

# The Resurgence of Yellow Fever in Oyo State, Nigeria: What's the Missing Link?

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## Research Article

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# Abstract

## Background:

Yellow Fever is an acute viral hemorrhagic disease endemic in tropical Africa and Latin America and transmitted through infected mosquitoes. The renewed onset of yellow fever outbreaks in Nigeria followed a global trend of reports and from other African countries marking the emergence of yellow fever as a brand-new re-emerging global threat in 2016 with giant outbreaks of yellow fever reports in Angola and the Democratic Republic of Congo. Nigeria has been battling successive yellow fever resurgence since September 2017. Yellow Fever disease has no cure, but control is through vaccination and vector control. Eliminating Yellow fever Epidemic (EYE) strategy to improve high risk countries' prevention, preparedness, detection, management and response to yellow fever outbreaks was developed by WHO in 2017 and launched in Nigeria in April 2018. Yet, poor vaccination coverage continues to be a cause for concern.

## Materials and Methods:

We conducted a retrospective cross-sectional study that examines the resurgence of Yellow fever cases and outbreaks from 2013-2020 in Oyo State, Nigeria. The Yellow Fever data for both surveillance and immunization were the focus of the review. Surveillance data were retrieved from the State's database reported by all 33 LGAs, maintained by the State and supported by the World Health Organization at the Zonal and State levels. The immunization data were retrieved from District Health Information Software (DHIS\_2). The proportion of LGAs reporting at least one case of suspected yellow fever with blood specimen, and the number of suspected cases reported for each year within the period under review was measured. We also assessed the trend of confirmed cases, and the incidence per 100,000 population. Also, suspected cases of yellow fever were categorized into four age groups and their vaccination status assessed. The State's annual administrative vaccination coverage for yellow fever vaccine was compared with the number of confirmed cases for each year.

## Results:

The proportion of LGAs reporting at least a case of suspected yellow fever, with blood sample collected, ranged from 6.1% to 84.9% between 2014 and 2020 while a total of 9 confirmed (8 cases) and probable (1 case) cases of yellow fever were recorded. However, there were no confirmed cases from the year 2013 to 2016, including 2018 but upward trend of incidence of the disease per 100,000 population from 0% in 2013 through 2018, to 3.5% in 2019 and then to 5.6% in 2020 was observed. 93 of 240 (39%) suspected yellow fever cases reported during the given period were observed to have received yellow fever vaccine

## Conclusion:

In conclusion, the resurgence of yellow fever cases in the State reiterate the State being high risk for yellow fever transmission and underline the need for viable interventions such as environmental hygiene to rid the environment of the disease vector's ecological niche and improving vaccination coverage to provide population immunity.

# Introduction

Yellow Fever is an acute viral hemorrhagic disease caused by single stranded RNA virus belonging to the genus flaviviridae. It is endemic in tropical Africa as well as Central and South America and transmitted through infected

mosquitoes (1). *Aedes* sp is mostly responsible for spread in Africa while the *Aedes*, *Haemagogus* and *Sabethes* spp are responsible in the South America (2). There are three transmission cycles of spread of the disease, the Jungle also referred to as Sylvatic, Intermediate, also called Savannah and the Urban transmission cycles. For the Jungle cycle, the vector, *Aedes* sp, *Haemagogus*/ *Sabethes* spp mosquitoes in the forest bite monkeys, which are primary reservoir of the yellow Fever virus and spread the virus between monkeys. Intermediate transmission cycle, common in Africa, involve infected mosquitoes biting humans that work or live close to forests while for the urban cycle, majorly responsible for sustained outbreaks, spread is from infected persons to other persons via same vector. (3, 4).

In Africa endemic areas, there is increased natural immunity with age, thus infants and children are at highest risk of infection whereas in the Americas, most cases reported were unimmunized men believed to be exposed to infected mosquitoes while working in forested areas. (2).

The global burden of Yellow Fever is estimated at 200,000 cases and 30,000 deaths annually with case fatality that may be as high as 50% in untreated severely affected (5) and Africa is said to accounts for greater than 90% of this burden (2).

The earliest reported Yellow Fever outbreak in Nigeria was in 1864 and between 1865 and 1996, the country continues to record outbreaks. After 21 years of no confirmed yellow fever case, a resurgence of yellow fever outbreaks was documented (6) in 2017, with recorded confirmed case within the Ifelodun Local Government Area (LGA) of Kwara State. These renewed onset of yellow fever outbreaks in Nigeria followed a global trend of reports from other African countries marking the emergence of yellow fever as a brand-new re-emerging global threat in 2016 (7). Giant outbreaks of yellow fever were reported in Angola and the Democratic Republic of Congo which highlighted the gaps and challenges of surveillance, rapid diagnosis due to lack of Medical Laboratory capacity and availability of global vaccine stockpiles resulting in poor routine vaccination coverage (7). In addition, factors like porous borders and increased migration, the widespread distribution of *Aedes* mosquitoes and lack of efficient health policies and surveillance system, favour this complex epidemiological scenario of reemergence yellow fever (7).

