

Review Article

Diphtheria outbreak triggered by low vaccine coverage and socioeconomic status in 2023: Nigeria

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ABSTRACT

Diphtheria is a highly contagious bacterial infection that primarily affects the throat and upper airways. Before the introduction of vaccines, there were many cases and fatalities from diphtheria. During the 1920s, over 150,000 cases of diphtheria with an average of 14,000 deaths reported each year in the United States of America. Ever since the diphtheria toxoid vaccine has been made available in the 1940s, there have been a massive decline in diphtheria morbidities and mortalities in developed countries as compared to developing and underdeveloped countries. The socioeconomic status of Nigeria could have contributed to the recent Outbreak of diphtheria. As a country, Nigeria has struggled to have a functioning Economy system but still no solution despite efforts from the government. For instance, the recent outbreak has been linked to low vaccine coverage especially in rural communities in the country. Poor access to healthcare has also played a role on the basis of insecurity and inadequate functioning health infrastructures. There is little or no awareness, conferences, workshops concerning the importance of vaccination all because of shortage of health workers in the country. Most of these factors above, have leads us to experiencing symptoms of diphtheria such as sore throat, low-grade fever, weakness, and difficulty breathing recently. Diphtheria can be prevented if vaccination is done as scheduled by the WHO (World Health Organization) and NPI (National programme for immunization). To prevent future outbreaks, low vaccine coverage and socioeconomic status must be tackled effectively by the Nigerian Government.

Keywords: Outbreak, Nigeria, Vaccine coverage, Socio-economic status

INTRODUCTION

The contagious disease diphtheria may be prevented through vaccination and once spread widely throughout the world. In many nations, especially affluent nations, the prevalence of diphtheria has significantly decreased as a result of the extensive use of vaccinations. Notwithstanding, diphtheria still poses a threat to public health in some regions of the world, particularly in those countries with poor vaccination rates or inadequate healthcare infrastructures. Although diphtheria can affect anyone, it tends to be more serious in small children and

elderly people. In populous areas like schools and densely populated housing, the disease can spread through intimate contact with an infected person or contaminated materials.¹

High levels of vaccine coverage, as well as rapid identification and treatment of patients, are necessary for effective diphtheria control. As part of national immunization programs, the World Health Organization (WHO) advises routine vaccination with the diphtheria, tetanus, and pertussis (DTP) vaccine. The group also offers recommendations for containing outbreaks and halting the disease's spread.²

Nigeria has lower diphtheria Immunization coverage compared to many high-income countries but higher than some other low- and middle-income countries. The exact coverage rate varies by region and demographic locations.

Nevertheless, Nigeria has been making progress in increasing access to immunization services. However, WHO recommends at least 95-96% coverage for full protection against diphtheria.³ Nigerian's socioeconomic crisis, including poverty, poor sanitation, and limited access to healthcare, has contributed to the spread of diphtheria by compromising the health and immunity of the population.⁴

These outbreaks were largely caused by low vaccination coverage and poor access to healthcare in affected areas. Ever since The World Health Organization (WHO) has been working with the Nigerian government and other partners to improve access to diphtheria vaccinations and to control and prevent future outbreaks of the disease. On the 20th January 2023 till date, 138 cases were reported by the national center for disease control, NCDC Nigeria. In Kano State 100 cases, 32 deaths; In Yobe state 17 cases, 3 deaths; Lagos state 5 cases, no deaths and Osun state a case with no death.⁵ Diphtheria cases reported in Nigerian states as far December 2022 till February 2023.⁵

AETIOLOGY

Diphtheria is a gram positive, encapsulated, non-acid fast bacteria with tendency to club at one end or both. On Electron microscope it is approximately $3-6 \times 0.6-0.8$ Nanometer in size.⁶ It was first described as a distinct disease in the early 19th century by French physician Pierre Bretonneau and first successfully cultured in 1883 by German physician Friedrich Löffler.⁷ In 1885, O'Dwyer tubes for laryngeal intubation in patients with laryngeal obstruction was introduced by Joseph P.O Dywer.

