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Two years of the pandemic: Impact of COVID-19 on tuberculosis management in Nigeria

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ABSTRACT

Tuberculosis case recognition and plotting is a key strategy employed by the National Tuberculosis and Leprosy Control Program in Nigeria to curtail the increasing gap of tuberculosis cases. Nigeria recorded its first case of COVID-19 in late January 2020, and since then Nigeria has currently recorded 255,753 confirmed cases with 3,143 deaths. It has currently recorded 2,699 new cases, as of 2 May 2022, among tuberculosis patients. Since the emergence of coronavirus, there has been a progressive decrease in clinic attendance and tuberculosis identification, detection, mapping, and management. The COVID-19 pandemic has impacted negatively on tuberculosis patients' services in Nigeria as well as the nutritional status of tuberculosis patients. The present review summarizes the impact of COVID-19 on the tuberculosis epidemic in Nigeria. The tuberculosis program could maximize potential resources employed to combat the pandemic, such as digital health technology and funds, and work toward strengthening the patient-centered approach of care to limit the challenges that COVID-19 presents to tuberculosis control.

INTRODUCTION

On 28 April 2022, 31 new coronavirus (COVID-19) confirmed cases were registered in Nigeria. Figures show that the highest number of cases in the country was registered between May and August 2020, as well as between December 2020 and January 2021 (NCDC, 2022). The coronavirus disease 2020–2022 (COVID-19 pandemic) has become the defining global health crisis of the century (Pollard *et al*., 2020). The impact of this pandemic, as underlined by the United Nations Development Program, claimed over four million lives and affected two million people worldwide (UNDP, 2021). The pandemic's impact has touched almost every aspect of modern life, upending public health systems, the global economy, travel, supply chains, community and social ties, and how we work. Therefore, request for various initiatives went beyond acute medical repercussions; the pandemic imparted long-lasting social and economic consequences that impacted people of all economic statuses across the globe (UNDP, 2020). Nigeria is among the underdeveloped nations which have suffered severe loss on social and economic platforms (OECD, 2020). In underdeveloped nations, including Nigeria, access to the food security and social safety have become inaccessible to the people and income losses exceeded USD 220 billion (UNDP, 2020). According to the recent research by the United Nations, the COVID-19 pandemic will result in the enhancement of people under poverty by 500 million, and majority of them will come from southeast Pacific and African regions (WHO, 2021). Although in the present scenario the focus is on COVID-19 management, the threat of tuberculosis as an epidemic in Nigeria has always been a cause of concern. The channelization of resources toward COVID-19 management has opened a window for impaired tuberculosis management in Nigeria, which may lead to adverse repercussions.

EPIDEMIOLOGY OF COVID-19 AND TUBERCULOSIS IN NIGERIA

Nigeria is ranked seventh among the 30 countries with the greatest tuberculosis burden, and second in Africa. Annually, about 470,000 people in Nigeria are identified with tuberculosis, culminating in over 150,000 tuberculosis-related mortalities in

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2017. Coinfection of tuberculosis with HIV is among the most serious threats to Nigerians (Fig. 1). Tuberculosis is 16–27 times considerably more probable in HIV-positive people than in HIV-negative people. In reality, every year in Nigeria, 63,000 HIV-positive persons are diagnosed with tuberculosis and 39,000 HIV-positive people die from tuberculosis. Nigeria has 3.2 million HIV-positive persons, making the nation's population vulnerable to tuberculosis. Another contributory factor to Nigeria's high tuberculosis rate is the country's high poverty rate. Nigeria's poverty rate is roughly 152 million people. Poor living circumstances, where diseases can sometimes roam free, as well as a lack of healthcare, sufficient food, and shelter, plague these individuals. Tuberculosis carries a negative connotation, which is why many people in low-income areas refuse to seek treatment (Jeremiah *et al*., 2021).

