

Systematic Review

Co-epidemics: implications of COVID-19 outbreak associated with human immune-deficiency virus, tuberculosis and Lassa fever in a low resource economy - a call for proactive measures

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ABSTRACT

As the global struggle to combat the quadruple burden of COVID-19, human immunodeficiency virus, tuberculosis and Lassa fever continues to increase, Sub-Saharan Africa has been the most affected region, especially Nigeria. There is a close interaction between these four diseases and a clear understanding of each of these diseases is very crucial. People living with chronic medical conditions such as HIV, TB and Lassa fever are more likely to experience poor outcomes from COVID-19 even though there are still some unknown facts as regards the burden of COVID-19 on patients with TB, Lassa fever and HIV in our low-middle-income nation. This study was conducted to review different researches on COVID-19 associated with HIV, TB and Lassa fever co-infections, to understand the interactions between them and its implications on clinical investigations and health management in high burden countries of COVID-19, especially Nigeria. The research was designed to accommodate research and reports from different geopolitical zones of Nigeria where the diseases has been reported and centering on Ondo State reports. This was done using search engines, with reference to valid studies from academic sources like ResearchGate, PubMed and Google Scholar. We also evaluated various related titles, abstracts and full reports for eligibility. Ondo state was the centre of study as it is one of the states with high prevalence of Lassa fever, TB, HIV and COVID-19 co-infections in Nigeria. Structured diagnostic algorithms and clinical management are suggested to improve COVID-19/HIV/TB/Lassa fever or COVID-19/Lassa fever co-infection outcomes. With low quality of health care facilities for laboratory diagnosis of COVID-19 and Lassa fever, reliance on clinical acumen and high index of suspicion may be the only process that health professionals may rely upon to make early diagnosis.

Keywords: COVID-19, Lassa fever, HIV, Tuberculosis

INTRODUCTION

Coronavirus disease otherwise known as COVID-19 is an illness caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has been a global concern since its emergence in December 2019. Different variants of the COVID-19 have been discovered

since the first wave with the Alpha variant being the first kind. Other variants that followed are; Beta, Gamma, Delta, Epsilon and the Omicron which have occurred between the first and the third wave of the outbreak. The Delta variant was first discovered in India in late 2020 while on 30 November 2021, the Omicron variant was identified in South Africa by the US government SARS-

CoV-2 Interagency Group (SIG) with other variants being monitored.¹

The Omicron variant has become the most dominant strain in the world. It was first reported to the World Health Organization (WHO) on 24 of November 2021 during the third wave of COVID-19. It has been suggested that the Omicron virus is less severe but more easily transmittable than other variants from early reports in South Africa.² According to WHO, the Delta variant is the dominant and most prominent strain in Nigeria among others and has been found in over 90% of samples tested.³

The first phase of COVID-19 in Nigeria emerged in February 2020 till March 2020. The Nigerian Centre for Disease Control (NCDC) reported that people who have contracted this virus were travelers from abroad who had just arrived the country within the first 30 days, with over 230 confirmed cases of the infection. Between February 6th and 8th 2020, the African Centre for Disease Control trained experts from Nigeria and 15 other African countries on how to diagnose the COVID-19 virus with the aid of polymerase chain reaction (PCR), but due to limited availability of testing and treatment centres, the Federal Government were constrained to the test only on those who are required to especially those departing and arriving the country, to curb further spread to other states. However, since the global decline in reported cases there has been improvement in the adherence to preventive measures and management.

During the second phase, between March 2020 and June 2020, the spread of the virus had increased to over 550 positive cases with Lagos state being the major concern since it has one of the most engaging international airports in Nigeria.⁴ Encounters from the Lassa fever outbreak should have guided the country on measures to undertake to manage the outbreak. But due to the delayed closure of entry points into the country, the virus soon began to grow across other states. Curfews and lockdown as well as interstate ban were however introduced on the 30 March, 2020 as a global measure.

Phase 3 measures have been in place since September 2020 and basic directives such as compulsory use of face masks, constant washing of hands, use of hand sanitizers, social distancing, checking of body temperatures at banks, offices, religious institutions and other public places has been in practice to prevent community transmission even to this present day. Vaccines have also been discovered and are being administered in different parts of the country. However, many other low- and middle-income countries are still struggling to obtain vaccines.⁵ The mortality rate of COVID-19 in Nigeria was however described to be the highest in West Africa as of June 2020.⁶

Lassa fever (LF) which is very common in the West Africa region is a viral hemorrhagic fever (VHF) transmitted by multi-mammate rats i.e. rats having several pairs of mammary glands. It can also be spread through direct

contact with the blood, tissue, secretions or excretions of infected individuals. It was named after a town in Borno state, Northeastern Nigeria where the first case occurred. Most people infected with the disease show little or no symptom while mild symptoms such as fever, weakness and headache may be noticed in others.⁶ There's no vaccine for the disease yet.⁷