The last decade show marked increase in the number of reported Yellow Fever outbreaks in the country with widespread viral transmission to many States between 2017 and 2019. In 2019 alone, 13 of the 36 States in Nigeria including Oyo State recorded at least one confirmed yellow fever case. (3).

Currently, there is no cure for Yellow Fever disease, but treatment by management of presenting complains, signs and symptoms and infection prevention and control through vaccination and vector control is the main method to prevent spread of the virus (8). There is availability of safe and highly effective yellow fever vaccine usually given routinely to infants at 9 months and emergency vaccination of population at risk during outbreaks, as well as to travelers to high risk areas to curtail the spread of the virus. A single dose of the vaccine provides effective immunity within 30 days of vaccination for 99% of vaccinee, conferring sustained immunity with life-long protection. (1). However, poor vaccination coverages continue to put a lot of population at risk of the disease especially in Africa.

Yellow Fever vaccination coverage in West African Countries under French rule was estimated to be over 80% as at 1960 with mandatory vaccination introduced by France (9), susceptible population however continue to grow after the Independence of these countries. It is noteworthy that other countries in the region are not included in the

mandatory vaccination. Estimations from study conducted by Shearer et al. (10) in 2017 shows increasing coverages since 1970, though with notable gaps within yellow fever risk zones, with about 472 million people still requiring yellow fever vaccination in high risk areas. Results from the rapid yellow fever vaccination coverage assessment carried out in Kwara State Nigeria following the confirmed case in 2017 produce a 46% yellow fever coverage in the LGAs. (6).

In 2017, World Health Organization developed the Eliminating Yellow fever Epidemic (EYE) strategy to improve high risk countries' prevention, preparedness, detection, management and response to yellow fever outbreaks. This was launched in April 2018 and Nigeria is considered as one of the high-risk countries for yellow fever disease in Africa (11).

This paper describes incidence and trend of yellow fever cases between 2013 and 2020 and examine the role of immunization coverage and quality of surveillance in the resurgence of yellow fever in Oyo state, after decades without an outbreak.

## Methodology

We conducted a retrospective cross-sectional study that examines the incidence and resurgence of Yellow fever outbreaks and immunization coverages from 2013-2020 in Oyo State, Nigeria

### Study area

Oyo State is in the South-West geopolitical zone of Nigeria with Ibadan city as her capital. The State is located in the Southern Guinea Savannah region characterized by trees and grasses with rainy season which lasts at least 7 months yearly. Oyo State has 33 Local Governments Areas (LGAs) and 29 Local Council Development Areas and a projected population of 9,233,010 with annual growth rate of 3.2 (12). The State is bounded to the North by Kwara State, to the East by Osun State and Southwest by Ogun State and the Republic of Benin.

### Data extraction

We reviewed the data for the state with primary focus on surveillance and immunization. Surveillance data were retrieved from the state's database reported by all 33 LGAs, maintained by the State and supported by the World Health Organization at the Zonal and State levels. Immunization data were retrieved from District Health Information Software 2 (DHIS2) platform for the state.

The study made use of already collected data from the yellow fever case-based surveillance system between January 2013 and December 2020. In this surveillance system, definition of suspected yellow fever is any person with acute onset of fever, with jaundice appearing within 14 days of onset of the first symptoms and a probable case is a suspected case that is epidemiologically linked to a confirmed case/ an outbreak or with positive post-mortem liver histopathology or both. Reported suspected case within the IDSR were investigated. Case investigation form is used to collect information about such cases. Blood samples are collected from the suspected cases with cases information collected on the standardized laboratory form. Serum were separated from the blood samples and sent to the accredited National laboratory with appropriately filled forms for testing. Presumptive positive and inconclusive samples are sent to yellow fever reference laboratory Institute Pasteur in Dakar (IPD) for confirmatory testing.

The routinely collected immunization data on DHIS2 was retrieved for Oyo State and the vaccination status of all the suspected cases were assessed through the surveillance system database.

**Measurements**

We measured the proportion of LGAs reporting at least one case of suspected yellow fever with blood specimen, and the number of suspected cases reported for each year within the period under review. We also assessed the trend of confirmed cases, and the incidence per 100,000 population. Also, suspected cases of yellow fever were categorized into four age groups and their vaccination status assessed.