On 27 February 2020, the first case of COVID-19 in Nigeria was confirmed as a 44-year-old Italian citizen landed in Nigeria via Murtala Mohammed International Airport in Lagos after flying from Milan, Italy. Public Health Emergency Operation Centers were activated just at national and subnational stages in reaction to this index case, with active case detections based on contact tracing. Only 217 contacts had been linked to this index case by 9 March 2020, with 136 (63.0%) being followed up and 1 contact being confirmed positive. The index case's 14-day follow-up period ended on 12 March 2020. In Nigeria, two more unrelated instances were documented during this time. Furthermore, 42 incidents were discovered in Nigeria's Federal Capital Territory, Edo, Kano, Lagos, Ogun, Rivers, and Yobe states. Since the first COVID-19 case was confirmed in Nigeria, the incidences and mortalities have steadily increased till today, as shown in Figure 2, despite the government's attempt to curb or mitigate the transmission of the virus through public health programs, such as the implementation of social separation, lockdown, and a prohibition on public gatherings (Dan-Nwafor *et al*., 2020).

COVID-19 and tuberculosis epidemiology relationship

Tuberculosis (TB) deleteriously affects the respiratory system (Gao *et al*., 2021). Therefore, when a patient suffers from a previous respiratory disease, the immune response offered by the lungs becomes very low, enhancing the tendency to develop COVID-19 infection (Mandal *et al*., 2020). Secondly, COVID-19 was first diagnosed as a respiratory illness which gradually progresses to acute necrotizing hemorrhage of brain, brain encephalopathy, and the presence of the virus in the cerebrospinal fluid (CSF), which is similar to the tuberculosis infection marked by the presence of tubercle bacilli in the CSF (Cherian and Thomas, 2011). The interaction between COVID-19 and tuberculosis clinico-immunological pathologies along with the mortality induced due to combinatorial effect remains nonelusive. However, global studies have indicated that the concomitant diagnosis and dual infection of both the diseases may be related to the enhanced fatality rate. Therefore, patients diagnosed with COVID-19 alongside TB have increased mortality risks equated to patients with only COVID-19 (Fig. 3).

The incubation time for tuberculosis is longer compared to COVID-19 and can be transmitted by droplets and fomites with slow onset (Cox *et al*., 2020). Both infections can cause mild to severe symptoms, such as dry cough, fever, and shortness of breath, which can become more complex with improper management (Lauretani *et al*., 2020). The relationship between COVID-19 and tuberculosis is most pronounced in sub-Saharan Africa, where tuberculosis is the leading infectious disease and cause of death. COVID-19 has had a catastrophic effect on tuberculosis, the prime infectious disease in the world. Until 1 April 2020, COVID-19 overhauled tuberculosis by significantly increasing the mortality/day (Hogan *et al*., 2020). It is no surprise that the sub-Saharan regions most likely to be impacted by COVID-19's social and economic effects also have the greatest tuberculosis burden (Datta *et al*., 2020). This is due to the fact that tuberculosis

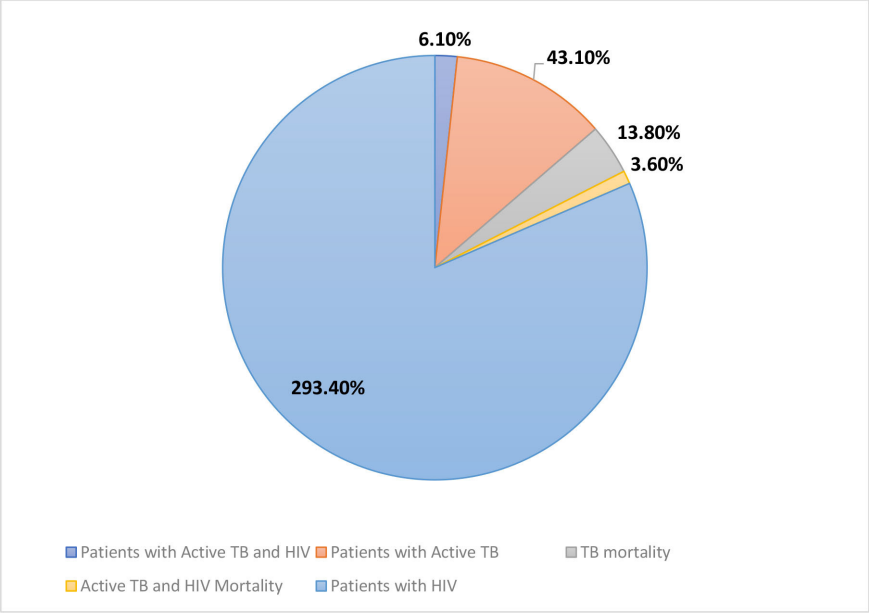

Figure 1. Tuberculosis epidemiology in Nigeria (Jeremiah *et al*., 2021).