The human immunodeficiency virus (HIV) is an infection that attacks the white blood cells (called CD4 cells) of the human body, thereby weakening the immune system of a person and making them susceptible to opportunistic infections like tuberculosis, fungal and bacterial infections.⁸ It was first recognized among homosexuals in United State of America in 1981. The first two cases in Nigeria were reported in 1985 in Lagos state. As of 2020, 1.7 million people in Nigeria were living with HIV with women being the most affected, and over 24,000 residents of Ondo state are living with the virus as of January 2022.⁹

Tuberculosis which was discovered in 1882 by Dr. Robert Koch is a bacterial infection that is spread through inhaling tiny droplets from the coughs or sneeze of an infected person. It mainly affects the lungs but can be cured if treated with the right anti-tuberculosis combination drugs. It is characterized by persistent cough that usually last more than 3 weeks, weight loss due to loss of appetite, high temperature and fatigue. Nigeria ranks fourth out of countries with the highest TB burdens in the world. The Bacillus Calmette-Guérin (BCG) vaccine protects against tuberculosis and is given once in a lifetime. The Damien Foundation Belgium (DFB), a non-profit medical organization has partnered with the Federal Government of Nigeria to provided support in the combat against TB in Nigeria.¹⁰

Ever since the onset of HIV, the occurrence of Tuberculosis has been increasing and has led to a high mortality rate among people living with HIV over the last ten years. While cases of COVID-19 continue to grow, the effort to control and provide treatment for HIV and TB continues to increase. The HIV epidemic reached its peak in Nigeria in 2001 when it was 5.8% compared to 1.8% in 1999.

WHO estimated that in 2020, 10 million people developed TB globally and 1.5 million died from the disease including 214,000 people with HIV.¹¹

In 2012, Nigeria had an estimated incidence of 338 cases of TB per 100,000 population. The number of people with HIV and TB in Nigeria is increasing, with an estimate of 570,000 cases in 2013.¹² The prevalence of HIV among TB patients in Nigeria has been established to be 22%. In 2021, Ondo State with an approximate population of 4,671,700, was estimated to have a TB burden of 10,231 from the incident rate of 219 in 100,000 population.

There have been cases of Lassa fever co-infection with HIV which has been reported among patients in southwest

Nigeria. Cases of Lassa fever occur throughout the year in Nigeria. Between 2018 and 2020, the number of people infected nearly doubled, if not for quick intervention in case identification and care provision. The number of cases usually peaks between January and May, during the dry season, when rodents increasingly enter into homes in search of food (Figure 1).

The geographical location of Ondo State been a transit states leading to some other states in Nigeria will be a major transmission zone for different types of emerging and re-emerging diseases like Lassa and SARS-CoV-2. Moreover, Ondo state borders Edo state with high level of interaction between people of both states as there are no demarcating borders between both states which puts Ondo State at a higher risk of influx of Lassa virus from Edo state. These also gives justification for this review as Ondo state and Nigeria is a low-income state and country, the burden of co-infection of these three diseases will seriously effect on the socio-economic growth the population.

METHODS

Study design

This is a systematic review bothering on COVID-19 and its attendant burden on association with HIV, TB and Lassa fever and its implication in the prevalent population. This study was designed to randomly access research publications and various desk report in each of the 6 geopolitical zones of Nigeria by picking states to sample by random. Emphasis was placed on Ondo State and other Southwest states of Nigeria with Ondo state as epicentre. Where research publications do not exist desk reports were reviewed.

Study setting

Nigeria is geographically situated between the Sahel to the north and the Gulf of Guinea to the south in the Atlantic Ocean. It is made up of 36 states and divided into 6 geopolitical zones (North West, North Central, North East, South East, South South, South West) having a population of over 200 million people. Each of the geopolitical areas are made up of 6 states. Ondo state is located in the southwestern part of Nigeria with about 3.5 million population and an area of 14,788 sq. It borders Ekiti state to the north, Ogun state to the southwest, Osun state to the northwest and the Atlantic Ocean to the south. The state is made up of 3 senatorial districts and has 18 local government areas.

The economy of Ondo state is the sixth largest in and crop production. Ondo state prevalence indices in the co-epidemics is of great significance having the highest number of confirmed cases of Lassa fever (63) which accounts for 30% of all Lassa fever, 1.1% of all HIV cases. Ondo State also borders Edo state which has been reported to have very high Lassa virus activity.

Data collection

We utilized formal methods of literature search, selection of articles for inclusion using search engines to review the literature with reference to PubMed, ResearchGate and Google Scholar databases. We also reviewed reports from the World Health Organization (WHO), Nigeria Centre for Disease Control (NCDC) and publications from other public health organizations. We also reviewed reports of cases of individuals with COVID-19 along with these co-epidemics Africa.

