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Current Trends of Yellow Fever in Nigeria: Challenges and Prospects

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Abstract

Yellow fever is a viral infection caused by yellow fever virus and is spread by the bite of an infected female mosquito (Aedes and Haemogogus species). The evolutionary origin of yellow fever lies in Africa, with transmission of the disease from nonhuman primates to human. Yellow fever remains a disease of significant public health importance. The earliest outbreak of yellow fever in Nigeria was reported in Lagos in 1864 with subsequent regular outbreaks reported until 1996 following which Nigeria has been responding to successive outbreaks. Since 15th September 2017, when the Nigeria Centre for Disease Control (NCDC) officially notified a confirmed case of yellow fever in Kwara state to WHO as per the International Health Regulations (2005). Currently the country has been responding to successive yellow fever outbreaks over a wide geographic area. As such, four-year (2018-2021) national yellow fever Preventive Mass Vaccination Campaign (PMVC) plan, supported by the Global Alliance for Vaccines and Immunization (GAVI) and partners, is currently being implemented to cover all states in the country. By 2025, it is anticipated that all states in Nigeria will have conducted PMVC activities to protect at-risk populations against yellow fever.

Keywords: *Yellow Fever, Mosquito, Outbreak, Vaccine and Challenges.*

INTRODUCTION

Yellow fever is a viral of typical short duration. The infection is caused by yellow fever virus and is spread by the bite of an infected female mosquito. Once infected, management is symptomatic with no specific measure effective against the virus and the death occurs in up to half of those who get severe disease (WHO, 2013). The evolutionary origins of yellow fever lies in Africa, with transmission of the disease from non-human primates to human. The virus is thought to have originated in East or Central Africa and it was endemic, the native have developed some immunity to it (Gould *et al.*, 2009). Yellow fever remains a disease of significant public health importance despite the availability of a safe and efficacious vaccine with an estimate of 200,000 cases and 30,000 deaths annually globally. A considerable epidemic occurs when people infected with the virus introduce it into densely populated areas with high mosquito density and where most people have little or no immunity from vaccination or prior infection.

The earliest outbreak of yellow fever in Nigeria was reported in Lagos in 1864 with subsequent regular outbreaks reported until 1996. For 21 years, no further confirmed cases were reported until September 2017 following which Nigeria has been responding to successive outbreaks. Yellow fever is an epidemic prone disease for immediate disease surveillance and response (IDSR) platform in Nigeria (Tomori, 2002).