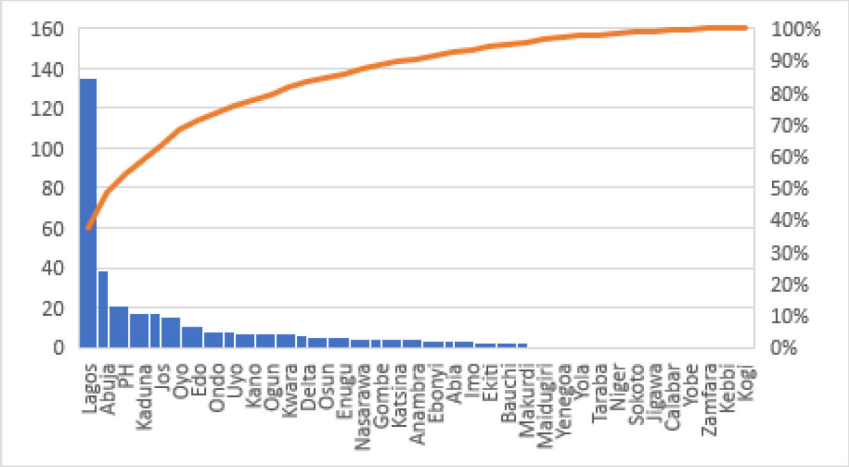

Figure 2. State-wise distribution of COVID-19 cases in Nigeria (Brandt and Botelho, 2020).

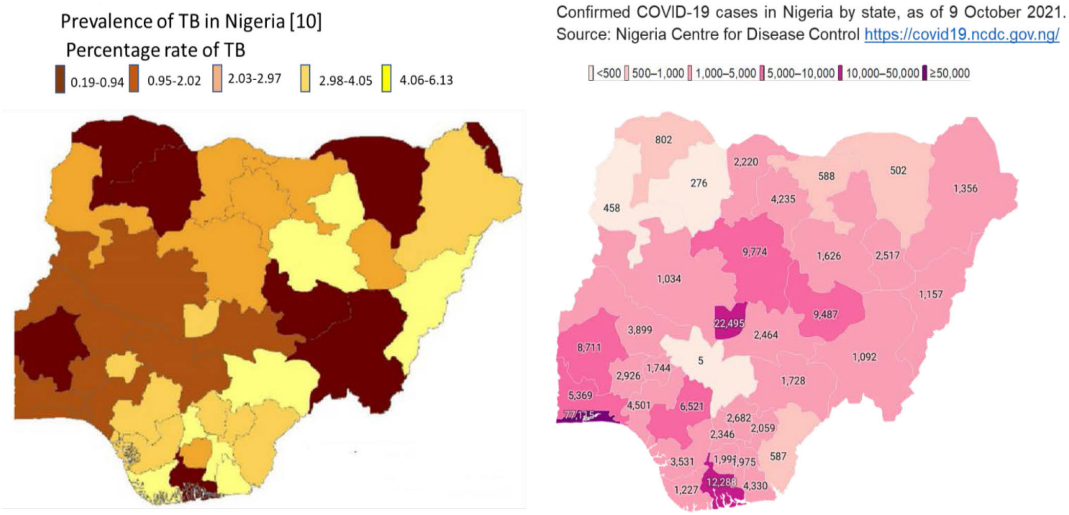

Figure 3. Epidemiological comparison of TB and COVID-19 in Nigeria (Akwafuo *et al*., 2020).

is both a social and an infectious disease: poorer, malnourished people living in densely populated areas are more likely to contact tuberculosis. Tuberculosis impacts society at socioeconomic levels by increasing cost of living, reducing income, and causing social discrimination (WHO, 2021; Wingfield *et al*., 2018). Indeed, scarcity of resources highlighted as poverty is a key factor underlining the tuberculosis pandemic, as evidenced by various studies (Saunders and Evans, 2016; Wingfield, 2014). Multiple studies have clearly indicated the correlation between tuberculosis incidence rates and socioeconomic development. This emphasizes the importance of pulmonary rehabilitation for TB patients (Carter *et al*., 2018; Dye *et al*., 2009).