Cases of co-epidemics across Africa

Since March 2020, COVID and LF have been occurring simultaneously in Ondo state southwestern Nigeria which has the highest burden of LF cases in Nigeria and the eleventh highest for COVID-19 (Figure 2).^{12,13}

Two cases of health care workers (HCWs), who were infected with both LF virus and COVID-19 virus at same time was reported and they were successfully managed after being admitted at the Federal Medical Centre, Owo a tertiary hospital in the state in 2020 (Figure 3). The first case was a 40-year-old medical doctor who was working at a LF treatment centre before he got admitted to the Infection Control Ward. He complained of severe headache, joint pains and fever that lasted for 3 days. His spouse, who was also a medical doctor, was managed as a confirmed COVID-19 carrier, 3 weeks before his presentation.¹⁴

Cases of COVID-19 associated with HIV as well as TB have also existed. This was the case of a 55-year-old man with WHO stage-3 HIV retroviral infection who have been on highly active anti-retroviral therapy (HAART) for over 3 years before he started receiving treatment in Wollega University Referral Hospital in western Ethiopia in May 2021. By the 6th day of admission, his condition had improved after being treated with anti-TB drugs, oral antibiotics and highly active antiretroviral therapy, and result for the PCR Follow-up test for COVID was negative. He was discharged after 10 days of hospital stay.¹⁵

RESULTS AND DISCUSSION

Implication of Lassa fever, TB and HIV

Lassa fever is one of the tropical VHF that has been overlooked over the years and very little research has been carried out on it in Nigeria, hence no vaccine for it yet.¹⁶ There has been high report of fever as a symptom compared to other symptoms which is common in these co-infections. The prominence of COVID-19 in Nigeria is a significant disadvantage in the fight against LF. This is because the major focus is on COVID-19 which has caused people to pay very little attention to the LF disease and has led to unreported cases due to less visit to clinics.¹⁷

Tuberculosis remains a global public health problem and one of the top ten leading causes of death, worldwide, with developing countries bearing the highest burden.¹⁸ Nigeria remains one of the 22 high burden countries in the world and comes third after India and China in terms of Tuberculosis cases. Every year, about 245,000 people die from TB and it accounts for more than 10% of all deaths in Nigeria. The risk of developing active TB is significantly increased following HIV infection, and nearly one in every four sufferers is also HIV-positive.¹⁹ In 2020, Nigeria was one of eight countries that accounted for two-thirds of people who developed TB. On the other hand, no fewer than 2,537 people were infected in Ondo state in 2021 (Figure 4).²⁰

TB and HIV constitute major public health problems in Nigeria. HIV infection accelerates progression of latent TB infection into active TB disease (Centers for Disease Control and Prevention, 2000).²¹ About 19,423 of the 88,317 TB cases tested were found to be HIV positive by the Nigerian National TB Prevalence survey in 2013. This represents a TB/HIV co-infection rate of about 22%. The prevalence of HIV among TB patients in Nigeria increased from 2.1% in 1991 to 19.1% in 2001 and 22% in 2013.¹³ Due to the high burden of HIV in Nigeria, 63,000 of TB cases were also co-infected with HIV in 2015. Over 20,000 new cases of drug-resistant TB have been recorded in 2016, with 4.3% new cases and 25% formerly treated cases.²² About 2.6 million new TB cases and 740,000 deaths have been recorded in Africa, while about 1 million (10%) of new TB cases and 374,000 TB-related deaths were recorded among people living with HIV (PLWHIV) globally in 2016 (Figure 5).

Effect of COVID-19 on HIV, Tb and LF co-infection

People living with HIV and who have also been infected with COVID have higher risk of complications and eventual death compared to those uninfected with COVID-19.²³ Likewise, those with TB and COVID-19 co-infection are at high risk of developing severe complications from COVID compared to those infected with COVID-19 only. Those having COVID-19 and HIV have a higher chance of recovery compared to those having COVID/HIV/TB and LF co-morbidity. COVID-19 could influence a transient suppression of cellular immunity that could revive new TB infections, as well as HIV.²⁴

Hypothesis by Mascolo et al made it known that correlative immunosuppression from HIV may make PLWHIV more susceptible to contracting COVID-19 but that lymphopenia, a disorder in which the blood does not have enough white blood cells may protect against severe manifestation of COVID due to the incapability to mount an overactive T-cell response.²⁵ Another study shows that HIV is distinguished by a chronically elevated inflammatory condition, which will lead to aggravated symptoms when combined with cytokine storm as observed in COVID.²⁶

Our medical services back-up is also poor but regardless the death rate we have experienced is minimal and our survival rate is quite outstanding compared to those recorded in other countries. This has been presumed to be due to the religious beliefs of some that Africans possess an innate or adaptive protective immune response to SARS-CoV-2 among the black communities. Others also believe that the virus could not withstand the tropical climate of the country which is not hundred percent true and these misconceptions have put the lives of many at risk.

