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Yellow fever outbreak in Ebonyi State, Nigeria, May-August 2019

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Abstract

An outbreak of Yellow fever (YF) occurred in Ebonyi State, Nigeria in the year 2019 and a Rapid Response Team (RRT) from the Nigeria Centre for Disease Control, Abuja was deployed to investigate and characterize the outbreak and institute control measures. All suspected cases were identified, line-listed and analyzed. Between May and August 2019, 78 suspected YF cases were identified from 5 LGAs in Ebonyi State. Of these, 17 (21.8%) confirmed YF cases [including 4 deaths (case fatality rate (CFR): 23.5%)] were reported in 4 LGAs, with majority 13 (76.5%) from Izzi LGA. Age groups mostly affected were 0-9 years 5(29.4%) and 20-29 years 5(29.4%) with mean age 19 ±12 years. Majority were males, 10 (58.8%). Overall, 50 eligible children participated in the YF VCS, 36(72.0%) had their vaccination cards available and only 24 (48.0%) of the cards had a record of YF vaccination. Aedeslarva was found in 9(90.0%) of 10 households surveyed and adult species Aedes simpsoni complexemerged from the collections. The 2019 YF outbreak in Ebonyi state was as a result of an abundance of Aedesmosquitoes and low vaccination coverage. We recommend a Statewide YF risk assessment, mass YF vaccination campaign, vector control and enhanced YF surveillance is important to prevent future outbreaks and mortality.

Introduction

The Ministry of Health, Ebonyi State reported to the Nigeria Centre for Disease Control (NCDC) rumours of cases and deaths from an unknown illness in two wards in Izzi Local Government Area of Ebonyi State. Ten persons were reported to have died and four on treatment at a General Hospital. All the patients presented with fever and jaundice. Blood samples were collected and tested in the Central Public Health Laboratory, Lagos, and the National Reference Laboratory Gaduwa, Abuja, Nigeria. One out of the samples tested positive for Yellow fever (YF) with real time polymerase chain reaction (RT PCR) while the remaining samples were sent to Institut Pasteur (IP) Dakar for further investigations. Yellow fever is transmitted by the bite of infected mosquito vector of the Aedes and Haemogogus spp. It is a vaccine-preventable disease and a single shot provides immunity for a lifetime [1]. The virus is found in tropical and subtropical areas of Africa and Central and South America with the illness being endemic in 34 African countries (including Nigeria) and 13 Central and South American countries [2]. In Africa, the burden of YF is estimated at 84,000-170,000 severe cases and 29,000-60,000 deaths annually [3,4]. In 2016, two linked urban YF outbreaks occurred in Angola and Democratic Republic of Congo with 965 confirmed cases and about 400 deaths. Additionally, 11 cases were exported to China. During this outbreak, 28 million doses of YF vaccines were urgently required and this exhausted the existing global vaccine supply and also diverted attention from other public health issues thereby impacting on the health systems. Nigeria has recorded some outbreaks of YF in the past [5]. The increasing number of YF cases is said to be attributable to multiple factors, which include decline in population immunity to infection, increasing human activities such as deforestation, farming, urbanization, migration, and climate change [6-9]. Since the reemergence of YF in Nigeria in September 2017, all states in the country have reported at least a suspected case. In view of the confirmation of YF outbreak, the NCDC deployed a multi-sectoral Rapid Response Team (RRT) on July 31, 2019, to assess the situation and determinants of the outbreak of YF in Ebonyi State and institute appropriate response actions. This paper describes the YF outbreak in Ebonyi State, Nigeria, May to August 2019.

Methods

Study design: this is a cross-sectional descriptive outbreak investigation of the Yellow Fever outbreak in Ebonyi State, Nigeria in 2019.

Outbreak setting: Ebonyi State is in the south-east geopolitical zone of Nigeria. It lies approximately

on longitude 07030´E and 08030´E and latitude 05040´N and 06045´N [10]. The state shares geographical boundaries with Cross River State to the east, Enugu State to the west, Benue State to the north and Abia State to the south. It has a land mass of 6,400 Km^2 with a 2018 projected population of 3,046,287 (Male- 1,553,606 and Female- 1,492,681) based on the 2006 population census [11]. Ebonyi State is made up of 13 LGAs; Abakaliki, Afikpo South, Afikpo North, Ebonyi, Ezza North, Ezza South, Ikwo, Ishielu, Ivo, Izzi, Ohaozara, Ohaukwu and Onicha. The majority of the population are subsistence farmers [11]. Others are civil servants, bankers and traders.