DIAGNOSTIC METHODS ADOPTED FOR TUBERCULOSIS DETECTION

The Center for Disease Control and Prevention (CDC) proposed two kinds of detections for tuberculosis, which are the skin test and the blood test, but they had some setbacks, which were the inability to detect if the patient had a latent tuberculosis infection or if the tuberculosis has progressed to a disease itself. As a result of these short-comings in accurately detecting tuberculosis, and also the strain getting very resistant to antibiotics treatment making recovery very difficult; other detection methods have been employed to detect the bacteria strain, and they are LED fluorescence microscopy, nucleic acid amplification, rapid liquid culture with adjunct drug susceptibility, and interferon gamma release assays, which give an improved accuracy of tuberculosis detection over the previous methods proposed by the CDC (Nyendak *et al*., 2009). However, in Nigeria, the method adopted for tuberculosis diagnosis is the use of microscopy examinations of three sputum samples which are collected in a span of 48 hours; first, the patient gives on-the-spot sputum and as a follow-up the patient is given a container to take home in which he/she will produce an early morning sample, which is to be brought to the clinic as early as possible, and on arrival again produce an "*on-the-spot*" sample under close supervision (Oladimeji *et al*., 2021). Second, the GeneXpert MTB/RIF assay, which is also recommended by the WHO, is an automated semi-quantitative

real-time PCR for the rapid detection of tuberculosis DNA and RIF resistance simultaneously, from unprocessed sputum within 2 hours giving a good diagnostic accuracy (Boehme *et al* 2010). Third, the skin test for diagnosis of latent tuberculosis is one of the oldest methods (Menzies, 2000) also used in Nigeria (Table 1). This method is used for patients who have no clinically manifested active tuberculosis disease (Diel *et al*., 2012). Finally, the chest radiography method which is also recommend by the WHO is used in Nigeria for diagnosis of tuberculosis among people living with HIV; this shortens the delay in diagnosis and early detection in suspected tuberculosis patient (WHO, 2007).

Impact of tuberculosis diagnosis

The COVID-19 pandemic has had substantial influence on the delivery of biomedical care pertaining to tuberculosis. Accessibility of diagnostic testing by the patients reduced significantly, because of limited resources, as well as the stigma of being a patient of respiratory malfunction associated with the COVID-19 symptoms (Chalmers *et al*., 2021). The COVID-19 pandemic has compounded this stigma with tuberculosis infection, possibly prompting tuberculosis people to hide their condition and wait until infection and infectiousness have advanced before seeking medication (Bonadonna *et al*., 2017). The COVID-19 pandemic may increase the number of these "missing" people, who are a key source of continuous transmission and are at a high risk of tuberculosis-related illnesses and death rate (Datta and Evans, 2019; Yuen *et al*., 2015).

COVID-19, TUBERCULOSIS, AND NUTRITION

Malnutrition and tuberculosis are both problems mostly found in developing countries, to which Nigeria is no exception (Dye, 2015). Poor nutrition, especially in protein-deficient diets, leads to protein–energy malnutrition over a long period of time and other micronutrients deficiencies which gives rise to tuberculosis infection when the immune system is weak to fight against opportunistic infections (Hussien and Ameni, 2021). A poor nutrition diet, like the constant intake of carbohydrates, e.g., rice, garri, fufu, and semovita, without a combination of animal protein, like meat, fish, crayfish or plant protein, like beans, fio-fio, oil-bean, etc., could lead to protein malnutrition and other micronutrient deficiencies, leading to inefficient immune responses during infection. This secondary immunodeficiency increases the host's susceptibility to infection and further predisposes the individual toward *mycobacterium*-based infection (Krishna *et al*., 2009). The symptoms of both COVID-19 and tuberculosis include weight loss, nutrient malabsorption, micronutrient malabsorption, and altered metabolism, resulting in wasting and low nutritional status (Tadolini *et al*., 2020). Patients in this category can improve their nutritional condition by eating a balanced diet, foods rich in green vegetables, fruits rich in vitamin C, spices like ginger and garlic that have antibiotic properties, and quality proteins from both animal and plant sources, which increases their resistance to infection during antituberculosis medication (Bhagya *et al*., 2018).