Suspected cases of COVID-19 and TB exhibit similar fever and/or respiratory symptoms such as difficult respiration, coughing, and chest pain. COVID-19 can conceal TB in HIV-infected people or the other way round. Therefore, it is important that screening is done for both COVID-19 and TB in HIV-infected people.²⁷ Disturbance to the provision and access to TB diagnosis and treatment caused by COVID-19 have been evaluated to have caused an increase of over 100,000 in the number of TB deaths globally between 2019 and 2020. It has been suggested that the impact will be greater on the incidence and mortality rate in the future.²⁸

The COVID-19 epidemic has impacted negatively on TB, HIV and LF case findings and services in Nigeria since there has been gradual decline in clinical attendance, probable identification and case detection since its onset.

Impact on the national economy

WHO reports that people living with HIV are 20 times more likely to develop TB than their counterparts.²⁹ It is estimated that 1.1 million people worldwide live with TB and HIV, 80% of whom live in sub-Saharan Africa.³⁰ Since the emergence of HIV, TB incidence is increasing and causing a high mortality rate among people living with HIV over the last ten years (Figure 6).³¹

Just before the global pandemic, Nigeria has already been dealing with some major economic issues such as increase in oil price with fuel scarcity, trade restrictions, insecurity and unemployment.³² The early phase of COVID-19 paved way for recession since it disrupted activities in lots of industries as well as organizations and this was majorly due to the lockdown measures limiting the movement of people to their places of work. The decrease in workforces, attention and measures did not allow the continuation of effective surveillance of LF during the lockdown.^{33,34} The population of Nigerians that were confronted with hunger doubled during the pandemic.³⁵ Considering the recession that was encountered in 2016 and a global recession in 2020, the impact still remains and the economy is yet to fully recover from it. Although Nigeria is combating HIV, TB and LF on a large scale, it is receiving less resources because it does not present as much economic threat in magnitude as COVID-19. These economic shocks have affected the financing of many different social sectors, including health.

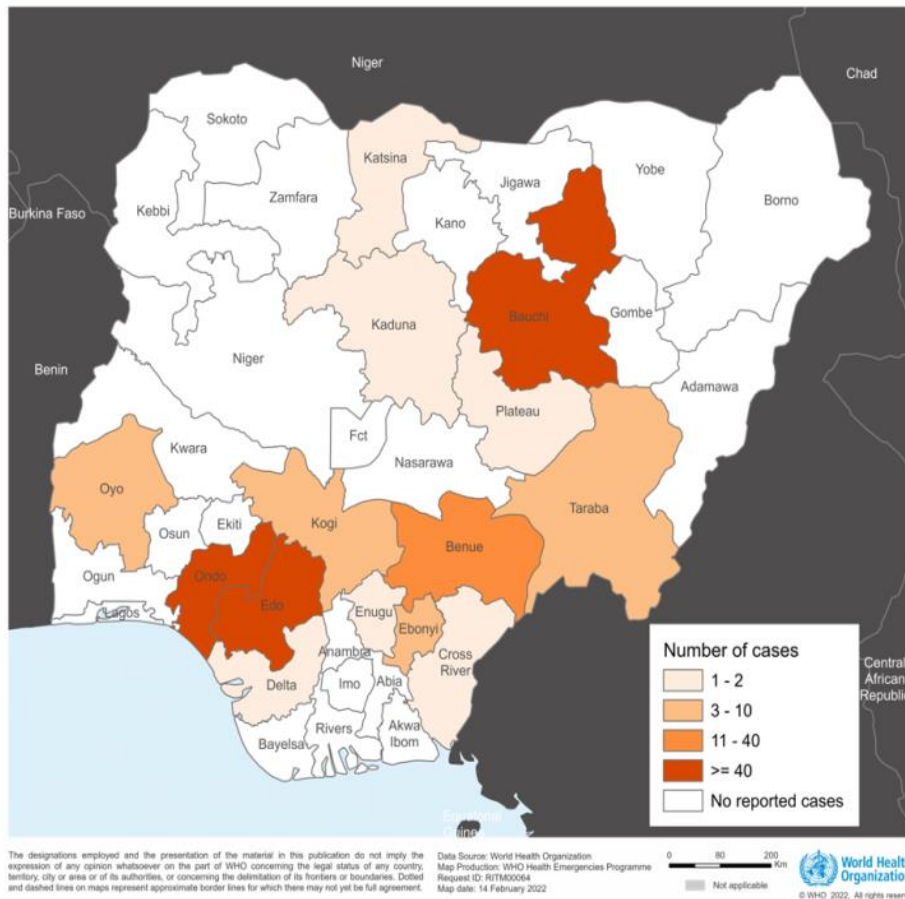


Figure 1: Map of Nigeria showing the number of Lassa fever cases across different states in January, 2022 (Source; World Health Organization (14 February 2022). Disease Outbreak News; Lassa Fever-Nigeria).