Study population: the study included persons who met the case definitions of yellow fever. The case definition is described below in detail.

Case definition: we adapted the standard case definition for YF as contained in the technical guidelines for integrated disease surveillance [12]. We described a suspected case as any person with acute onset of fever, with jaundice appearing within 14 days of onset of the first symptoms and residing in Izzi LGA or any of its contiguous LGAs from May 1st to August 10th, 2019. A probable case was defined as a suspected case AND one of the following: a) IgM positive/PCR positive in a national laboratory in the absence of YF vaccination within 30 days of onset of illness, b) Epidemiological link to a confirmed case or an outbreak, c) Positive post-mortem liver histopathology. A confirmed case was defined as a probable case AND one of the following: a) Detection of YF-specific* IgM, b) Detection of four-fold increase in YF IgM and/or IgG antibody titres between acute and convalescent serum samples, c) Detection of YFV-specific* neutralizing antibodies at World Health Organization (WHO) Regional Reference Laboratory.

Active case search: we conducted active case search for suspected cases of YF in health facilities and the affected communities. In the health facilities, we conducted a retrospective review of medical and laboratory records from the period May to August 2019. We extracted the following information from suspected cases: signs and symptoms, biodata, outcome, date of onset, vaccination history, travel history, date of presentation at the facilities. In the communities, we asked households for history of jaundice and fever. All suspected cases were line-listed, verbal autopsy conducted, and samples collected for laboratory testing.

Laboratory: all blood samples collected during the study were sent to the Central Public Health Laboratory (CPHL Lagos) and National Reference Laboratory, Gaduwa (NRL), Abuja for testing using Reverse Transcription Polymerase Chain Reaction (RT-PCR) and the monoclonal antibody capture enzyme linked immunosorbent Assay (MAC-ELISA) analysis techniques. The testing platform used was determined by the timeline between the date of symptom onset and the date of sample collection. Samples which were collected less than or equal to (≤) ten (10) after the date of symptom onset were first tested by RT-PCR and when negative were subjected to MAC-ELISA test while samples which were collected more than 10 days after the date of onset of symptoms are tested using the MAC-ELISA testing method. Samples which tested positive, equivocal or inconclusive in the Nigerian laboratories were sent to the WHO regional reference laboratory Institute Pasteur (IP) in Dakar, Senegal. The WHO reference laboratory (IP Dakar) retested these samples using the IgM ELISA, RT PCR as well as Plaque Reduction Neutralization Test (PRNT) methods.

Rapid yellow fever vaccination coverage survey: we conducted a rapid YF vaccination coverage survey of children aged 1-10 years of age in Izzi LGA (most affected LGA) to determine their YF routine immunization (RI) vaccination status and coverage. A systematic sampling of alternate houses was used to identify those to be included. The process was explained to the caregivers, who were asked to produce the immunization card of the children. Eligible children whose immunization cards could not be produced by their caregivers were excluded. Sighting of the immunization card

and date of YF vaccination was evident that the child received YF vaccination. Every firstborn child in each household was sampled until the communities were covered. A checklist developed by the RRT was used to collect data on YF vaccination status. The result was used to develop a YF vaccine request for the International Coordinating Group (ICG) on vaccine provision to support a reactive vaccination campaign.

Risk communication and social mobilization: we conducted advocacy to key stakeholders, community engagement, radio and television phone-in programmes and use of key messages to targeted audience. We also visited heads of secondary and tertiary healthcare facilities and conducted trainings of healthcare workers on the epidemiology, reporting and management of YF.

Entomological survey: entomological survey was conducted in Ndingele, Nkumoro and Ndienwogu communities in Izzi LGA to establish the presence of the YF vectors and identify their breeding sites in the areas. These included a larval survey which was conducted in ten (10) households (in the communities where positive cases were found), to collect the larval stage of *Aedes*mosquitoes. This method was then used to measure two key larval indices (including House and Breteau indices), to determine vector infestation in the area. Larval index was considered high when House Index ≥4% and/or Breteau Index ≥5%. Also, Biogent Sentinel (BGS) trapping for adult *Aedes*mosquito collection.

