Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Review Article

A Systematic Review of Yellow Fever Outbreaks and Public Health Responses in Nigeria

Wilson Chukwukasi Kassy[1], *Casmir Ndubuisi Ochie[1], Anne Chigedu Ndu[1,2],Olanike R Agwu-Umuahi[1,2], Charles Ntat Ibiok[1,2], Ifeoma Juliet Ogugua[1,2], Onyinye Hope Chime[3,4], Chinonye Orji[3,4], Sussan Uzoamaka Arinze-Onyia[3,4], Emmanuel Nwabueze Aguwa[1,2], Theodora Adaeze Okeke[1,2].

[1]Department of Community Medicine, UNTH Ituku-ozalla , Enugu, Nigeria.[2]Department of community Medicine, University of Nigeria Ituku-Ozalla, Enugu, Nigeria.[3]Department of Community of Medicine, Enugu State University of Science and Technology, College of Medicine, Park Lane GRA Enugu, Nigeria.[4]Department of Community of Medicine, Enugu State University of Science and Technology Teaching Hospital, Park Lane GRA Enugu, Nigeria.

Abstract

Background: Yellow fever (YF) outbreaks continue to occur in Nigeria with a high mortality rate despite a well-established mode of transmission and the availability of a potent vaccine. This review is aimed at describing the epidemiology, determinants, and public health responses of yellow fever outbreaks in Nigeria from 1864 to 2020.

Methodology: The guidelines for the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) were used to conduct the review from November 2020 to April 2021. PubMed database, WHO library databases, and Google Scholar were used to search for relevant published materials including original and reviewed articles, conference papers and case reports from 1864 to 2020

Results: Forty – eight articles and reports were included in the final reviews. Twenty – three outbreaks were described involving 33,830 suspected, presumptive, or confirmed cases of yellow fever and 8,355 deaths. The outbreaks occurred in every state of Nigeria including the Federal Capital Territory mostly during the rainy season. Low immunity in the population or low vaccination coverage, poor vector control, rainforest or savanna vegetation, rural–urban migration, and imported virus by travelers were common determinants noted. Public health responses have been through, centrally coordinated laboratory support, case management, emergency immunization, vector control, and surveillance.

Conclusion: Yellow fever outbreaks have increased in frequency and geographical spread with associated mortality rates. To stem the tide, mass immunization with 17D vaccines is encouraged, planned urbanization with adequate vector control measures enforced, effective case definition, vector surveillance, and effective awareness campaigns should be emphasized.

Keywords: Yellow Fever, Outbreaks, Determinants, Public Health Response, Nigeria.

***Correspondence**: Ochie, Casmir N Department of Community Medicine, UNTH, Ituku-Ozalla, Enugu, Nigeria.
Email: drcasmirnf@gmail.com

How to cite this article: Kassy WC, Ochie CN, Ndu AC, Agwu-Umuahi OR, Ibiok CN, Ogugua IJ, Chime OH, Orji C, Arinze-Onyia SU, Aguwa EN, Okeke TA. A Systematic Review of Yellow Fever Outbreaks and Public Health Responses in Nigeria. Niger Med J 2023;64(4): 427-447. Accepted: August 29, 2023. Published: September 21, 2023.

Quick Response Code:

Introduction

Yellow fever (YF) is an acute viral haemorrhagic disease caused by the yellow fever virus, an arbovirus, belonging to the family Flaviviridae and genus Flavivirus.[1 - 3] Historically, the origin of the disease is uncertain but believed by consensus to have been in Africa 500 years ago where it has remained endemic and was disseminated to the Americas and other parts of the world through sailing ships and the slave trade.[3 – 5] The colonial expeditions and imperial activities of non–immune Europeans and Americans led to the early recorded outbreaks of YF disease in West Africa.[4, 6, 7] The earliest recorded yellow fever outbreak in Nigeria was reported in Lagos in 1864, followed by repeated outbreaks in 1894, 1905, 1906, 1925, and 1926, and have continued to the present among the indigenous population.[8 - 10] By the end of the 20th century, the viral origin of the disease was identified, its means of spreading, and possible ways of prevention were found. These were evidenced by the works of Carlos Finlay and Walter Reed in the discovery of the disease urban mosquito vector which set the stage for a successful eradication programme.[11, 12] As vector control proved effective and urban epidemics were controlled in the Americas, the West African yellow fever commission was established in 1925 by the international health division of Rockefeller Foundation in collaboration with British colonial authorities purely on yellow fever research.[6, 7] By 1927, the first isolation of the yellow fever virus called the Asibi strain from a patient Asibi was achieved followed by the identification of the rhesus monkey used for the important protection test, a method used to identify individuals exposed to yellow fever and developed immunity.[7]From 1931 to 1937, Max Theiler, successfully used the Asibi strain and the protection test method propagated on mice using intracerebral injections to produce a vaccine called 17D (Rockefeller) vaccine of the Asibi strain. The combined discoveries of the vector and safe vaccine implied that the disease and epidemic could be effectively controlled and possibly eradicated.[6, 7, 11]

Yellow fever is transmitted through a cycle that involves a vector (Mosquito), humans, and monkeys. The cycles are categorized into sylvatic / jungle/forest cycle which is in the natural or endemic zone. The virus is transmitted or circulated by the wild species of mosquitoes (Aedesafricanus and furcifer) and arboreal monkeys. The monkeys are resistant but if infected, are immune. Man is accidentally infected following a short forest stay leading to sporadic or limited local epidemics causing immune protection of the population. The second cycle is the intermediate / savannah cycle which is in the border zone of emergence with settlements near the forest where there are some human activities. The virus is transmitted by monkeys to humans or humans to humans via mosquitoes. (Aedesluteocephalus, Aedesfurcifer, Aedesmetallicus, Aedesopok, Aedestaylori, Aedesvittatus, and members of the Aedessimpsoni complex), anthropization of the environment through deforestation, population growth, and global warming. Lastly is the urban cycle which is the epidemic zone characterized by low population immune status or poor immunization coverage, no presence of wild mosquitoes, and circulation of virus. The virus is imported by an infected person from the jungle or savanna zones and transmitted from human to human transmission through urban mosquitoes; Aedes aegypti.[3, 5, 10]