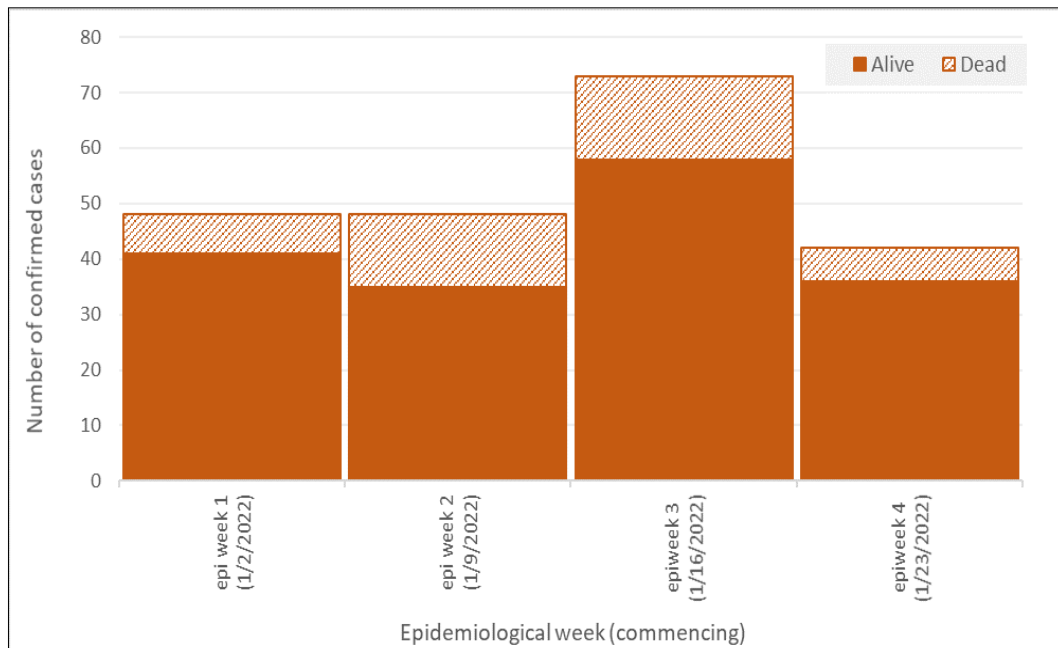


Figure 2: Weekly number of reported confirmed Lassa fever cases and deaths in Nigeria during the epidemiological weeks one through four in 2022

(Source; World Health Organization (14 February 2022). Disease Outbreak News; Lassa Fever-Nigeria).