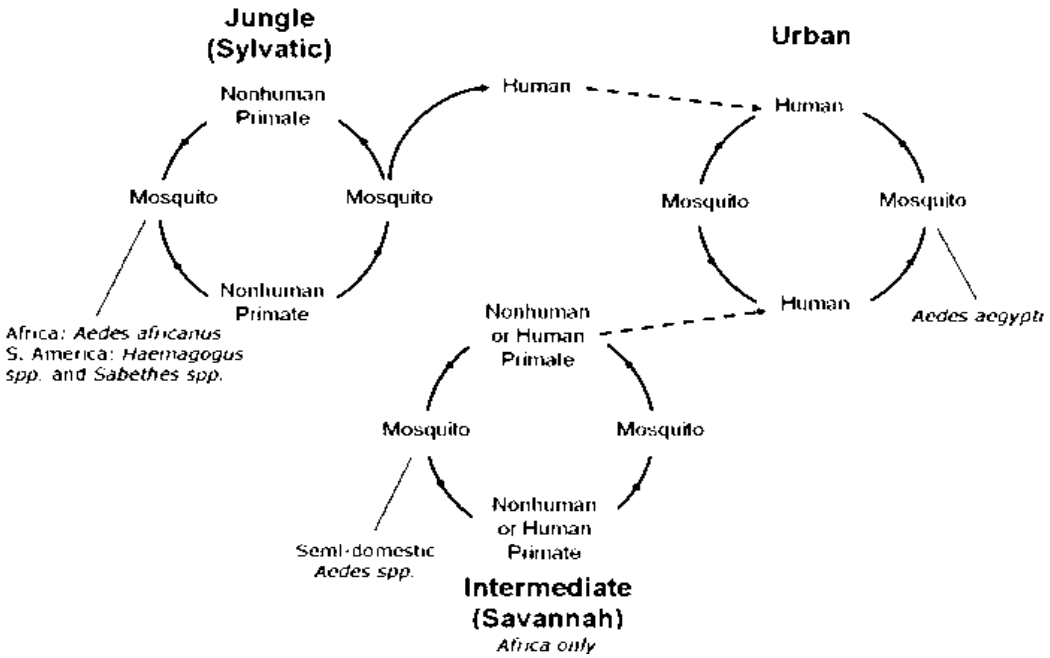
Pathogenesis of Yellow Fever Virus

Yellow fever is caused by yellow fever virus and enveloped RNA virus, 40-50mm in width; the species belong to the family flavivirdae. The positive-sense-single stranded RNA is around 11,000 nucleotides long and has a single open reading frame encoding a polyprotein (Siva and Patrica, 2010). Yellow fever belongs to the group of hemorrhagic fever and the viruses infect amongst others, monocytes, macrophages, Schwann cell and dendritica cell. The viruses attach to the cell surface via specific receptors and are taken up by an endosomal vesicle. Inside the endosome, the decreased pH induces the fusion of the endosomal membrane with the virus envelope. The capsid enters the cytosol, decays, and releases the genome (Dhiman *et al.*, 2019).

After entering the host cell, the viral genome is replicated in the rough endoplasmic reticulum (ER), at first are immature form of the viral particles produced inside the ER, whose m-protein is not yet cleared to its mature form so is denoted as precursor metabolite (prm) and forms a complex with protein E. the immature particles are processed in the Golgi apparatus by the host protein, which cleave prm to mature and releases ER from the complex which can now take its place in the mature infectious virus (Sampath and padmanabhan, 2009).

Mode of Transmission of Yellow Fever

Yellow fever virus is transmitted by mosquitoes (both Aedes and Haemogogus species) and has three transmission cycles, namely jungle (sylvatic), intermediate (savannah), and urban. The jungle/sylvatic cycle occurs in tropical rainforests where monkeys, which are the primary reservoir of the virus, are bitten by mosquitoes of the Aedes and Haemogogus species, passing the virus on to other monkeys. Occasionally humans working or travelling in the forest are bitten by infected mosquitoes and develop yellow fever. The intermediate/savannah cycle which is the most common in Africa involves transmission of virus from mosquitoes to humans living or working in jungle border areas. The virus can be transmitted from monkey to human or from human to human via mosquitoes. The urban cycle involves transmission of the virus between humans by urban mosquitoes, primarily Aedes aegypti. The virus is usually brought to the urban setting by a person who has been infected in the jungle or savannah (Barrett and Higgs, 2007). Transmission in Africa is maintained by a high density of Aedes mosquito populations that are in close proximity to largely unvaccinated human populations. Occasionally, infected travellers from areas where yellow fever occurs have exported cases to countries that are free of yellow fever (Fontenille *et al.*, 1997).



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Clinical features of yellow fever

Following infection, the virus incubates in the body for three to six days. Many people do not experience symptoms but when these occur they vary from mild, nonspecific, febrile illness to a fulminant, sometimes fatal disease. The clinical symptoms associated with the early stages of infection are indistinguishable from those of influenza or malaria, mainly fever, muscle pain backache, headache, loss of appetite and nausea or vomiting. In most cases, symptoms disappear after 3 to 4 days. A small percentage of patients, however, enter a second, more toxic phase within 24 hours of recovering from initial symptoms. High fever returns, and several body systems are affected, usually the liver and the kidneys, and also the heart and occasionally brain. In this phase people are likely to develop jaundice (yellowing of the skin and eyes), dark urine and abdominal pain with vomiting (Monath, 2008).