The incubation period is 3 – 6 days with a case fatality rate of 20 – 50 % or higher.[2, 3] The symptoms range from mild symptoms (first phase) to severe illness or fatal disease (toxic phase). Only about 15% of those infected will be in this phase. Those with mild symptoms develop sudden onset of fever, headache, muscle pain, backache, general weakness, red eyes (injected conjunctiva), nausea and vomiting. During this phase, patients quickly recover though they have viraemia, and are infectious to mosquitoes. This is followed by 24 hour period of remission. The second and toxic phase includes high fever, vomiting, epigastric pains, jaundice, hemorrhagic diathesis (hematemesis), coma, and death. YF virus is usually absent from the blood of patients during the toxic phase, and anti-YF virus antibodies appear.[3] Confirmation of yellow is by viral isolation, serology test (Enzyme–Linked Immunosorbent Assay [ELISA], reverse transcription polymerase chain reaction [RT – PCR], Plaque reduction and neutralization test [PRNT]). Serology has the challenges of cross–reaction with other flaviviruses.[10, 13]Yellow fever outbreaks are controlled through an effective

and timely surveillance system, laboratory capability, routine, and mass immunization, supportive management of cases, environmental and vector control using registered insect repellents for the outdoors, bed nets, long-sleeved clothing, long pants, and socks are necessary. In 2018, the Eliminate Yellow Fever Epidemics (EYE) was launched in Nigeria to eliminate yellow fever by 2026. The strategic objectives are to protect at-risk populations, prevent international spread, and contain outbreaks rapidly.[9, 10, 14]

Yellow Fever is endemic in the tropical areas of Africa, Central and South America with more than 90% global burden in Africa. The World Health Organization (WHO) estimates the burden of YF in Africa to be at 84,000 – 170,000 severe cases and 29,000 – 60,000 deaths annually.[1, 14] Nigeria has over the century experienced a series of outbreaks of yellow fever which have been associated with various public health response measures. Despite these public health responses, the current increased frequency of the epidemics is of great concern, especially for a disease marked for elimination. This study review will help to understand the current drivers and gaps in public health response measures for the effective control of the epidemics and possible elimination by 2026 through EYE. The study is aimed at describing the epidemiology, determinants, and public health responses of yellow fever outbreaks in Nigeria from 1864 – 2020.

Methodology

The guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used to conduct a systematic search of Yellow fever outbreaks in Nigeria. The strategy is detailed in Figure 1.[15]The search was conducted between November 2020 and April 2021. PubMed database, WHO library databases, and Google Scholar were used to search for relevant published materials including original and reviewed articles, conference papers, and case reports from 1900 to 2020. Other websites such as the World Health Organization, and Center for Disease Control were searched for outbreaks and were included if they contained information on each reporting year. The main themes considered were Yellow fever outbreaks in Nigeria, the epidemiological profile, the determinants, and the public health responses.

Data Abstraction and Synthesis

Data abstraction and synthesis included the following 4 steps: identification, screening, eligibility, and inclusion. Articles were identified using the search strategy described above. Titles and abstracts were then screened to assess their suitability to the study objectives. Then the full texts of the articles were reviewed to determine eligibility for the study. Detailed information relevant to the study was extracted and tabulated according to; outbreak year, time of year (month), states affected, persons affected, laboratory confirmation, mortality or case fatality rates, determining factors, and public health responses. Studies were then categorized by epidemiological profile, determinants, and public health response.

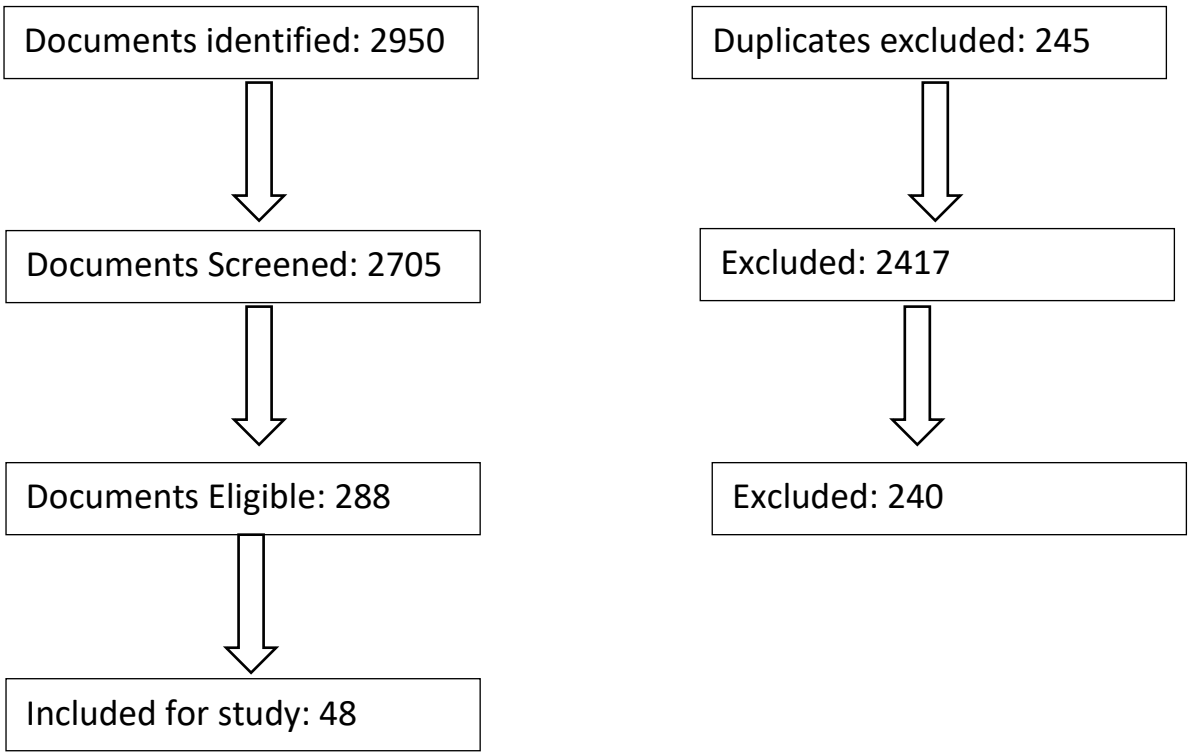
Inclusion and Exclusion Criteria

Articles that described Yellow fever outbreak epidemiology, determinants, and public health response were included while outbreaks outside Nigeria and those conducted in animals were excluded.