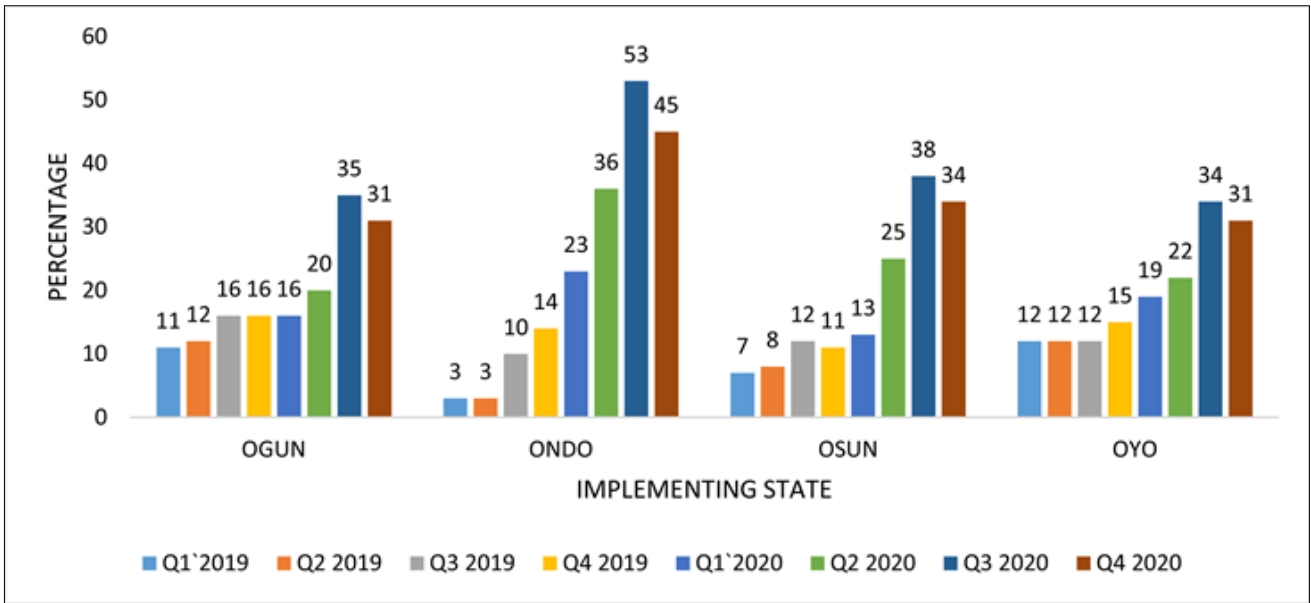


Figure 3: Quarterly contributions of Global Fund Private Public Mix (GF PPM) total state TB notification on four states in South West Nigeria. 2019-2020.

(Source: Journal of Tuberculosis Research > Vol.9 No.3, September 2021).

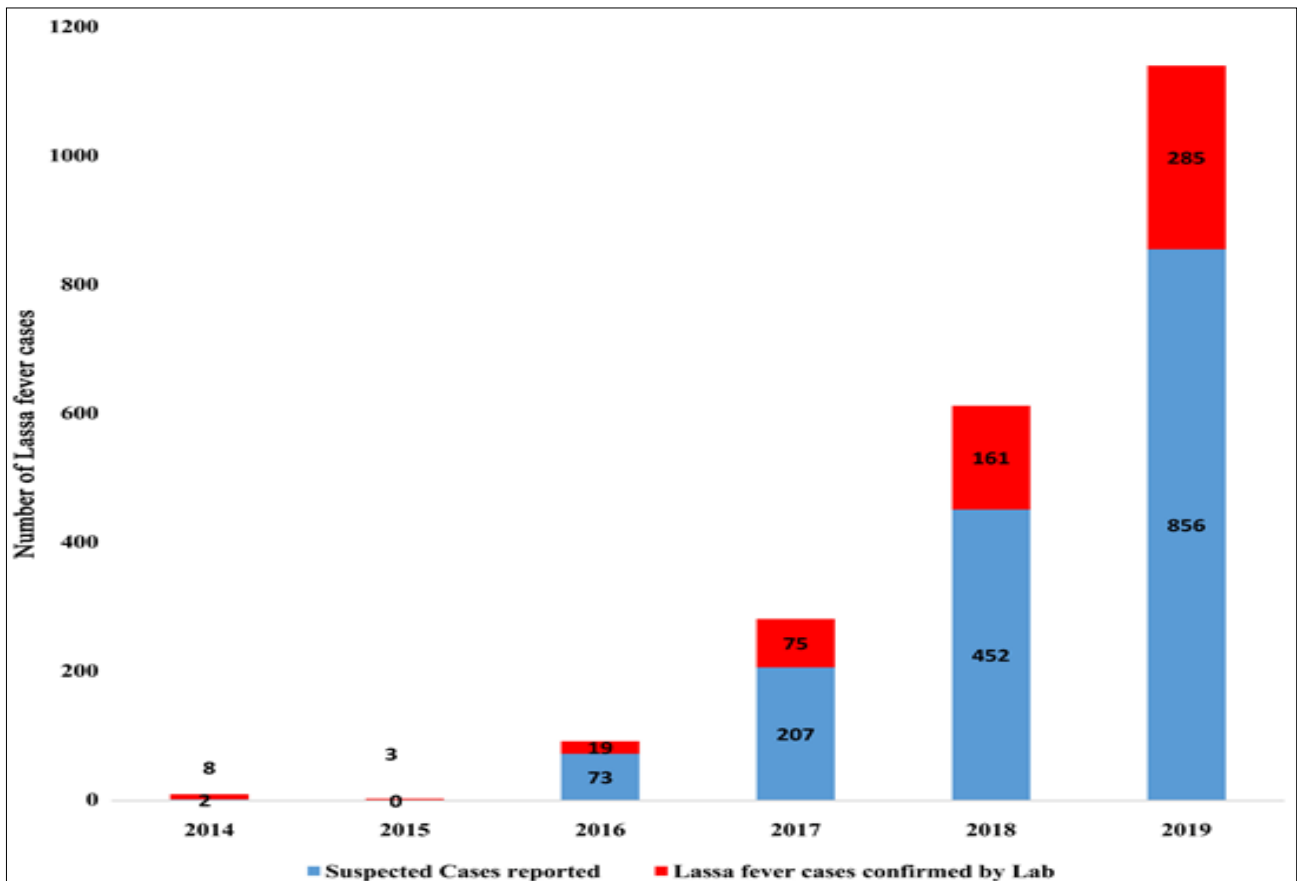


Figure 4: A chart of suspected and confirmed Lassa fever cases in Ondo state, Nigeria, from 2014 to 2019.