It later replaced tracheotomy as a method used in emergency diphtheria intubation. In the 1920s, there were approximately 100,000 -200,000 diphtheria cases per year causing over 13,000 fatalities per year in the United States. In 1926, the Addition of Aluminium Salts by Alexander Thomas Gleeney to the diphtheria toxoid increased its effectiveness. In 1974, The World Health Organization incorporated the diphtheria toxoid vaccine in their program for immunization. Outbreak of cutaneous diphtheria was reported in Seattle, Washington, United States of America in 1975. In 1994, 39,703 cases of diphtheria were reported in Russian Federation. In 2006, 22 cases of Diphtheria were reported with 5 fatalities.⁸

EPIDEMIOLOGY

In the past, diphtheria was a leading cause of death among children worldwide. Diphtheria is fatal on the average of 7.5% of cases. Fatality rate in children less

than 5 years of age and adults over 40 years can be about 20%. However, widespread vaccination efforts have led to a significant decline in the incidence of the disease. Global diphtheria incidence has decreased by over 80% since the 1980s, and in many countries, the disease is now considered to be endemic. Subsequently, outbreaks of diphtheria still occur in some regions with low vaccination coverage.⁹

In Nigeria, they have been under-reported cases of diphtheria. In December, 2011 experimental research was carried out by Besa et al. in which 98 cases of diphtheria was reported with 21% death in Kimba village, Miringa, Biu local government area of Borno state, Nigeria.¹⁰ Recently 138 confirmed cases were reported with 38 fatalities on the 20th January 2023.⁵

Mode of transmission

Typically, diphtheria can spread from one individual to another via generated respiratory droplets from coughs or sneezes of an infected person.¹¹ It can occur from skin lesions that are infected with diphtheria or from contaminated discharges that come from the lesions, although not usually common. In some situations, contaminated Objects or surfaces that have come into contact with an infected person's secretions can indirectly spread the disease, if the Organism remains viable. Those who have received the diphtheria vaccine have a lower risk of contracting the illness and transmitting it to others if they do get infected.¹²

Signs and symptoms

The symptoms of diphtheria can be mild, Moderate, or severe and typically appear 2 to 5 days after exposure to the bacterium. The following are typical respiratory diphtheria signs and symptoms.

Sore throat

This is often the initial sign of diphtheria and may come with a slight fever and hoarseness.

Grayish or whitish patches in the throat

A thick, sticky membrane makes up these gray or white patches in the throat, which can make it challenging to swallow or breathe.

Swollen glands

The neck's glands may swell, become sensitive, and even enlarge.

Difficult breathing

Diphtheria can make it difficult to breathe if the throat membrane thickens excessively.

Muscle weakness

Diphtheria can lead to weakness and weariness, especially in severe cases.

Nausea and vomiting

Diphtheria patients occasionally experience nausea and vomiting.^{13,14}

Cutaneous Diphtheria infection is usually commingled in country with low hygiene status. Signs and symptoms include, areas of upper and lower limbs with pus filled blisters. Red sores skin with large ulcer located centrally.¹⁴

Types of diphtheria

Tonsillar and pharyngeal

Signs and symptoms include, the present of fever, anxiety, halitosis and tachycardia. Pharyngeal erythema and edema in tonsils and pharynx, thick, gray, leathery membrane variably covers the tonsils, oropharynx, uvula, nasopharynx, and soft palate.

Cracks at scraping the pseudomembrane cause bleeding of the underlying mucosa. Presence of respiratory distress manifesting as wheezing, stridor, cyanosis, accessory muscle use and retractions. Cervical lymphadenopathy imparts a bull's neck appearance.^{15,16}

Nasal

Presence of serosanguineous or seropurulent nasal discharge, white nasal membrane characterized by a clear nasal discharge initially, but later becomes blood-stained.¹⁷

Laryngeal

The downward spread of infection from nasopharynx to the larynx results in laryngeal diphtheria, it caused the airway to blocked, resulting in "tracheotomy"-restoring the airway by inserting a tube or cutting an opening in the trachea.¹⁹

Cutaneous

Cutaneous diphtheria starts as a painful lesion resembling an erythematous pustule, which breaks down to form an ulcer covered with a gray membrane.

