Stratton CW (2020) The Laboratory Diagnosis of COVID-19 Infection: Current Issues and Challenges [published online ahead of print, 2020 Apr 3]. J Clin Microbiol, JCM.00512-20.
81. Holshue ML, DeBolt C, Lindquist S, et al. (2020). First case of 2019 novel coronavirus in the United States. The New England Journal of Medicine, 382:929-936.
82. Chan JF, Yuan S, Kok KH, Kelvin Kai-Wang To, Hin Chu et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395: 514-523.
83. Than TM, Saw YM, Khaing M, Win EM, Cho SM et al. (2017) Unit cost of healthcare services at 200-bed public hospitals in Myanmar: what plays an important role of hospital budgeting? BMC Health Serv Res 17: 669.
84. Diao B, Wen K, Chen J, Liu Y, Yuan Z et al. (2020) Diagnosis of Acute Respiratory Syndrome Coronavirus 2 Infection by Detection of Nucleocapsid Protein. medRxiv.
85. Zhang W, Du RH, Li B, Zheng XS, Yang XL et al.(2020) Molecular and serological investigation of 2019-nCoV infected patients: Implication of multiple shedding routes. Emerg Microbes Infect 9: 386-389.
86. Chen X, Zhou B, Li M, Liang X, Wang H, et al. (2004) Serology of severe acute respiratory syndrome: implications for surveillance and outcome. J Infect Dis 189: 1158-63.
87. Chan CM, Tse H, Wong SS, Woo PC, Lau SK et al. (2009) Examination of seroprevalence of coronavirus HKU1 infection with S protein-based ELISA and neutralization assay against viral spike pseudotyped virus. J Clin Virol 45: 54-60.
88. Chaolin H, Yeming W, Xingwang L, Lili Ren, Jianping Zhao et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet, 395: 497-506.
89. Fuk-Woo CJ, Shuofeng Y, Kin-Hang K, Kelvin Kai-Wang To, Hin Chu et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet 395: 514-523.
90. Chung M, Bernheim A, Mei X, Zhang N (2020) CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV) Radiology 295: 202-207.
91. The Guardian (2020) UK sends 50,000 coronavirus samples to US for testing after technical problems. https://www.theguardian.com/world/2020/may/10/uk-sends-coronavirus-samples-to-us-for-testing.
92. Schraer R (2020). Coronavirus: Why did the UK need 100,000 tests a day? Available at: https://www.bbc.com/news/health-51943612.
93. Russian News Agency (2020) Russia delivers over 100,000 COVID-19 test kits to 13 states – officials. https://tass.com/russia/1133483.
94. Worldometer (2020) Italy Population (LIVE). https://www.

worldometers.info/world-population/italy-population/.

95. Crisanti A, Cassone A (2020). In one Italian town, we showed mass testing could eradicate the coronavirus. https://www.theguardian.com/commentisfree/2020/mar/20/eradicated-coronavirus-mass-testing-covid-19-italy-vo.
96. Campbell J, McCaslin J (2020) How Nigeria has responded to COVID-19 so far. Available at: https://www.cfr.org/blog/how-nigeria-has-responded-covid-19-so-far.
97. Nigeria Centre for Disease Control and Prevention (2020) An update of COVID-19 outbreak in Nigeria for Week 16. https://ncdc.gov.ng/diseases/sitreps/?cat=14&name=An%20update%20of%20COVID-19%20outbreak%20in%20Nigeria.
98. Nigeria (2020) List of State Governors: Governors and their parties. Available at: http://www.nigeriaembassyusa.org/index.php?page=state-governors.
99. WHO (2020) WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020. Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020?fbclid=IwAR25Aw5IrZOqg7znGfG3OdUKBN2Hw8WL4kHHVTPEv8EdJOqg3JD-vLz1HQY .
100. WHO (2020) Emergencies preparedness, response. https://www.who.int/csr/don/archive/country/nga/en/.
101. Azuonwu O and Chuku E.C (2015) Emergence and Re-emergence of 2014 Ebola outbreak in Sub- Sahara Africa: 'Challenges and lessons learned' from Nigerian epidemic outbreak. Scholars Journal of Applied Medical Sciences 3: 2802-2814.