(Source: Elvis Efe Isere et al Scientific research; Epidemiological Pattern of Lassa Fever Outbreak in Ondo State, Southwest Nigeria, 2014 to 2019).

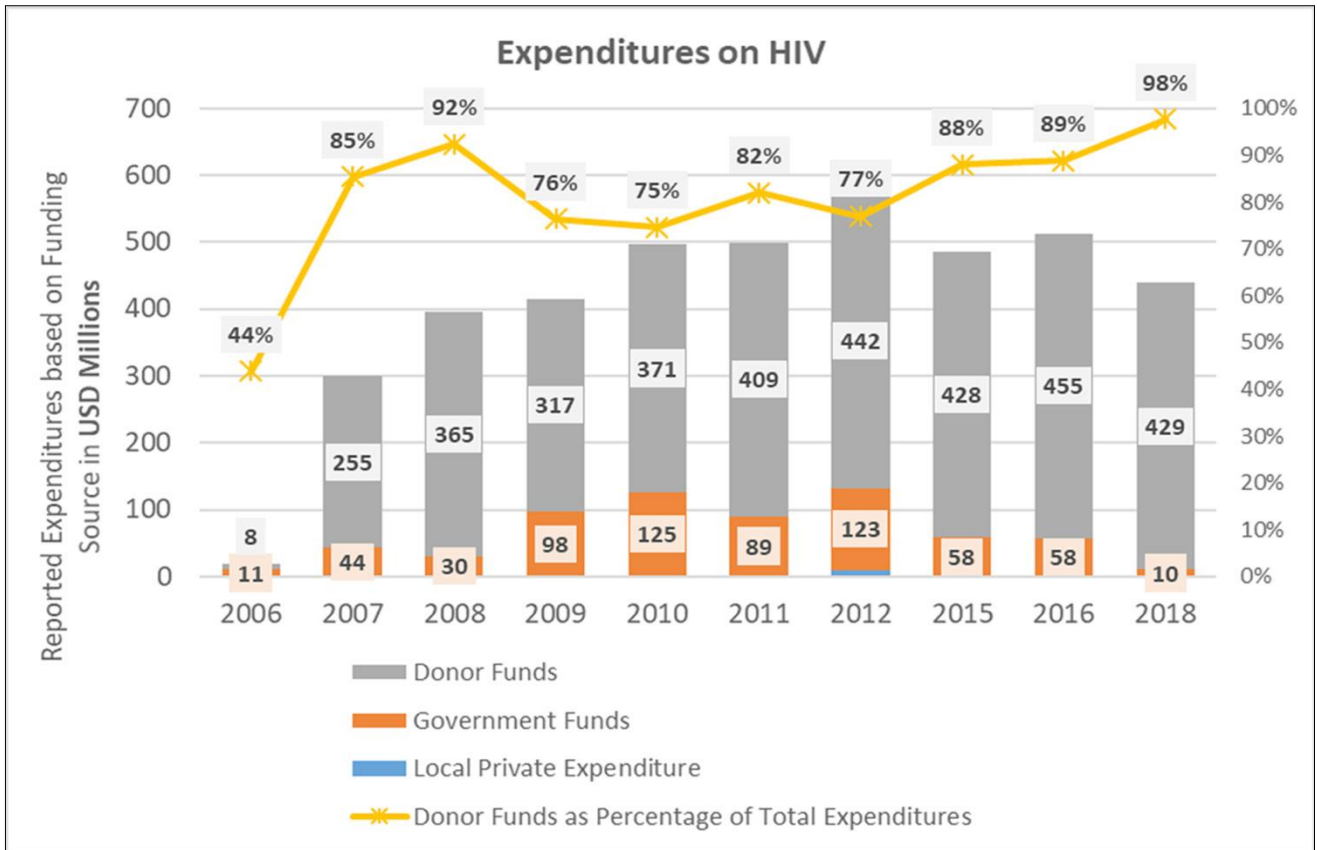


Figure 5: HIV expenditures from all funding sources, Nigeria, 2006–2018.

(Source: UNAIDS HIV Financial Dashboard - <http://hivfinancial.unaids.org/hivfinancialdashboards.html#>).