Bleeding can occur from orifices such as mouth, nose or eyes. Only 15 percent of people with yellow fever enter this phase, but of those that do, approximately half die within 7 - 10 days (WHO, 2016). Surviving the infection provides lifelong immunity (Modrow, *et al.*, 2002)and normally no permanent organ damage results (Rogers *et al.*, 2006).

Laboratory Diagnosis of yellow fever

It is clinically difficult to distinguish yellow fever from many other infectious diseases, and often impossible when the condition is mild or atypical. The diagnosis of yellow fever is made by detection of the virus or of its genetic material in serum or tissue, or by means of serological testing for the detection of antibodies. Polymerase chain reaction (PCR) testing in blood and urine can sometimes detect the virus in early stages of the disease. In later stages, testing to identify antibodies is needed. The necessary tests needed for laboratory confirmation of yellow fever during an outbreak are:

• Enzyme-linked immunosorbent assay (ELISA) to measure yellow fever virus IgM – a single positive gives an early diagnosis, with a rising titre over paired sera establishing recent infection from vaccination or cross-reaction with other viruses (WHO, 2016).

• If yellow fever is suspected, the virus cannot be confirmed until 6–10 days after the illness. A direct confirmation can be obtained by reverse transcription polymerase chain reaction (RT-PCR), where the genome of the virus is amplified (Tolle, 2009).

Treatment

There is currently no specific treatment for yellow fever. Early supportive treatment in hospitals including treating dehydration and under nutrition, management of metabolic acidosis, liver and kidney failure, and antibiotic treatment for secondary bacterial infections improves survival rates. Infection Prevention and Control (IPC) are usually adopted (WHO, 2016). Different methods for acute treatment of the disease have been shown not to be very successful; passive immunization after the emergence of symptoms is probably without effect. Ribavirin and other antiviral drugs, as well as treatment with interferons, do not have a positive effect in patients (Monath, 2008).

Prevention and control of yellow fever in Nigeria

Vaccination with the yellow fever vaccine provides life-long protection, and is the most important means of preventing yellow fever. Routine infant immunization and mass vaccination campaigns designed to increase coverage in countries at risk. Prompt recognition and control of outbreaks using mass vaccination is critical in high-risk areas where vaccination coverage is low. It is important to vaccinate most (80% or more) of the population at risk to prevent transmission. Therefore, prompt detection of yellow fever and rapid response through emergency vaccination campaigns are essential for controlling outbreaks (WHO, 2016).The risk of transmission in urban areas can be reduced by eliminating potential mosquito breeding sites e.g. places and containers where standing water collects. Vector surveillance and control are components of transmission control in epidemic situations. Targeting *Aedes aegypti* and other *Aedes* species in terms of vector surveillance will help inform where there is a risk of an urban outbreak. Vaccination of travellers going to yellow fever endemic areas makes them insusceptible host and therefore preventing the spread of the disease. Programmes for distribution of mosquito nets for use in homes provide reductions in cases of both malaria and yellow fever. Use of EPA-registered insect repellent is recommended when outdoors. Long-sleeved clothing, long pants, and socks are useful for prevention (CDC, 2016).

Factors Responsible for the Resurgence of Yellow Fever in Nigeria

Some of the factors responsible for the resurgence of yellow fever are;

- Collapse of health care delivery systems
- Poor or inadequate disease surveillance, inappropriate disease control measures
- Urban poverty with overcrowding and massive population movements,-poor environmental management and indiscriminate deforestation.
- Where an outbreak is promptly reported, confirmation of the clinical or presumptive diagnosis is generally impossible, because of the poor state of laboratory diagnostic facilities (Oyewale, 2002).

Current Trends of Yellow Fever in Nigeria

Since 15th September 2017, when the Nigeria Centre for Disease Control (NCDC) officially notified a confirmed case of yellow fever in Kwara state to WHO as per the International Health Regulations (2005), the country has been responding to successive yellow fever outbreaks over a wide geographic area (WHO, 2019). On 29 August 2019, a suspected yellow fever case was reported from Kano state with a travel history to Yankari game reserve, Alkaleri Local Government Area (LGA), Bauchi state, Nigeria.