Subsequently, cutaneous diphtheria often develops at a site of previous infection, trauma, or a primary dermatologic disease. It follows an indolent course, usually appears as small ulcers on exposed limbs-particularly the legs, typically lasting for weeks to months.¹⁸

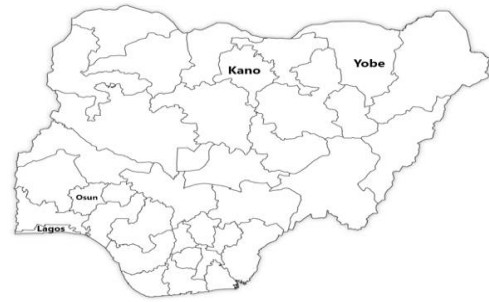


Figure 1: Map of Nigeria showing the States affected by the outbreak.

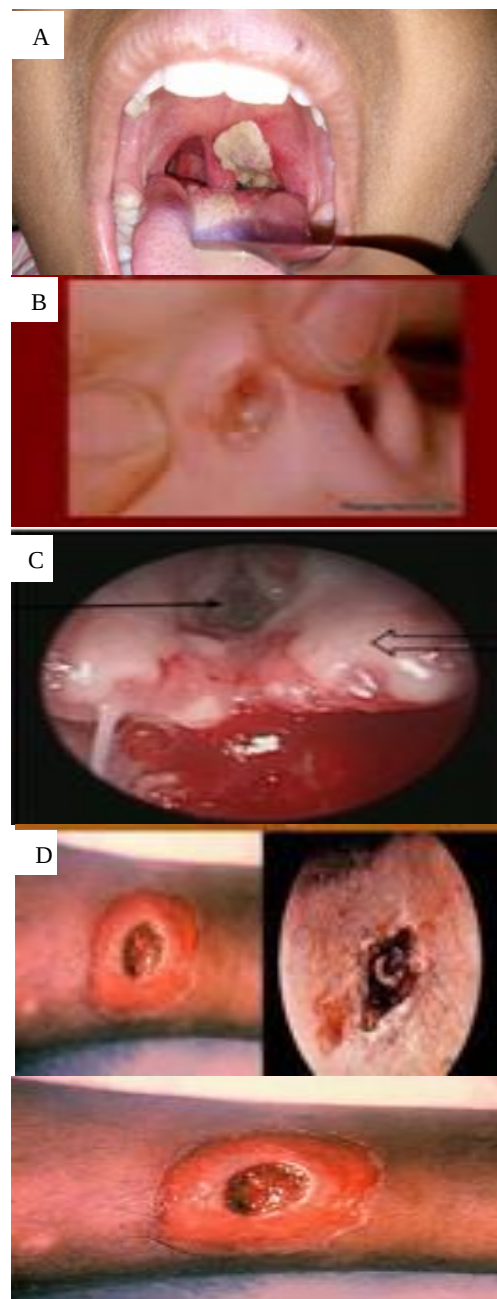


Figure 2: Types of diphtheria. A) Tonsillar and pharyngeal. B) Nasal. C) Laryngeal. D) Cutaneous.¹⁵⁻¹⁹