In addition, we also retrieved the data on annual administrative vaccination coverage for yellow fever vaccine, juxtaposing it with the number of confirmed cases for each year during the period under review.

**Results**

**Table 1 shows Age Distribution of Suspected Yellow Fever and Surveillance Performance 2013-2020.**

The proportion of LGAs reporting at least a case of suspected yellow fever, with blood sample collected, ranged from 6.1% to 84.9% between 2014 and 2020. The findings further indicate a positive directional movement and upward trend was observed from 2014 to 2019. The year 2020 however had report of suspected yellow fever case from 75.8% of LGAs in the State.

Overall, the lowest number, only 2 cases, of suspected yellow fever cases were recorded in 2014 while the highest, 94 suspected cases were recorded in 2019. A decline was observed in 2020 with only 51 suspected cases reported, though still considerably higher than other years.

In the period under review, a total of 9 confirmed (8cases) and probable (1 case) cases of yellow fever were recorded. However, there were no confirmed cases from the year 2013 to 2016, including 2018. One Probable case was recorded in the State in 2017 before the surge in 2019 to 2020, thus indicating an upward trend, which could also be observed in the upward trend of incidence of the disease per 100,000 population from 0% in 2013 through 2018, to 3.5% in 2019 and then to 5.6% in 2020.

The age group 15 years+ was observed to have the highest number of reported suspected Yellow Fever cases for each year from 2013 to 2020, with a total of 125 cases, accounting for 52% of all suspected cases reported. The descending order in number of cases for the specified age groups was observed as 15 years+, 5 – 9 years, <5 years, with the age group 10 – 14 years being the least with 31 suspected cases reported.

**Table 2 illustrates the Vaccination Status of suspected yellow fever cases 2013 to 2020.**

The vaccination status was classified into 3 categories: vaccinated, unvaccinated and unknown.

In total, 93 of 240 (39%) suspected yellow fever cases reported during the given period were observed to have received yellow fever vaccine. Furthermore, 61 of the 240 (25%) were unvaccinated, and 86 (36%) had unknown vaccination status. At least, half of the suspected yellow fever cases reported in the year 2013 to 2016 had received yellow fever vaccine while less than 50% of suspected cases in 2017 to 2020 had been vaccinated against Yellow Fever with year 2017 and 2020 recording only about a quarter 26% and 22% respectively, of all suspected cases who had received Yellow Fever vaccine.

**Figure 1 indicates the number of confirmed yellow fever cases and the annual administrative vaccination coverage 2013 to 2020.**

According to the data collected, a total of 8 confirmed and 1 probable cases of yellow fever were recorded. The highest number of confirmed cases, 5 cases, was recorded in the same year, 2020 which happens to have the lowest (41%) annual administrative coverage, followed closely by 2013 with 42% yellow fever annual routine immunization administrative coverage. Greater than 65% annual coverage was reported in 2014 to 2019.

## Discussion

In recent years, there has been increase in the suspected and confirmed yellow fever cases in Oyo state. From 2016, there has been a gradual increase in the number of suspected cases and the proportion of LGAs reporting at least a suspected case with blood sample collected, which is an indication of improved surveillance system. The highest number of cases, 94 and the highest proportion of LGAs reporting, 84.9% were both recorded in 2019. The gradual increase could be linked with an increasing capacity of surveillance officers, expansion of the surveillance network characterized by the inclusion of assistant disease surveillance and notification officers as well as an increase in the number of community informants at the LGA level, and provision of incentives to other components of the surveillance system. These interventions have increased the sensitivity of the surveillance system to detect cases of Yellow fever in health facilities and the community. In addition, the visit of the African Regional Certification Committee (ARCC) in 2019 to the country and state led to the conduct of a number of key surveillance activities such as intensified active case search, and intensified and extensive sensitization activities, which increased the sensitivity of the surveillance system.

After many years of no confirmed yellow fever case in Oyo State, a probable case was recorded in 2017 and this coincide with the same period for the same year of Nigeria's first confirmed case in 21 years (13) which was reported in neighboring Kwara State. Then followed another 3 confirmed cases in year 2019 and yet another 5 new cases in 2020 with incidence rate per 100000 population rising from 0% in 2013 to 3.5% in 2019 and 5.6% in 2020. Though the year 2019 had 12 other States in Nigeria recording yellow fever outbreaks (3), most of which were linked to the Yankari game reserve in Bauchi State, but majority of the State are Northern parts of the Country, nonetheless, Oyo State was one of the few Southern Nigeria States that recorded an outbreak. All these points at the re-emergence of the disease in the State and an indication of Oyo State being high risk for Yellow fever transmission.