Results.

The initial search generated 2950 results. After the removal of 245 duplicates, 2705 articles and reports remaining were screened based on titles and abstracts resulting in the further exclusion of 2417 papers. Content review of the 288 full texts articles and reports led to the exclusion of an additional 240 papers. Finally, 48 full-text articles and reports were included based on yellow fever outbreaks in Nigeria from 1864 to 2020, epidemiological profiles, determinants, and public health responses. (See Figure 1)

Figure 1: Flow Chart selection of relevant documents for review of literature.



From our review of the literature, the Yellow fever outbreak occurred 23 times from the years 1864 to 2020 under review. About 33,830 cases (suspected, presumptive, or confirmed) and 8,355 deaths of yellow fever were observed. There were no observed age or sex predilections from the reviewed materials. The highest number of cases and deaths were reported in 1950 – 52, 1986 – 87, 1991, and 2019 while the lowest were from 1864 – 1937. The highest case fatality rate was 84.1% reported in 1990. (See Table 1 and Figure 2).

Table 1. Description of yellow fever outbreaks in Nigeria 1864-2020

Outbreak year	Season	States	Cases	Deaths	Case fatality rates (%)	Lab. confirmed	References
1864 – 1900	------	Lagos	-----	------	---------	-----	(7) (9) (16)
1905-1906	-----	Lagos	-----	------	--------	------	(17) (9)
1913 – 1914	Jan – Feb & Oct	Lagos, Onitsha	9	1	--------	-------	(18)
1925 – 1926	April – Sept	Lagos	17	7	--------	------	(19) (20)
1934 – 1937	July – Dec	Ogbomosho, Kano	4	------	-------	Lab. Confirmed	(21) (22) (23) (6)
1946	April	Ogbomosho	75	9	< 1%	Lab. Confirmed	(6)
1950 – 1952	-------	Onitsha	12, 000	500 - 600	-----	Lab. Confirmed	(6) (24)
1969	Sept-Dec	Benue – Plateau	100,000 (252 hospitalized)	123	40%	Lab. Confirmed	(25)
1970	Aug – Dec	(Okwaga) Benue	786	3	1.6% - 14.4%	Lab. Confirmed	(26)
1976	--------	Akwa – Ibom	------	-------	56%	Isolation & Serology	(27)
1979	Jan – Feb	Bauchi (Azare)	11	None	----	------	(28)
1986	June – July	Benue, Cross river, Anambra, Imo	9800 Benue alone	5600 Benue alone	2.8%	Serology	(29), (30)
1987	April – Dec	Oyo, Niger.	805 + 644 = 1449	416 + 149 = 565	0.6%	Viral isolation & serology	(31) (32) (30)
1988	----	Potiskum (Yobe)	30	---	------		(33)
1990	Aug – Dec	Borno	102	83	84.1%	Serology	(33)

1991	April – Dec	Delta, Anambra, Kaduna, Kastina& Plateau	2561	661	26%		(34) (35)
1992	-------	-----	149	8	5%		(36)
1993	------	------	152	8	5%		(36)
1994	Sept-Dec	Imo, Anambra	1227	415	34%		(37)
2017	July – Dec	Kwara State, Abia, Anambra, Borno, Edo, Enugu, Kano, Katsina, Kogi, Kebbi, Lagos, Nassarawa, Niger, Oyo, Plateau and Zamfara.	341 suspected cases. 32 confirmed cases	45 among suspected cases while 9 among confirmed cases.	21.1% in suspected cases and 28.1% in confirmed cases	Serology using IgM ELISA and RT – PCR	(9) (38)
2018	Nov – Dec	Edo State	146 suspected, 42 presumptive, and 32 confirmed cases	26 deaths	18%	IgM and RT – PCR and Plaque Reduction Neutralization Test (PRNT)	(39) (16)
2019	Jan – Dec	All 36 + FCT	4189 suspected cases.	23 deaths from Bauchi, Katsina and Benue states	12.2% for confirmed cases	207 confirmed by IgM, 197 by RT – PCR.	(40) (41)
2020	Nov – Dec	Enugu, Delta, Ebonyi, Benue and Bauchi	530 suspected cases, 48 laboratory-confirmed	178 deaths among the suspected	------	RT – PCR and IP Dakar	(42)

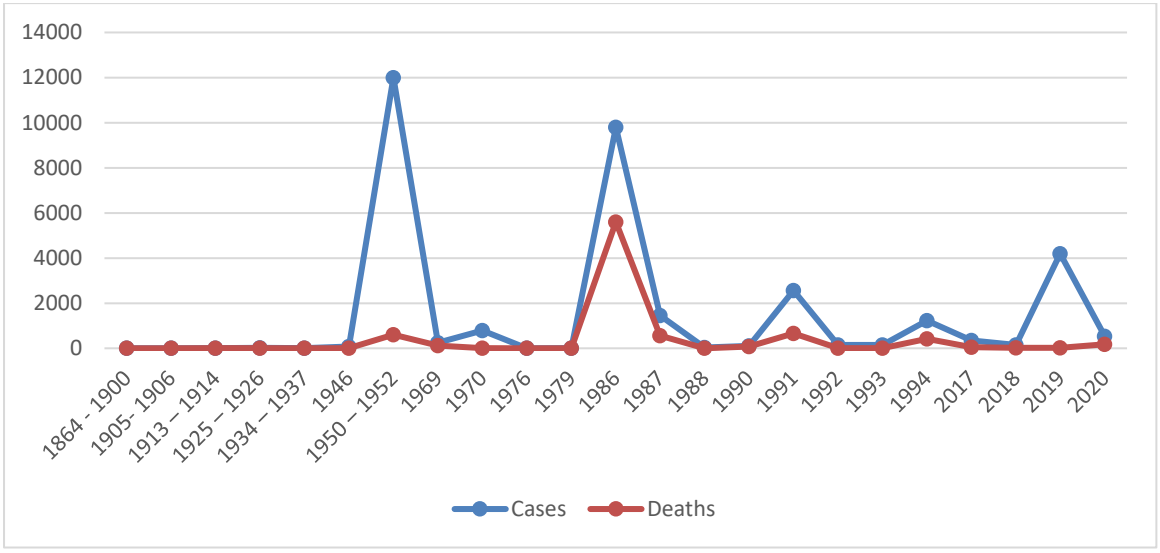


Figure 2: Time Trend of Yellow Fever Outbreaks in Nigeria 1864-2020

Between 1864 and 2020, all the states plus the Federal Capital Territory recorded an outbreak of yellow fever. Most outbreaks in Nigeria were reported in the southern states while few were in the northern states. Anambra, Lagos, and Benue had the highest recorded outbreaks with 5 – 7 outbreaks of yellow fever. (See table 2 and figure 3).