COVID-19 INFLUENCE ON TUBERCULOSIS PREVENTION AND TREATMENT

The pandemic has bought down the polished supply chain of goods pertaining to medicines and associated support like foodstuff, hand sanitizers, and nose masks. Impaired mental and nutritional health due to disruptions in the manufacture and distribution of medicines, limited availability of adverse drug reaction monitoring, clinical care facilities, and coinfections have augmented the risk of poor management of tuberculosis patients in Nigeria. This has further led to impaired diagnosis and management settings of the patients with drug-resistant *Mycobacterium tuberculosis* infection. Furthermore, in the general population, these comorbidities are probable to increase the likelihood of development from dormant tuberculosis infection to active disease. In addition, tuberculosis prevention treatment for household members is expected to be significantly debilitated, as overburdened healthcare management have channelized the resources on diagnosis and treatment. The tagged nonemergency visits to healthcare facilities were reduced in Nigeria. This in particular calls for concern because the prevalent COVID-19 is anticipated to promote tuberculosis transmission to household members via delayed transmission (Saunder *et al*., 2017, 2020). Unfortunately, for majority of the global population inhabiting congested dwellings with high population density, where most tuberculosis occurs, isolation and quarantine of patients within families poses a herculean task. COVID-19-related economic issues, such as the inability to buy sufficient food for family consumption because of the hike in price, constant struggle to sell the goods and foodstuff as a result of little or no buyers, undernutrition as a result of poor feeding, and increased tuberculosis susceptibility as a result of an immunocompromised immune system, are all anticipated to exacerbate this increased tuberculosis transmission (Saunder *et al*., 2017, 2020). In the management of tuberculosis in Nigeria, the following measures have been classified into three categories: the administrative control, which drafted the protocol measures that will be followed by all staff working in tuberculosis centers or hospital; the environmental control, which reduces the concentration of the infectious droplets in the atmosphere; and personal protective devices (respiratory protection) to protect individuals in areas with a high concentration of the infectious droplets. Also, there are facility assessments, assigning of roles and responsibilities, implementation of activities, monitoring, and evaluation (Paul, 2020; Rudgard *et al*., 2017).

INTERVENTIONS IN SOCIAL PROTECTION AND SAFEGUARDS

Global tuberculosis rates were driven by socioeconomic development and poverty, hence combating tuberculosis in the context of COVID-19 necessitates addressing social determinants as well as biomedical care (Saunders and Evans, 2016; Wingfield *et al*., 2018). While people are not able to work during the pandemic, national and local governments gave finances to give social support to susceptible groups at increased risk of poverty, and hence COVID-19 and tuberculosis patients are not exempted to lower their chance of further infection (Carter *et al*., 2018; Rudgard *et al*., 2017). With the current prevailing tuberculosis scenario in Nigeria, tuberculosis-specific social protection was also provided in the form of cash transfers, food supply, sanitizers, and masks for tuberculosis-burdened households (WHO, 2019; Wingfield *et al*., 2018). Importantly, most of the financial assistance collaborated with patient civil society organization and local government councils, as they play an important role in giving psychosocial