In the period under review, the most affected age group was observed to be above 15 years. This could also be as a result of the level of exposure of individuals in this age group to the disease vector as observed in Delta and Enugu state. On the contrary, findings from the Kwara state outbreak in 2017 show that individuals below 15 years (55%) were mostly affected (13). Children below the age of 10 years accounted for 35 % of all reported suspected cases between 2013 and 2015 and this is similar with observation by Tomashek et al, 2019 that due to increasing natural immunity with age in Africa, infants and children are often mostly affected during yellow fever outbreaks. This is especially important because children can most likely be the major unprotected group in areas with poor yellow fever routine immunization coverage and especially the unprotected cohort where preventive or reactive mass yellow fever vaccination campaign had previously been conducted.

Furthermore, it was observed that 3 out of the confirmed cases in 2020 were domiciled in agrarian communities. This is a major factor affecting level of exposure to the disease vector and is in tandem with findings from the

outbreak reported in Delta and Enugu state in 2020 (14) with majority of the cases being farmers. In addition, it was observed that males were more affected than females. This could be directly linked to the farming occupation and by extension, higher level of exposure of the males to the ecological niche of the disease vector. This is in sync with the 7894 cases reported in 20 states in the country from September 2017 to October 2019, with 57% being males. Findings from Brazil between 2017 and 2018 (15) also show that majority of those affected were males.

The vaccination status of all suspected cases between 2013 and 2020 was assessed and it was observed that only 39% of all suspected cases were vaccinated with at least 1 dose of yellow fever vaccine. This could be linked to the number of confirmed cases detected. Furthermore, with WHO recommendation of 60% to 80% vaccination coverage to prevent outbreaks (8), a comparison of the yellow fever vaccination coverages for each year in the period under review with the laboratory confirmed cases was conducted in a bid to assess a link between both parameters. The finding revealed that the highest number of laboratory confirmed cases were recorded in 2020, which was the year with the lowest vaccination coverage (41%). This is not surprising, as previous findings follow similar pattern (6) and the yellow fever vaccine is said to be highly efficacious, conferring life-long immunity to 99% of persons vaccinated (8). The low vaccination coverage and high number of confirmed cases recorded in 2020 is largely linked to the disruption of service delivery, immunization and health education on hygiene and vector control inclusive, due to the COVID-19 pandemic. The pandemic can thus be said to have contributed to outbreaks of other diseases including yellow fever in the country.

Greater than 65% annual yellow fever vaccination coverage was reported in 2014 to 2019, yet there was record of yellow fever outbreak in 2019. This may be because the vaccination data available for this study was that of the routine immunization data for the under 1/ under 2 years of age and so vaccination coverage for the whole population at risk may be less than the recommended 60-80% which can prevent occurrence of outbreaks (5) and less than 80% that should prevent viral transmission (1). This is a limitation of this work and future studies may incorporate data from the recently concluded mass yellow fever vaccination campaign and travelers' yellow fever vaccination data.

In conclusion, the resurgence of yellow fever cases in the period under review in the State reiterate the State being high risk for yellow fever transmission and underline the need for viable interventions such as environmental hygiene in a bid to rid the environment of the disease vector's ecological niche and improving vaccination coverage to provide population immunity. Another alternative to improve immunization coverage may be to make the vaccine available at strategic locations at no cost to people above 2 years old who may have missed being vaccinated during mass vaccination campaigns. In addition, the introduction of a second dose of the yellow fever vaccine targeted to boost the immunity of individuals previously vaccinated could be essential in reducing the incidence of positive cases of yellow fever particularly in endemic areas, as there has been debates on seroconversion rates after yellow fever vaccination, waning immunity and primary vaccine failure. (15).

## Abbreviations

ARCC: African Regional Certification Committee; EYE: Eliminating Yellow fever Epidemic; WHO: World Health Organization; (DHIS2): District Health Information Software 2; LGAs: Local Government Areas; RNA: Ribonucleic acid; IDSR: Integrated Disease Surveillance and Response; IPDs: Institute Pasteur in Dakar; COVID-19: Coronavirus Disease 2019.

# Declarations

## Ethics approval and consent to participate

The analysis for this work is based on secondary data. This data is available at the WHO server [api.who.int/whohub](https://api.who.int/whohub) and permission was given by WHO country office. Data collected, collated and used were readily accessed from the available database for yellow fever surveillance and DHIS2.