Table 2: Frequency of yellow fever outbreaks among states in Nigeria 1864-2020.

State	Number
Abia	2
Adamawa	1
Akwaibom	2
Anambra	7
Bauchi	2
Bayelsa	1
Benue	5
Borno	3
Cross River	2
Delta	3
Ebonyi	2
Edo	3
Ekiti	1
Enugu	3
Gombe	1
Imo	3
Jigawa	1
Kaduna	2
Kano	3
Katsina	3
kebbi	2
Kogi	2
Kwara	2
Lagos	6

Nasarawa	2
Niger	3
Ogun	1
Ondo	1
Osun	3
Oyo	3
Plateau	4
Rivers	1
Sokoto	1
Taraba	1
Yobe	2
Zamfara	2
Fct	1

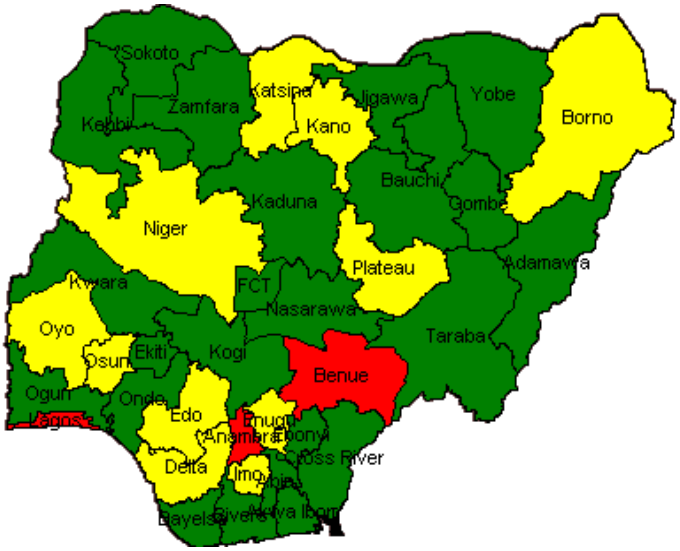


Fig 3. Map showing frequency of yellow fever outbreaks among the states in Nigeria 1864 – 2020.

Key

States with a total of 5 - 7 outbreaks

States with a total of 3 - 4 outbreaks

States with a total of 1 - 2 outbreaks

From 1864 to 2020, outbreaks occurred every decade except in 2000 to 2010. The seasonality of the outbreaks as reported from reviewed materials showed that most outbreaks happened in the rainy seasons of July to November. (See table 3 and figure 4).

Table 3: Determinants of Yellow fever outbreaks in Nigeria from 1864 – 2020.

Outbreak year	Inference	References
1864 – 1900	*Non immune European and American expeditions. *Endemic disease among indigenous population. *No knowledge of the disease epidemiology (aetiology and transmission). *presence of few foreign doctors competent to make diagnosis.	(7)
1905 - 1906	*Non immune European and American expeditions. *Endemic disease among indigenous population. *earliest awareness and recorded case of the disease *presence of few foreign doctors competent to make diagnosis.	(7)
1913 – 1914	*Non immune European and American expeditions. *presence of few foreign doctors competent to make diagnosis. *Poor sanitary conditions for mosquito – breeding Field	(7)
1925 – 1926	*Non immune European and American expeditions. *presence of few foreign doctors competent to make diagnosis. *Poor sanitary conditions for mosquito bleeding	(20) (7)
1934 - 1937	-------	
1946	*Water pots for storage following droughts, dye pits from the dyeing industry acted as a mosquito breeding grounds. *Prior vaccination program were largely to colonial military	(6)
1950 – 1952	*Waning immunity or non – immune population due deforestation / forest disappearance in the densely populated south eastern and south southern Nigeria. *some cities are in transitional belt. *infected travelers entering the northern Region from the south. * Unchecked and unplanned urbanization *trade *Rural – urban migration *low vaccination coverage	(6) (24) (43)
1969	*Low immunization coverage to surrounding areas to JOS city. *epidemic was preceded by rainfall to aid mosquito breeding *Rural transmission *Suspected to be imported from Benue province south of Plateau province. *Vector was believed to be Aedesleteocephalus (Wild breeding Stegomyia mosquitos) *Absence of Aedesaegypti mosquitoes	(25)
1970	*Rainfall with breeding sites of mosquitos in the forest *Rural transmission by wild breeding Stegomyia mosquitos *many species of mosquitoes, A. africanus, A. argenteoventralis, A. ingrami, A. simpsoni,	(26)
1976	*First reported outbreak in the area. *Forest vegetation	(27)
1979	--------	

1986	*Aedesafricanus *Sylvatus transmission *Savanna and rainforest vegetation *Rainy season and water collection in cans *Poor Immunization coverage	(29)
1987	*AedesEgypti breeding in domestic water containers. *Urban type transmission following the sylvatic yellow fever in eastern Nigeria the previous year imported by viraemic travelers.	(31)
1990	*Non – immune status of the population evidence from affectation of all ages. *Sporadic vaccination *Sylvatic spread from the rural border town of Bama, Gwoza *water storage habits	(33)
1991	*Aedesaegypti *Aedesalbopictus *Aedesafricanus *Low immunization coverage	(34) (35)
1992 - 1993	*Low immunization coverage < 50%, 1% for Nigeria.	(36)
1994	*Sylvatic transmission / Exposure. *Low immunization coverage < 50%, 1% for Nigeria.	(37)
2017	*low index of suspicion *poor reporting of cases *fear of treatment of cases *low vaccination coverage *Sylvatic (Aedesafricanus and leuteocephalus) and Urban (Aedesaegypti) exposures. *Water collection *Priorities 1 and 2 high risk areas	(9)
2018	*Low immunity, vaccine coverage < 50% *Land use practices, cultivation close to dwellings	(39)
2019	*low index of suspicion of yellow fever among health care workers *low but improving immunization coverage *Poor documentation of yellow fever surveillance in many health facilities. *	(41)
2020		

The commonest determinants of yellow fever outbreaks in Nigeria as noted from the reviewed articles were low immune – population or low vaccination coverage, poor sanitary conditions with available collected water for breeding of mosquitos, wild mosquitos vectors in the rainforest or savanna, rural–urban migration and importation of virus by travelers. (See Tables 3 and 4).