NATIONAL IMMUNIZATION COVERAGE BRIEF														
Percentage (%) of children aged 12-23 months who received:														Children age 12- 23 mo.
BCG	Hep B at birth	Polio at birth	Polio ¹			Penta			Yellow fever	Measles MCV1 ¹	Full ²	Card seen		
			1	2	3	1	2	3						
NIGERIA	53.5	30.2	47.4	49.7	42.5	33.2	48.7	39.9	33.3	38.8	41.7	22.9	29.0	6,268
North Central	63.0	38.3	56.1	59.2	53.3	37.3	58.6	48.3	39.0	49.9	52.4	26.5	30.9	900
FCT-Abuja	87.5	68.7	84.4	71.8	65.6	55.6	87.7	71.9	65.7	73.7	76.3	46.8	55.2	46
Benue	66.4	53.9	62.9	66.4	62.7	45.1	68.3	59.5	57.4	50.6	53.6	37.0	37.9	132
Kogi	73.3	46.9	62.7	60.3	46.9	36.4	63.7	47.6	38.4	55.7	65.0	29.9	41.5	89
Kwara	72.1	46.9	61.6	69.8	64.1	41.0	70.8	61.3	49.1	67.5	66.9	33.9	19.7	66
Nasarawa	63.8	33.7	59.6	57.6	48.7	32.8	56.4	44.7	34.9	46.5	49.7	21.4	26.3	127
Niger	38.1	20.8	33.5	44.6	39.8	24.5	36.3	30.6	20.0	28.8	31.2	13.8	24.7	255
Plateau	80.1	39.5	67.8	67.9	64.3	46.8	69.9	57.1	45.2	65.5	65.3	30.6	30.7	186
North East	52.6	19.2	41.7	46.4	36.7	29.8	46.7	37.3	28.2	32.8	36.0	19.6	24.4	1,346
Adamawa	67.4	35.0	54.5	60.3	50.8	40.9	56.6	50.3	37.9	44.5	48.8	29.0	46.2	134
Bauchi	41.2	14.2	28.9	37.6	33.4	26.5	35.3	25.2	18.5	22.0	22.2	13.9	19.7	345
Borno	80.6	24.1	66.1	69.4	50.7	41.5	72.9	63.9	47.7	50.8	58.1	31.5	31.9	421
Gombe	54.4	29.9	45.0	50.1	41.2	35.9	44.7	29.1	25.0	30.5	32.4	16.7	25.8	122
Taraba	39.7	23.8	34.4	31.0	21.3	17.7	35.9	20.0	16.4	25.1	29.2	11.5	22.0	70
Yobe	16.3	2.8	12.1	15.2	12.6	9.4	17.5	11.3	8.7	14.6	14.7	6.5	7.0	253
North West	30.0	14.1	28.6	29.4	23.6	19.3	25.3	17.4	13.7	19.1	22.4	8.5	15.6	2,468
Jigawa	25.6	11.2	26.0	15.8	10.2	6.7	19.5	9.0	7.1	9.0	10.4	1.8	11.8	337
Kaduna	51.4	26.8	40.9	39.8	36.7	34.4	43.7	32.5	29.5	42.7	43.1	24.9	23.1	376
Kano	33.7	11.4	29.4	27.3	18.9	13.7	27.9	20.9	15.9	22.3	24.1	9.5	19.6	554