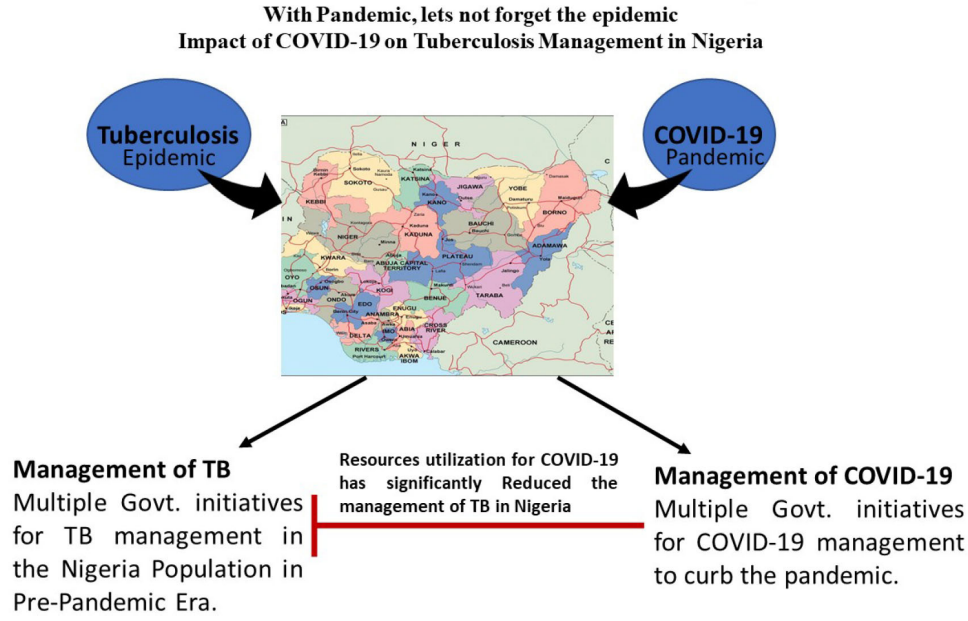

Figure 4. Impact of COVID-19 on Tuberculosis management in Nigeria.

Table 1. Symptoms common to COVID-19 and tuberculosis (Gao *et al*., 2021).

Parameters	COVID-19	Tuberculosis
Main transmission route	Through respiratory droplets	Through respiratory droplets
Main target	The lungs	The lungs
Symptoms	Cough, fever, and difficulty breathing, loss of weight, night sweat, persistent fever, loss of smell and taste	Cough, fever, and difficulty breathing, loss of weight, night sweats, persistent fever, loss of smell and taste
Diagnosis	GeneXpert (Nuclear acid amplification test, NAAT), radiological analysis, microbial analysis	GeneXpert (NAAT), radiological analysis, microbial analysis

sustenance to tuberculosis-burdened families to decrease stigma and discrimination (Datta *et al*., 2020; Wingfield *et al*., 2015). The use of digital technology was also employed to increase fairness and efficiency while also addressing the infection control issues that both tuberculosis and COVID-19 posed (Saunder *et al*., 2018). Tuberculosis-specific social protection was provided to the burdened individual in the form of equal access to the treatment and prevention for reducing the associated risk factors (Saunders *et al*., 2019b; Wingfield *et al*., 2016). Also, during the COVID-19 in Nigeria, the government set out a number of measures through the Central Bank of Nigeria, and it included the release of funds to reduce the impact of COVID-19 on households, micro and small businesses, loans with longer period of paybacks were granted, some restrictions on importation were lifted, and electricity tariffs were lifted (Amanzee*t al*., 2020).

In the management of tuberculosis, the Nigerian government through various agencies came up with some strategy plans like the DOT strategy, access to diagnosis centers, patient-centered treatment, and prevention strategies (Ogbuabor and Onwujekwe, 2019). More so, to offset the consequences of the COVID-19 pandemic, provisions of healthcare for tuberculosis-burdened household were organized by nongovernmental organizations that collaborated with governments and national tuberculosis programs. To support care delivery, there was sharing of diagnostic equipment and recruiting of an efficient laboratory that has the capacity to carry out testing and enhance caregiver and community health worker responsibilities. National tuberculosis programs used regionally derived, simple risk stratification techniques to target treatments like active case discovery. The preventative treatment to members of the highest risk families increased the impact and cost-effectiveness (Paul, 2020; Rudgard *et al*., 2017).