From 29 August through 22 September 2019, Nigeria reported an outbreak of yellow fever with an epi-centre in the Yankari game reserve of Alkaleri LGA, Bauchi state. According to Nigeria Centre for Disease Control (NCDC), 231 suspected cases have been reported in four states including Bauchi (110), Borno (109), Gombe (10), and Kano (2), of which there have been 13 presumptive positive by IgM testing and 24 cases positive by reverse-transcriptase polymerase chain reaction (RT-PCR) at national laboratories. Of 24 cases confirmed by RT-PCR (20 cases in Bauchi, three in Gombe and one in Kano state), six deaths were reported, all from Alkaleri LGA, Bauchi state, resulting in a case fatality ratio of 25% among the confirmed cases. The vaccination history for the 231 suspected yellow fever cases is not known, and the results of follow-up testing from regional reference laboratory Institute Pasteur Dakar (IPD) are not yet available (WHO, 2019).

This is the first time that cases have been reported in relation to this area since the outbreak started in Nigeria in September 2017. This outbreak is unique in the broad geographic distribution of cases, most with linkage through travel, work or residence in, or close to, the Yankari game reserve, which is an ecological zone highly prone to yellow fever virus circulation (vectors, reservoir) (WHO, 2019).

From January to September 2019, a total of 2,254 suspected yellow fever cases have been reported in 535 LGA's. All states including Federal Capital Territory (FCT) have reported at least one suspected case of yellow fever. Samples have been collected for 2,197 suspected cases, and according to Nigerian laboratories 74 tests were presumptive positive and 29 inconclusive for yellow fever. A total of 103 (74 presumptive positive and 29 inconclusive) samples were sent to yellow fever reference laboratory Institute Pasteur in Dakar (IPD) for confirmatory testing, of which 29 tested positive. Eight additional cases were confirmed by the Nigerian laboratories including National Reference Laboratory (7), Lagos University Teaching Hospital (1). These 40 confirmed cases were from the states of Edo (13), Ebonyi (8), Ondo (4), Katsina, (23), Kebbi (2), Anambra (1), Cross River (1), Imo (1), Osun (1), Oyo (1), Kano (2), Gombe (3) and Sokoto (1). Forty-four (44) deaths have been recorded from the states of Katsina (66), Edo (1), Adamawa (1) and Ebonyi (26) with an overall CFR of 2% among suspected cases (NCDC; WHO, 2019).

On 4th November, 2019 an outbreak of yellow fever virus was reported with 10 mortality cases and more than 20 suspected cases in different communities of Ningi LGA, it was recalled that in October 2019, there was 22 cases of mortality in Alkaleri LGA of bauchi state (Hassan, 2019).

Table 1: Summary of Suspected, Confirmed and Mortality cases of yellow fever in Nigeria 2019.

S/N	States	Cases		
		Suspected	Confirmed	Mortality
1.	Edo	00	13	01
2.	Ebonyi	84	08	26
3.	Ondo	00	04	00
4.	Katsina	66	23	14
5.	Kebbi	00	02	00
6.	Anambra	00	01	00
7.	Cross River	00	01	00
8.	Imo	00	01	00
9.	Osun	00	01	00
10.	Oyo	00	01	00
11.	Kano	02	02	00
12.	Sokoto	00	01	00
13.	Bauchi	110	00	22
14.	Borno	109	00	00
15.	Gombe	10	03	00
16.	Adamawa	01	00	01
	Total	**382**	**61**	**64**

Public Health Response to Current Outbreak in Nigeria

The outbreak response activities are being coordinated by a multi-agency national yellow fever emergency operation Centre (EOC) hosted at NCDC. On 5th September, 2019, a national Incident Management System (IMS) was activated to coordinate the response activities.

A national rapid response team (RRT), including NCDC and National Primary Health Care development Agency (NPHCDA), have been deployed to Bauchi and other affected states to support outbreak response activities such as case finding, case management and risk communication. The state with the support of partners has successfully conducted a reactive yellow fever vaccination campaign in Alkaleri LGA and is now planning to conduct a similar campaign in contiguous LGAs across the affected states (WHO, 2019).