The common public health response to the outbreaks in Nigeria observed from the reviewed material was team coordination, laboratory support, case management and emergency immunization, vector control, and surveillance. (See Tables 4 and 5).

Figure 4: Seasonality of Yellow fever outbreaks in Nigeria 1864 - 2020

	RAINY SEASON					DRY SEASON							
	JULY	AUG	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APRIL	MAY	JUNE	JULY
OUTBREAK YEAR													
1864 – 1900													
1905 – 1906													
1913 – 1914				***			***	***					
1925 – 1926	***	***	***							***	***	***	***
1934 – 1937	***	***	***	***	***	***							***
1946										***			
1950 – 1952													
1969			***	***	***	***							
1970		***	***	***	***	***							
1976													
1979							***	***					
1986												***	***
1987	***	***	***	***	***	***				***	***	***	***
1988													
1990		***	***	***	***	***							
1991	***	***	***	***	***	***				***	***	***	***
1992													
1993													
1994			***	***	***	***							
2017	***	***	***	***	***	***							***
2018					***	***							
2019	***	***	***	***	***	***	***	***	***	***	***	***	***
2020					***	***							

Table 4: Summary of determinants of Yellow Fever Outbreaks in Nigeria 1864 – 2020.

Year	Determinants									
	Ignorance	**Low index of suspicion**	**Low immunity / Vaccination**	**Sanitary condition**	**Rainforest or savanna**	**Imported travellers**	**R – U Migration**	**rainfall**	**Case reporting**	**Farming near dwelling**
1864 – 1900	+	+	+	-	+	----	-----	----	----	-----
1905 - 1906	+	+	+	----	+	-------	------	----	--------	-------
1913 - 1914	+	+	+	+	+	-------	-------	-------	-------	--------
1925 - 1926	+	+	+	+	+	------	--------	+	------	-------
1934 - 1937	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info
1946			+	+	+			+		
1950 – 1952			+	+	+	+	+			+
1969			+	+	+	+	+	+		+
1970				+	+			+		+
1976	+	+			+					
1979	No info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info
1986			+	+	+			+		+
1987				+		+		+		
1990			+	+		+	+			

1991			+							
1992 - 1993			+							
1994			+		+		+			+
2017		+	+	+	+			+	+	
2018			+							+
2019		+	+						+	
2020	No info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info	No Info

Table 5: Public Health Response to yellow outbreaks in Nigeria 1864 – 2020.

Outbreak years	Inferences	References
1864 – 1900	None	(7)
1905 – 1906	None	(7)
1913 – 1914	*British Commission on Yellow fever in 1913. * 1st West African Yellow Fever Commission (Rockefeller Foundation) in 1920.	(7)
1925 – 1926	* 2nd West African Yellow Fever Commission (Rockefeller Foundation) in July 1925 with a laboratory in Yaba. Lagos. *The commission was site of research, not public health intervention *Sanitation awareness to clear mosquito breeding containers *Field studies for intensive search of the disease in the African population both clinically and entomology for yellow fever eradication. * YF protection test experiment was conducted which identified those exposed to YF and developed immunity. *Isolation of the Yellow fever virus from Asibi and development of vaccine.	(20) (6) (4) (7)
1934 – 1937	Mass vaccination were initiated from 1939.	[44]
1946	*Outbreak management *Supportive treatment *Autopsy *DDT spraying *Emptying water pots *Restriction of movement in and out of the town	[6]

	*Community involvement of school teachers, *school records for absenteeism *verbal autopsy *Home visitations *mass vaccination *Thirty – four isolated strains of the virus were included in vaccine development.	
1950 – 1952	No available Record	
1969	*Attempt at immunization that covered up to 20% of the population of Plateau province. *Response was from virus research laboratory of the university of Ibadan. *rapid case finding *Autopsy *viral isolation *ELISA test and complement fixation test	(25)
1970	*Late response in December when the epidemic was waning *House to House survey using verbal autopsy to obtain data on cases and deaths *viral isolation *complement fixation *75% vaccination coverage using 17D vaccine.	(26)
1976	Viral isolation and serology	(27)
1986	*Vaccination *containment outbreak and epidemiological assessment. *Yellow fever vaccination to be included in Expanded Programme on Immunization *control environmental sanitation	(29)
1987	*Yellow fever vaccination to be included in Expanded Programme on Immunization	(31)
1988	No available record	
1990	*Patient survey, case finding and assessment *outbreak investigation and entomology investigation. *Virus Isolation and Serology test. *increase vaccination through EPI.	(33)
1994	*vaccination by the Local PHC department. * Dry weather	(37)
2017	*Active case search	(9) (38)

	*Rapid yellow fever vaccination coverage assessment *Verbal autopsy *human blood sample collection *Entomological Surveillance *Risk communication and social mobilization *Data management *Vaccination campaigns and mass *Surveillance *One week training on diagnosis of Yellow fever in Lagos *Strengthen Laboratory capacity *WHO advised Vaccination and Mosquito control as the primary means for prevention and control.	
2018	*Multi – agency, multi – partner incident management system (IMS), *National Emergency Operation Centre (EOC) at NCDC *Rapid Respond Teams *Yellow Fever Surveillance and active case findings *Strengthen Laboratory capacity *Vaccination campaigns *Entomological Survey.	(39) (16)
2019	*NCDC activated National EOC *Partners *Risk communication and community Engagement through social mobilization *Prevention and Active case finding. *Case management support * Vector control – destruction of breeding grounds of mosquitoes. *New laboratories. *Immunization	(40)
2020	*National EOC *partners *Prevention and Active case search *Immunization	(42)

Table 5. Public Health Response Summary to yellow fever outbreaks in Nigeria from 1864 – 2020