Katsina	28.5	16.6	32.6	33.0	27.8	21.5	28.2	18.3	12.1	17.0	21.1	5.9	18.7	478
Kebbi	22.6	11.2	23.1	26.0	18.1	12.1	20.2	16.7	11.3	12.6	25.5	4.8	12.6	202
Sokoto	16.3	4.6	12.6	15.1	10.1	7.1	9.4	5.2	2.9	6.4	9.8	2.2	5.2	218
Zamfara	19.0	11.0	23.4	42.8	37.9	35.2	14.7	9.5	8.9	12.2	16.2	4.9	8.2	303
South East	90.1	64.9	82.5	79.6	70.9	52.4	85.3	73.9	65.9	69.9	72.6	44.4	47.1	353
Abia	87.1	65.5	81.1	76.9	68.9	43.3	81.6	68.6	54.8	66.3	70.4	33.9	39.9	57
Anambra	88.5	74.6	84.7	84.1	80.7	62.1	89.5	82.4	76.2	76.4	75.0	55.2	44.6	74
Ebonyi	82.5	61.5	77.6	69.6	60.6	46.9	79.7	66.2	54.4	56.4	57.6	35.0	49.7	59
Enugu	93.2	69.2	88.2	79.8	70.4	60.2	84.9	78.6	73.8	74.5	81.2	50.5	52.8	73
Imo	95.6	55.3	80.2	83.9	71.2	47.7	88.1	71.7	65.6	72.0	74.6	43.5	47.5	91
South South	83.9	58.2	72.3	77.6	69.1	53.1	79.9	72.0	64.8	68.2	69.0	42.5	51.6	503
Akwa Ibom	82.4	59.3	70.6	75.8	70.9	58.7	80.2	73.4	68.4	64.2	63.7	44.2	46.8	120
Bayelsa	65.9	33.9	48.2	63.8	55.3	35.4	61.2	50.3	42.6	45.8	51.6	28.5	37.0	41
Cross River	88.2	44.7	69.3	82.7	77.1	58.8	83.5	76.9	69.5	69.6	73.7	49.9	54.5	76
Delta	80.9	64.8	70.7	71.6	58.2	47.8	75.7	63.7	57.2	67.5	63.7	36.3	51.1	102
Edo	96.7	69.5	89.4	86.9	78.1	52.7	88.6	86.1	74.5	83.8	86.1	45.7	55.9	81
Rivers	82.0	61.7	75.0	80.7	70.4	56.0	82.0	72.8	66.0	69.4	70.7	44.8	60.0	82
South West	85.6	60.4	78.3	80.1	72.9	59.7	81.6	73.2	66.4	68.4	71.7	50.2	57.3	698
Ekiti	86.5	56.1	84.3	76.5	71.7	57.9	87.1	80.1	72.2	70.3	80.1	48.0	65.5	30
Lagos	92.9	70.8	88.5	91.0	86.2	74.7	93.6	85.6	80.2	84.9	88.0	68.1	67.5	244
Ogun	80.0	57.2	75.7	69.2	57.8	48.0	71.1	58.9	52.1	56.5	58.7	35.0	45.0	72
Ondo	83.1	44.2	66.5	76.8	71.4	53.4	76.4	71.4	66.2	68.5	72.2	44.8	47.8	102
Osun	87.5	60.4	79.0	76.8	67.6	54.2	83.1	65.7	60.0	65.7	67.0	43.0	53.7	96
Oyo	77.1	56.9	69.7	72.7	63.6	49.5	69.1	64.9	54.1	49.2	53.1	37.4	53.9	155