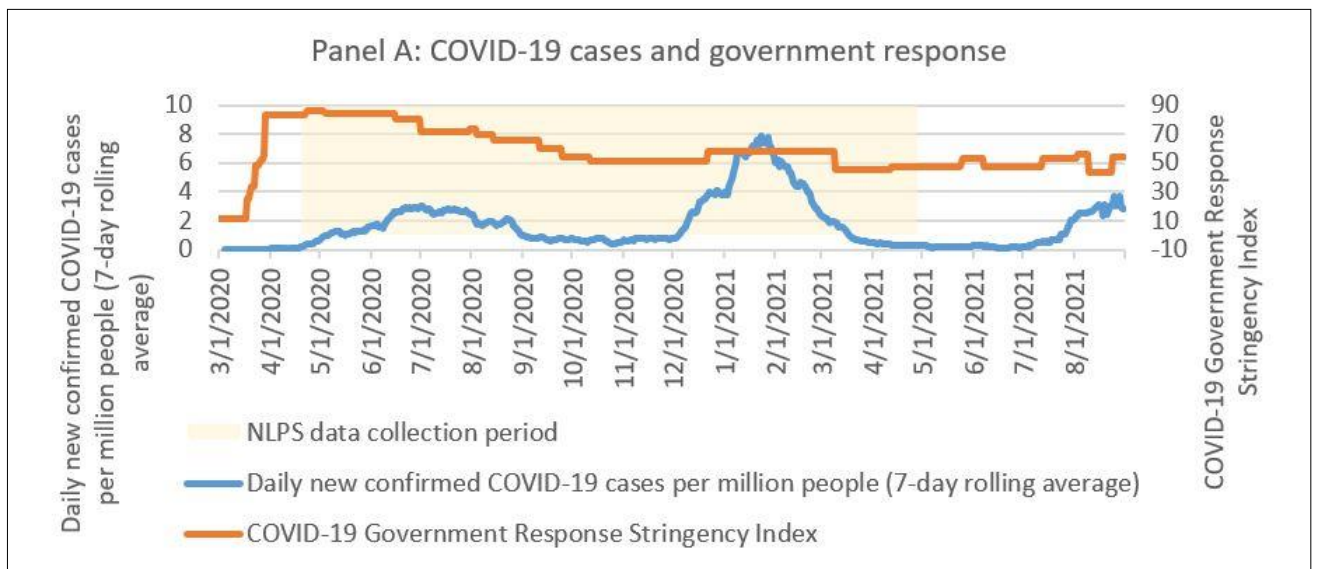


Figure 6: Government response to COVID on COVID-19 cases between March 2020 and August 2021.

(Source; worldbank.org).

PROACTIVE MEASURES TO BE TAKEN BY GOVERNMENT

The following measures should be carried out by the three tiers of government, communities and individuals to stem

down the incidence of these co-infections: a national response plan should be integrated into the National Health Insurance Scheme (NHIS) to help control and manage future resurgence of COVID-19 and other emergent disease; government at various levels of governance should provide preventive and control measures in all

public arenas in preparedness for any other impending epidemic; the government should create awareness and sensitize the general public on the dangers of these diseases, and necessary measures they should take to prevent themselves from getting infected, and this should be done from time to time on a regular basis; National health Insurance schemes should be structured and well-funded at national, state, and local government levels in Nigeria to provide proper support for the management of these diseases; trust funds should be organized to support and encourage the treatment of the epidemics in Nigerian hospitals; the national health policy should be expanded to accommodate these emerging diseases with clear strategies for funding so as to tackle this menace; all medical professionals/healthcare providers in the health sector should be provided with personal protective equipment (PPE) in times of emergent epidemics and they should apply standard infection prevention and control (IPC) measures when caring for individuals, regardless of their presumed diagnosis; samples taken for diagnosis from suspected patients with these co-infections should be handled by trained staff and processed in suitably equipped laboratories under maximum biological containment conditions; more researches are needed to be carried out and regular disease surveillance should be done for seasonal outbreaks to explore and improve the management of the coexistence of these epidemics; and political leaders and policy makers should be beckoned on to make sure control of COVID-19 and co-infection are included in the national health policy to strengthen the health system through proper budgeting funding.

CONCLUSION

The COVID-19 pandemic has been a challenging experience in Nigeria and has brought major changes in the public health response to infectious disease outbreaks in Nigeria and throughout the globe. There is lack of sufficient medical services, personnel and we have poor medical emergencies to meet up with the present epidemic and co-infections. The economic meltdown, social crisis and morbidities experienced during the COVID-19 crisis has awakened our consciousness to see the need for urgent attention and proper measures to be adequately put in place and a huge responsibility lies on the government.

In the future, the potential of overwhelming COVID-19 as well as other epidemic is still imminent in Nigeria and could lead to a major crisis within the country, especially to people with HIV, TB and LF. Therefore, public health control measures must be strictly adhered to. Generally, in sub-Saharan region, particularly in Nigeria, government of the three tiers should brace up to their responsibilities since we are sitting on a time bomb. It is imperative to focus on preventive strategies to alleviate the spread of these epidemics as it is a key concern. There is a need for public health interventions by conducting trainings and administering vaccinations among the vulnerable groups including health care workers who serve as front liners during case investigation, testing and care management.

Finally, the control efforts of the various programs must be maintained during COVID-19 or else Nigeria could see a resurgence and subsequently a combined catastrophe across the country.

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