Year	Public Responses									
	Coordina – tion	Lab. support	isolation	Case mgt	awareness campaign	Emergency Iz	Mass Iz	Envt& rodent control	Case surveillance	Vector surveillance
1864 – 1900	-----	------	------	-----	-------	-------	-----	------	-------	--------
1905 – 1906	-----	------	------	-----	-------	-------	-----	------	-------	--------
1913 – 1914	+	------	------	-----	-------	-------	-----	------	-------	--------
1925 – 1926	+	+						+	+	
1934 – 1937							+			
1946	+	+	+	+	+		+	+		
1950 – 1952	-----	------	------	-----	-------	-------	-----	------	-------	--------
1969	+	+		+		+			+	
1970	---	+				+			+	
1976		+								
1979	-----	------	------	-----	-------	-------	-----	------	-------	--------
1986						+ (EPI)		+		
1987						+ (EPI)				
1990		+		+			(EPI)		+	+
1991										
1992 – 1993										
1994						+				
2017	+	+		+	+	+			+	+
2018	+	+		+	+	+			+	+
2019	+	+		+	+	+		+	+	
2020	+	+		+		+			+	

Discussions

The findings of our review revealed that from 1864 to 2020, Yellow fever has had an uneven pattern of distribution in the frequency of cases and deaths. There were periods of slowed frequency in cases and deaths in the years 1864 - 1946, 1976 – 1979, and 1988 – 1990, and periods of increased frequency in 1950 – 1969, 1986 – 1987, 1991 – 1994, and 2017 – 2020. The periods of slowed frequency (1864 – 1946) were characterized by the period of poor scientific knowledge of the disease, transmission, and vaccine production. The reported outbreaks were mostly among the non–immune foreign populations with a low index of suspicion of the disease. The developed vaccines were initially limited to the European–American military before mass vaccination was advocated.[6 – 7] The outbreaks occurred in states and cities of the southern to middle belt region of Nigeria whose vegetation is respectively Rainforest and Savanna. The outbreaks were commoner in the rainy season, but in 2019, the outbreaks occurred throughout the year. This is because the reports were of suspected cases of YF from 1st January to 10th December, however, only 207 of the 4189 suspected cases were confirmed. Our review could not ascertain the months that had the confirmatory test. Public health implications are that the vegetation constitutes the endemic, emergency, and epidemic zones. The zones are known for the sylvatic (mosquito or monkey to human) and urban (human to human) transmission of yellow fever virus causing sporadic and epidemic cases.[3, 5, 10] The Northern states and cities characterized by Sahel vegetation had fewer numbers and frequency of outbreaks. Even though this vegetation has a high temperature suitability index for yellow fever transmission, the low rainfall creates an unfavorable atmosphere for mosquito breeding which requires high rainfall and water dependency.[45] Outbreaks in these states and cities are due to imported virus by travelers and trade.[6, 24]

The review showed that the majority of the yellow fever outbreaks from 1864 to 2020 were driven by mostly low immunity or vaccination coverage, poor sanitary conditions, and Rainforest and Savanna vegetation. Others are rainy season, ignorance of the disease, low index of suspicion in identifying the disease, international travel, rural–urban migration, inadequate case reporting system, and cultivating near dwellings. In the earlier years from 1864 to 1906, the outbreaks were driven by the presence of non–immune European and American colonialists. The disease was already endemic among the indigenous population. There were generally poor or no knowledge of the disease. The few foreign doctors available had a low index of suspicion in making the diagnosis of the disease as there were similar diseases with similar presentations. The consequence of the above was a poor case reporting system further increasing the associated high mortality rate of yellow fever disease outbreak.[7] By 1913 – 1926, an understanding of the route of transmission and the life cycle of the mosquito was known. Poor sanitary conditions became known as a driving factor as the mosquito breeds in collected water cans, stagnated water, etc. Campaigns for environmental sanitation were advocated and implemented as a public health intervention for the elimination and possible eradication which was successful in controlling urban transmission. However, sylvatic transmission by the wild species of Aedes was able to maintain the transmission of yellow fever.[7, 20] After the discovery of the 17D vaccine, there was no widespread implementation of vaccination leading to consequent outbreaks. Available vaccines were largely limited to the colonial military. This coupled with the presence of water pots and dye pits from the dyeing industry led to the outbreak in Ogbomosho in 1946.[6] From 1950 upwards, there were many reported determinants of the outbreaks. Cities began to spring up in different parts of the country, increasing economic activities with connecting roads, railways, and other means of transportation making travel easier, rural–urban migration for better economic power. Other activities of deforestation, population increase, unchecked urbanization, and farming close to human dwellings increased. The implication was that the wild Aedes mosquitoes either from monkey to human or human to human transmission became possible as they were transported or imported by travelers and migrants to the cities. The increased activities also led to poor sanitary conditions as industries increased. The healthcare system became overwhelmed and stretched, characterized by a poor reporting system and fewer doctors. Another implication was the low immunization coverage that was consistently < 50%. This

was because most of the immunization response following outbreaks was mainly emergency immunization and most covered the population where the outbreaks occurred.[24 – 26, 31, 43]