¹Does not include vaccines administered through campaigns. ²BCG, OPV1-3 & measles from health system.

¹Does not include vaccines administered through campaigns. ²BCG, OPV1-3, penta1-3 & measles from health system.

Figure 3: National Immunization Coverage Survey in Nigeria from 2016 -2017.²²

COMPLICATIONS

Diphtheria toxin are responsible for these complications. When absorbed, toxins affect distant vital organs distant from the site of infection. Diphtheria can cause serious and potentially life-threatening complications if left untreated. The most common complications of the disease, includes myocarditis, peripheral neuropathy and kidney related symptoms including death.

Myocarditis which can lead to heart failure, irregular heartbeats and other heart disease conditions can present early or weeks later as the illness progress. Peripheral Neuropathy often involves motor nerves resulting to weakness, difficulty swallowing, and breathing difficulties which usually resolves completely. Kidney related symptoms may present as proteinuria, hematuria and Reduced kidney function. Other complications

include Pneumonia, septicemia, otitis media and Airways obstruction particularly in infants.

Antibiotics should be used as a prompt treatment in the preventing Diphtheria complications. Therefore, in order to ensure timely and efficient management, it is crucial to seek medical attention if you suspect diphtheria. Vaccination is also a crucial strategy in preventing diphtheria and its complications.²⁰

EXAMINATION AND TESTING

Diagnosing respiratory diphtheria is made by clinical presentation because it's essential to commence management immediately. On the other hand, cutaneous diphtheria may not be clinically confirmed but through laboratory testing. The confirmation test includes culture to identify the bacterial species. These species can be

distinguished by culture on selective media containing tellurite. Diphtheria toxin production by the bacteria is confirmed by Elek test.

In a case of presumed *C. diphtheria* and culture was negative or no response to Antibiotic therapy, A positive polymerase chain reaction (PCR) for the tox gene of *C. diphtheria* and isolation of the organisms from close contact via culture of specimen will support our presumed diagnosis.^{21,9}

PROPHYLAXIS

In comparison to the global average, Nigeria has lower immunization coverage. The average immunization rate in Nigeria is roughly 37%, which is lower than the 85% global average. Nevertheless, the nation has been making an effort to increase vaccination rates through a number of programs, such as expanding vaccine access and enhancing routine immunization services.²²

Vaccination is the gold standard for the prevention of Diphtheria. In Nigeria, 3 doses of Pentavalent vaccine (containing diphtheria toxoid) are given in the first year of life usually at the 6th, 10th and 14th weeks. It is imperative parent ensure that their children are properly vaccinated. Health workers should be on the outlook for any signs and symptoms of the disease. However, Health workers with high level of exposure to the diphtheria should also get vaccinated.²³

MEDICAL MANAGEMENT

Organisms producing toxins has been taking advantage of by humans in biological warfare and one of them is diphtheria. In the 1980s, The Soviet Union was suspected of having developed a biological weapons program that included anthrax, botulinum toxin, tularemia, small pox, plague and diphtheria as a potential agent.

It's crucial to remember that using biological weapons is forbidden by international law and is regarded as a war crime. The use of diphtheria has made many governments in the world store up Diphtheria vaccines, Diphtheria Antitoxin and Antibiotics in the event of any occurrence.²⁴

Diphtheria Antitoxin are derived from horses (horses antibodies that have been challenged with diphtheria toxin). The antitoxin does not neutralised toxin that is already tissue bound but circulating toxin. Hence, any delay in its administration risks death. diphtheria antitoxin is not administered in the case of non-respiratory form of diphtheria and also not used in prophylaxis with diphtheria patients contact. In a suspected case of diphtheria, a person should urgently receive diphtheria antitoxin and antibiotics while awaiting confirmatory diagnosis.²⁵ Antibiotics such as Erythromycin (injection or orally), procaine Penicillin G, and Metronidazole can be administered.²⁶

Table 3: States affected by the outbreak, number of case and fatalities.⁵

States	Number of cases	Number of fatalities
KANO	100	32
YOBE	17	3
LAGOS	5	-
OSUN	1	-

Table 2: Vaccine schedule of Diphtheria Toxoid vaccine in the first year of life in Nigeria.²³

Vaccines	Schedules
Diphtheria, Pertussis and Tetanus I	6th weeks
Diphtheria, Pertussis and Tetanus II	10th weeks
Diphtheria, Pertussis and Tetanus III	14th weeks

CONCLUSION

This re-emergence of diphtheria should set out as a warning of how potentially the DPT epidemic in Nigerian populations is, which is accompanied by inadequate or interrupted routine immunization facilities. This can however, be tackle or prevent the disease re-occurrence, via intensive vaccine awareness and epidemiological metrics, as done in most developed countries that were previously affected by the disease (DPT).

Furthermore, the Nigerian government should also be reminded that diphtheria may still have a great negative impact on overall communities' health and sustainable growth if left neglected. Additionally, creation of proper/functioning healthcare system, possible solution to insecurity, improve a strong or reliable partnership with national and international health organizations, organising more conferences, workshops and vaccine campaign programs will surely serve as a first step forward in preventing a forthcoming DPT resurgence. However, progress is being made in controlling diphtheria but sustainable vaccination efforts are necessary to put an end to future outbreaks and maintain progress against the disease.

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