Data management: we collected data using line-list for active case search and the checklist for rapid YF vaccination coverage assessment. Variables analyzed where age, sex, LGAs and vaccination status and clinical outcome. Data was entered into Microsoft Excel and analyzed using IBM SPSS statistics 25 [13]. We calculated frequencies and proportions for categorical variables, mean and standard deviation (SD) for numeric variables, and calculated the attack rate per 100,000 population by dividing the number of new cases by the projected population 3,046,287 (male: 1,553,606 and female: 1,492,681). We generated a choropleth map; and an epi-curve showing number of suspected cases, confirmed cases and deaths.

Ethical consideration: the manuscript approved by the Ebonyi State Ministry of Health. The study was part of the YF outbreak response activities, participation in the survey was voluntary, and confidentiality of respondents was maintained. The survey process was fully explained to the respondents, and proper interpretation made to respondents who did not understand English language. All respondents gave a written consent before administration of data tools.

Results

The index case: the index case was a 7-year-old male child who fell ill on June 7, 2019. He was being managed at home with herbs until his condition deteriorated. He was brought to the Primary Health Center (PHC) Ndingele on July 12, 2019, with symptoms of fever and jaundice and was referred to General Hospital Iboko where YF was suspected. Sample was collected for testing and patient care commenced. The patient´s sample test result returned positive for yellow fever.

Summary of yellow fever cases in Ebonyi State, May to August 2019: from May to August 2019, 78 suspected cases of YF were identified, of which 17 (21.8%) were confirmed positive with 4 deaths, giving a CFR of 23.5%. Majority were in the age groups 0-9 years 5 (29.4%) and 20-29 years 5 (29.4%) with mean age was 19±12 years while majority 10 (58.8%) also, were males (Table 1). At the initial period in the epidemic curve, the number of suspected cases sharply increased in week 19 (8 cases), followed by a sharp decline. In week 22, there was a slight increase with 1 case and in week 23, a sharp rise in number of suspected cases (6 cases), confirmed cases (2 cases) and deaths (1 case) were seen. The slope declined continuously until week 26 when the number of suspected cases continued to rise, with

a sharp increase (1 case) in number of confirmed cases in week 28 and in week 29; there was 1 death which also led to a sharp rise in number of deaths. The curve rose steeply and peaked in epidemiological week 30 (6 confirmed cases and 1 death). Thereafter, the number of cases continuously declined steeply until week 32 with a sharp rise in the number of suspected cases (11 cases). Afterwards, the number of cases continued to decline steadily for the period (Figure 1). Five LGAs reported at least one suspected case of YF with majority 70 (89.7%) from Izzi LGA. However, 17 confirmed cases were identified in 4 LGAs, and majority 13 (76.4%) were in Izzi LGA, followed by Ebonyi 2 (11.8%), Abakiliki 1 (5.9%) and Ishielu 1 (5.9%) LGAs. Of the 4 reported deaths, 3 (75%) were in Izzi LGA and 1 (25%) in Ishielu LGA (Figure 2).

Rapid yellow fever vaccination coverage survey: a total of 50 children between the age group 1-10 years, 25 (50.0%) males and 25 (50.0%) females, participated in the YF vaccine coverage survey. The survey was conducted in four wards in Izzi LGA, and majority 29 (58.0%) were from Ndingele ward (**Table 2**). Of the 50 participants, 36 (72.0%) had their vaccinations cards available and 24 (48.0%) cards had a record of YF vaccination (**Table 2**).

Entomological survey/spot check: the larva of *Aedes*mosquitoes were found in 9 (90.0%) of the 10 households in Ndingele, Nkumoro and Ndienwogu during the larval survey/spot check. At least one water container was found to harbour the immature stages of *Aedes*mosquitoes in each of the 9 households. Also, almost all cocoyam leaf axils in farms around the houses had the immature stages of *Aedes*mosquitoes. An adult *Aedes*mosquito identified as a member of *Aedes simpsoni*complex emerged from the collection. Both House and Breteau indices were very high (>4% and >5% respectively).

Discussion

We conducted a descriptive analysis of the YF outbreak in Ebonyi State between May and August 2019. Seventy-eight suspected cases, with 17 confirmed positive cases, were recorded, with the majority of the cases found in Izzi LGA. The YF vaccination coverage survey found low vaccination coverage in Izzi LGA, and this called for mass vaccination and improvement in RI. The epi-curve shows a propagated transmission. The retrospective analysis identified suspected cases long before the arrival of the RRT in the State. This suggests that the outbreak in 2019 may have been going on for a few months undetected by local health authorities. The cases found during active case search were majorly among severely affected persons who visited the health facility during the outbreak. This suggests that more persons than reported may have been affected. Michael Johansson Icerberg estimation found that for any severe case of YF there is an additional 3-20 asymptomatic or mild infections [14]. Our finding may also suggest a low index of suspicion for YF as found by W. Nwachukwu *et al*. 2020 [15]. Since the re-emergence of the disease in September 2017, Nigeria has recorded suspected cases of YF in all states in the country [16].