The commonest public health response to the various outbreaks from our review of the literature was team coordination and laboratory support followed by case management, emergency immunization, and case surveillance. Environmental and vector control, isolation of cases, mass immunization, awareness campaigns, and vector surveillance were other public health interventions that lagged behind in the frequency of responses to the outbreaks. The public health implications were increased repeated outbreaks as evidenced by the occurrence of the yellow fever epidemics in every decade meaning there are gaps in responses that aren't fully implemented. In 1864 – 1906, no public response was offered as nothing was known of the disease then.[7] Immediately after the discovery of the vehicle of transmission through the works of the Reed Commission (built upon the works of Carlos Finlay), the British Commission and West African Yellow Fever Commission represented a team coordination for public health response whose task was to study the yellow fever in west Africa with laboratory in Yaba, Lagos, to serve as center for distribution of vaccine to troops and non – African settlements and lastly to serve as consultative unit to British government on problems of yellow fever.[6, 7] Presently, the team coordination response is headed by the Nigerian Center for Disease Control (NCDC) through their national Emergency Operation Center (EOC) to respond to cases of outbreaks in the country. Also, they have established national laboratory support and growing laboratories among the states to enhance fast diagnosis.[38 – 40] The management of outbreaks are multi–agency, multi–partners incident management like the National Primary Healthcare Development Agency (NPHCDA), Ministry of Environment, and Ministry of Information.[16] However, there are still poor responses from key public health interventions in control of yellow fever outbreaks like adequate immunization coverage, environmental and vector control, surveillance, and awareness campaigns. Since the discovery of the 17D vaccine, Immunization coverage has been mainly emergency immunization following outbreaks till 1986 when it was included in the Expanded Immunization Program (EPI) and later the National Program on Immunization.[29, 31] The other form of immunization was the yellow card for travelers which didn't serve its intended purpose because of corruption.[46] Immunization coverage of yellow fever has consistently been < 50% (the 2006 – 2016 study was 45%) and the Yellow fever – measles vaccine difference of – 3%.[47] There is a need, because of increasing population, and porous borders, to have an effective mass immunization and supplemental immunization by the NPHCDA as was done in polio that yielded tremendous results. This will improve yellow fever immunization coverage and help prevent the frequency of outbreaks with consequent mortality. Another response is effective surveillance to have continuous reporting of all factors that will enable possible outbreaks of yellow fever disease. This should include both case and vector reporting. Regarding environmental and vector control, there should be a checked and planned urbanization that is receptive to modernized sanitary measures of sewage and refuse disposal and treatment. Good drainage system to avoid collection of water and recycling of cans and biodegradable materials in the environment. Finally, in every outbreak with a high mortality rate, there are misconceptions that affect desired control outcomes. There are need for awareness campaigns through Risk Communication and Community Engagement that are permissive and community participatory. These key responses should be emphasized in the Eliminate Yellow Fever Epidemic (EYE) vision 2026.

Conclusion

YF outbreaks have increased in frequency and geographical spread from 1864 to 2020. It is commoner in the southern and middle belt states that are characterized by Rainforest and Savanna vegetation. The outbreaks are commonly determined by low immune – population or low vaccination coverage, poor sanitary conditions with available collected water for breeding of mosquitoes, wild mosquito vectors in the rainforest or savanna, rural–urban migration, and importation of virus by travelers. The common public

health response to the outbreaks in Nigeria observed from the reviewed material was team coordination, laboratory support, case management and emergency immunization, vector control, and surveillance.

Recommendations

In other to achieve vision EYE 2026, there should be mass and emergency immunization with 17D vaccines, adequate environmental and vector control, effective surveillance and reporting system, risk communication, and community participation in the control of the outbreaks.

Limitations: Different articles or reports gave varying accounts for the same outbreak. The most recent in terms of time was used. Only articles available online and in the databases we searched were used for this study.

Conflict of interest: There is no declared conflict of interest.

References

1. WHO | World Health Organization – Yellow fever. https://www.who.int/news-room/fact-sheets/detail/yellow-fever
2. Lucey D, Gostin LO. Yellow Fever Epidemic: A New Global Health Emergency? *JAMA.* 2016;**315**(24):2661 – 2662.
3. Mutebi JP, Barrett AD. The epidemiology of yellow fever in Africa. *Microbes Infect.* 2002**(14)**:1459-68.
4. Beeuwkes H, Bauer JH, Mahaffy AF. Yellow Fever Endemicity in West Africa, with Special Reference to Protection Test. *The American Journal of Tropical Medicine 1930; s1*-**10**(5):305-333.
5. Chippaux, JP., Chippaux, A. Yellow fever in Africa and the Americas: a historical and epidemiological perspective. *J Venom Anim Toxins Incl Trop Dis* **24,** 20 (2018). https://doi.org/10.1186/s40409-018-0162-y.
6. Vaughan M. A Research Enclave in 1940s Nigeria: The Rockefeller Foundation Yellow Fever Research Institute at Yaba, Lagos, 1943-49. *Bull Hist Med.* 2018;**92**(1):172-205.
7. "Yellow Fever": the Complete Symposium" (1955). Yellow fever, a symposium in commemoration of Carlos Juan Finlay, 1955. Page 12. https://jdc.jefferson.edu/yellow_fever_symposium/12. Accessed 31st March 31, 2021.
8. Olumade TJ, Adesanya OA, Fred-Akintunwa IJ, Babalola DO, Oguzie JU, Ogunsanya OA, et al. Infectious Disease Outbreak Preparedness and Response in Nigeria: History, Limitations and Recommendations for Global Health Policy and Practice. *AIMS public health* 2020;**7**(4):736–757.
9. Nwachukwu WE, Yusuff H, Nwangwu U, Okon A, Ogunniyi A, Imuetinyan-Clement J, et al. The response to re-emergence of yellow fever in Nigeria, 2017. *Int J Infect Dis.* 2020; **92:189**-196.
10. Abdulkadir B, Dazy DB, Abubakar MA, Farida AT, Samira IG, Aladelokun J et al. Current Trends of Yellow Fever in Nigeria: Prospects and Challenges. *UMYU journal of Medical Research* 2020;**4**(2):105-110.
11. Cattan D. Yellow fever--cause for concern? *Br Med J (Clin Res Ed)*. 1981**;283**(6289):499.
12. Norrby E. Yellow fever and Max Theiler: the only Nobel Prize for a virus vaccine. *J Exp Med*. 2007;**204**(12):2779-2784.
13. Nomhwange T, Baptiste A, Ezebilo O, Nomhwange E, Bathondeli B, Adejoh K. Resurgence of Yellow Fever Outbreaks in Nigeria, A Two Year Review 2017 – 2019. Research Square 2020. https://doi.org/10.21203/rs.3.rs-112727/v1. https://www.researchsquare.com/article/rs-112727/v1. Accessed April 2, 2021.
14. Yellow fever | WHO | Regional Office for Africa. https://www.afro.who.int/health-topics/yellow-fever.