COVID-19 AND INTEGRATED HEALTHCARE FOR TUBERCULOSIS

Some group of authors gave an account of the first patients who had both tuberculosis and COVID-19, and suggested the importance for healthcare integration for both disorders (Datta *et al*., 2017; Tadolini *et al*., 2020). They said that patients with tuberculosis who eventually recovered are at a serious risk of getting the COVID-19 infection which would result in chronic lung injury (Yuen *et al*., 2015). As a result of this, there needs to be a compulsory test for these categories of patients. Secondly, those patients who survived the severe effects of COVID-19 that had affected their lungs may be at risk of tuberculosis, which is likely to progress from latent to active tuberculosis infection. Intensive

research is needed to give more insights and understanding about the transmission as well as mutations of COVID-19, as well as adopt new diagnostic methods that are authentic, reliable, and give results in real time (Rangaka *et al*., 2015). Thirdly, when an acute symptom of COVID-19 is diagnosed, the possibility of chronic subclinical symptoms of tuberculosis could present itself, owing to overlapping symptoms, these could definitely drive affected patients to seek medical attention before tuberculosis symptoms emerge (Datta and Evans, 2019; Saunders *et al*., 2019). Because of these, areas with high burden of tuberculosis as well COVID-19 would require constant presence of healthcare personnel for persons presented with respiratory symptoms so as to get them tested for both infections. Finally, as evident with the parallels between COVID-19 and tuberculosis, there is an obvious prospect to harness tuberculosis healthcare workers' ensuring that they have substantial knowledge, expertise, and infrastructure for the control of COVID-19.

COMMUNITY MOBILIZATION AND ADVOCACY

In the context of the COVID-19 pandemic, it is important that scientific and wider global campaigns should be carried out in both rural and urban communities, not excluding civil society organizations, for the rights of tuberculosis-burdened families. Also, the response of these populations as a whole to COVID-19 is quite interesting to note, not forgetting that the western nations were at the forefront of combating the spread of the disease. It should serve as an example for the world's oldest pandemic, tuberculosis, which generates a huge load of disease and associated mortality in impoverished nations (Matthew and Carlton, 2020). The WHO's prediction implied that tuberculosis would have induced more than double the mortality caused by SARS CoV-2 by 2020, but as time went on, COVID-19 currently has caused over 2556 deaths in Nigeria and 4,585,598 deaths globally (Datta *et al*., 2020).The "perfect storm" analogy has been criticized for putting less focus over the effectiveness of public health monitoring and prevention initiatives. Instead, the international community must be proactive and foresee the possibly harmful cooperation between COVID-19, tuberculosis, and poverty. If we have the prudence and vision to act now to combat tuberculosis via investment, research, and great leadership, we can avoid being caught in the eye of the storm and potentially save millions of lives.

Strategies employed by the National Tuberculosis and Leprosy Control Program are to curtail the widespread of tuberculosis in Nigeria with the advent of COVID-19 in 2020 till date. The tendency is that most of the patients affected with COVID-19 possess similar symptoms as tuberculosis; while some are tuberculosis patients before the invasion of COVID-19. This has negatively impacted the entire government sectors, financial stability, health sector, and educational sector (Fig. 4).

As a result of the negative impact, infected patients (tuberculosis and COVID-19) as well as patients who show symptoms reluctantly decide to go to the healthcare centers as a result of previous experiences encountered by some other infected patients in these healthcare centers. Food insecurity became very high owing to the fact that the prices of food stuffs have greatly increased and there is no sufficient money in circulation to buy these food items.

CONCLUSION

There is no doubt that patients who are symptomatic with either tuberculosis or COVID-19 were tested using a more accurate testing method. The gene expert test which was used in detecting the tuberculosis bacteria was also employed in the COVID-19 testing as well in Nigeria, making it difficult for tuberculosis patients to get tested because of the increasing number of COVID-19 patients. Moreover, tuberculosis patients as well as COVID-19 patients need good nutrition to build strong resistance to diseases, and they were given food recommendations that would aid them combat both infections. The government employed some relief programs and interventions to reduce the scourge of both infections, especially the COVID-19 infection. The National Center for Disease Control also made provisions of treatment/quarantine centers, especially for COVID-19 patients who have tested positive, but these centers were being avoided because of the stigmatization associated with been tested positive as well as quarantined. Therefore, awareness should be created about the COVID-19 infection, as well as the purpose of quarantine. And then proper education should be given to patients who have recovered from both infections to avoid a re-infection of either of the infections (Brandt and Botelho, 2020).

CONFLICT OF INTEREST

The authors have no actual or potential conflict of interest.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included within this research article.

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