More than half of the confirmed positive cases were from Izzi LGA, which is a forest farming settlement, dominated by farmers. YF has been found to be associated with agricultural activities in and near forests and swampy fields, where *Aedes*spp can breed well [17-19]. The outbreak started in June which was peak of rainy season when mosquitoes´ population would have greatly increased, and farming activities increased. There would be frequent human exposure to the *Aedes*mosquitoes. This finding disagrees with previous works which found sylvatic transmission [20]. It, however, agrees with the findings of W. Nwachukwu *et al*. 2020 [15] and Y. SO *et al*. 2018 [21], who reported urban transmission in Nigeria. The overall CFR (23.5%) agrees with previous studies which also found CFR

to be 20% - 60% [22,23]. Children below 10 years, young adults and men (which may be persons engaged in farming activities) were majorly affected by the outbreak. This agrees also with previous findings in Nigeria [15]. We suggest this might be an urban yellow fever spread by *Aedes* mosquitoes in the affected areas, although we were unable to prove these claims through entomological and environmental surveys. Our YF vaccination coverage survey found low vaccination coverage among children 1-10 years old as less than 50% of the children surveyed showed evidence of YF vaccination, despite the introduction of YF vaccine in the RI schedule for children up to 9 months old and the YF mass vaccination campaign [24]. This agrees with a previous study in Nigeria which also found low vaccination coverage [15]. Vaccination is the most important measure for preventing and containing YF outbreaks [25,26]. Immediately after the outbreak investigation, a reactive mass vaccination campaign was conducted in Ebonyi State in September 2019, following recommendations of the RRT [27].

The affected communities were rural areas, and the major occupation of the people is farming. Vegetation of the area is mainly derived savannah, interspersed with rain forest areas which harbour monkeys (the main reservoir hosts of the YF). Interestingly, one of the main agricultural products of the areas is cocoyam but unfortunately, the cocoyam leaf axils provided breeding grounds for *Aedes*mosquitoes. Larva of *Aedes*mosquitoes were found in 90% of the households visited during the survey, while the adult mosquito, *Aedes*simpsoni complex, emerged from the collections. These species have been established as transmitter of YF (it can transmit yellow fever from monkeys to humans at the edge of the forests). Additionally, House index was >4% while Breteau index was >5%. The presence of *Aedes*mosquito was established, which indicated a high risk of YF transmission in the area and for unimmunized persons. Previous studies within and outside Nigeria have shown that the abundance of the yellow fever vector, *Aedes* mosquitoes, increases the possibility of local yellow fever transmission, particularly when infected persons introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination [15,17,28].

Study limitations: we were unable to ascertain the vaccination status of the positive cases. This would have helped to support the administration of vaccination as an important control of the outbreak; however, this does not affect the validity of our conclusions following support of our findings by previous publications

Conclusion

We confirmed an outbreak of YF in Ebonyi State. The outbreak occurred among susceptible populations, which include children below 10 years and young-adult men. Additionally, there was low vaccination coverage. The presence of Aedes mosquito was established following the entomological survey. This indicated a high risk of YF transmission in the area and for unimmunized persons.

Recommendations: we recommend the State Ministry of Health, Ebonyi State and other relevant stakeholders to strengthen YF surveillance and YF vaccination through improving RI, mass vaccination campaign, especially in high-risk areas. Sustenance of a state-wide health education (focusing on YF transmission, signs, symptoms, preventive and control measures, including vaccination, and the importance of vaccination card retention and safety) is also important, targeted especially at mothers. Additionally, vector control using insecticide space spraying or fogging for adult mosquitoes, larval source reduction using larvicides/ destruction of breeding sites and clearing of bushes around homes to reduce vector resting sites around human dwellings are urgently recommended.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have read and agreed to the final manuscript.