15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: *Explanation and Elaboration. 2009;* **6**(7):6(7):e1000100.doi: 10.1371/journal.pmed.1000100.
16. Adogo LY, Ogoh MO. Yellow Fever in Nigeria: A Review of the Current Situation. Afr. *J. Clin. Exper. Microbiol.*2020; **21**(1): 1 – 13.
17. Yellow Fever: Global Status: 2020 Edition. Page 128. Availablefrom : https://www.google.com/search?tbm=bks&q=yellow+fever%3A+global+Status%3A+2020+edition.
18. Public health weekly reports 1914, June 12; 29 (24):1485 – 1610. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1999929/pdf/pubhealthreporig03459-0001.pdf/?tool=EBI.
19. Aitken AB, Connal A, Gray GM, Smith EC. Yellow fever in Lagos during 1925. Clinial and pathological notes, *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 1926;**20**(3):166–184
20. Rockefeller Annual Report of colonies, Nigeria 1925. Available from https://libsysdigi.library.illinois.edu/ilharvest/Africana/Books2011-05/3064634/3064634_1925/3064634_1925_opt.pdf.
21. Public Health Weekly Reports. 1935 Feb 8;50(6):163-201.Available from.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1996141/pdf/pubhealthreporig01924-0004.pdf.
22. Public Health Weekly Reports. (1937) 13;52(33):1105-1134. PMID: 19315621; PMC2024694. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2024694/pdf/pubhealthreporig01028-0001.pdf.
23. Public Health Rep. 1937 Dec 17;52(51):1851-1874. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2024733/pdf/pubhealthreporig01046-0001.pdf.
24. Monath T.P. Yellow Fever in Nigeria: Summary of the past, present and possible future status. *Skr. Ent. med, et Parasifol* 1972;**10**(2): 169 – 175.
25. Carey DE, Kemp GE, Troup JM, White HA, Smith EA, Addy RF, et al. Epidemiological aspects of the 1969 yellow fever epidemic in Nigeria. *Bull World Health Organ.* 1972**;46**(5):645-51.
26. Monath TP, Wilson DC, Lee VH, Stroh G, Kuteyi K, Smith EA. The 1970 yellow fever epidemic in Okwoga District, Benue Plateau State, Nigeria. I. Epidemiological observations. *Bull World Health Organ.* 1973;**49**(2):113-21.
27. Fagbami A.H, Attah B, Fabiyi A, O'Connor E.H. Yellow Fever Outbreaks in South – Eastern Nigeria – Virological and Serological Studies. *Nigerian Medical Journal 1976;* **6**(1):38 – 41.
28. World Health Organization. (1980). Yellow fever in 1979. *WeeklyEpidemiological Record= Relevé épidémiologique hebdomadaire*, *55*(45), 345-351. https://apps.who.int/iris/bitstream/handle/10665/223276/WER5545_345-351.PDF.
29. De Cock KM, Monath TP, Nasidi A, Tukei PM, Enriquez J, Lichfield P, et al. Epidemic yellow fever in eastern Nigeria. *Lancet 1986. Lancet.* 1988;**1**(8586):630-3
30. World Health Organization. (1992). Yellow fever in 1989 and 1990. *WeeklyEpidemiological Record= Relevé épidémiologique hebdomadaire*, *67*(33), 245-251.https://apps.who.int/iris/bitstream/handle/10665/228453/WER6733_245-251.PDF. Accessed 12th April 12, 2021.
31. Nasidi A, Monath TP, DeCock K, Tomori O, Cordellier R, Olaleye OD, et al. Urban yellow fever epidemic in western Nigeria, 1987. *Trans R Soc Trop Med Hyg.*1989 ;**83**(3):401-6.
32. Vainio J, Cutts F, World Health Organization. Yellow fever. World Health Organization; 1998. https://apps.who.int/iris/bitstream/handle/10665/64455/WHO_EPI_GEN_98.11.pdf.
33. Ekenna O, Chikwem JO, Mohammed I, Durojaiye SO. Epidemic yellow fever in Borno State of Nigeria: characterisation of hospitalised patients. *West Afr J Med.* 2010**;29**(2):91-7.

34. Centers for Disease Control (CDC). Aedesalbopictus introduction into continental Africa, 1991. *MMWR Morb Mortal Wkly Rep*. 1991;**40**(48):836-8.
35. World Health Organization. Yellow fever in 1991. WeeklyEpidemiological Record= Relevé épidémiologique hebdomadaire. 1993;68(29):209-15. https://apps.who.int/iris/bitstream/handle/10665/228775/WER6829_209-215.PDF
36. World Health Organization. Yellow fever in 1992 and 1993. WeeklyEpidemiological Record Relevé épidémiologique hebdomadaire. 1995;70(10):65-70. https://apps.who.int/iris/bitstream/handle/10665/229332/WER7010_65-70.PDF.
37. World Health Organization. Yellow fever in 1994 and 1995. WeeklyEpidemiological Record Relevé épidémiologique hebdomadaire. 1996;71(42):313-8. https://apps.who.int/iris/bitstream/handle/10665/229925/WER7142_313-318.PDF.
38. World Health Organisation: Yellow Fever- Nigeria. Available from https://www.who.int/csr/don/22-december-2017-yellow-fever-nigeria/en/
39. World Health Organisation Yellow fever – Nigeria. Available from https://www.who.int/csr/don/09-january-2019-yellow-fever-nigeria/en/
40. World Health Organisation. Yellow fever – Nigeria. Available from https://www.who.int/csr/don/17-december-2019-yellow-fever-nigeria/en/.
41. Nigeria: Yellow Fever Final Report – DREF n° MDRNG027. https://reliefweb.int/report/nigeria/nigeria-yellow-fever-final-report-dref-n-mdrng027.
42. World Health Organisation. Responding to yellow fever outbreak in Nigeria amidst a global pandemic. Available from https://www.afro.who.int/news/responding-yellow-fever-outbreak-nigeria-amidst-global-pandemic.
43. Karunamoorthi K. Yellow fever encephalitis: an emerging and resurging global public health threat in a changing environment. Croatia*: licensee InTech*. 2013 Jan **9**:207-30. https://doi.org/10.5772/46041.
44. Tomori O. Yellow fever in Africa: public health impact and prospects for control in the 21st century. *Biomedica*. 2002;**22(**2):194-210.
45. Hamlet A., Jean K., Perea W, Yactayo, S, Biey, J., Van Kerkhove M., Ferguson, N., Garske T. The seasonal influence of climate and environment on yellow fever transmission across Africa. *PLoS neglected tropical diseases* 2018;**12**(3):1-17. e0006284.
46. Adepoju P. The yellow fever vaccination certificate loophole in Nigeria. *Lancet (London, England).* 2019;**394**(10194):203-204.
47. Adrien N, Hyde TB, Gacic-Dobo M, Hombach J, Krishnaswamy A, Lambach P. Differences between coverage of yellow fever vaccine and the first dose of measles-containing vaccine: A desk review of global data sources. *Vaccine*. 2019;**37**(32):4511-