102. Nigeria Centre for Disease Control and Prevention (2020) We're pleased to announce the activation of 2 new labs for inclusion in the NCDC Molecular Laboratory Network: Afriglobal Medicare Lab, Ogun; Sahel Centre for Molecular Diagnostics & Research, Katsina. This brings the total number of labs with #COVID19 testing capacity to 28 [Tweet]. Available at: https://twitter.com/NCDCgov/status/1265278581720133632?ref_src=twsrc%5Etfw%7Ctwcamp%5Eembeddedtimeline%7Ctwterm%5Eprofile%3ANCDCgov%7Ctwcon%5Etimelinechrome&ref_url=https%3A%2F%2Fcovid19.ncdc.gov.ng%2F.
103. Tafirenyika, M. (2014). Ebola: A wake-up call for leaders. https://www.un.org/africarenewal/magazine/december-2014/ebola-wake-call-leaders
104. World Bank (2019) Current health expenditure (% of GDP) - Sub-Saharan Africa, Worldhttps://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?contextual=max&locations=ZG-1W.
105. WHO (2020). How does corruption affect health care systems, and how can regulation tackle it? Available at: http://www.euro.who.int/en/data-and-evidence/evidence-informed-policy-making/publications/hen-summaries-of-network-members-reports/how-does-corruption-affect-health-care-systems,-and-how-can-regulation-tackle-it.
106. Tormusa DO, Idom AM (2016). The impediments of corruption on the efficiency of healthcare service delivery in Nigeria. Online Journal of Health Ethics.
107. Espy MJ, Uhl JR, Sloan LM et al. (2006) Real-Time PCR in Clinical Microbiology: Applications for routine laboratory testing. Clinical Microbiology Reviews 19: 165-256.
108. Ravi V, Madhusudana SN, Desai A, et al. (2011). Establishment of PCR laboratory in developing countries. World Health Organisation: ResearchGate.
109. Sambo A, Garba B, Zarma IH & Gaji MM (2010) Electricity Generation and the Present Challenges in the Nigerian Power Sector. Available at: https://www.researchgate.net/publication/228399732_Electricity_Generation_and_the_Present_Challenges_in_the_Nigerian_Power_Sector/stats.
110. World Health Organization (2010) World Health Report 2010—health systems financing: The path to universal coverage. Geneva: World Health Organization.
111. Oleribe OO, Ezieme IP, Oladipo O, Akinola EP, Udofia D et al. (2016) Industrial action by healthcare workers in Nigeria in 2013-2015: an inquiry into causes, consequences and control-a cross-sectional descriptive study. Human Resources for Health 14: 46.
112. Abimbola S, Olanipekun T, Schaaf M, Negin J, Jan S et al. (2016) Where there is no policy: governing the posting and transfer of primary health care workers in Nigeria. Int J Health Plann Manage. The International Journal of Health Planning and Management 32: 492-508.
113. Adeloye D, David RA, Olaogun AA et al. (2017) Health workforce and governance: the crisis in Nigeria. Hum Resour Health.
114. Alubo O, Hunduh V (2016) Medical dominance and resistance in Nigeria's health care system. Int J Health Serv, 47: 778-794.
115. Obokoh A (2019) Examining Nigeria's healthcare challenges. Available at: https://businessday.ng/why-nigeria-is-broke/article/examining-nigerias-healthcare-challenges/amp/.
116. Mathews T (2018) Where do countries get their money? Available at: https://www.quora.com/Where-do-countries-get-their-money [Accessed 16 May 2020].
117. BBC (2020) Coronavirus: The world in lockdown in maps and charts. Available at: https://www.bbc.com/news/world-52103747 .
118. Abu-bashal A (2020) Nigeria: 113 healthcare workers infected with COVID-19. Available at: https://www.aa.com.tr/en/africa/nigeria-113-healthcare-workers-infected-with-covid-19/1825398 [Accessed 18 May 2020].
119. Ghinai I, Woods S, Ritger KA, Tristan D. McPherson , Stephanie R. Black et al. (2020) Community transmission of SARS-CoV-2 at two family gatherings — Chicago, Illinois, February–March 2020. MMWR Morb Mortal Wkly 69: 446–450.
120. European Centre for Disease Prevention and Control (2020). Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – eighth update. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-rapid-risk-assessment-coronavirus-disease-2019-eighth-update-8-april-2020.pdf.