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Tables and figures

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Table 2: characteristics of children assessed in the rapid YF vaccination coverage survey, Izzi LGA, Ebonyi State, May - August 2019 (N=50)

Figure 1: epi-curve of yellow fever cases in Ebonyi State, May - August, 2019

Figure 2: distribution of yellow fever cases in Ebonyi State, May - August, 2019

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Table 1: age and sex distribution of yellow fever cases in Ebonyi State, May-August 2019 (N = 17)					
Age (years)	**Total number of cases N = 17**	**Males**		**Females**	
		Number of cases (%) n =10	**Deaths (CFR%) n = 4**	**Number of cases (%) n = 7**	**Deaths (CFR%) n = 0**
0 - 9	5 (29.4)	2 (20.0)	2 (50.0)	3 (42.8)	0 (0.0)
10 - 19	4 (23.5)	2 (20.0)	0 (0.0)	2 (28.6)	0 (0.0)
20 - 29	5 (29.4)	4 (40.0)	1 (25.0)	1 (14.3)	0 (0.0)
30 - 39	2 (11.8)	1 (10.0)	0 (0.0)	1 (14.3)	0 (0.0)
40 - 49	1 (5.9)	1 (10.0)	1 (25.0)	0 (0)	0 (0.0)

Table 2: characteristics of children assessed in the rapid YF vaccination coverage survey, Izzi LGA, Ebonyi State, May - August 2019 (N=50)	
Variables	**Frequency (%)**
Ward	
Ndingele	29 (58.0)
Mgbabeluzor	4 (8.0)
Igbeagu	2 (4.0)
Nkumoro	15 (30.0)
Sex	
Female	25 (50.0)
Male	25 (50.0)
Age	
1	8 (16.0)
2	5 (10.0)
3	9 (18.0)
4	7 (14.0)
5	4 (8.0)
≥6	17 (34.0)

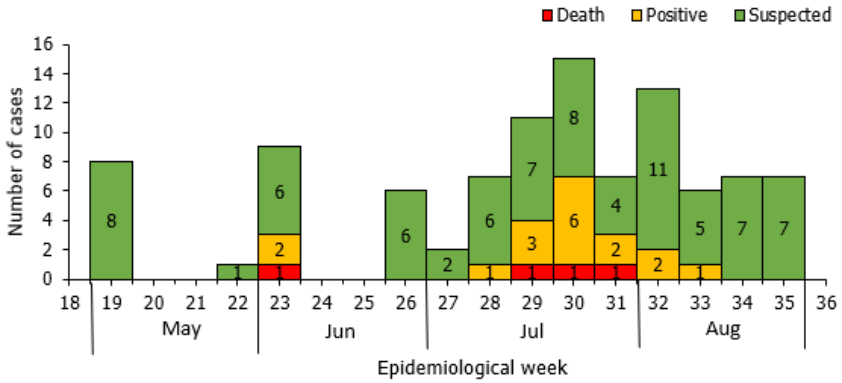

Figure 1: epi-curve of yellow fever cases in Ebonyi State, May - August, 2019

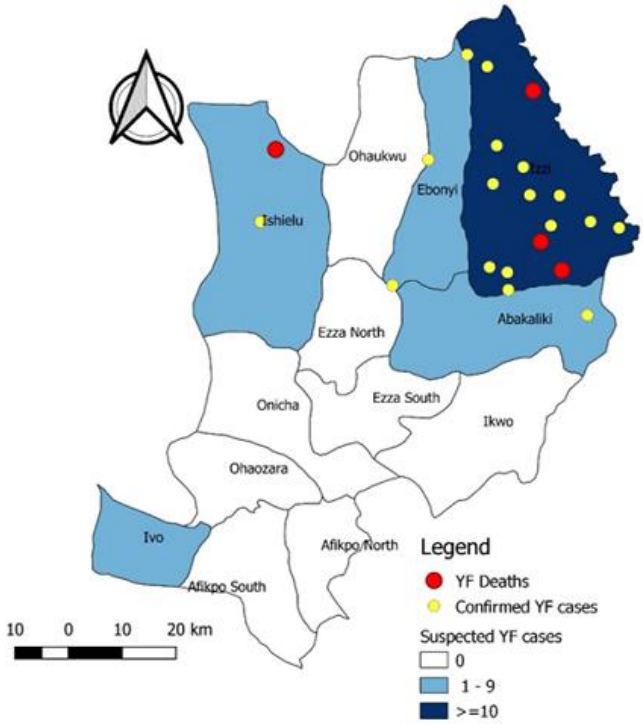

Figure 2: distribution of yellow fever cases in Ebonyi State, May - August, 2019