Challenges

Although the prospects are high, the challenges are enormous and require total commitment and focused strategies to overcome. These challenges include;

- **Mal-orientation of communities, politicians and health workers**

Many decision-makers and caregivers reject routine immunization due to rumour, incorrect information, and fear. Attempts to increase coverage must include awareness of people's attitudes and the influence of these on behaviour. Fears regarding routine immunization are expressed in many parts of Nigeria. Fathers of partially immunised children in Muslim rural communities in Lagos State see hidden motives linked with attempts by non-governmental organisations (NGOs) sponsored by unknown enemies in developed countries to reduce the local population and increase mortality rates among Nigerians. Belief in a secret immunization agenda is prevalent in Jigawa, Kano and Yobe States, where many believe activities are fuelled by Western countries determined to impose population control on local Muslim communities (Feilden, 2005; Yola, 2003).

- **Politicization of health issues**

Low and differential routine and supplemental immunization coverage below the threshold required for interruption of transmission. These immunity gaps allow viruses to persist in smaller areas and population sub-groups. The downward trend in the coverage of all the antigens appears to be associated with political problems. These political problems included low government commitment to ensure the fulfilment of EPI policy as well as over-centralization in the administration of EPI at the federal level of governance in Nigeria (Obioha *et al.*, 2010).Some positions offer potential for patronage due to the large payments for NID activities. This has led to political appointments and frequent changes in personnel as some LGA chairmen wish to bestow or repay political favours. Even at the state government level, increased political interference has been reported to be in the appointment of civil servants, also resulting in frequent changes of staff and the appointment of inappropriately qualified staff (Babalola and Adewuyi, 2005).

- **Influence of religion**

Very large population and high population growth rate with cultural, religious and geographical barriers. In Nigeria, the greatest challenge to the acceptance of immunization is a religious one especially among the northern Nigerian Muslims. Generally, the Muslim north has the low immunization coverage, the least being 6% (northwest) and the highest being 44.6% (southeast). In Ekiti state (southwest), for example, the northeast and west of Ekiti, with a stronger Islamic influence, has low immunization coverage and also poor educational attainment. Christians have 24.2% immunization coverage as compared to only 8.8% for Muslims (Ankrah and 2005).

- **Shortage of vaccines and immunization supplies**

Under the NPI's the first mandate is to "support the states and local governments in their immunization programmes by supplying vaccines, needles and syringes, cold chain equipment and other things and logistics as may be required for those programmes". However, the supply of vaccines has always been problematic for Nigeria, primarily because funds were not sufficient and were not released on time (FBA, 2005).

- The continuing cases of yellow fever (WHO, 2019).

Prospective Approach for Preventing Re-emergence of Yellow Fever in Nigeria

A four-year (2018-2021) national yellow fever Preventive Mass Vaccination Campaign (PMVC) plan, supported by the Global Alliance for Vaccines and Immunization (GAVI) and partners, is currently being implemented to cover all states in the country. By 2025, it is anticipated that all states in Nigeria will have conducted PMVC activities to protect at-risk populations against yellow fever (WHO, 2019).

This year's phased preventive campaigns will target the following states, Anambra, Ekiti, Katsina, and Rivers, with specialized activities in Borno. Bauchi has not yet been covered by the phased PMVCs, and the states planned for the next phase are undergoing through a review process to consider the evolving epidemiology (WHO, 2019).

CONCLUSION

Nigeria has been responding to successive yellow fever outbreaks over a wide geographic area. A four-year (2018-2021) national yellow fever Preventive Mass Vaccination Campaign (PMVC) plan, supported by the Global Alliance for Vaccines and Immunization (GAVI) and partners, is currently being implemented to cover all states in the country. By 2025 it is anticipated that all states in Nigeria will have been vaccinated. Therefore the prospects for yellow fever eradication in Nigeria are high but the current challenges require urgent, sustained and focused attention so as to shorten the journey from now to eradication time.

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