## Consent for publication.

Not Applicable

## Availability of data and materials

The data were generated as part of the activities supporting disease surveillance and routine immunization in Nigeria. The data are kept at the WHO server and are subject to protection.

## Competing Interests

The authors declare that they have no competing interests.

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This work did not receive funding from any organization

## Authors' Contributions

BEB and OAI conceived and led the study design, interpretation of results, and manuscript conceptualization and preparation. FB RO, OOK, MO, AO, AAT, and OSO, reviewed the first draft BEB, OAI, OSO conducted a systematic literature review data management and interpretation, and manuscript conceptualization. All authors read and approved the final manuscript.

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## Tables

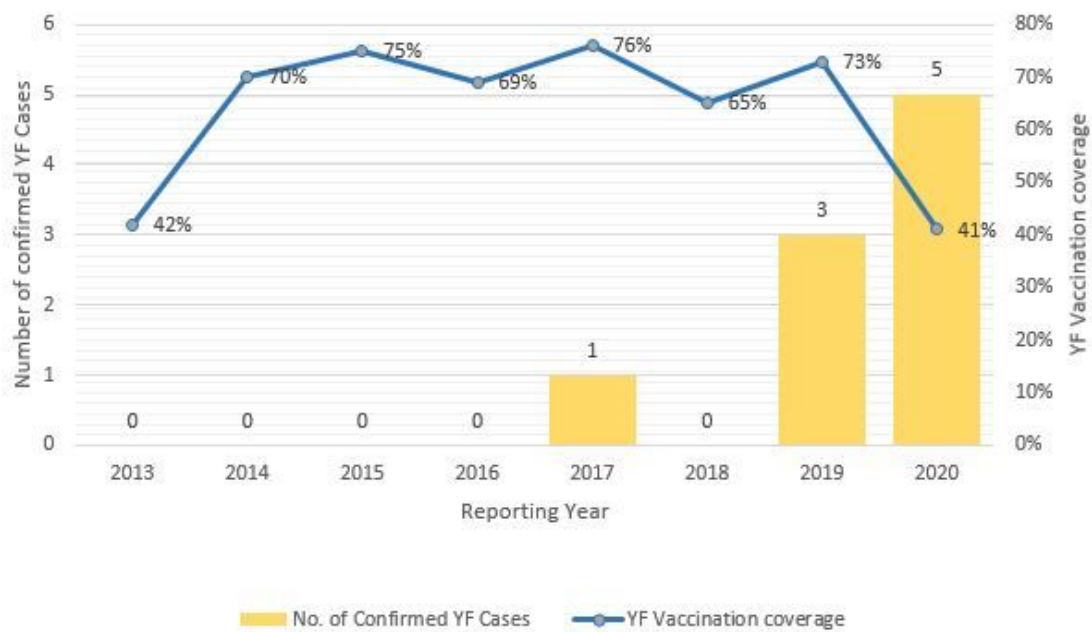
**Table 1: Surveillance Performance and Age Distribution of Suspected Yellow Fever 2013-2020**

<i>Parameter</i>	<i>2013</i>	<i>2014</i>	<i>2015</i>	<i>2016</i>	<i>2017</i>	<i>2018</i>	<i>2019</i>	<i>2020</i>
<b>Basic Indicators</b>								
Proportion of LGAs reporting at least 1 case with blood specimen	15.2%	6.1%	33.3%	18.2%	39.4%	51.5%	84.9%	75.8%
Number of suspected YF Cases	6	2	20	8	19	40	94	51
Probable YF Cases	0	0	0	0	1	0	0*	0*
Confirmed YF Cases	0	0	0	0	0	0	3	5
Incidence per 100,000 population	0	0	0	0	0	0	3.5	5.6
<b>Age Groups</b>								
< 5 years	2	0	3	3	4	3	20	6
5 - 9 years	0	0	5	1	2	8	18	9
10 - 14 years	1	1	3	1	2	8	10	5
15 years +	3	1	9	3	11	21	46	31

**Table 2: Vaccination Status of Suspected Yellow Fever Cases 2013-2020**

Status	2013	2014	2015	2016	2017	2018	2019	2020	Cumulative	Proportion
Vaccinated	3	1	15	6	5	18	34	11	93	39%
Unvaccinated	3	1	5	2	14	5	12	19	61	25%
Unknown	0	0	0	0	0	17	48	21	86	36%
Proportion of vaccinated	50%	50%	75%	75%	26%	45%	36%	22%	39%	

## Figures



**Figure 1**

indicates the number of confirmed yellow fever cases and the annual administrative vaccination coverage 2013 to 2020